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Efficient palladium-catalyzed amination of aryl chlorides using di(dicyclohexylamino)phenylphosphine as a PN_2 ligand

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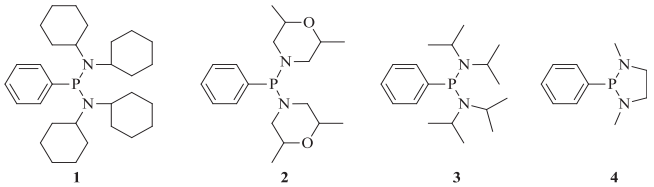
ABSTRACT

The palladium-catalyzed amination of a variety of aryl chlorides has been accomplished by using di(dicyclohexylamino)phenylphosphine (**1**) as a bulky electron-rich monoaryl phosphine ligand. The optimized condition for the palladium-catalyzed amination of aryl chloride is the followings: aniline (3.0 mmol, 1.0 equiv), chlorobenzene (3.15 mmol, 1.05 equiv), ligand **1** (1 mol %, 0.03 mmol), KO^{t}Bu (4.5 mmol, 1.5 equiv), $Pd_2(dba)_3$ (1 mol %, 0.03 mmol), and toluene as solvent at reflux temperature. We report on couplings of various amines or chloroamines with chlorobenzenes and heteroaryl chloride.

1. Introduction

Over the past decade, one of the foremost accomplishment in the field of catalysis has been the discovery of the palladium-catalyzed carbon–nitrogen bond forming process commonly known as the Buchwald–Hartwig amination reaction.[1] The palladium-catalyzed formation of C–N bonds is also a rapidly expanding area of research.[1a,2] Since the first general procedures were discovered,[3] efforts have been made toward increasing the substrate scope and efficiency. Although the use of alternative bases or solvents can be beneficial, electronic, and steric tuning of the supporting ligand has the most impact on increasing efficacy and reactivity in these processes.[1c,2] A major impetuses to this field was provided by the ability to activate the notoriously unreactive but relatively cheap aryl chlorides. Not surprisingly, a plethora of palladium-catalyst systems featuring a palladium-bound ligand is now accessible for achieving the aforementioned transformation involving aryl chlorides. Typically, the electronically rich sterically hindered ligands belonging to the trialkylphosphine,[4–6] ferrocenyldialkylphosphine,[7] aryldialkylphosphine,[8–10] phosphinous acid,[11] palladacycle,[12,13] heterocyclic carbene[14–16] or triaminophosphine (PN_3)[1d,17–20] classes have been investigated for these reactions. While several ligands exhibiting improved abilities in assisting the palladium-catalyzed aryl aminations are now available, a general solution has not yet been completely found for the metal-catalyzed aryl aminations of all substrates.

Thus, as part of our ongoing efforts to develop efficient methods for the amination of aryl chloride, we investigated the synthesis and coupling reaction of novel air stable phenyl backbone-derived PN_2 ligands that are easily prepared. The reaction setup is experimentally simple and does not require the use of a glove box for these reactions. In previous paper,[21] amination of aryl chlorides using dicyclohexylamino[(2,6-dimethyl)morphorino]phenylphosphine as a PN_2 ligand has been reported (Scheme 1).



Scheme 1. Bulky electron-rich ligands used in the amination of aryl chlorides.

We designed ligand **1**–**4** as novel phenyl backbone-derived PN_2 ligands. Ligand **4** is commercially available, and ligand **3** was

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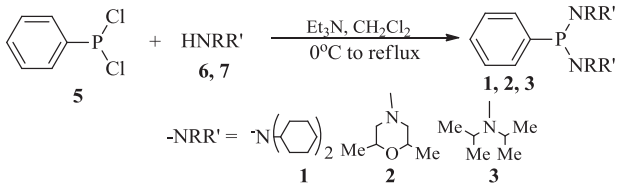
prepared by the literature method.[22] Ligands **1** and **2** were synthesized from dichlorophenylphosphine (**5**) according to reported method.[21] Here, we report the results for amination of aryl chloride with amines by using compound **1** as a novel PN_2 ligand.

2. Results and discussion

Reaction of dichlorophenylphosphine (**5**) with dicyclohexylamine (**6**) or 2,6-dimethylmorphorine (**7**) in the presence of triethylamine in refluxing dichloromethane or toluene gave the corresponding ligands **1** (78%) or **2** (85%). Ligands **1**–**3** in coupling reaction was used without further purification. The structures of ligands **1** and **2** were established by IR, NMR, and elemental analysis (Scheme 2).

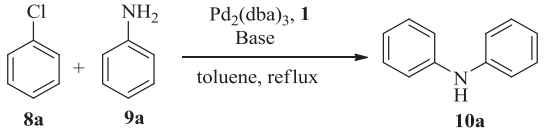


Scheme 2. Synthesis of ligands **1**, **2**, and **3**.

To test the feasibility of the ideas described above, we initially conducted a reaction of chlorobenzene (**8a**) with aniline (**9a**) in refluxing toluene. We used 1 mol % of $Pd_2(dba)_3$ in combination with 1 mol % of ligand **1**, and this reaction proceeded successfully to afford the desired product **10a** in a 93% isolated yield after 4 h. This result was encouraging, and we evaluated the efficiency of the three ligands **2**–**4** in the same screening. This reaction did not occur when ligands **2**–**4** were used.

Next, we investigated a variety of solvents and bases for the aforementioned coupling reaction catalyzed by the $Pd_2(dba)_3$/ligand **1** system. Toluene was found to be the most efficacious solvent among six solvents, such as toluene, acetonitrile, ethanol, 1,4-dioxane, THF, and water. This reaction, however, in other solvents did not occur. Among the bases explored, potassium *tert*-butoxide gave the best result (entry 1 in Table 1). However, reaction involving Cs_2CO_3, K_3PO_4, K_2CO_3, and Rb_2CO_3 as a base failed to provide complete conversion even after 49–60 h (entry 2–5 in Table 1).

Table 1
Screening of bases[a]

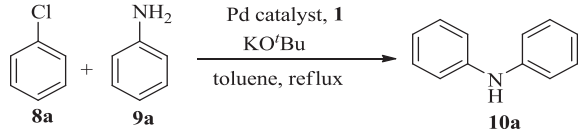


Entry	Base	Time (h)	**10a**[b] (%)
1	KO^tBu	4	93
2	Cs_2CO_3	49	56[c]
3	K_3PO_4	56	55[c]
4	K_2CO_3	60	5[c]
5	Rb_2CO_3	60	3[c]

[a] Reaction conditions: aniline (**9a**, 3.0 mmol, 1.0 equiv), chlorobenzene (**8a**, 3.15 mmol, 1.05 equiv), ligand **1** (1mol%, 0.03 mmol), base (1.5 equiv), $Pd_2(dba)_3$ (1 mol %, 0.03 mmol), toluene (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.
[c] The starting materials were recovered.

Also, we investigated the effect of a variety of palladium compounds for this reaction. Among the palladium compounds explored, $Pd_2(dba)_3$ gave the fastest reaction rates and the excellent yields although $PdCl_2$ and $Pd(OAc)_2$ were also a suitable reagent (entry 2 and 3 in Table 2). However, reaction using $Pd(PPh_3)_4$ or Pd/C failed to provide complete conversion even after 24 h (entry 4 and 6 in Table 2).

Table 2
Screening of Pd-catalysts[a]

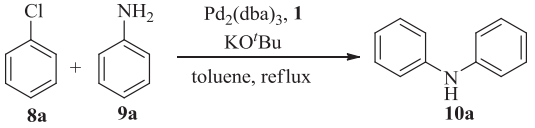


Entry	Palladium-catalyst	Time (h)	**10a**[b] (%)
1	$Pd_2(dba)_3$	4	93
2	$PdCl_2$	5	91
3	$Pd(OAc)_2$	5	90
4	$Pd(PPh_3)_4$	24	5[c]
5	$PdCl_2(PPh_3)_2$	8	85
6	Pd/C	24	4[c]

[a] Reaction conditions: aniline (**9a**, 3.0 mmol, 1.0 equiv), chlorobenzene (**8a**, 3.15 mmol, 1.05 equiv), ligand **1** (1 mol %, 0.03 mmol), KO^tBu (1.5 equiv), Pd-catalyst (1 mol %, 0.03 mmol), toluene (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.
[c] The starting materials were recovered.

We next optimized the coupling of chlorobenzene (**8a**) with aniline (**9a**) by the $Pd_2(dba)_3$/**1**/KO^tBu in toluene. The $Pd_2(dba)_3$ (2 mol %)/**1** (1 mol %)/KO^tBu (1.5 equiv) system in toluene showed the best result (entry 6 in Table 3). On the other hand, the yields are low at below the reflux temperature. Applying the $Pd_2(dba)_3$ (1 mol %)/**1** (1 mol %)/KO^tBu (1.5 equiv)/toluene system (entry 2 in Table 3), however, we evaluated the scope of the coupling of aryl chlorides with various amines because it requires the small amount of catalyst.

Table 3
Optimization for the coupling of chlorobenzene (**8a**) with aniline (**9a**) using **1**[a]

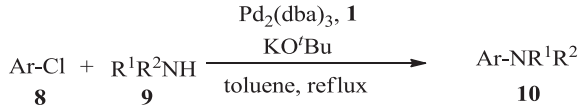


Entry	**1** (mol %)	$Pd_2(dba)_3$ (mol %)	Time (h)	**10a**[b] (%)
1	1	0.5	17	84
2	1	1	4	93
3	2	1	4	89
4	5	1	4	90
5	10	1	4	90
6	1	2	2	91

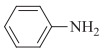
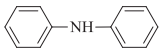
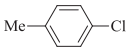
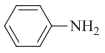
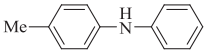
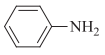
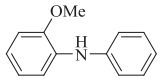
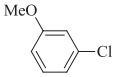
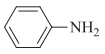
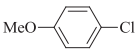
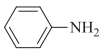
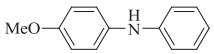
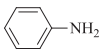
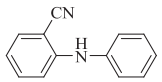
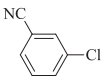
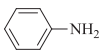
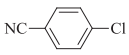
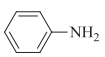
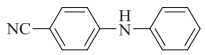
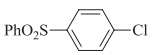
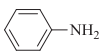
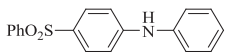
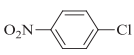
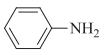
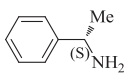
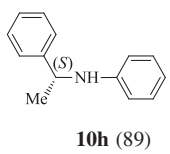
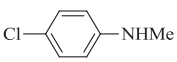
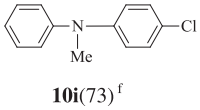
[a] Reaction conditions: aniline (**9a**, 3.0 mmol, 1.0 equiv), chlorobenzene (**8a**, 3.15 mmol, 1.05 equiv), ligand **1**(1 mol %, 0.03 mmol), KO^tBu (1.5 equiv), $Pd_2(dba)_3$, toluene (20 mL) at reflux temperature.
[b] Isolated yield after silica gel chromatography.

It is clear from Table 4 that chlorobenzenes containing electron-withdrawing groups, such as cyano and benzenesulfonyl groups are coupled fast with aniline (**9a**) (entries 8 and 9 in Table 4), whereas chlorobenzene containing electron-donating groups, such as methyl and methoxy groups are coupled slowly with aniline (**9a**) (entries 2 and 5 in Table 4). The position effect of the substituents for MeO and CN in benzene was evaluated. The *para* substituted-chlorobenzene **8e** (*p*-OMe) and **8h** (*p*-CN) showed the best results (entries 5 and 8 in Table 4), but the *ortho* or the *meta* substituted derivatives gave the products in the low yield (entries 3 and 6 in Table 4) or unknown products (entries 4 and 7 in Table 4). On the other hand, the coupling 4-nitrochlorobenzene (**8j**) with aniline under our system gave 2-chlorophenazine as the main product instead of the corresponding coupling product (entry 10 in Table 4). This is similar to Pachter's result.[24] The coupling of chlorobenzene (**8a**) with various amines using our optimized system gave the

Table 4
Palladium-catalyzed amination of aryl chlorides[a]

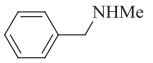
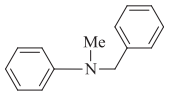
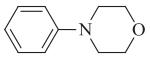
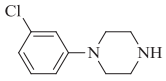
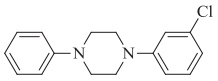
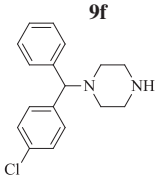
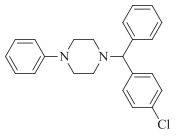
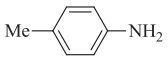
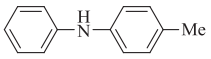
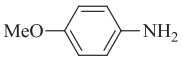
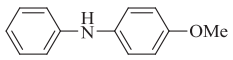
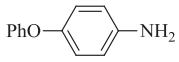
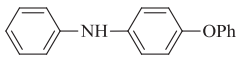
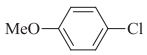
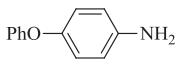
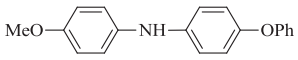
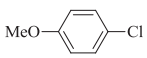
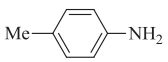
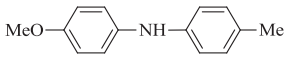
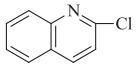
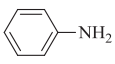
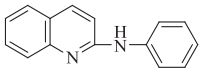
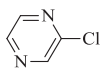
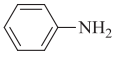
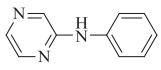


8 **9** **10**

Entry	Ar–Cl **8**	Amine **9**	Time (h)	Product **10**[b] (%)
1	 **8a**	 **9a**	4	 **10a**(93)
2	 **8b**	 **9a**	34	 **10b** (25)[c]
3	 **8c**	 **9a**	32	 **10c** (10)[c]
4	 **8d**	 **9a**	32	—[d]
5	 **8e**	 **9a**	32	 **10d** (32)[c]
6	 **8f**	 **9a**	5	 **10e** (48)[c]
7	 **8g**	 **9a**	3	—[d]
8	 **8h**	 **9a**	2	 **10f** (82)
9	 **8i**	 **9a**	4	 **10g** (89)
10	 **8j**	 **9a**		—[e]
11	 **8a**	 **9b**	5	 **10h** (89)
12	 **8a**	 **9c**	3	 **10i**(73)[f]

(*continued on next page*)

Table 4 (*continued*)

Entry	Ar—Cl **8**	Amine **9**	Time (h)	Product **10**[b] (%)
13	 **8a**	 **9d**	4	 **10j** (84)
14	 **8a**	 **9e**	0.5	 **10k** (93)
15	 **8a**	 **9f**	10	 **10l** (67)[f]
16	 **8a**	 **9g**	11	 **10m** (53)[f]
17	 **8a**	 **9h**	16	 **10b** (93)
18	 **8a**	 **9i**	15	 **10d** (75)
19	 **8a**	 **9j**	3	 **10n** (90)
20	 **8e**	 **9j**	5	 **10o**(71)
21	 **8e**	 **9h**	6	 **10p** (56)
22	 **8k**	 **9a**	16	 **10q** (52)
23	 **8l**	 **9a**	5	 **10r** (59)

[a] Reaction condition: amine (**9**, 3.0 mmol, 1.0 equiv), aryl chloride (**8**, 3.15 mmol, 1.05 equiv), ligand **1** (1 mol %, 0.03 mol), KO^{t}Bu (4.5 mmol, 1.5 equiv), $Pd_2(dba)_3$ (1 mol %, 0.03 mmol), toluene (20 mL) at reflux temperature.

[b] Isolated yield after silica gel chromatography.

[c] The unreacted starting materials were recovered.

[d] Some unknown products were detected.

[e] The main product is 2-chlorophenazine.[24]

[f] Double-coupling product was also detected on TLC.

corresponding mono-coupling products involving the double-coupling products as the traces in moderate to excellent yields (entries 11–19 in Table 4). Although chlorobenzene (**8a**) of coupling with various amines do not show a general tendency that depended on the kind of amines, the reaction of amines containing chlorine gave the corresponding double-coupling products by the coupling of the first product with starting chloramines or chlorobenzene (entries 12, 15, and 16 in Table 4).

The coupling of chloroheterocycles, such as 2-chloroquinoline (**8k**) and 2-chloropyrazine (**8l**) with aniline (**9a**) using our system also gave the corresponding C–N coupling products **10q** and **10r** (entries 22 and 23 in Table 4). The structures of all products were established by IR, NMR, HMRS, and elemental analysis. The structures of the known compounds also were confirmed by comparing the literature data.

3. Conclusion

In conclusion, we developed ligand **1** as a new PN_2 ligand for Pd-catalyzed amination of aryl chloride. This ligand **1** also has some advantages: as an efficient ligand for Pd-catalyzed amination of aryl chlorides, it is stable in air at high temperature, and easily prepared from cheap and commercially available dichlorophenylphosphine.

4. Experimental

4.1. General

Melting points were determined with a capillary apparatus and uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer with chemical shift values reported in δ units (ppm) relative to an internal standard (TMS). IR spectra were obtained on a Mattson Genesis Series FT-IR spectrophotometer. Elemental analyses were performed with a Perkin–Elmer 240C. Mass spectra were obtained on a JMS-700, JEOL. The open-bed chromatography was carried out on silica gel (70–230 mesh, Merck) using gravity flow. The column was packed with slurries made from the elution solvent.

4.2. Typical preparation of PN_2 ligands

A mixture of amine (2 equiv), triethylamine (2.2 equiv), and dichloromethane (50 mL) was stirred for 10 min at room temperature. A dichloromethane solution of dichlorophenylphosphine **5** (20 mmol of **5** in 200 mL dichloromethane) was slowly dropped to the above amine solution, and the mixture was refluxed for 24 h until phosphine **5** disappeared. After evaporating the solvent under reduced pressure, the resulting residue was triturated in *n*-hexane, filtered, and washed with *n*-hexane. The filtrates-containing the product were combined and evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (3.0×7 cm). The column was eluted with dichloromethane/diethyl ether (10/1, v/v). Fractions containing the product were combined and evaporated under reduced pressure to give di(dicyclohexylamino)phenyl phosphine (**1**), 4,4′-(phenylphosphinediyl)bis(2,6-dimethylmorpholine) (**2**) or di(diisopropylamino)-phenylphosphine (**3**) as a PN_2 ligand. Ligand in coupling reaction was used without further purification.

*4.2.1. Di(dicyclohexylamino)phenylphosphine (**1**).* Yield: 78%. Colorless oil. IR (KBr) 2926, 2846, 2776, 2740, 1460, 1378, 1042 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83–2.02 (m, 40H), 2.93–2.98 (m, 4H), 7.34–7.43 (m, 3H), 7.69–7.74 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.07, 22.63, 25.48, 31.57, 128.10, 129.15, 130.54, 130.82. Anal. Calcd for $C_{30}H_{49}N_2P$: C, 76.88; H, 10.54; N, 5.98. Found: C, 76.93; 10.61; N, 6.01.

*4.2.2. 4,4′-(Phenylphosphinediyl)bis(2,6-dimethylmorpholine) (**2**).* Yield: 85%. Colorless oil. IR (KBr) 3012, 2904, 1436, 1366, 1120, 1048 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.8 (s, 6H), 1.10 (s, 6H), 2.40–2.44 (m, 2H), 2.99 (d, 4H, J=12.16 Hz), 3.44–3.51 (m, 2H), 3.78–3.87 (m, 4H), 7.30–7.81 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.69, 47.92, 68.71, 128.15, 128.32, 129.60, 129.40. Anal. Calcd for $C_{18}H_{29}N_2O_2P$: C, 64.26; H, 8.69; N, 8.33. Found: C, 64.30; H, 8.60; N, 8.37.

4.3. Typical C–N coupling of amines and aryl chlorides

A dried resealable Schlenk tube was charged with $Pd_2(dba)_3$ (0.03 mmol, 1 mol % of Pd), amine (3.0 mmol), ligand **1** (1 mol %) and KO^{t}Bu (4.5 mmol) in dried toluene (20 mL). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with nitrogen. This evacuation/backfill sequence was repeated two or three additional times. Aryl chloride (3.15 mmol) and toluene (2 mL×2) were added through the septum. After the septum was replaced with a Teflon screwcap, the mixture was refluxed until the starting amine had been completely consumed as judged by GC or TLC. The reaction mixture was then cooled to room temperature, diluted with dichloromethane (10 mL×2), filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel using *n*-hexane/dichloromethane (1/1, v/v) to afford C–N coupled product.

*4.3.1. Diphenylamine (**10a**).* Mp 53–54 °C (lit.[21] mp 53–54 °C). IR (KBr) 3392, 3318, 1602, 1486, 1324, 740 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (br s, NH, D_2O exchangeable), 6.87–6.93 (m, 2H), 7.01–7.04 (m, 4H), 7.19–7.26 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.96, 121.10, 129.43, 143.27. Anal. Calcd for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.14; H, 6.54; N, 8.27. HRMS (*m*/*z*): $[M]^+$ calcd for $C_{12}H_{11}N$ 169.0891. Found: 169.0891.

*4.3.2. Phenyl-p-tolylamine (**10b**).* Mp 87–88 °C (lit.[21] mp 87–88 °C). IR (KBr) 3400, 3010, 2912, 1596, 1508, 1304, 744 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 3H), 5.55 (br s, NH, D_2O exchangeable), 6.84–6.89 (m, 1H), 6.97–7.00 (m, 4H), 7.06–7.08 (m, 2H), 7.19–7.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.69, 116.95, 118.99, 120.35, 129.33, 129.88, 130.97, 140.39, 144.04. Anal. Calcd for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.20; H, 7.13; N, 7.65. HRMS (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{13}N$ 183.1048. Found: 183.1048.

*4.3.3. (2-Methoxyphenyl)phenylamine (**10c**).* Yellow oil. IR (KBr) 3414, 2923, 2850, 1637, 1594, 1518, 1495, 1462, 1420, 1296, 1235, 1176, 1115, 1026 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88 (s, 3H), 6.14 (br s, NH, D_2O exchangeable), 6.83–6.95 (m, 4H), 7.14 (d, 2H, J=7.51 Hz), 7.23–7.32 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.57, 110.51, 114.67, 118.59, 119.88, 120.82, 121.15, 129.27, 133.00, 142.73, 148.27. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.37; H, 6.60; N, 7.02. HRMS (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{13}NO$ 199.0997. Found: 199.1008.

*4.3.4. (4-Methoxyphenyl)phenylamine (**10d**).* Mp 98–99 °C (lit.[21] mp 99–100 °C). IR (KBr) 3428, 3056, 2992, 2950, 1600, 1502, 1300, 1242, 1038, 744 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H), 5.46 (br s, NH, D_2O exchangeable), 6.80–6.91 (m, 5H), 7.05–7.08 (m, 2H), 7.18–7.23 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.61, 114.74, 115.73, 119.61, 122.24, 129.32, 135.84, 145.24, 155.36. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.35; H, 6.60; N, 7.01. HRMS (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{13}NO$ 199.0997. Found: 199.1008.

*4.3.5. 2-(Phenylamino)benzonitrile (**10e**).* Mp 48–49 °C (lit.[23]mp 50–51 °C). IR (KBr) 3343, 3048, 2926, 2216, 1625, 1593, 1573, 1515,

1497, 1472, 1456, 1318, 1292, 1163 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 6.98–7.02 (m, 2H), 7.13 (d, 2H, J=7.65 Hz), 7.24–7.33 (m, 3H), 7.48–7.54 (m, 1H), 7.65–7.68 (m, 1H), 8.46 (br s, NH, D_2O exchangeable). ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.17, 117.87, 118.26, 119.56, 120.98, 122.33, 129.71, 134.39, 134.65, 142.36, 147.36. Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.40; H, 5.21; N, 14.40. HRMS (m/z): $[M]^+$ calcd for $C_{13}H_{10}N_2$ 194.0844. Found: 194.0842.

*4.3.6. 4-(Phenylamino)benzonitrile (**10f**).* Mp 134–135 °C (lit.[21] mp 134–135 °C). IR (KBr) 3246, 2248, 1634, 1600, 1390, 1098 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.81 (br s, NH, D_2O exchangeable), 6.95–6.99 (m, 2H), 7.04–7.10 (m, 1H), 7.36–7.43 (m, 4H), 7.81–7.84 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.53, 123.22, 128.24, 128.72, 129.58, 130.50, 134.23, 136.64, 149.32. Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.38; H, 5.19; N, 14.39. HRMS (m/z): $[M]^+$ calcd for $C_{13}H_{10}N_2$ 194.0844. Found: 194.0837.

*4.3.7. N-Phenyl-4-(phenylsulfonyl)benzenamine (**10g**).* Mp 206–207 °C. IR (KBr) 3369, 3022, 1581, 1520, 1490, 1340, 1290, 1146, 1100 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (s, NH, D_2O exchangeable), 6.95–6.99 (m, 2H), 7.06–7.15 (m, 3H), 7.30–7.35 (m, 2H), 7.44–7.55 (m, 3H), 7.73–7.76 (m, 2H), 7.89–7.92 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 114.72, 121.25, 123.93, 127.14, 129.60, 129.75, 130.65, 132.62, 140.08, 142.79, 148.69. Anal. Calcd for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 69.86; H, 4.84; N, 4.50. HRMS (m/z): $[M]^+$ calcd for $C_{18}H_{15}NO_2S$ 309.0823. Found: 309.0825.

*4.3.8. Phenyl-((S)-1-phenylethyl)amine (**10h**).* Coloress oil. IR (KBr) 3426, 3056, 3044, 2996, 1606, 1504, 1320, 750, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.69 (d, 3H, J=6.72 Hz), 4.21 (br s, NH, D_2O exchangeable), 4.69 (q, 1H, J=6.72 Hz), 6.72–6.76 (m, 2H), 6.89–6.92 (m, 1H), 7.30–7.60 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.15, 53.65, 113.60, 117.49, 126.09, 127.09, 128.71, 128.86, 145.49, 147.56. Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10. Found: C, 85.21; H, 7.64; N, 7.09. HRMS (m/z): $[M]^+$ calcd for $C_{14}H_{15}N$ 197.1204. Found: 197.1203.

*4.3.9. N-(4-Chlorophenyl)-N-methylbenzenamine (**10i**).* Colorless oil. IR (KBr) 3050, 2900, 1592, 1498, 1342, 1260, 1136, 820, 750, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.22 (s, 3H), 6.83–6.87 (m, 2H), 6.94–7.01 (m, 3H), 7.12–7.17 (m, 2H), 7.20–7.27 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.40, 120.59, 120.72, 121.64, 122.40, 125.70, 129.19, 129.32, 129.51. Anal. Calcd for $C_{13}H_{12}ClN$: C, 71.72; H, 5.56; N, 6.43. Found: C, 71.71; H, 5.53; N, 6.43. HRMS (m/z): $[M]^+$ calcd for C $C_{13}H_{12}ClN$ 217.0658. Found: 217.0659.

*4.3.10. N-Benzyl-N-methylphenylamine (**10j**).* Colorless oil. IR (KBr) 3026, 1902, 1600, 1502, 1450, 1346, 748, 722, 690 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.95 (s, 3H), 4.48 (s, 2H), 6.66–6.74 (m, 3H), 7.16–7.30 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.60, 56.80, 112.60, 116.77, 126.93, 127.02, 128.71, 129.34, 139.20, 149.96. Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10. Found: C, 85.21; H, 7.65; N, 7.07. HRMS (m/z): $[M]^+$ calcd for $C_{14}H_{15}N$ 197.1204. Found: 197.1213.

*4.3.11. 4-Phenylmorpholine (**10k**).* Mp 51–53 °C (lit.[21] mp 51–53 °C). IR (KBr) 3062, 2970, 2865, 2826, 1600, 1494, 1444, 1222, 1110, 920, 864 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.12–3.16 (m, 4H), 3.83–3.86 (m, 4H), 6.85–6.92 (m, 3H), 7.23–7.30 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.41, 66.96, 115.74, 120.05, 129.19, 151.34. Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.60; H, 8.01; N, 8.55. HRMS (m/z): $[M]^+$ calcd for $C_{10}H_{13}NO$ 163.0997. Found: 163.0997.

*4.3.12. 1-(3-Chlorophenyl)-4-phenylpiperazine (**10l**).* Thin yellow liquid. IR (KBr) 3028, 1592, 1484 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.32 (s, 8H), 6.81–6.98 (m, 6H), 7.15–7.20 (t, J=8.07 Hz, 1H), 7.25–7.31 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.92, 49.29, 114.13, 116.04, 116.41, 119.62, 120.22, 129.62, 130.10, 135.06, 151.13, 152.30. Anal. Calcd for $C_{16}H_{17}ClN_2$: C, 70.45; H, 6.28; N, 10.27. Found: C, 70.44; H, 6.25; N, 10.25. HRMS (m/z): $[M]^+$ calcd for $C_{16}H_{17}ClN_2$ 272.1080. Found: 272.1080.

*4.3.13. 1-((4-Chlorophenyl)(phenyl)methyl)-4-phenylpiperazine (**10m**).* Thin yellow liquid. IR (KBr) 3044, 1578, 1422 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.51–2.54 (m, 4H), 3.15–3.19 (m, 4H), 4.24 (s, 1H), 6.79–6.89 (m, 3H), 7.16–7.30 (m, 7H), 7.35–7.41 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.25, 51.94, 75.52, 115.88, 119.61, 127.31, 127.92, 128.72, 128.79, 129.14, 129.27, 132.73, 141.35, 142.15, 151.33. Anal. Calcd for $C_{23}H_{23}ClN_2$: C, 76.12; H, 6.39; N, 7.72. Found: C, 76.10; H, 6.38; N, 7.70. HRMS (m/z): $[M]^+$ calcd for for $C_{23}H_{23}ClN_2$ 362.1550. Found: 362.1550.

*4.3.14. (4-Phenoxyphenyl)phenylamine (**10n**).* Mp 95–98 °C. IR (KBr) 3374, 3048, 3020, 1594, 1492, 1200, 740 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (br s, NH, D_2O exchangeable), 6.86–7.59 (m, 14H). ^{13}C NMR ($CDCl_3$) δ 117.25, 118.31, 120.65, 120.82, 122.99, 129.41, 129.70, 130.03, 144.26, 144.26, 151.46, 158.56. Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.72; H, 5.77; N, 5.35. HRMS (m/z): $[M]^+$ calcd for $C_{18}H_{15}NO$ 261.1154. Found: 261.1155.

*4.3.15. (4-Methoxyphenyl)(4-phenoxyphenyl)amine (**10o**).* Mp 81–82 °C. IR (KBr) 3422, 3047, 2952, 1594, 1508, 1490, 1240, 1130, 820 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 3H), 5.39 (br s, NH, D_2O exchangeable), 6.81–7.05 (m, 11H), 7.25–7.32 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.63, 114.81, 117.64, 117.79, 120.81, 121.29, 122.37, 129.59, 136.60, 141.19, 149.91, 155.07, 158.58. Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.30; H, 5.89; N, 4.80. HRMS (m/z): $[M]^+$ calcd for $C_{19}H_{17}NO_2$ 291.1259. Found: 291.1259.

*4.3.16. 4-Methoxy-N-p-tolylbenzenamine (**10p**).* Mp 81–83 °C (lit.[21] mp 81–83). IR (KBr) 3396, 3028, 1588, 1500 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 3H), 3.78 (s, OCH_3), 5.36 (br s, NH, D_2O exchangeable), 6.81–6.85 (m, 4H), 6.98–7.04 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.53, 55.62, 114.72, 116.63, 121.14, 129.35, 129.80, 136.71, 142.45, 154.86. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.80; H, 7.10; N, 6.56. HRMS (m/z): $[M]^+$ calcd for $C_{14}H_{15}NO$ 213.1154. Found: 213.1155.

*4.3.17. N-Phenylquinolin-2-amine (**10q**).* Mp 162–163 °C. IR (KBr) 3305, 3057, 3045, 1593, 1504, 1423, 1344, 1328, 1294, 823, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 6.36 (br s, NH, D_2O exchangeable), 7.23–7.98 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.81, 124.80, 125.68, 125.89, 127.21, 127.90, 128.16, 129.38, 129.50, 136.99, 144.54, 147.39, 156.61. Anal. Calcd for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.78; H, 5.47; N, 12.71. HRMS (m/z): $[M]^+$ calcd for $C_{15}H_{12}N_2$ 220.1000. Found: 220.1000.

*4.3.18. N-Phenylpyrazin-2-amine (**10r**).* Mp 133–135 °C. IR (KBr) 3302, 3072, 3122, 3026, 2950, 1636, 1592, 1530, 1454, 1360, 1144, 1014, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.04–7.09 (m, 1H), 7.37 (br s, NH, D_2O exchangeable), 7.30–7.46 (m, 4H), 7.94 (d, 1H, J=2.67 Hz), 8.08 (d, 1H, J=1.22 Hz), 8.23 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 120.22, 123.41, 129.32, 133.21, 134.57, 139.44, 141.87, 152.52. Anal. Calcd for $C_{10}H_9N_3$: C, 70.16; H, 5.30; N, 24.54. Found: C, 70.15; H, 5.30; N, 24.51. HRMS (m/z): $[M]^+$ calcd for $C_{10}H_9N_3$ 171.0796. Found: 171.0795.

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References and notes

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