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Strategies for fine-tuning the catalytic activity of pincer-complexes

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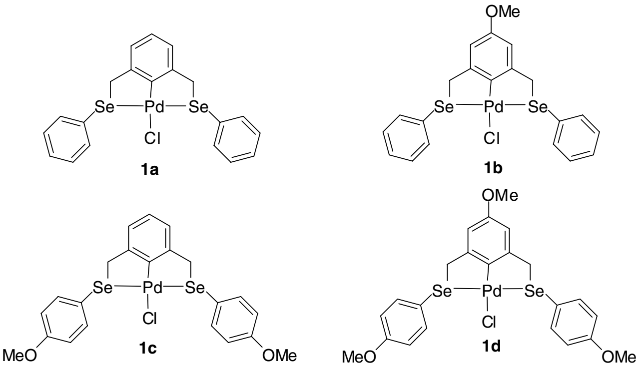
Abstract—Various methoxy substituted pincer-complexes were prepared in order to study the substituent effects on the catalytic activity in palladium catalyzed opening of vinyl epoxides and boronation of cinnamyl alcohol. The results clearly show that methoxy substitution at the *para*-position of the pincer-complex leads to up to fourfold acceleration of the catalytic reactions, while substitution of the side-arms does not change the activity of the complex or leads to a slight deceleration of the catalytic processes.

Palladium pincer-complexes[1] (such as **1a**[2a]) have been extensively applied as catalysts in organic transformations.[2,3] One of the most important features of these complexes is the strong terdentate coordination between palladium and the pincer-ligand. Thus, when a pincer-complex is the active catalyst in a transformation, the ligand remains tightly bound to the metal center for the entire reaction, which allows an efficient transmission of the ligand effects to the catalyst. Accordingly, the activity and selectivity of pincer-complex catalysts are expected to be efficiently fine-tuned by substitution of the pincer-ligand. However, the electronic effects of the ligand depend on the location of the substituent in the pincer-complex catalyst. Therefore, we decided to study the influence of various substitution patterns on the catalytic activity of **1a**, which proved to be a useful catalyst in several organic transformations,[2a,3a–c,j] such as in the opening of vinyl epoxides with organoboronic acids[3a] and in allylic boronation reactions.[3b,c] Our mechanistic studies[3a–c] suggested that the catalytic activity of **1a** can be increased for several catalytic transformations by increasing the electron-density on palladium. These studies inspired us to prepare several analogs of **1a** (Scheme 1) to investigate the electronic effects of the electron-donating methoxy substituents on the catalytic activity of the complex. In complex **1b** the methoxy substituent is located *para* to the metal, while in **1c** the side-arms are substituted. Expecting a synergic effect on the methoxy substitution, we also prepared complex **1d**, which is substituted both at the *para* position and in the side-arms.



Scheme 1.

Pincer-complexes **1b–d** were synthesized by a slightly modified version of the procedure reported by Yao et al.[2a] Dibromoxylene derivatives **2a–b** were reacted with the appropriate diselenide (**3a** or **3b**) to obtain pro-ligands **4b–d**, which underwent a transcyclometallation reaction[1a,c] with **5** to give complexes **1b–d** in good to excellent yields (Scheme 2). Characterization of the complexes by ^{77}Se NMR spectroscopy revealed an interesting trend. The ^{77}Se NMR shift values obtained for **1a**[3j] (427.1 and 424.9 ppm[4]) and **1b** (427.1 and 425.7 ppm) were almost identical, while methoxy substitution of the side-arms led to an increase of the shielding of the selenium nuclei (**1c**, 420.5 and 419.3 ppm; **1d**, 420.7 and 419.1 ppm). This indicates that only methoxy

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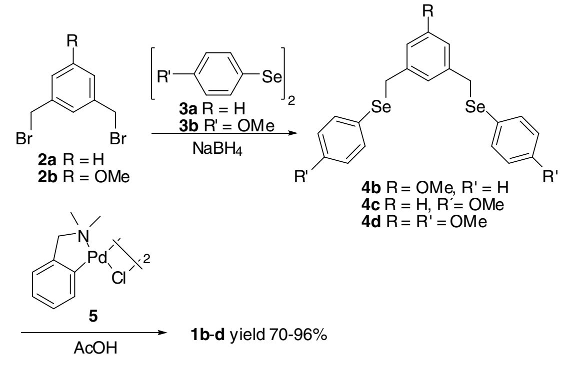


Scheme 2.

substitution of the side-arms affects the electron-density of the selenium atoms.

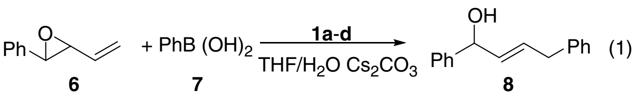
Previously, we have shown that **1a** catalyzes the ring-opening of vinyl epoxides and aziridines with organoboronic acids.[3a] In this reaction, an electron-rich palladium center was expected to increase the catalytic activity of the applied pincer-complex.[3a] Therefore, we investigated the effects of the methoxy substituted pincer-ligands on the catalytic ring-opening (Eq. 1) of vinyl epoxide **6** with phenylboronic acid **7**. The progress of the reaction (formation of **8**) was monitored by ^{1}H NMR spectroscopy (Fig. 1).

Under the reaction conditions applied, the complete conversion of **6**–**8** required about 10 h using the parent catalyst **1a**. Application of **1b** led to a dramatic (four-fold) acceleration of the process, which was completed in only 2 h. Surprisingly, methoxy substitution of the catalyst on the side-arms led to a weak and deactivating effect. Complex **1c** proved to be slightly less reactive than the parent complex **1a**, and the trimethoxy substituted catalyst **1d** was less efficient than the monomethoxy complex **1b**.

Subsequently, we studied the rate of boration[3b,c] of cinnamyl alcohol **9** with diboronic acid **10**, in the presence of catalytic amounts of **1a**–**b** and **1d** (Fig. 2). The reaction[3c] was complete in about 8 h using the parent catalyst **1a**. Similar to the catalytic ring-opening of **6**, the boronation reaction was significantly accelerated using *para*-methoxy complex **1b**. Although, the acceleration in the boronation reaction (Fig. 2) was less extensive than in the ring-opening process (Fig. 1), the catalytic transformation with the methoxy complex **1b** proceeded about twice as fast as with the parent catalyst **1a**. On the other hand, the reaction rate was unaffected by the methoxy substituents on the side-arms, as the reaction was completed about as quickly with **1d** as with **1b**.

The above results clearly indicate that the catalytic activity of **1a** (and probably other pincer-complexes as well) can be efficiently fine-tuned by *para*-substitution of the complexes. The ^{77}Se NMR shifts (see above) indicate that methoxy substitution of the side-arms (**1c** and **1d**) increases the electron-density on the selenium atom, nevertheless complexes **1c** and **1d** do not display higher reactivity than the corresponding analogs **1a** and **1b**. Accordingly, the most efficient fine-tuning of the catalytic activity of pincer-complexes can be achieved by *para*-substitution of the aromatic ring, while substitution of the side-arms has much weaker effects on the catalytic activity. These results are also in line with previous studies on the electronic and magnetic properties of pincer-complexes. Van Koten and co-workers[1c] have shown that the ^{195}Pt NMR shifts and the natural charges on the platinum atom are in excellent correlation with the Hammett substituent constants of the *para*-substituents in platinum pincer-complexes.

In summary, we have shown that in arylation and boronation reactions, the catalytic activity of pincer-complex **1a** can be effectively increased by *para*-methoxy substitution of the catalyst **1b**. On the other hand, methoxy substitution of the side-arms does not increase the catalytic activity of the complexes or even has a slight deactivation effect. These substituent effects probably apply to other pincer-complex catalyzed substitution



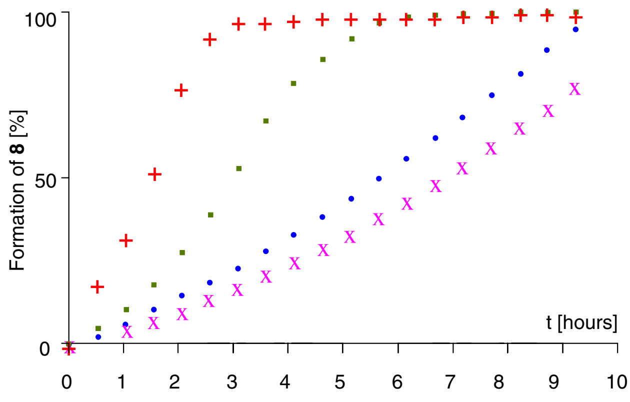
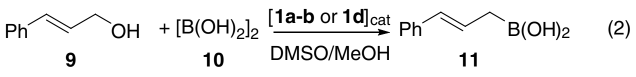


Figure 1. Catalytic ring-opening of **6** affording **8** at rt. Catalysts (2.5 mol %): **1a** (●), **1b** (+), **1c** (X), and **1d** (■).



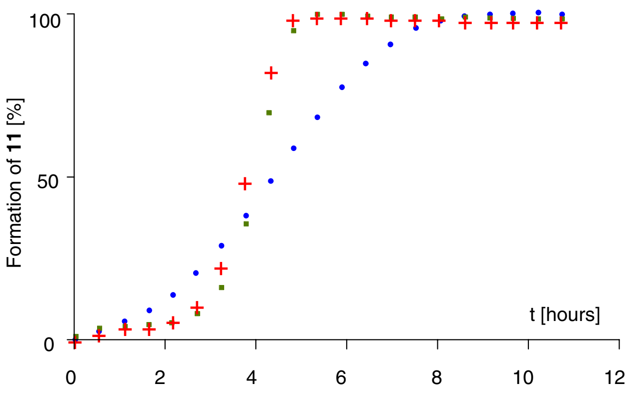


Figure 2. Catalytic boronation of **9** to obtain cinnamyl boronic acid **11** at 55 °C. Catalysts (5 mol %): **1a** (●), **1b** (+), and **1d** (■).

reactions, in which charge accumulation on the metal atom is required to increase the catalytic activity of the complex.

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Supplementary data

Experimental procedures, NMR data as well as ^{1}H, ^{13}C, and ^{77}Se NMR spectra of complexes **1b–c** are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.08.141.

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4. Each complex exists in two diastereomeric forms[2a] in about a 1:1 ratio, and therefore two ^{77}Se NMR shifts were observed.