

# Palladium/Proazaphosphatrane-Catalyzed Amination of Aryl Halides Possessing a Phenol, Alcohol, Acetanilide, Amide or an Enolizable Ketone Functional Group: Efficacy of Lithium Bis(trimethylsilyl)amide as the Base

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**Abstract:** A commercially available catalyst system comprising  $\text{Pd}(\text{OAc})_2$  or  $\text{Pd}_2(\text{dba})_3$  and the proazaphosphatrane ancillary ligand  $\text{P}(i\text{-BuNCH}_2\text{CH}_2)_3\text{N}$  (**1**) for the amination of aryl halides substituted with a phenol, alcohol, acetanilide, amide or ketone group containing an enolizable hydrogen is described. The reaction is performed in the presence of  $\text{LiN}(\text{SiMe}_3)_2$

as the base. Other bases tested were either less effective or completely non-functional.

**Keywords:** aryl amination; homogeneous catalysis; lithium amides; palladium; P,N ligands; proazaphosphatranes

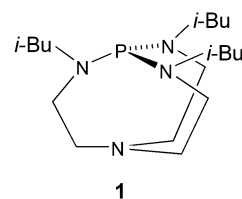
## Introduction

Lithium bis(trimethylsilyl)amide [ $\text{LiN}(\text{SiMe}_3)_2$ ] is a well known sterically hindered non-nucleophilic base that has played an increasingly important role in organic synthesis.<sup>[1]</sup> In one such application, Hartwig recently employed  $\text{LiN}(\text{SiMe}_3)_2$  as the base in the palladium-catalyzed reaction of aryl halides with amines.<sup>[2]</sup> In 1997, Brüning reported that  $\text{LiN}(\text{SiMe}_3)_2$  can be utilized as a nitrogen source (nucleophile) in palladium-catalyzed aminations of allyl chloride.<sup>[3]</sup> Building on this observation, Hartwig, in 2001, demonstrated the use of  $\text{LiN}(\text{SiMe}_3)_2$  as an ammonia equivalent for the  $\text{Pd}(\text{dba})_2/\text{P}(t\text{-Bu})_3$ -catalyzed conversion of aryl halides to anilines.<sup>[4]</sup> Later that year, Buchwald used  $\text{Pd}_2(\text{dba})_3$  and (*o*-biphenyl)PCy<sub>2</sub> for the same transformation.<sup>[5]</sup> More recently, Buchwald<sup>[6]</sup> showed the utility of  $\text{LiN}(\text{SiMe}_3)_2$  as a base for amination reactions of aryl halides possessing substituents such as acetanilide, alcohol, and phenol; functional groups that were not compatible with either the original protocol utilizing  $\text{NaO}-t\text{-Bu}$  as the base or with the modified procedure wherein weaker bases such as  $\text{K}_3\text{PO}_4$  or  $\text{Cs}_2\text{CO}_3$  were employed. The inefficient amination reactions using these bases when the aforementioned functional groups were present may be due to binding of the deprotonated species to the palladium with resulting deactivation of the catalyst. This reaction inefficiency may also be due to the ineffectiveness of the commonly employed ligands to support such transformations as is indicated in a recent report by Buchwald wherein amination reactions of aryl halides

substituted by amide and acetanilide functional groups were accomplished with the use of a sterically hindered biaryl monophosphine ligand.<sup>[7]</sup>

Our recent investigation of palladium-catalyzed reactions (e.g., Suzuki,<sup>[8]</sup> amination,<sup>[9]</sup> and alpha-arylation<sup>[10]</sup>) led us to the discovery of a new bicyclic triaminophosphine ligand, namely, **1** (2,8,9-triisobutyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane, a member of the proazaphosphatrane class of compounds<sup>[11]</sup>) for these transformations (Figure 1).

In the case of aryl amination reactions, the  $\text{Pd}/\mathbf{1}$  catalyst system, in combination with  $\text{NaO}-t\text{-Bu}$  as the base, displays very high activity for the coupling of aryl halides with amines.<sup>[9]</sup> However, there were limitations for the types of functional groups that could be present in the substrates. Thus, the conversion of substrates possessing amide, alcohol, phenol, and ketone substituents into desired products proved difficult. The use of a weaker base, such as  $\text{Cs}_2\text{CO}_3$ , failed to promote this reaction. Following the report of Buchwald that  $\text{LiN}(\text{SiMe}_3)_2$  functions as an unique base for the aforementioned substrate



**Figure 1.** Bicyclic triaminophosphine ligand.

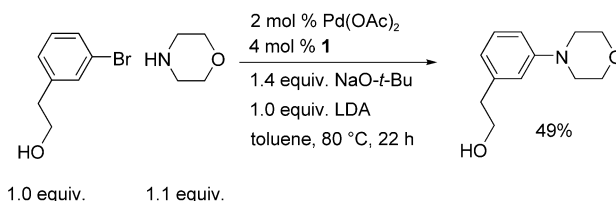
types,<sup>[6]</sup> we were interested in its application to amination reactions catalyzed by **1**/Pd. Here we report the results of that study.

## Results and Discussion

We first examined the coupling of 3-bromophenol with morpholine using 2 mol % of Pd(OAc)<sub>2</sub> and 4 mol % of ligand **1** in the presence of various bases in toluene at 80 °C (Table 1). As expected, bases such as NaO-*t*-Bu, LiO-*t*-Bu and Cs<sub>2</sub>CO<sub>3</sub> afforded either trace or undetectable amounts of the desired coupled product (Table 1, entries 1–3).

However, the combination of LDA (1.0 equiv.) and NaO-*t*-Bu (1.4 equiv.) provided a good yield of the product (Table 1, entry 4). Here, initial deprotonation of the acidic proton from the phenol by an equivalent of LDA would be followed by typical palladium-catalyzed amination chemistry<sup>[12]</sup> with NaO-*t*-Bu playing the role of the base. Changing the base to a commercially available solution of LiN(SiMe<sub>3</sub>)<sub>2</sub> in THF resulted in a higher yield of the product (Table 1, entry 5). Other silylamide bases such as KN(SiMe<sub>3</sub>)<sub>2</sub> and NaN(SiMe<sub>3</sub>)<sub>2</sub> were also effective in providing good yields (Table 1, entries 6 and 7). Isolation of the product was readily achieved by direct loading of the reaction mixture onto a silica gel column for chromatography. It was further determined that the LDA/NaO-*t*-Bu system could also be used in the coupling of aryl bromides possessing a primary alcohol functionality (Scheme 1).

Although the protocol involving the combination of LDA and NaO-*t*-Bu as the deprotonating agent and the base, respectively, was effective for bromophenols, its utilization in the reactions of 4-bromobenzamide, 4'-bromoacetanilide, and 4'-bromoacetophenone yielded undetectable amounts of the desired product. These results are in accord with those of Buchwald's group, except in the case of 4'-bromoacetanilide, wherein the



**Scheme 1.**

LDA/NaO-*t*-Bu protocol was also effective in their hands.<sup>[6]</sup>

From the above results it is clear that lithium bis(trimethylsilyl)amide is a highly effective base in amination reactions using the **1**/Pd catalyst system. In examining the scope of this methodology, it was found that functionalities such as phenol, alcohol, amide, keto, and acetanilide were compatible (Table 2). Although a standard palladium loading of 2 mol % was used for aryl bromides, some substrate combinations gave good to excellent yields even with substantially lower catalyst loadings. For example, while the reaction of 4-bromophenol with *N*-methylaniline and with morpholine in the presence of 2 mol % of palladium afforded 95% (Table 2, entry 6) and 83% (Table 2, entry 3) yields of the desired products, respectively, these reactions also occurred with about equal efficiency with 1 mol % of Pd (92% and 75%, respectively) as well as with 0.5 mol % of Pd (88% and 72%, respectively) as is seen in entries 7, 4, 8 and 5, respectively, of Table 2. Similarly, the amination of 4'-bromoacetanilide with *N*-methylaniline and with morpholine proceeded in high yields even with low palladium loadings (Table 2, entries 14–19). Reactions of bromoacetophenone were slightly less effective and required longer reaction times (Table 2, entries 21–24). Aryl bromides possessing a primary alcohol substituent were also transformed into the desired product in acceptable yields (Table 2, entries 12 and 13) and the amination of 4-bromobenzamide was also achieved in high yield (Table 2, entry 25). This protocol was also successful when *N*-BOC-piperazine was used as the coupling partner, leading to the formation of a highly functionalized aryl amine (Table 2, entry 33).

We were pleased to find that aryl chlorides were also suitable substrates, although a higher catalyst loading (4 mol % Pd) and reaction temperature (100 °C) were necessary (Table 2, entries 26–32). In these reactions, Pd<sub>2</sub>(dba)<sub>3</sub> was more effective as a palladium source than Pd(OAc)<sub>2</sub>. In one case, the reaction proceeded in good yield even at 80 °C. Thus 4'-chloroacetanilide reacted with morpholine at 100 °C and at 80 °C, providing 82% and 80% yields of the desired product, respectively (Table 2, entries 29 and 30).

Although the **1**/Pd catalyst system is quite general, several limitations were encountered which are summarized as follows: (a) the reaction proceeded sluggishly when the functional groups amide, acetanilide, alco-

**Table 1.** Survey of bases

| Entry | Base                                 | Yield <sup>[a]</sup> [%] |
|-------|--------------------------------------|--------------------------|
| 1     | NaO- <i>t</i> -Bu                    | trace                    |
| 2     | Cs <sub>2</sub> CO <sub>3</sub>      | nr <sup>[c]</sup>        |
| 3     | LiO- <i>t</i> -Bu                    | nr <sup>[c]</sup>        |
| 4     | NaO- <i>t</i> -Bu <sup>[b]</sup>     | 80                       |
| 5     | LiN(SiMe <sub>3</sub> ) <sub>2</sub> | 92                       |
| 6     | KN(SiMe <sub>3</sub> ) <sub>2</sub>  | 85                       |
| 7     | NaN(SiMe <sub>3</sub> ) <sub>2</sub> | 88                       |

<sup>[a]</sup> Isolated yields (average of two runs).

<sup>[b]</sup> 1.0 equiv. of LDA was also added.

<sup>[c]</sup> nr = no reaction.

**Table 2.** Pd/P(*i*-BuNCH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>N-catalyzed amination of aryl bromides and chlorides.<sup>[a]</sup>

| Entry | Aryl halide | Amine | Mol % Pd | Product | Time [h] | Yield <sup>[b]</sup> [%] |
|-------|-------------|-------|----------|---------|----------|--------------------------|
| 1     |             |       | 2        |         | 20       | 95                       |
| 2     |             |       | 2        |         | 27       | 88                       |
| 3     |             |       | 2        |         | 22       | 83                       |
| 4     |             |       | 1        |         | 22       | 75                       |
| 5     |             |       | 0.5      |         | 22       | 72                       |
| 6     |             |       | 2        |         | 23       | 95                       |
| 7     |             |       | 1        |         | 23       | 92                       |
| 8     |             |       | 0.5      |         | 23       | 88                       |
| 9     |             |       | 2        |         | 28       | 82                       |
| 10    |             |       | 1        |         | 20       | 76                       |
| 11    |             |       | 2        |         | 28       | 78                       |
| 12    |             |       | 2        |         | 25       | 60                       |
| 13    |             |       | 2        |         | 26       | 73                       |
| 14    |             |       | 2        |         | 24       | 94                       |
| 15    |             |       | 1        |         | 24       | 85                       |
| 16    |             |       | 0.5      |         | 24       | 85                       |
| 17    |             |       | 2        |         | 24       | 95                       |
| 18    |             |       | 1        |         | 24       | 92                       |
| 19    |             |       | 0.5      |         | 24       | 79                       |
| 20    |             |       | 2        |         | 28       | 78                       |
| 21    |             |       | 2        |         | 30       | 65                       |
| 22    |             |       | 2        |         | 30       | 88                       |
| 23    |             |       | 2        |         | 32       | 60                       |
| 24    |             |       | 2        |         | 29       | 89                       |
| 25    |             |       | 2        |         | 20       | 93                       |
| 26    |             |       | 4        |         | 29       | 97 <sup>[c,d]</sup>      |
| 27    |             |       | 4        |         | 31       | 66 <sup>[c,d]</sup>      |
| 28    |             |       | 4        |         | 24       | 97 <sup>[c,d]</sup>      |
| 29    |             |       | 4        |         | 32       | 82 <sup>[c,d]</sup>      |
| 30    |             |       | 4        |         | 32       | 80 <sup>[c]</sup>        |
| 31    |             |       | 4        |         | 34       | 52 <sup>[c,d]</sup>      |
| 32    |             |       | 4        |         | 28       | 95 <sup>[c,d]</sup>      |
| 33    |             |       | 2        |         | 20       | 72                       |

<sup>[a]</sup> Conditions: 1.0 equiv. of aryl halide, 1.1 equiv. of amine, cat. Pd(OAc)<sub>2</sub>, cat. ligand **1** (2L/Pd), 2.4 equivs. of LiN(SiMe<sub>3</sub>)<sub>2</sub> (1 M in THF), 80 °C. Reaction times have not been optimized.

<sup>[b]</sup> Isolated yields (average of at least two runs).

<sup>[c]</sup> Pd<sub>2</sub>(dba)<sub>3</sub> was used in place of Pd(OAc)<sub>2</sub>.

<sup>[d]</sup> The reaction was carried out at 100 °C.

hol, ketone or phenol were present in the amine component; (b) the amination reactions of aryl halides substituted with these groups at the *ortho* position yielded none of the desired product; and (c) primary amines and acyclic amines were not compatible under these conditions. Data associated with these limitations are therefore not included in Table 2.

In all the reactions presented here, a commercially available solution of LiN(SiMe<sub>3</sub>)<sub>2</sub> in THF (1 M) was used for convenience. Interestingly, when solid LiN(SiMe<sub>3</sub>)<sub>2</sub> was used with toluene as the only solvent, reactions proceeded slowly and provided inferior yields compared with reactions carried out with THF<sup>[13]</sup> and toluene as a binary solvent system. This observation may stem from the insolubility of the lithium alkoxide or lithium enolate formed during the reaction in toluene. Furthermore, additional experiments showed that KN(SiMe<sub>3</sub>)<sub>2</sub> can be substituted for LiN(SiMe<sub>3</sub>)<sub>2</sub>, although lower yields were usually observed. Here also,

THF as a co-solvent was essential because when toluene was used as the sole solvent, a precipitate was observed.

The exceptional activity displayed by silylamide bases, especially LiN(SiMe<sub>3</sub>)<sub>2</sub>,<sup>[14]</sup> might be due to deprotonation of the substrate with resultant formation *in situ* of a covalently bound lithium which acts as a protecting group that inhibits coordination of an alcohol or amide group to palladium. The highly aggregated state and tight ion pairing which is characteristic of lithium alkoxides, might provide some degree of stability to such intermediates,<sup>[15]</sup> even at the elevated temperatures used in our protocol. Another factor in the efficacy of silylamide bases in these reactions is the possible formation of a silylated alcohol or silylated amide intermediate via migration of a trimethylsilyl (TMS) group from the silylamide base to the alcohol or amide, thus protecting the oxygen or nitrogen, respectively, from coordination to the palladium. On the basis of the experiments discussed herein, it may be concluded that the latter option

is favored with the amide, acetanilide, and ketone functionality because these functional groups are compatible with  $\text{LiN}(\text{SiMe}_3)_2$  but not with the  $\text{LDA}/\text{NaO}-t\text{-Bu}$  system. Because the  $\text{LDA}/\text{NaO}-t\text{-Bu}$  base system as well as silylamide bases are effective in the case of an aryl halide bearing an alcohol or phenol functionality, two types of oxygen protection may be operating. Thus protection via covalent binding ( $\text{Li}^+$ ) or ion pairing ( $\text{Na}^+$ ,  $\text{K}^+$ ) may be occurring, or TMS protection may be at play.

## Conclusion

In summary, we have demonstrated the utility of  $\text{LiN}(\text{SiMe}_3)_2$  as a base in  $\text{Pd}/\mathbf{1}$ -catalyzed aminations of aryl chlorides and bromides containing a relatively acidic functional group, namely, a phenol, an alcohol, an amide, an acetanilide or a ketone possessing enolizable hydrogens. This new catalyst system (wherein the ligand  $\mathbf{1}$  is also commercially available<sup>[16]</sup>) significantly expands the repertoire of methodologies enabling such transformations.

## Experimental Section

### General Considerations

All reactions were performed under an atmosphere of argon in oven-dried glassware. Toluene was collected from a solvent purification system and stored over 4 Å molecular sieves.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 300 and 75 MHz, respectively, unless otherwise noted. The yields reported are isolated yields and are the average of at least two runs. All commercially available reagents were used as received. Although ligand  $\mathbf{1}$  is commercially available,<sup>[16]</sup> we synthesized it according to our previously reported procedure.<sup>[17]</sup> For convenience, a stock solution of  $\mathbf{1}$  in toluene (2 mM) was prepared and stored under argon. All products in Tables 1 and 2 are known in the literature and were characterized by comparing their  $^1\text{H}$  and  $^{13}\text{C}$  NMR or mass spectra to the previously reported data. In all cases, the comparisons were very favorable.

### General Procedure for the Coupling of Aryl Halides with Amines

An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with  $\text{Pd}(\text{OAc})_2$  or  $\text{Pd}_2(\text{dba})_3$  ( $x$  mol %, see Table 2), amine (1.2 mmol) and aryl bromide (1.0 mmol). The flask was capped with a rubber septum, evacuated and then flushed with argon. This cycle was repeated three times. Ligand  $\mathbf{1}$  (2x mol %, see Table 2),  $\text{LiN}(\text{SiMe}_3)_2$  solution (1 M in THF) (2.3 mmol) and toluene (5 mL) were then successively added by a syringe. The reaction mixture was heated at the temperature indicated in Table 1 and reaction progress was monitored by TLC. After completion of the reaction, the crude reaction mixture was cooled to room temperature, adsorbed onto silica

gel and then purified by column chromatography (hexanes/ethyl acetate as eluent).

***N*-(3-Hydroxyphenyl)-morpholine<sup>[18]</sup> (product in Table 1 and Table 2, entry 26):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.14–7.09 (m, 1H), 6.50–6.47 (m, 1H), 6.36–6.34 (m, 2H), 6.23 (bs, 1H), 3.86 (m, 4H), 3.11 (m, 4H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 157.0, 152.9, 130.4, 108.4, 107.5, 103.3, 67.0, 49.5.

**3-Hydroxy-*N*-methyl-diphenylamine<sup>[19]</sup> (Table 2, entries 1 and 28):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.36–7.31 (m, 2H), 7.15–7.04 (m, 4H), 6.48–6.40 (m, 2H), 5.10 (bs, 1H), 3.30 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 156.7, 150.8, 149.0, 130.3, 129.6, 122.7, 122.6, 111.7, 107.8, 106.2, 40.6.

***N*-(3-Hydroxyphenyl)-piperidine<sup>[20]</sup> (Table 2, entries 2 and 27):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.11–7.06 (m, 1H), 6.55–6.51 (m, 1H), 6.36–6.29 (m, 2H), 5.76 (bs, 1H), 3.09–3.05 (m, 4H), 1.72–1.53 (m, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 156.8, 153.6, 130.2, 109.4, 107.1, 104.4, 51.0, 25.7, 24.4.

***N*-(4-Hydroxyphenyl)-morpholine<sup>[6]</sup> (Table 2, entries 3, 4 and 5):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.86–6.75 (m, 4H), 4.99 (bs, 1H), 3.87 (m, 4H), 3.05 (m, 4H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 150.2, 145.8, 118.4, 116.2, 67.2, 51.2.

**4-Hydroxy-*N*-methyldiphenylamine<sup>[6]</sup> (Table 2, entries 6, 7 and 8):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.28–7.22 (m, 2H), 7.09–7.06 (m, 2H), 6.86–6.83 (m, 5H), 5.45 (bs, 1H), 3.28 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 152.3, 150.0, 142.7, 129.3, 12.6, 118.8, 116.6, 116.2, 40.8.

***N*-(4-Hydroxyphenyl)-piperidine<sup>[21]</sup> (Table 2, entry 9):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.89–6.69 (m, 4H), 5.09 (bs, 1H), 3.01 (s, 4H), 1.73–1.53 (m, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 150.2, 146.6, 119.6, 116.0, 53.0, 26.2, 24.3.

***N*-(4-Hydroxyphenyl)-piperazine<sup>[22]</sup> (Table 2, entry 10):**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.97 (bs, 1H), 6.82–6.68 (m, 4H), 3.10–3.08 (m, 4H), 2.66–2.65 (m, 4H), 2.37 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 151.0, 145.0, 119.0, 116.4, 55.3, 50.7, 46.1.

***N*-(4-Hydroxyphenyl)-*p*-toluidine<sup>[23]</sup> (Table 2, entry 11):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.06–6.96 (m, 4H), 6.87–6.76 (m, 4H), 5.30 (bs, 2H), 2.29 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 150.7, 142.6, 137.0, 130.0, 129.7, 121.6, 116.9, 116.3, 20.8.

**2-(3-Morpholin-4-yl-phenyl)-ethanol<sup>[6]</sup> (Table 2, entry 12):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.26–7.19 (m, 1H), 6.79–6.73 (m, 3H), 3.86–3.80 (m, 6H), 3.16–3.13 (t,  $J$  = 4.8 Hz, 4H), 2.81 (t,  $J$  = 6.6 Hz, 2H), 2.03 (bs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 151.7, 139.8, 129.6, 120.9, 116.7, 114.0, 67.1, 63.8, 49.6, 39.8.

**2-(4-Morpholin-4-yl-phenyl)-ethanol<sup>[6]</sup> (Table 2, entry 13):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.15–7.12 (m, 2H), 6.88–6.86 (m, 2H), 3.86–3.78 (m, 6H), 3.13–3.12 (m, 4H), 2.81–2.76 (m, 2H), 1.81 (bs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 150.2, 130.2, 130.0, 116.3, 67.2, 64.0, 49.8, 38.5.

***N*-(4'-Morpholin-4-yl-phenyl)-acetanilide<sup>[24]</sup> (Table 2, entries 14, 15, 16, 29 and 30):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.36 (d,  $J$  = 8.9 Hz, 2H), 7.21 (bs, 1H), 6.88 (d,  $J$  = 8.9 Hz, 2H), 3.87–3.83 (m, 4H), 3.11–3.09 (m, 4H), 2.14 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 168.4, 148.5, 130.8, 121.8, 116.5, 67.1, 50.0, 24.6.

***N*-[(4'-(*N*-Phenyl-*N*-methylamino)-phenyl]-acetanilide<sup>[6]</sup> (Table 2, entries 17, 18, 19 and 32):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.93 (bs, 1H), 7.43–7.40 (m, 2H), 7.27–7.22 (m, 2H), 7.00–6.88 (m, 5H), 3.27 (s, 3H), 2.15 (s, 3H);  $^{13}\text{C}$  NMR

(75 MHz, CDCl<sub>3</sub>):  $\delta$  = 169.0, 149.3, 145.8, 132.5, 129.4, 122.2, 121.9, 120.8, 119.4, 40.6, 24.5.

**N-[4'-(4-Methylphenyl)-amino]-acetanilide**<sup>[6]</sup> (Table 2, entry 20): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.86 (bs, 1H), 7.36–7.33 (m, 2H), 7.07–7.04 (m, 2H), 6.95–6.91 (m, 4H), 5.65 (bs, 1H), 2.29 (s, 3H), 2.12 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 169.0, 141.0, 140.7, 131.2, 130.7, 130.1, 122.2, 118.4, 118.0, 24.5, 20.9.

**4'-(N-Phenyl-N'-methylamino)-acetophenone**<sup>[25]</sup> (Table 2, entry 21): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.83–7.80 (m, 2H), 7.44–7.38 (m, 2H), 7.26–7.20 (m, 3H), 6.77–6.74 (m, 2H), 3.37 (s, 3H), 2.51 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 196.6, 152.9, 147.5, 130.4, 130.1, 127.3, 126.4, 125.9, 113.6, 40.5, 26.4.

**3'-(Morpholin-4-yl)-acetophenone**<sup>[26]</sup> (Table 2, entry 22): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.49–7.31 (m, 3H), 7.11–7.07 (m, 1H), 3.86–3.82 (m, 4H), 3.20–3.16 (m, 4H), 2.56 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 198.6, 151.7, 138.2, 129.5, 120.5, 114.6, 67.0, 49.3, 27.0.

**3'-(Piperidin-4-yl)-acetophenone**<sup>[27]</sup> (Table 2, entry 23): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.51–7.50 (m, 1H), 7.38–7.28 (m, 2H), 7.14–7.10 (m, 1H), 3.22–3.18 (m, 4H), 2.57 (s, 3H), 1.74–1.67 (m, 4H), 1.62–1.54 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 198.9, 152.5, 138.1, 129.3, 121.3, 119.5, 115.4, 67.0, 50.6, 27.0, 25.9, 24.4.

**3'-(N-Phenyl-N'-methylamino)-acetophenone**<sup>[6]</sup> (Table 2, entry 24): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.56–7.55 (m, 1H), 7.48–7.44 (m, 1H), 7.35–7.27 (m, 3H), 7.15–7.03 (m, 4H), 3.36 (s, 3H), 2.56 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 198.6, 149.6, 148.7, 138.5, 129.8, 129.4, 123.5, 122.7, 120.6, 117.6, 40.6, 27.0.

**4-(N-Phenyl-N'-methylamino)-benzamide**<sup>[28]</sup> (Table 2, entry 25): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.68–7.65 (m, 2H), 7.41–7.35 (m, 2H), 7.20–7.18 (m, 3H), 6.81–6.78 (m, 2H), 6.04 (bs, 2H), 3.35 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 169.6, 152.1, 147.8, 130.0, 129.0, 125.7, 125.3, 122.6, 114.6, 40.4.

**N-(4'-Piperidin-4-ylphenyl)-acetanilide**<sup>[29]</sup> (Table 2, entry 31): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.62 (bs, 1H), 7.35 (d, *J* = 8.9 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 3.09–3.06 (m, 4H), 2.10 (s, 3H), 1.72–1.65 (m, 4H), 1.58–1.52 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 168.7, 149.6, 130.2, 121.8, 117.2, 51.3, 26.1, 24.5, 24.4.

**N-tert-Butoxycarbonyl-4-(4-hydroxyphenyl)-piperazine**<sup>[30]</sup> (Table 2, entry 33): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 6.84–6.75 (m, 5H), 3.58–3.55 (m, 4H), 2.98–2.94 (m, 4H), 1.48 (m, 9H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 155.2, 151.2, 145.2, 119.5, 116.2, 80.5, 51.4, 28.7.

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