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Intramolecular Pd(0)-Catalyzed Reactions of β-(2-Iodoanilino) Carboxamides: Enolate Arylation and Nucleophilic Substitution at the Carboxamide Group

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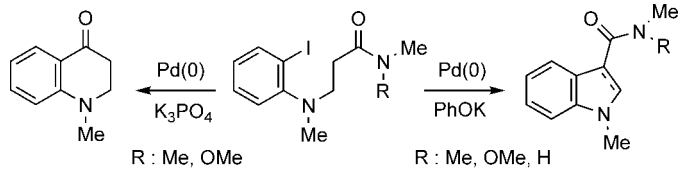

Two different reaction pathways, the enolate arylation and the acylation of the aryl halide, can be promoted by a Pd(0) catalyst starting from β-(2-iodoanilino) carboxamides. The intramolecular acylation of β-(2-iodoanilino) carboxamides reported here is the first example of a nucleophilic attack of a σ-arylpalladium species at the carboxamide group, a framework that is usually inert toward organopalladium reagents.

Introduction

During the past decades, there has been continuous interest in developing reliable Pd-catalyzed coupling reactions to form carbon−carbon bonds.[1] Among the different cross-coupling processes, the Pd-catalyzed arylation[2−8] and alkenylation[9−13] of enolate-type nucleophiles are emerging as extremely powerful tools in organic synthesis. In particular, the intramolecular versions of these reactions[14−18] have found growing application in the synthesis of complex natural products.[9,10,19−29]

Parallel with the progress in this field, there also has been growing interest in the direct addition of the aryl- and vinyl palladium species to electrophilic carbon−heteroatom multiple bonds. So far, the intramolecular attack of these relatively low nucleophilic species on the carbonyl group of aldehydes,[30] ketones,[31] and esters[32] and on the imino,[33] cyano,[34] and isocyanate[35] groups has been described.

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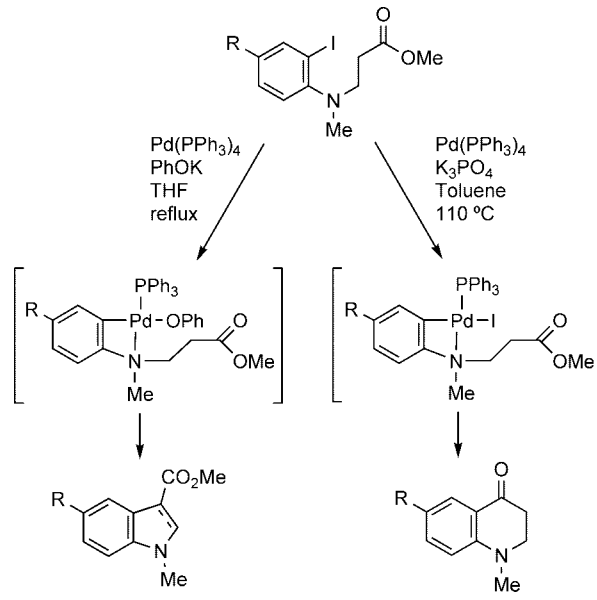
Although both the reaction at the α position and the nucleophilic attack on the carbon−heteroatom multiple bond probably involve similar σ-C-bonded palladium(II) intermediates, these two reaction pathways seem to operate quite independently of each other, and almost no competition between the two processes has been reported.[36] In fact, such competition has been observed only in the Pd-catalyzed intramolecular coupling of aryl halides with aldehydes[17,37] and in reactions starting from β-(2-haloanilino) ketones.[14c,31c]

In this context, we have reported recently that starting from β-(2-iodoanilino) esters either the enolate arylation[18b] or the nucleophilic substitution at the alkoxycarbonyl group[32] catalyzed by Pd(0) could be selectively promoted by changing the reaction conditions only slightly (Scheme 1). The acylation reaction shown in Scheme 1 constitutes the first example of palladium-catalyzed substitution at the alkoxycarbonyl group by an aryl halide.[38] The intermediacy of a four-membered azapalladacycle,[39] which strongly modifies the interaction of the metal center with the carbonyl group,[31c] was invoked to explain the otherwise unexpected attack of the σ-arylpalladium species at the less electrophilic ester carbonyl.

SCHEME 1



Continuing our research on this aspect of palladium chemistry, we were interested to see whether changing the ester to an amide moiety could modify the course of the palladium-catalyzed reactions on this type of substrate. We expected that the higher pK_as of the amides would make the α arylation a more challenging task, while the less electrophilic character of the amide carbonyl could avoid the direct nucleophilic attack of the σ-arylpalladium species.

Herein, we report that starting from β-(2-iodoanilino) carboxamides the two alternative pathways, involving either the enolate arylation or the nucleophilic substitution at the amide group, can be promoted by a Pd(0) catalyst. This has allowed us to develop new synthetic entries to both indole-3-carboxamides[40] and dihydroquinolin-4-ones,[41] which constitute important classes of compounds in medicinal chemistry.

Results and Discussion

We commenced our investigation by studying the α arylation of amides **1a**−**d**, **2**, and **3**, which were synthesized from the

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(36) It should be noted that in the majority of the examples in which the nucleophilic attack takes place the formation of the α-arylation products is prevented either by the substitution pattern of the substrate or by the size of the ring to be formed.

(37) The formation of the carbonyl arylation products was explained in this case by means of the insertion of the σ-arylpalladium species into the formyl C−H bond. However, the alternative mechanism involving the addition of the σ-arylpalladium species to the C=O bond of the aldehyde, followed by β-hydride elimination from the resulting palladium(II) alkoxide, also could be possible.

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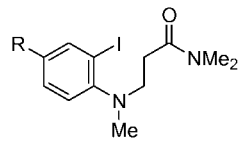
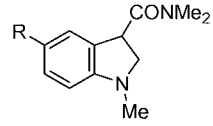
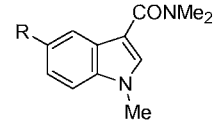
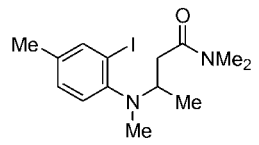
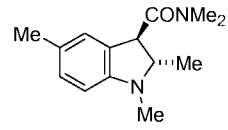
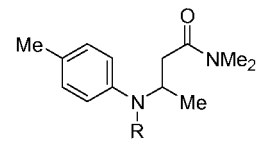
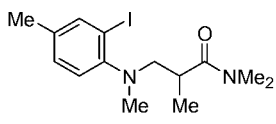
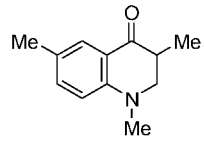
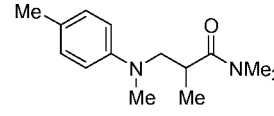
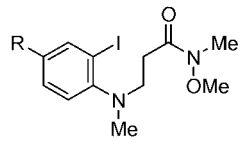
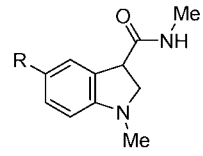
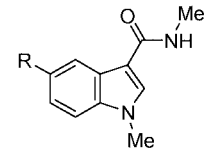
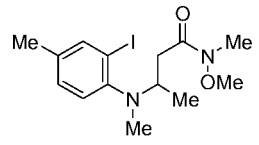
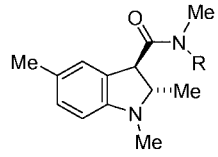
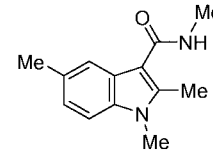
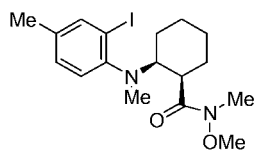
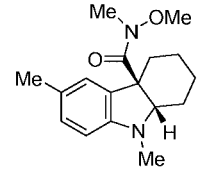
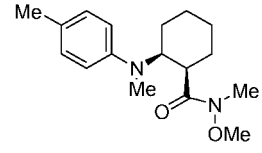
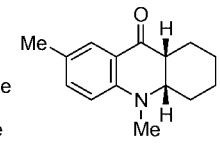
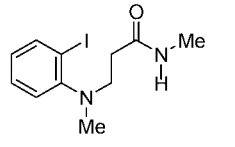
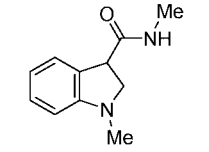
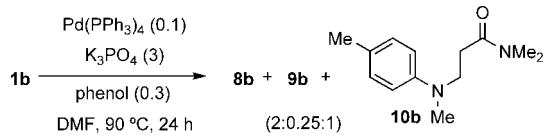
TABLE 1. Pd(0)-Catalyzed α Arylation of *β*-(2-Iodoanilino) Carboxamides[a]

	amide	time	products (yield)[b]	
				
1	**1a**, R = H	30 h	**8a** (68%)	
2	**1b**, R = Me	36 h	**8b** (76%)	**9b**[c]
3	**1c**, R = OMe	40 h	**8c**[d]	**9c** (58%)
4	**1d**, R = F	48 h[e]	**8d** (43%)	
				
5	**2**	41 h	**11** (65%)[f]	**12a** (R = Me) + **12b** (R = H) (1:1.4, 30%)
				
6	**3**	72 h[e]	**13** (4%)	**14** (42%)
				
7	**4a**, R = H	8 h	**15a** (37%)	**16a** (58%)
8	**4b**, R = Me	8 h	**15b**[g]	**16b** (59%)
9	**4c**, R = Cl	18 h	**15c**[h]	**16c** (78%)
				
10	**5**	12 h	**19a** (R = OMe) (18%) **19b** (R = H)[f,i]	**20** (58%)
				 
11	**6**	48 h[e]	**21** +	**22** (1:2, 35%) **23** (15%)[j]
				
12	**7**	48 h[k]	**15a** (43%)[l]	

[a] Reaction conditions: 5 mol % of $Pd(PPh_3)_4$, phenol (2.75 equiv), and KO-*t*-Bu (2.25 equiv) in THF at reflux. [b] Unless otherwise indicated, yields refer to pure products isolated by flash chromatography. [c] Indoline **8b** suffered partial air oxidation to indole **9b** during ^{13}C NMR experiments. [d] ^1H NMR analysis of the crude reaction mixture gave indoline **8c** as the only reaction product. [e] At 20 mol % of $Pd(PPh_3)_4$. [f] Stereochemistry is based on ^1H and ^{13}C NMR. See ref 18b. [g] ^1H NMR analysis of the crude reaction mixture gave a 1:1.3 mixture of **15b** and **16b**. [h] ^1H NMR analysis of the crude reaction mixture gave a 1:1.4 mixture of **15c** and **16c**. [i] ^1H NMR analysis of the crude reaction mixture gave a 1:2:1 mixture of **19a**, **19b**, and **20**. [j] *N*-Methyl-*p*-toluidine also was isolated (10%). [k] At 10 mol % of $Pd(PPh_3)_4$. [l] The hydrodehalogenation compound also was detected in the reaction mixture, although it could not be isolated.

SCHEME 2



corresponding esters by reaction with the dimethylaluminum chloride dimethylamine complex.[42] The most representative results are summarized in Table 1.

We were pleased to find that the conditions we have previously employed in the Pd(0)-catalyzed intramolecular arylation of amino-tethered esters, using 5 mol % of $Pd(PPh_3)_4$ and 2.25 equiv of PhOK in refluxing THF,[18b] allowed iodoaniline **1a** to undergo the α arylation to give indoline **8a** in 68% yield (Table 1, entry 1). Under the same reaction conditions, iodoanilines **1b**−**d**, bearing electron-donating or electron-withdrawing groups at the arene ring, afforded reaction mixtures in which the corresponding indolines **8b**−**d** were also the only detected products (Table 1, entries 2−4). While indolines **8b**[43] and **8d** could be isolated and characterized, indoline **8c** oxidized spontaneously during the purification process to give indole **9c**.[44]

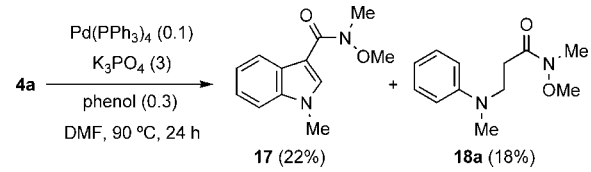
The use of K_3PO_4 as the base in the presence of a catalytic quantity of phenol in DMF, which also allowed the Pd(0)-catalyzed cyclization in the ester series,[18b] was found to be less effective for the present α-arylation reaction. For example, treatment of **1b** under these reaction conditions resulted in the formation of significant amounts of the reduction product **10b** together with indoline **8b** and indole **9b** (Scheme 2). The use of a stronger base such as LiO-*t*-Bu was completely ineffective in promoting the cyclization and led to the formation of complex reaction mixtures.

The arylation reaction also was used successfully for the preparation of 2,3-disubstituted indolines (Table 1, entry 5). However, amide **3** failed to give the α-arylation reaction and afforded the reduction compound **14** together with small amounts of dihydroquinolone **13**, the latter resulting from the nucleophilic substitution at the carboxamide group (Table 1, entry 6). In this case, the slowness of the reaction at the more hindered α-methine position allowed competitive processes such as reduction or an attack on the carbonyl group to occur.

The palladium-catalyzed α arylation was extended to the Weinreb amides **4a**−**c**, **5**, and **6**. Weinreb amides are important carbonyl equivalents that have found many applications in the synthesis of carbonyl compounds.[45] However, there are few examples of the use of *β*-amino Weinreb amides.[46]

Treatment of amide **4a** under the optimized reaction conditions afforded a mixture of indoline **15a** and indole **16a**, resulting from the α arylation and demethoxylation of the Weinreb amide

SCHEME 3



(Table 1, entry 7). It should be noted that on standing in a chloroform solution indoline **15a** quantitatively oxidized to indole **16a**.

Similar results were obtained from iodoanilines **4b** and **4c**, which also afforded mixtures of the corresponding indolines and indoles. In these cases, however, the oxidation was completed during the purification process and only the indoles **16b** and **16c** were isolated (Table 1, entries 8 and 9, respective).

Once again, the use of K_3PO_4 as the base in the presence of a catalytic quantity of phenol in DMF was less effective for the arylation reaction. Thus, for example, under these reaction conditions, **4a** afforded a nearly equimolecular mixture of indole **17** and the reduction product **18a**. Interestingly, the Weinreb amide moiety remained unchanged in both products (Scheme 3).

The Pd-catalyzed α arylation of amide **5** afforded a mixture of indolines **19a** and **19b** and indole **20** (∼1:2:1), but after flash chromatography only **19a** (18%) and **20** (58%) were isolated because indoline **19b** quantitatively oxidized to indole **20** (Table 1, entry 10). The attempt at α arylation of Weinreb amide **6** resulted in the formation of a complex reaction mixture (Table 1, entry 11). After column chromatography, the main products could be identified, although not all of them were completely characterized. Thus, the three main fractions consisted of an unseparated mixture of the α arylation product **21** and the hydrodehalogenation compound **22**; hexahydroacridinone **23**, which resulted from the substitution at the carboxamide group; and *N*-methyl-*p*-toluidine. As with the simple amides, the α arylation at the more-hindered α-methine position of a Weinreb amide was troublesome.

Finally, it is noteworthy that the α arylation also could be extended to the secondary amide **7**, which under the optimized reaction conditions afforded indoline **15a** in an acceptable yield (Table 1, entry 12). The alternative pathway involving lactamization by formation of the C−N bond[47] was not observed.

At this point, we turned our attention to the unexpected formation of minor amounts of dihydroquinolones **13** and **23**, resulting from the nucleophilic substitution at the carboxamide group, in the attempts at α arylation of amides **3** and **6** (vide supra). The lower electrophilic character of the amide carbonyl group surprisingly did not avoid the nucleophilic attack.

To our delight, when amide **3** was treated with $Pd(PPh_3)_4$ in the presence of K_3PO_4 as the base in toluene, the formal nucleophilic substitution at the carboxamide group became the main reaction, with dihydroquinolone **13** being obtained in 40% yield (Table 2, entry 1). Similar behavior was observed starting from amides **1a,b** and **2**, which afforded the corresponding dihydroquinolones in low to moderate yields together with the hydrodehalogenated anilines (Table 2, entries 2−4). As expected from the less electrophilic character of the amide carbonyl group, the Pd(0)-catalyzed intramolecular acylation reactions starting from amides afforded lower yields than those obtained in the reactions of the corresponding esters.[48] Interestingly, when

(42) Hughes, D. L.; Bergan, J. J.; Amato, J. S.; Bhupathy, M.; Leazer, J. L.; McNamara, J. M.; Sidler, D. R.; Reider, P. J.; Grabowski, J. J. *J. Org. Chem.* **1990**, *55*, 6252–6259.

(43) It should be noted that indoline **8b** suffered partial air oxidation to indole **9b** during ^{13}C NMR experiments.

(44) Chou, S.-S. P.; Yuan, T.-M. *Synthesis* **1991**, 171–172.

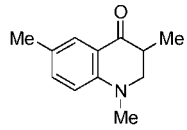
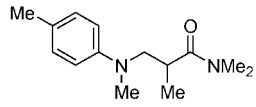
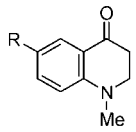
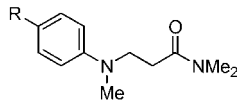
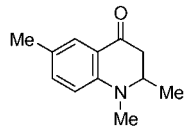
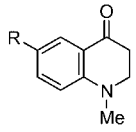
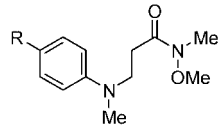
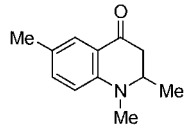
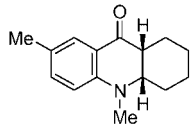
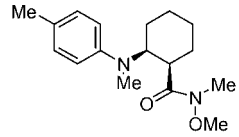
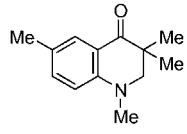
(45) See for a review: Sibi, M. P. *Org. Prep. Proced. Int.* **1993**, *25*, 15–40.

(46) See for an example: Davis, F. A.; Nolt, M. B.; Wu, Y.; Prasad, K. R.; Li, D.; Yang, B.; Bowen, K.; Lee, S. H.; Eardley, J. H. *J. Org. Chem.* **2005**, *70*, 2184–2190.

(47) (a) Yang, B. H.; Buchwald, S. L. *Org. Lett.* **1999**, *1*, 35–37. (b) Kitamura, Y.; Hashimoto, A.; Yoshikawa, S.; Odaira, J.-I.; Furuta, T.; Kan, T.; Tanaka, K. *Synlett* **2006**, 115–117.

(48) For example, the acylation reaction from the ester analog of amide **1b** afforded dihydroquinolone **24b** in 65% yield, and the acylation from the ester analog of **3** gave **13** in 49% yield. See ref 32.

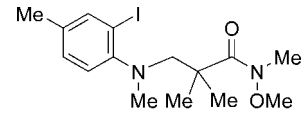
TABLE 2. Pd(0)-Catalyzed Intramolecular Acylation from *β*-(2-Iodoanilino) Carboxamides

	amide	products (yield)[b]	
			
1	**3**	**13** (40%)	**14** (22%)
			
2	**1a**	**24a**, R = H (41%)	**10a**, R = H (49%)
3	**1b**	**24b**, R = Me (35%)	**10b**, R = Me (25%)
			
4	**2**	**25** (22%)[c]	
			
5	**4a**	**24a**, R = H (49%)	**18a** (29%)
6	**4b**	**24b**, R = Me (65%)[d]	**18b**[e]
7	**4c**	**24c**, R = Cl (43%)	**18c** (31%)
			
8	**5**	**25** (50%)	
			
9	**6**	**23** (41%)[f]	**22** (20%)[g]
			
10	**26**	**27** (89%)[h]	

[a] Reaction conditions: 20 mol % of $Pd(PPh_3)_4$, K_3PO_4 (3 equiv), and Et_3N (10 equiv) in toluene at 110 °C in a sealed tube for 72 h. [b] Yields refer to pure products isolated by flash chromatography. [c] *N*-Methyl-*p*-toluidine also was isolated, although not quantified. [d] After 48 h. [e] Not quantified. [f] Stereochemistry is based on ^1H and ^{13}C NMR. [g] *N*-Methyl-*p*-toluidine also was isolated (8%). [h] At 10 mol % of $Pd(PPh_3)_4$ and 48 h.

starting from Weinreb amides, the intramolecular acylation reaction proceeded with better yields (compare Table 2, entries 2, 3, and 4 with 5, 6, and 8, respectively). Starting from Weinreb amide **6**, hexahydroacridinone **23** was obtained in 41% yield (Table 2, entry 9).

The acylation reaction of amide **26**, lacking hydrogen atoms α to the carbonyl group, afforded dihydroquinolone **27** in excellent yield (Table 2, entry 10).



26

Finally, secondary amide **7** failed to produce acylation when submitted to the usual reaction conditions and afforded the hydrodehalogenation compound as the main product.

The effectiveness of PhOK in the Pd(0)-catalyzed α-arylation reaction of *β*-(2-iodoanilino) carboxamides is somewhat surprising because the pK_a of phenol is considerably lower than that of the amides.[49] Especially interesting is the α arylation of amide **7**, which has the more acidic N−H bond.

Possible mechanisms for these Pd(0)-catalyzed α arylations are shown in Scheme 4. The oxidative addition of the aryl iodide to Pd(0) followed by ligand exchange would give the arylpalladium phenoxide complex **A**. A related four-membered azapalladacycle in which the iodo ligand has been replaced by TfO^- has been previously reported.[50] The formation of this transient intermediate would not only stabilize the arylpalladium moiety, preventing the nucleophilic attack at the carbonyl (vide infra), but also assist the enolization reaction. Thus, the intramolecular reaction of the phenoxide ligand[51] with the coordinated carboxamide group would facilitate the deprotonation with concomitant formation of an O-bonded Pd(II) enolate **B**. Reductive elimination from this Pd(II) complex[52] would produce indoline **8a** and the regeneration of the reactive Pd(0) species.

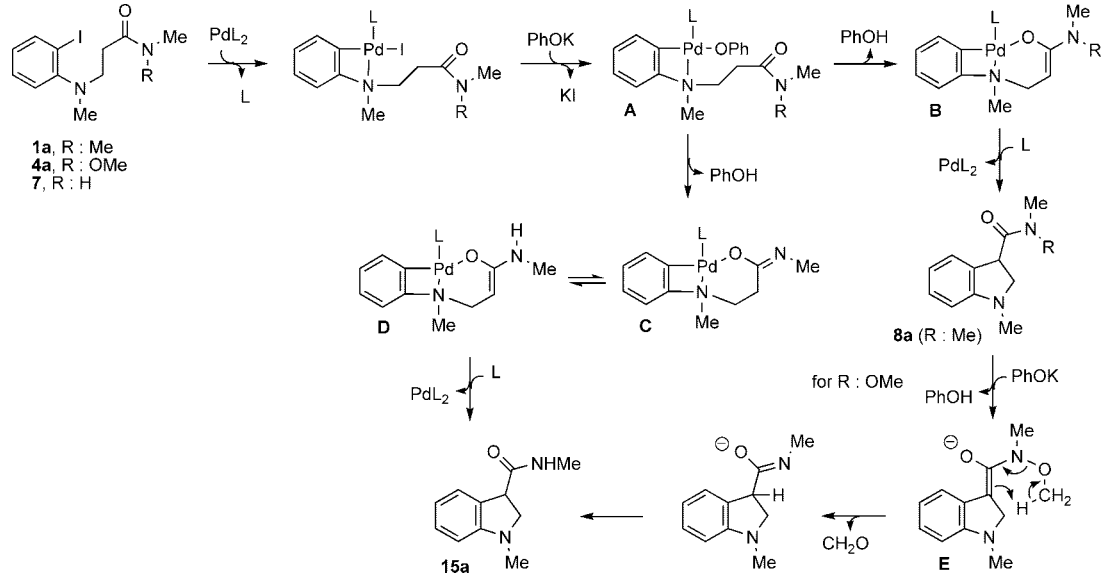
On the other hand, for secondary amide **7**, the deprotonation of the more acidic N−H bond of **A** (R:H) would afford an O-bonded Pd(II) amidate **C**. In the basic reaction conditions, this amidate would be in equilibrium with the O-bonded Pd(II) enolate **D**,[53] which by reductive elimination would give rise to indoline **15a**.

Two possibilities can be considered to account for the observed α arylation/demethoxylation of Weinreb amides. A sequence of reactions involving the initial demethoxylation of the Weinreb amide was dismissed as inconsistent with the experimental evidence. Thus, for example, Weinreb amide **4a** was recovered unchanged when treated with KO-*t*-Bu/phenol in the absence of a Pd catalyst,[54] and moreover both the α arylation compound **21** and the hydrodehalogenation compound **22**, which were formed when **6** was treated with KO-*t*-Bu/phenol/$Pd(PPh_3)_4$, maintained the Weinreb amide moiety.

However, the alternative sequence, which involves demethoxylation of the indoline resulting from the α-arylation reaction of the Weinreb amide, could explain the experimental results

(49) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.
(50) Solé, D.; Díaz, S.; Solans, X.; Font-Bardia, M. *Organometallics* **2006**, *25*, 1995–2001.
(51) Rutherford, J. L.; Rainka, M. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 15168–15169.
(52) Isolation and study of the reductive elimination reaction of arylpalladium enolates: Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 5816–5817.
(53) Related process: Altman, R. A.; Hyde, A. M.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 9613–9620.
(54) Moreover, no reaction was observed when *N*-methoxy-*N*-methylacetamide was treated with KO-*t*-Bu/phenol/$Pd(PPh_3)_4$.

SCHEME 4. Proposed Mechanisms for the α-Arylation Reactions



obtained in this work. In fact, treatment of indoline **19a** with KO-*t*-Bu/phenol in refluxing THF for 36 h resulted in the demethoxylation reaction to give an equimolecular mixture of indoline **19b** and indole **20**.

Two mechanisms can be proposed for this demethoxylation on the basis of related reactions of Weinreb amides.[55,56] A simple E2 mechanism was an unlikely explanation of why demethoxylation takes place after the arylation reaction only, so it was rejected. However, a mechanism involving the formation of an enolate, **E**, and its further decomposition via unimolecular fragmentation with the loss of formaldehyde appears more reasonable on chemical grounds, considering the following:

(A) The facile demethoxylation of the indolines resulting from the α-arylation reaction is consistent with the higher acidity of the benzylic α hydrogens.

(B) Weinreb amide **21**, which lacks α hydrogens, was the α-arylation product obtained in the reaction of amide **6** (Table 1, entry 11) and was recovered unchanged after further treatment with KO-*t*-Bu/phenol in refluxing THF.

(C) The isolation of Weinreb amide **19a** is probably a consequence of the steric hindrance exerted by the methyl group, which would hinder the concerted fragmentation.

(D) The formation of indole **17** in the α-arylation reaction of **4a** when using K_3PO_4 as the base could be understood considering that the low enolization promoted by such a mild base makes the competitive oxidation the main reaction.

Returning to the acylation reaction reported in this work, we note that it is the first example of a nucleophilic substitution at the carboxamide group by a *σ*-arylpalladium species. This reaction is quite surprising because the carboxamide group has long been considered inert toward organopalladium reagents. Moreover, although different carbopalladation reactions of carbon−heteroatom multiple bonds have been reported, these species generally show a low propensity to undergo the insertion process because of their coordination characteristics. The migratory insertion must be preceded by *π* coordination, but in carbon−heteroatom multiple bonds the *σ* donation of the lone pair of electrons on the heteroatom is the preferred mode of interaction with the metal center. The larger negative charge and consequent stronger coordination ability of the carbonyl oxygen of an amide fragment[57] should hinder the required *σ* to *π* isomerization and thus prevent the carbonyl insertion.

The formal nucleophilic substitution reported here probably proceeds through a mechanism similar to that of the Pd(0)-catalyzed acylation by the alkoxycarbonyl group.[32] The key steps here would be (1) oxidative addition of the aryl iodide to a Pd(0) species and (2) carbopalladation between the *σ*-arylpalladium moiety and the carbonyl of the amide group. The intermediacy of the four-membered azapalladacycle, which strongly modifies the interaction of the metal center with the carbonyl group,[31c] is invoked again to explain the otherwise unexpected attack of the *σ*-arylpalladium species onto the barely electrophilic amide carbonyl. Thus, the coordination of the N atom to the palladium in the four-membered azapalladacycle not only brings the carbonyl group nearer to the metal to facilitate the required *π* coordination but also increases the electron density on the palladium center to enable the otherwise unfavorable carbopalladation reaction to occur. The remaining key steps would be (3) *β*-amide elimination from the Pd(II) alkoxide formed in the carbopalladation step to give the dihydroquinolone and a Pd(II) amide complex and (4) *β*-hydride elimination from the latter to regenerate the Pd(0) catalyst.

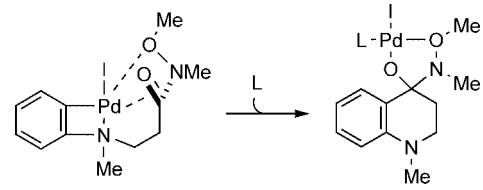
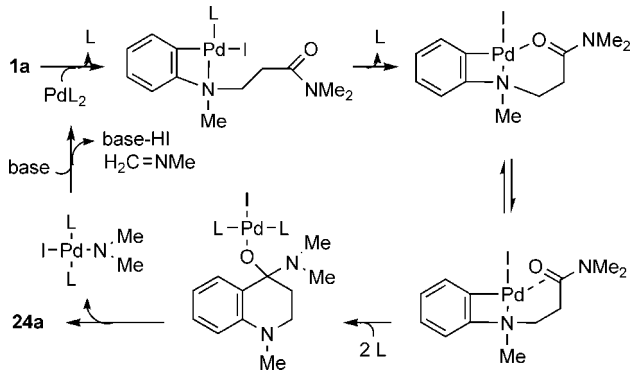


FIGURE 1. Stabilization of Pd(II) intermediates by chelation.

The better results obtained in the acylation reactions when using Weinreb amides are probably due to the chelation ability of the second oxygen atom (Figure 1). Thus, the coordination of this oxygen with the Pd center would not only facilitate the

(55) Keck, G. E.; McHardy, S. F.; Murry, J. A. *Tetrahedron Lett.* **1993**, *34*, 6215–6218.
(56) Graham, S. L.; Scholz, T. H. *Tetrahedron Lett.* **1990**, *31*, 6269–6272.
(57) For the coordination ability of the−N(R)−$(CH_2)_n$−CO−$N(R)_2$ framework in *σ*-arylpalladium(II) complexes, see ref 50.

SCHEME 5. Proposed Mechanism for the Intramolecular Acylation Reaction



formation of the carbonyl π complex required for the carbopalladation but also stabilize the Pd(II) alkoxide resulting from this reaction.

Conclusions

In summary, we have reported that two different Pd(0)-catalyzed reactions, involving either enolate arylation or the acylation of the aryl halide, can be promoted from β-(2-haloanilino) carboxamides by slightly changing the reaction conditions. The Pd(0)-catalyzed acylation reaction described in this work constitutes the first reported example of the formal nucleophilic substitution at the carboxamide group by a σ-arylpalladium species. Besides the potential synthetic application of the above methodologies, this work highlights how the presence of a strong coordinating group can modify the reactivity of organic compounds, allowing the development of unknown palladium-catalyzed reactions with otherwise "unreactive" functional groups. In particular, the formation of transient four-membered azapalladacyclic intermediates is invoked to explain how σ-arylpalladium species can react with nucleophiles such as enolates, as well as electrophiles such as the carbonyl of the amide group.

Experimental Section

Representative Procedure for the Pd(0)-Catalyzed α Arylation (Table 1, Entry 1). To a solution of amide **1a** (100 mg, 0.30 mmol) in THF (7 mL) were added under argon phenol (78 mg, 0.83 mmol), KO-*t*-Bu (0.68 mmol, 0.68 mL of 1 M solution in *tert*-butyl alcohol), and $Pd(PPh_3)_4$ (17 mg, 0.015 mmol). The solution was heated at reflux for 30 h. After being cooled at room temperature, the mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and 1 N aqueous NaOH. The organic layer was dried and concentrated. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2-MeOH 1%) to give indoline **8a** (41 mg, 68%).

Representative Procedure for the Pd(0)-Catalyzed Acylation (Table 2, Entry 1). A mixture of amide **3** (75 mg, 0.21 mmol), K_3PO_4 (135 mg, 0.63 mmol), Et_3N (0.3 mL, 2.1 mmol), and $Pd(PPh_3)_4$ (48 mg, 0.042 mmol) in toluene (6 mL) was stirred at 110 °C in a sealed tube for 72 h. The reaction mixture was poured into water and extracted with Et_2O. The organic extracts were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2-MeOH 1%) to give dihydroquinolin-4-one **13** (16 mg, 40%) and aniline **14** (11 mg, 22%).

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Supporting Information Available: Characterization data for all new compounds and experimental procedures for preparation of starting materials and ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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