

Heterogeneous catalysis in organic chemistry. Part 10¹. Effect of the catalyst support on the regiochemistry of the heck arylation reaction

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Abstract

Data have been presented which show that dispersed metals can be considered as viable catalysts for synthetically useful organometallic reactions. In addition, the material used as the catalyst support has been shown to influence the regiochemistry of the reaction. In the Heck arylation an acidic support, such as silica, withdraws electrons from the palladium and this leads to predominant β enol ether formation. Palladium supported on a basic support, such as magnesia, which is electron donating, produces primarily the α product. Electron withdrawal also increases the rate of the reaction. As with a number of other synthetically useful reactions the heterogeneously catalyzed Heck arylation takes place on the coordinately unsaturated corner atoms and adatoms on the metal surface. These single atom active sites are the only ones having a sufficient number of orbitals available for interaction with both the aryl species and the enol ether at the same time, a procedure needed for the reaction to take place. A mechanism for the reaction on a tetrahedral corner atom is proposed. This is based on the Frontier Molecular Orbitals of this site and the corresponding mechanism established for the homogeneously catalyzed reaction.

Keywords: Effect of support; Heck arylation; Palladium; Supported catalysts

1. Introduction

Organometallic reactions have become increasingly important in organic synthesis with soluble complexes being used as catalysts for a wide range of C–C bond forming reactions. The presence of such species in the reaction medium can, however, present problems concerned with the separation, recovery and regeneration of the organometallic species. Such problems could be minimized by using heterogeneous catalysts for these reactions. While polymer or oxide supported complexes can

have some advantages in this regard [2–4] these materials can dissociate to leave the metallic species and/or ligands in the reaction mixture. If supported metals were to be used as catalysts for these reactions this problem would not arise, but about the only exposure a synthetic chemist has to supported metals is their use as hydrogenation catalysts. Dispersed metals have, however, been used to promote some of the C–C bond forming reactions that are catalyzed by soluble complexes. It was reported that Pd/C would promote the allylation of aniline with allyl acetate in the presence of triphenylphosphine [5]. While it was considered that this reaction was probably catalysed by

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a soluble palladium complex formed by dissolution of the supported palladium by the phosphine [5] we have recently shown that allylations are readily catalyzed by supported palladium metal catalysts without added phosphine. It was established that the reaction occurs on the metal surface rather than being catalyzed by a soluble catalyst [6].

Supported palladium catalysts are also effective for promoting the Heck arylation [7–9] of enol ethers. Here, too, it was shown that the reaction takes place on the metal surface [10–12]. In these reactions an amine is used to remove the acid produced in the arylation from the catalyst. In a homogenous reaction it is sometimes desirable to use a solvent in which the amine salt is insoluble so it can be more easily removed from the reaction mixture. With a heterogeneous catalyst, however, the salt will precipitate over the catalyst surface blocking it from further reaction so the solvent used must be capable of keeping the amine salt in solution. Dioxane was particularly effective in this regard [10] but the more polar solvents such as acetonitrile, DMF and DMSO are also useful [13]. It was also found that the heterogeneously catalyzed reaction proceeds with a 1:400 (Pd:substrate) ratio at the same rate as one catalyzed by palladium acetate with a 1:100 (Pd:substrate) ratio [10].

The most significant difference between heterogeneous and homogeneous catalysts is concerned with the nature of the active sites on these species. Since a homogeneous catalyst is a discrete chemical entity there is only one type of catalytically active species in the reaction medium. The surface of a dispersed metal catalyst, however, is composed of a number of different types of atoms which are distinguished by the number and geometry of their neighboring atoms [14–16]. A representative metal particle is shown in Fig. 1. Since most of the catalytically active metals have the fcc crystalline orientation, the bonding angles for the metal – metal bonds are either 60° or 120° . There are no square, 90° , bonding angles in such crystals. For simplicity these different types of sites can be classified as corner, edge and face atoms but it has

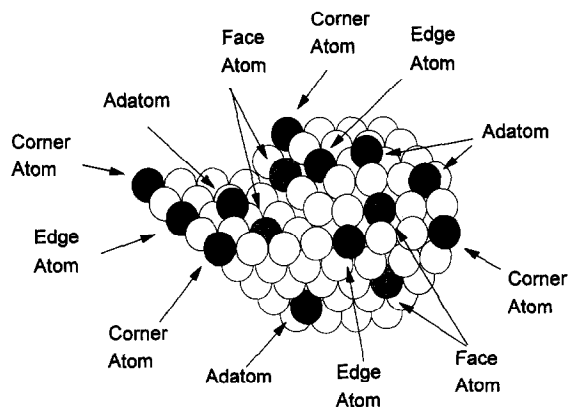


Fig. 1. Representation of some different types of surface atoms on a metal catalyst particle.

to be recognized that there are two different types of face atoms, those on a 111 face and those on a 100 face. In addition there are four different types of edge atoms and seven different corner atoms all differing in the degree of coordinative unsaturation and the accessibility to the surface orbitals [14–16].

The two most coordinately unsaturated surface atoms are the tetrahedral and octahedral corners depicted in Fig. 2. The same orbital arrangement as a tetrahedral corner is also found on an atom (adatom) placed on top of a 111 plane and an adatom on a 100 plane has the same orbital arrangement as an octahedral corner. The number of corner atoms on a metal crystallite may be limited by the particle geometry but there is no limit to the number of adatoms which may be present on the various faces of these crystallites.

While our previous report was concerned with the various reaction parameters involved in the heterogeneously catalyzed Heck arylation [10], there are still some questions about this reaction which need to be answered. In the first place there is the problem of regiochemistry. The reaction gives a mixture of the α product, **2**, and the *E* and *Z* isomers of the β product, **3**. In homogeneous systems it has been shown that decreasing the electron density of the aromatic ring increases the tendency for β product formation while an increase in electron density favors the production

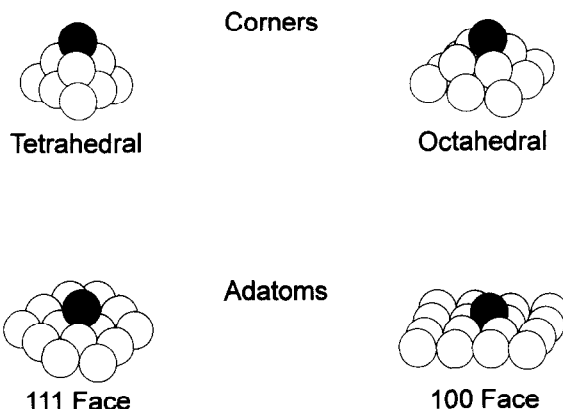
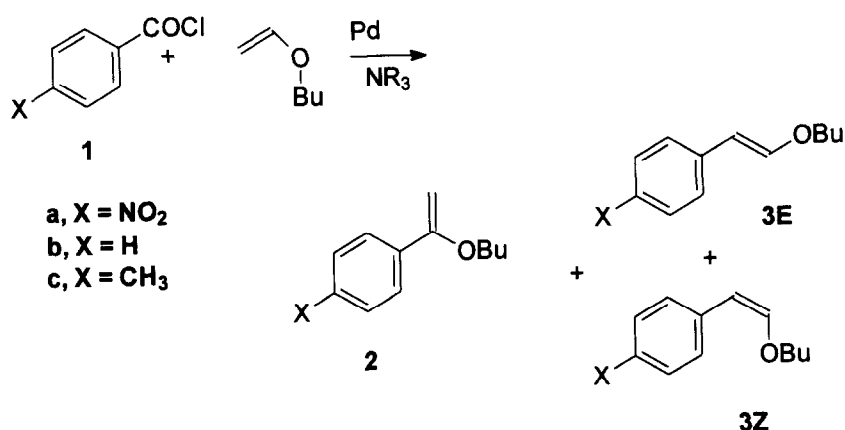


Fig. 2. Relationship between some corner atoms and adatoms on metal crystallite faces.



Scheme 1.

of the α isomer [17]. The previous work used *p*-nitro-iodobenzene and *p*-nitro-benzoyl chloride as arylating agents and in both cases the β enol ethers, **3a**, were the predominant product. It remains, then, to see if electron donating substituents will shift the regiochemistry of the reaction toward α isomer formation in the heterogeneously catalyzed reactions as well. Metal catalysts dispersed on a support material also have an electronic interaction with the support so it would also be interesting to determine what effect acidic and basic supports have on the regiochemistry of the arylation (Scheme 1).

The second question is concerned with the molecular processes taking place on the metal surface and, thus, provide a mechanistic understand-

ing of the reaction. Central to this problem is the determination of the type or types of sites on which the arylation is taking place. The present manuscript is concerned with both of these matters.

2. Experimental

General information concerning the materials and analytical procedures used has been published [10] as has the experimental description of the STO procedure [14,18,19].

The 1% Pd/MgO catalyst was prepared by stirring 3.0 g of MgO, 20 ml of triply distilled water and 4 ml of 0.14 M NaOH solution in a two-neck flask, equipped with a buret and magnetic stirring

bar, for 10 min. Then, 10 ml of a 0.028 M $\text{Pd}(\text{NO}_3)_2$ solution was added dropwise over 30 min keeping the mixture at room temperature. The resultant slurry was stirred for an additional 30 min and then centrifuged, decanted and washed four times until the supernatant was clear. The supported salt was dried overnight at 110°C and then reduced in a stream of hydrogen at 250°C. The procedure for the preparation of the 1.2% Pd/SiO₂ catalyst has been reported [19] as has the preparation of the 6% Pd/Al₂O₃ catalyst [10]. The samples of the 6% Pd/Al₂O₃ catalyst used for the STO characterization were reduced in hydrogen at 200°, 250°, 300° and 400°C.

The arylations were run in a dry 50 ml three-necked flask fitted with a magnetic stirring bar, condenser, thermometer and septum. The catalyst (0.25 mol% of Pd based on the starting aryl compound), dodecane as internal standard (33.3 mol% of the aryl compound) and 15.0 ml of dioxane were added to the flask. The reactor was purged twice with nitrogen and a positive pressure of nitrogen was maintained in the flask during the reaction. A mixture of the aryl chloride (2.5 mmol), *n*-butyl vinyl ether (5 mmol) and *N*-ethyl morpholine (3 mmol) in 5.0 ml of dioxane were added to the flask by syringe under nitrogen. The reaction mixture was heated to 100°C with vigorous stirring and was monitored by GC analysis of samples withdrawn at periodic intervals. The stirring was suspended for 10 sec before taking each sample to allow the catalyst to settle. The samples were partitioned between ethyl ether and dilute aqueous acid before analysis of the organic phase by gas chromatography. The reaction products were isolated for spectral analysis by flash chromatography through silica gel. The spectral data obtained were consistent with the assigned structures and agreed with published data for these compounds. [20]

3. Results and discussion

3.1. Support effect

It was originally thought that the primary purpose of the support material in a dispersed metal

Table 1

Effect of the aryl substituent and the catalyst support on the regiochemistry of the heterogeneously catalyzed Heck arylation

Reagent	Support	% α (2)	% β (3)	β/α (3/2)	3Z/3E	Reaction rate ^a
1a	SiO ₂	5	46	9.1	0.48	9.08
1a	Al ₂ O ₃	6	49	7.1	1.10	7.35
1a	MgO	2	14	7.0	0.67	2.10
1b	SiO ₂	12	70	5.8	0.89	2.72
1b	Al ₂ O ₃	11	55	5.0	0.57	2.06
1b	MgO	10	3	0.3	0.5	1.74
1c	SiO ₂	20	41	2.0	0.48	2.03
1c	Al ₂ O ₃	32	33	1.0	0.83	2.31
1c	MgO	12	1	0.1	0.5	1.77

^a Moles of product (2 and 3) / mole of Pd/hour.

catalyst was to keep the metal crystallites separated from each other so they would not agglomerate or sinter into larger, less efficient particles on heating. The concept of an 'inert' support has now been replaced by one in which the metal particles are anchored to the support by interfacial bonds between some of the metal atoms and the surface functionalities of the support. The electronic character of the support can, thus, be transmitted to the metal through these bonds [21]. The extent of this 'metal-support interaction' depends on both the nature of the metal and the type of support used.

To determine whether a support effect were operative in this reaction Pd/SiO₂, Pd/Al₂O₃ and Pd/MgO catalysts were prepared and used to promote the reactions between butyl vinyl ether and *p*-nitrobenzoyl chloride, 1a, benzoyl chloride, 1b, and *p*-toluoyl chloride, 1c. The reaction rates and product compositions obtained after 36 h reactions are listed in Table 1. Over each catalyst the β/α product (3/2) ratio decreased (*p*-NO₂ > *p*-H > *p*-CH₃) as the electron density on the aromatic ring increased. Of the three supports used here, silica is the most acidic with an isoelectric point (IEP) of about 2, magnesia is the most basic with an IEP near 12 and alumina is intermediate with an IEP of about 9 [22,23]. The Pd/SiO₂ catalyst gave the highest β/α ratio and the basic Pd/MgO the lowest β/α ratio with each substrate. This effect is least pronounced with the *p*-nitro benzoyl chlo-

is least pronounced with the *p*-nitro benzoyl chloride. Here it appears that the strong electron withdrawing capability of the *para* nitro group predominates and overshadows the electronic contribution of the support. With the other two substrates, **1b** and **1c**, though, the effect of the support is more evident. For comparison a commercial 5% Pd/C catalyst gave a product composed of 7% of the α product, **2**, and 70% of the β material, **3** [10]. A direct comparison with the present data is, however, difficult since there are a number of different types of carbons used as catalyst supports [24], each with their own IEPs, but all of them are acidic having on their surfaces phenolic and carboxylic acid groups. Even though the type of the carbon used in this commercial catalyst is not known the acidic nature of the support is evident by the β/α ratio of 10 for this reaction.

The nature of the support also has a pronounced effect on the rate of the reaction. The acidic silica supported catalyst is the most reactive while the basic magnesia slows the reaction down as does the presence of an electron releasing substituent on the aromatic ring. These results show that the electronic nature of the aryl halide and the catalyst support both can influence the regiochemistry of the reaction. There does not appear to be any clear relationship between the nature of the support and the **3Z/3E** product ratio, however.

3.2. Active sites

The determination of the nature of the active site(s) involved in this reaction requires a different approach. We have developed a single turnover (STO) reaction sequence which is used to characterize dispersed metals catalysts with respect to the numbers of alkene saturation sites, double bond isomerization sites and hydrogenation inactive sites they have present on their surfaces [14,18,19]. Data have been obtained which shows that these alkene saturation sites are the corner atoms or adatoms on the metal crystallite [25]. Mechanistic considerations indicate that the double bond isomerization sites are edge atoms

and that the face atoms on the metal particle do not take part in a hydrogenation reaction [14,19]. When a series of STO characterized catalysts are used to promote the same reaction under the same reaction conditions, plots of reaction rates versus the individual site densities (moles of site/mole of metal) for each catalyst can be prepared. A linear relationship between the reaction rate observed with each catalyst and the amount of a specific STO site present on each catalyst will show the type of site on which the reaction is taking place. This approach has been used to show that alkene [25,26] and ketone [27] hydrogenations as well as carbon monoxide [15] and alcohol [28] oxidations all take place on the STO saturation sites, the coordinately unsaturated corner atoms and adatoms on the metal surface.

A series of STO characterized Pd/Al₂O₃ catalysts were used to promote the reaction between butyl vinyl ether and **1a**. The STO site densities and the reaction rates are listed in Table 2. Also listed are the catalyst dispersions which are the ratios of surface atoms to the total atoms contained in the catalyst. Since the STO site densities are given as moles of site/mole of metal the dispersions are the sum of the site densities. This factor, which is also routinely obtained from the extent of hydrogen chemisorption on the metal, is commonly used for catalyst comparisons.

A plot of the saturation site densities versus the reaction rates (Fig. 3) shows a good correlation between these two factors and strongly supports the conclusion that the arylation reaction is taking place on the corner atoms and adatoms on the metal particles. The data in Fig. 4 show that there is no relationship between the isomerization and hydrogenation inactive site densities and the reaction rates. This indicates that the reaction cannot be taking place on these sites. Further, the lack of any correlation between the catalyst dispersions and the reaction rates rules out any generalized process in which the reaction can be considered to take place over essentially all of the surface atoms on the metal.

The conclusion that the corner atoms and adatoms are responsible for this reaction also follows

Table 2
STO site densities and reaction rates in the Pd/Al₂O₃ catalyzed Heck arylation

Catalyst	Saturation sites	Isomerization sites	Non-hydrogenation sites	Dispersion ^a	Reaction rate ^b
200 ^c	0.037	0.161	0.165	0.363	0.076
250 ^d	0.091	0.155	0.088	0.334	0.188
300 ^e	0.067	0.165	0.161	0.393	0.177
400 ^f	0.047	0.137	0.223	0.407	0.108
Com ^g	0.108	0.191	0.040	0.339	0.221

^a Moles of surface Pd/mole of total Pd.

^b Moles of product/mole of Pd/hour.

^c 6% Pd/Al₂O₃ reduced at 200°C.

^d 6% Pd/Al₂O₃ reduced at 250°C.

^e 6% Pd/Al₂O₃ reduced at 300°C.

^f 6% Pd/Al₂O₃ reduced at 400°C.

^g Commercial 5% Pd/Al₂O₃.

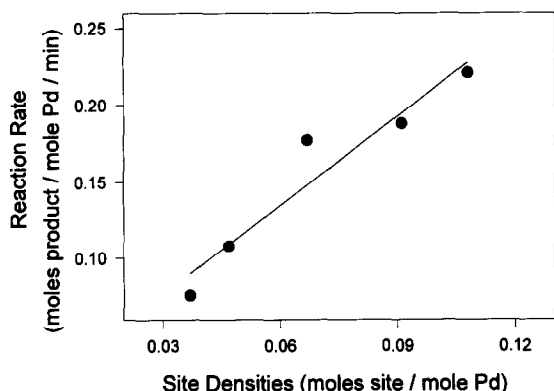


Fig. 3. Relationship between the STO saturation site densities and the rates of the Heck arylation run over various Pd/Al₂O₃ catalysts.

logically from the degree of coordinate unsaturation of the various types of surface sites. We have developed an Angular Overlap Method approach for the calculation of the s, p and d electron energies for each possible type of surface site on a number of different fcc metals and have used these data for frontier molecular orbital considerations of the reaction capabilities of each type of site [15,16]. Face atoms have the largest numbers of neighboring atoms and, thus, low coordinate unsaturation. With edge atoms the coordinate unsaturation increases somewhat but there still is not enough for the complexation of both the aryl halide and the enol ether as would be required for this

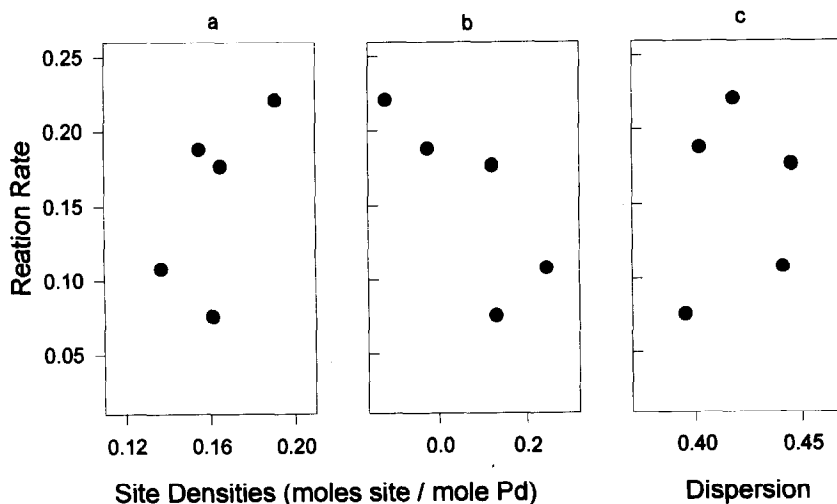


Fig. 4. Relationships between some STO surface site densities and the rates of the Heck arylation run over various Pd/Al₂O₃ catalysts. (a) STO isomerization sites. (b) STO non-hydrogenation sites. (c) Catalyst dispersions.

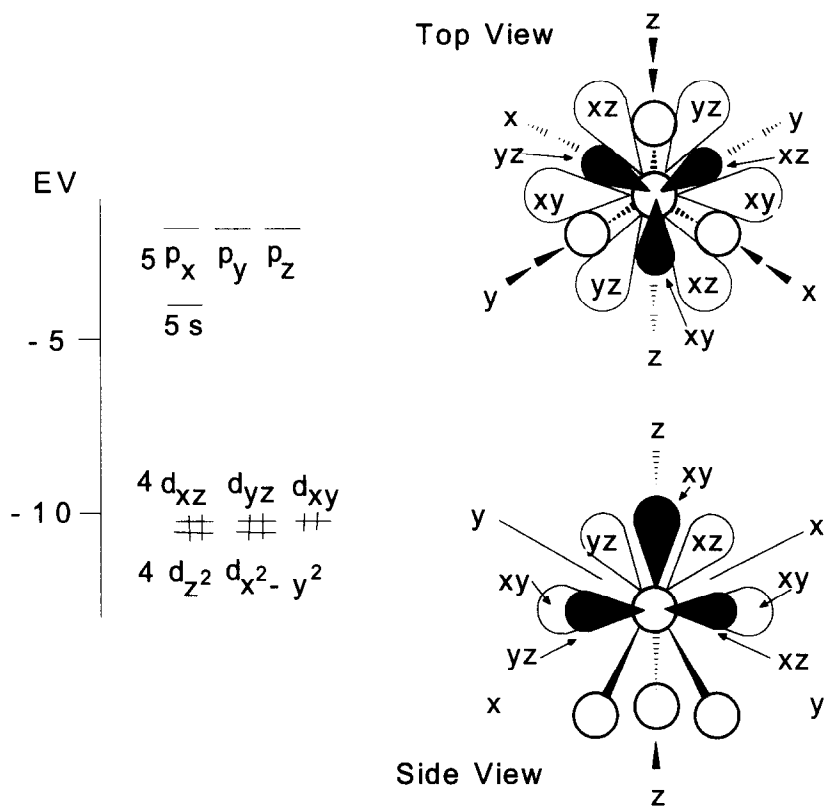
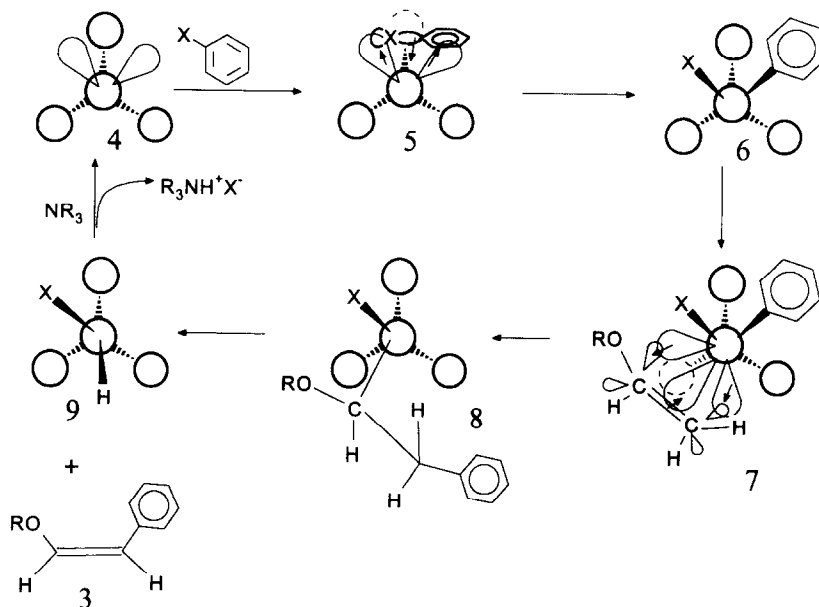


Fig. 5. Energy levels of the 5s, 5p and 4d electrons of a palladium tetrahedral corner atom.



Scheme 2.

appear to have this ability. The geometry of the metal surface and the interatomic spacing of the metal atoms also mitigates against the possible collaboration of two or more metal atoms as a multi-atom site for reactions of this type.

As an illustration the energy levels of the 5s, 5p and 5d electrons of a palladium tetrahedral corner atom are depicted in Fig. 5 along with a representation of the surface orbitals on this type of site. Scheme 2 illustrates the mechanistic pathway for the Heck arylation as it is proposed to take place on these tetrahedral corners and adatoms on the 111 faces of the Pd crystallites. This mechanism is based on that established for soluble palladium catalysts [7]. Adsorption of the aryl halide takes place by electron donation to the 5s LUMO with back bonding from one of the degenerate, d_{xy} , d_{xz} or d_{yz} , HOMO to give the aryl palladium halide **6** by way of the adsorbed intermediate, **5**. If the d_{xz} HOMO is used, vinyl ether adsorption, as in **7**, takes place by π donation to the now LUMO 5 p_y , followed by back bonding from the d_{xy} HOMO. Aryl insertion gives the halometalalkyl, **8**, which on β elimination to an available d orbital gives the enol ether, **3**. The resulting halo palladium hydride, **9**, then reacts with the tertiary amine to give the amine salt and regenerates the tetrahedral corner, **4**, for further reaction. A similar pathway for a reaction taking place on an octahedral corner or an adatom on a 100 face has been published [11].

4. Conclusions

The results presented here show that dispersed metals can be considered as viable catalysts for synthetically useful organometallic reactions. Further, the material used as the catalyst support can influence the regiochemistry of the reaction. In the Heck arylation studied here an acidic support such as silica withdraws electrons from the palladium and this leads to predominant β enol ether, **3**, formation. Palladium supported on a basic support, such as magnesia, which is electron donating, produces primarily the α product, **2**.

Electron withdrawal also decreases the rate of the reaction.

As with a number of other synthetically useful reactions [26–28] the heterogeneously catalyzed Heck arylation takes place on the coordinately unsaturated corner atoms and adatoms on the metal surface. These single atom active sites are the only ones having a sufficient number of orbitals available for interaction with both the aryl species and the enol ether at the same time, a procedure needed for the reaction to take place.

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