# A DFT study on Mor-DalPhos ligand in ammonia monoarylation by Buchwald-Hartwig amination

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Abstract: The use of ancillary ligands with palladium catalysts is very important for the Buchwald-Hartwig amination (BHA). As shown by Stradiotto[1], the use of Mor-DalPhos (Scheme 1) ligand for selective monoarylation of ammonia can achieve excellent yields of aniline at room temperature (Scheme 1) compared to its analogue, which has a dimethyl amine instead of the morpholine group (MorG).
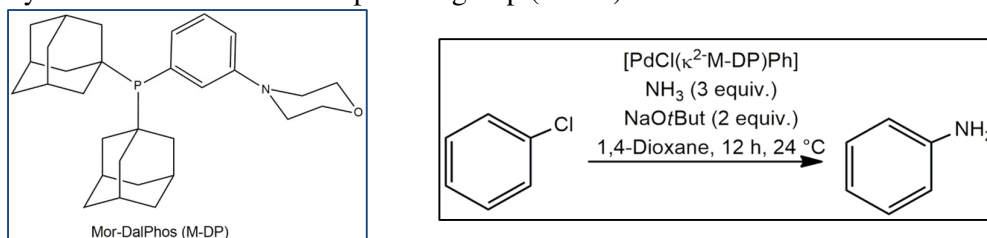
Scheme 1. Mor-DalPhos sketch (left) and Ammonia monoarylation reaction equation (right)

To verify the relevance of MorG in BHA, our research group suggested to investigate how the conformation affects intermediates and transition using Density Functional Theory (DFT).

All possible conformation are shown in Scheme 2. The codes *C* or *B* stand for chair or boat conformation, *eq* or *ax* correspond to equatorial or axial position of phenyl group bonded to N of MorG and + or - represents if the oxygen atom of MorG points towards or away from the Palladium center.
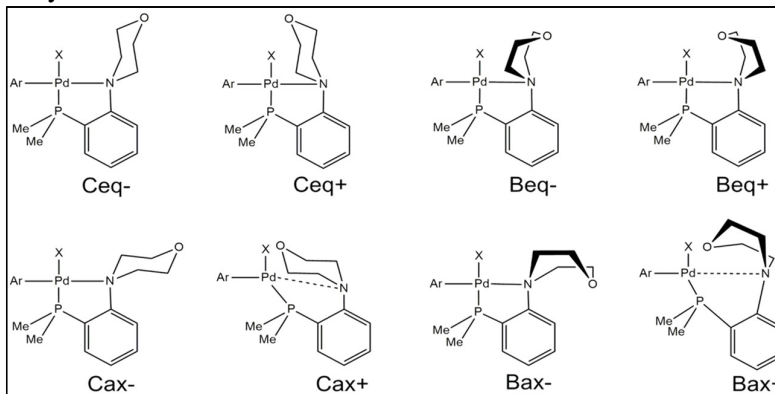
Scheme 2. Possible conformations and their codes for MorG in the Palladium catalyst.

All optimizations were done under Gaussian09 package with B3LYP/SDD(Pd)/6-31+G(d,p), adding Grimme's dispersion correction "D3" and solvent effect for 1,4-

dioxane were introduced by SMD model. The 1-Adamantyl groups were replaced by methyl groups to simplify the system. All energies reported are Gibbs Free energies at 273.15 K and 1 atm.

Intermediates 1 and 2 have at least two conformations which are almost isoenergetic in Gibbs Free Energy, indicating there isn't a preferential conformation for those intermediates. However in **IM3** and **IM4**, Ceq- conformation is the most stable compared to the others, 1.2 and 4.0 kcal.mol^{-1} for **IM3** and **IM4,** respectively.

Table 1. Relative Gibbs Free Energy (kcal.mol^{-1}) comparing conformations for intermediates 1, 2, 3 and 4

[Pd<u>Cl</u>(κ^2-M-DP)Ar] – IM1		[Pd<u>NH$_3$</u>(κ^2-M-DP)Ar]$^+$ – IM2		Pd<u>NH$_2$</u>(κ^2-M-DP)Ar – IM3		Pd(κ^1-P-M-DP) – IM4	
Confor.	**ΔG**	**Confor.**	**ΔG**	**Confor.**	**ΔG**	**Confor.**	**ΔG**
-	-	**-**	-	**Beq-**	13.5	**-**	-
Beq-	17.0	**Ceq+**	10.5	**Ceq+**	8.3	**-**	-
Ceq+	11.4	**Bax-**	3.6	**Beq+**	3.2	**Bax-**	8.6
Bax-	0.9	**Cax-**	2.1	**Bax-**	2.8	**Beq-**	7.9
Cax-	0.7	**Ceq-**	0.5	**Cax-**	1.2	**Ceq+**	4.0
Ceq-	0	**Beq+**	0	**Ceq-**	0	**Ceq-**	0

Transitions states (**TS**) were found for Chloride Substitution step (**IM1→IM2**) and Reductive Elimination step (**IM3→IM4**). Both **TSs** shows a clearly preference for **Ceq-** conformations by 3 kcal.mol^{-1} than others conformations.
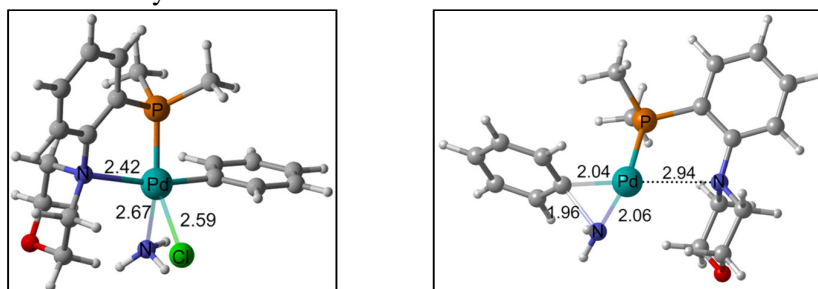
Figure 1. Transition state of Chloride Substitution step (left) and Transition State of Reduction Elimination step (right). Both TSs with the most stable conformation.

This work shows that steric hindrance rules over the formation of weak interaction to determine Morpholine Group conformations for the intermediates and transition states calculated so far.

Key-words: Buchwald-Hartwig Amination, Transition State, mechanism, Mor-DalPhos

References:

[1] J; Stradiotto, M. and cowokers, Chem. Eur. J. 2013 , 19 , 2131–2141.