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Development of a New Arylamination Reaction Catalyzed by Polymer Bound 1,3-(Bisbenzimidazolyl) Benzene Co(II) Complex and Generation of Bioactive Adamanate Amines

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Abstract: We herein report the preparation and characterization of an inexpensive polymer supported 1,3-bis(benzimidazolyl)benzeneCo(II) complex [PS-Co(BBZN)Cl_2] as a catalyst by using the polymer (divinylbenzene cross-linked chloromethylated polystyrene), on which 1,3-bis(benzimidazolyl) benzeneCo(II) complex (PS-Co(BBZN)Cl_2) has been immobilized. This'catalyst was employed to develop arylamination reaction and robustness of the same reaction was demonstrated by synthesizing various bioactive adamantanyl-tethered-biphenylamines. Our synthetic methodology was much improved than reported methods due to the use of an inexpensive and recyclable catalyst.

Keywords: arylamination reactions; adamantanyl-tethered-biphenylamines; polymer-supported catalyst; cobalt complex; Buchwald–Hartwig reaction

1. Introduction

Transition metal-catalyzed cross-coupling reactions between aryl halides and primary/secondary amines to obtain aminated aryl compounds has been an area of interest due to the wide applications of arylamines in the synthetics and pharmaceutical industries [1–5]. In this direction, the Buchwald–Hartwig cross-coupling reaction was performed by using transition metal catalysts, ligands and bases

with substrates to obtain the desired arylamine products [6–8]. The disadvantage of this reaction is the use of expensive catalysts, which offers the chemist the opportunity to discover cheaper, reusable catalysts to drive the arylamination reactions. Inspired by major developments in cobalt-catalyzed arylamination reactions, we developed a complementary method to perform an arylamination reaction using cobalt as a metal catalyst [9–11]

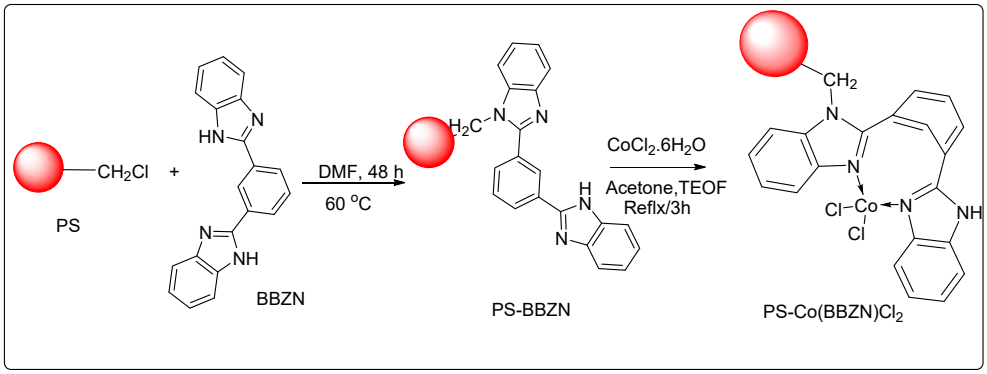
In addition, benzimidazole ligand coordinated metal complexes are widely used as catalysts in arylamination reactions [12]. Since these catalysts were found to be less hydrophobic, immobilization of such metal complexes with polymer support was observed to be stable, selective, and recyclable, attributed to the steric, electrostatic, hydrophobic and conformational effects of the polymer support [13]. Hence, several reports pertaining to the synthesis of arylamines using polymer-supported transition metal complexes are found [14–16]. Specifically, chloromethylated polystyrene cross-linked with divinyl-benzene was employed as a macromolecular support to perform the arylamination reactions [17–22].

In medicinal chemistry, an adamantane-coupled bicyclical core structure was used as an important pharmacophore, which was inserted in many drugs [23]. Hence, the adamantane structure was recognized as a readily available "liphophilic bullet" for providing critical liphophilicity to known pharmacophoric units. Given the remarkable importance of adamantane chemistry, we recently reported the synthesis and biology of adamantyl-tethered biphenylic compounds as potent anticancer agents [24]. In our continued efforts to synthesize newer bioactive agents [25–31], we herein report a practical, economically feasible and efficient arylamination reaction using polymer-supported 1,3-bis(benzimidazolyl)benzeneCo(II) complex (PS-Co(BBZN)Cl_2) as a catalyst. Interestingly, the recovered (PS-Co(BBZN)Cl_2) could be reused three times without a significant loss of activity.

2. Results

2.1. Chemistry of Catalyst Design and Method Development

We initially synthesized polymer-supported 1,3-bis(benzimidazolyl)benzeneCo(II) complex [PS-Co(BBZN)Cl_2] as shown in Scheme 1.



Scheme 1. Schematic representation to show synthesis of PS-Co(BBZN)Cl_2.

For this, 1, 3-bis(benzimidazolyl)benzene was treated with chloromethylated polystyrene divinylbenzene and followed by the addition of cobalt chloride. The obtained PS-Co (BBZN)Cl_2 was characterized by analytical techniques including CHNS, UV-Vis, FT-IR, SEM-EDX and TGA as presented in supporting information (Figure 1, Supplementary SI-02). Based on N% and Co% obtained through elemental and metal ion analysis, the complex formed on the polymer support was about 0.0053 moles per 1 g of the polymer support which corresponded to 7.16% of Co intake. This further confirmed the formation of the complex on the polymer support.

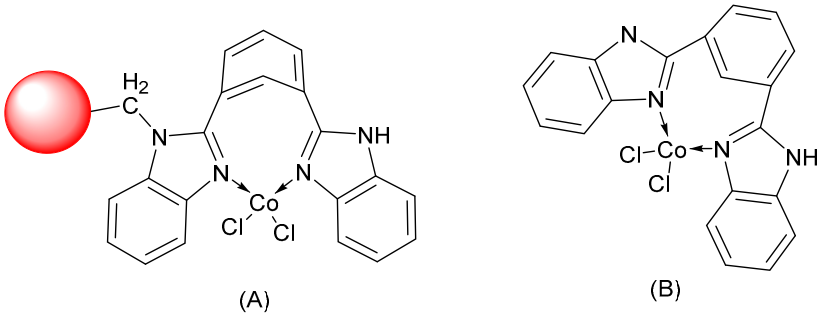
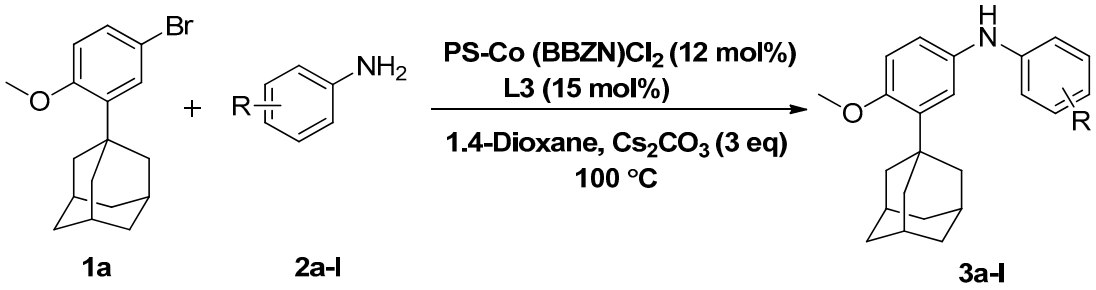


Figure 1. Structure of (**A**) PS-Co (BBZN)Cl_2 and (**B**) unbound Co(BBZN)Cl_2.

Motivated by the increased understanding of the Co-catalyzed amination reaction, we next investigated the applicability of (PS-Co (BBZN)Cl_2) in the arylamination reaction. To examine this hypothesis, 1-(5-bromo-2-methoxyphenyl)adamantine (**1a**) and 4-chloro aniline (**2a**) were selected as model substrates and reagents for the reaction in 1,4-dioxane media and Cs_2CO_3 as a base (Scheme 2).



Scheme 2. General scheme of arylamination reaction between adamantane bromide and various amines using PS-Co(BBZN)Cl_2 as a catalyst.

Control experiments established the importance of both PS-Co(BBZN)Cl_2 and ligand, as no product was obtained (Table 1, entry **1**). Gratifyingly, the substrate was transformed into the desired product 3-(adamantan-1-yl)-N-(4-chlorophenyl)-4-methoxyaniline (**3a**) with 51% yield in the presence of catalyst (PS-Co(BBZN)Cl_2) (10 mol%) and ligand **L3** (Table 2, entry **10**). Screening of various classes of ligands (Figure 2) to improve the yield revealed that the use of phosphine based ligand BINAP (**L3**) or Xphose (**L4**) gave improved yields at different catalyst concentrations (Table 1, entry **10**, **11**, **14**, **15**), whereas the other ligands such as bidentate ligands (**L1**, **L2**) and N-heterocyclic carbine ligands (**L5**, **L6**) yielded no products indicating the high role of selectivity of ligands in the forward reaction. The most robust reaction was achieved by the use of 12 mol% of PS-Co(BBZN)Cl_2 in the presence of BINAP with an 86% yield at 10 h reaction condition (Table 1, entry **14**). Further investigation revealed that there was no considerable improvement in yield when the catalyst load was increased to 15 mol% (Table 1, entry **18**, **19**) whereas the yield dropped to 69% when the reaction time was reduced to 6 h with 15 mol% catalyst (Table 1, entry **20**). Using the above better protocol, we further synthesized ABTAs by reacting adamantine bromo compounds (**1a**) and various amines (Table 2). It was observed that all amine partners productively coupled with good yields of around 70–86%.

All novel compounds exhibited spectral properties consistent with the assigned structures and were fully characterized by their spectroscopic data (mass, elemental, ^{1}H and ^{13}C NMR analysis).

The majority of reactions were done by keeping time point for 16 h and when the concentration of the catalyst was increased to 12%, the reaction was completed in 12 h and in many cases pure product was produced with excellent yield. The above developed method tolerated the presence of substituent in the aromatic amino-compounds. Specifically, we observed that the electron-donating para-substituted aromatic amine partners were well-tolerated to produce corresponding products in

good to excellent yields (Table 2, entries **1**–**12**). However, ortho-substituted and electron-withdrawing group bearing compounds were not productive giving lower yields (Table 2, entries **5**, **11**, **12**, **13**).

Table 1. PS-Co(BBZN)Cl_2-catalyzed coupling of 1-(5-bromo-2-methoxyphenyl)adamantane with 4-Chloro aniline [a].

Entry	PS-Co(BBZN)Cl_2	Ligand [b]	Time	Yield (%) [c]
1	5 mol%	—	16	NR
2	5 mol%	L1	16	NR
3	5 mol%	L2	16	NR
4	5 mol%	L3	16	NR
5	5 mol%	L4	16	NR
6	5 mol%	L5	16	NR
7	5 mol%	L6	16	NR
8	10 mol%	L1	16	NR
9	10 mol%	L2	16	NR
10	10 mol%	L3	16	51
11	10 mol%	L4	16	42
12	10 mol%	L5	16	20
13	10 mol%	L6	16	26
14	12 mol%	L3	10	86
15	12 mol%	L4	12	78
16	12 mol%	L5	16	36
17	12 mol%	L6	16	41
18	15 mol%	L3	10	86
19	15 mol%	L4	12	79
20	15 mol%	L3	6	69

[a] Conditions: admantane-bromo compounds (1 mmol), 4-chloro aniline (1 mmol) (PS-Co (BBZN)Cl_2) (12 mol%); Cs_2CO_3 (3 eq); 1, 4 dioxane (10 mL); N_2 atmosphere: 100 °C. [b] ligands (15 mol%): L1 = 2, 2′-bipyridine, L2 = 1,10-phenanthroline; L3 = 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene, L4 = dicyclohexyl(2-(2,4,6-trisopropylphenyl)cycohexyl)phosphine, L5 = 2,6-bis(3-methylimidazoline-1yl)pyridine, L6 = 1,3-dimessityl-4,5-dihydro-1H-imidazole-3-ium chloride; [c] isolated yield; NR = no reaction.

Table 2. PS-Co(BBZN)Cl_2 composite-catalyzed coupling of various substituted halo aromatic compounds with various substituted aromatic amines [a].

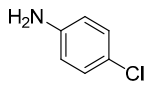
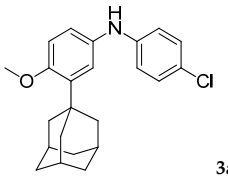
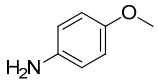
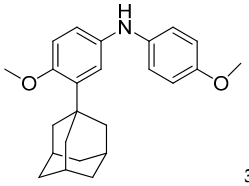
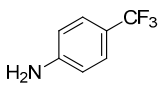
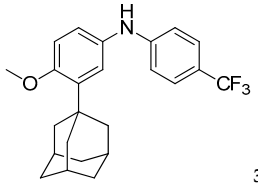
Entry	Amine	Product [b] and Yield (%) [c]
1	 **2a**	 **3a(86)**
2	 **2b**	 **3b(82)**
3	 **2g**	 **3c(79)**

Table 2. *Cont.*

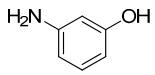
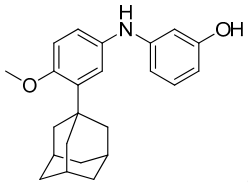
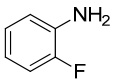
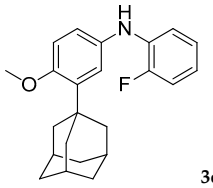
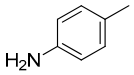
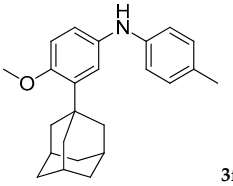
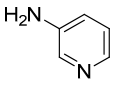
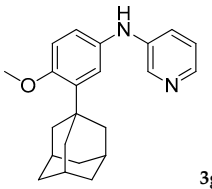
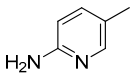
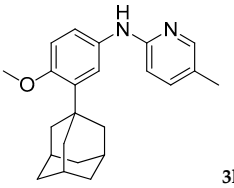
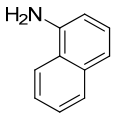
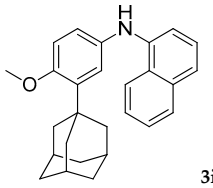
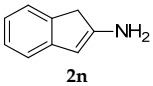
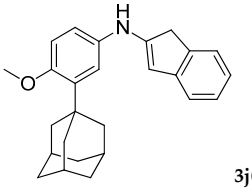
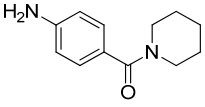
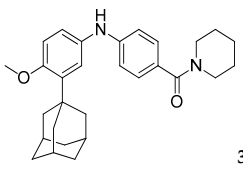
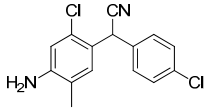
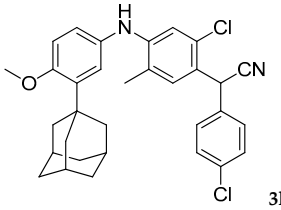
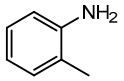
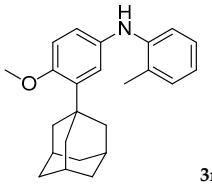
Entry	Amine	Product [b] and Yield (%) [c]
4	 **2h**	 **3d(84)**
5	 **2i**	 **3e(62)**
6	 **2j**	 **3f(87)**
7	 **2k**	 **3g(84)**
8	 **2l**	 **3h(80)**
9	 **2m**	 **3i(83)**
10	 **2n**	 **3j(76)**
11	 **2o**	 **3k(64)**

Table 2. *Cont.*

Entry	Amine	Product [b] and Yield (%) [c]
12	 **2p**	 **3l(61)**
13	 **2q**	 **3m (64)**

[a] Reaction conditions—Aromatic halo compounds (1 mmol), aromatic amine (1 mmol), BINAP(15 mol%), PS-Co(BBZN)Cl_2 (12 mol%), CS_2CO_3(3 mmol), 1,4-dioxane (5 mL), N_2 atmosphere 10 h, 100 °C. [b] All new compounds were characterized by their spectroscopic data shown in supporting information; [c] isolated yield.

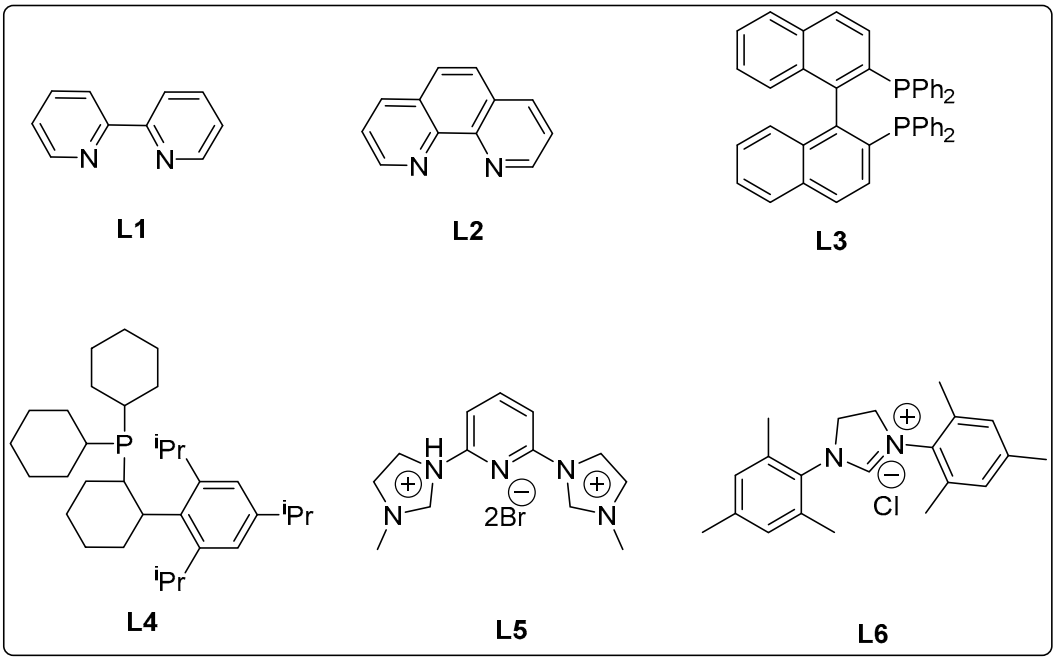
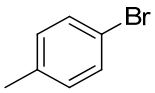
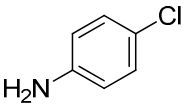
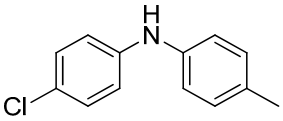
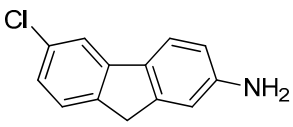
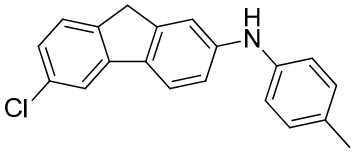
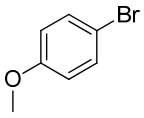
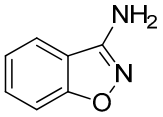
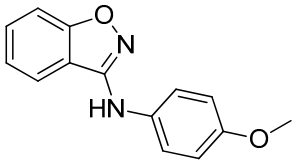
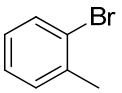
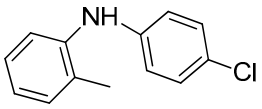
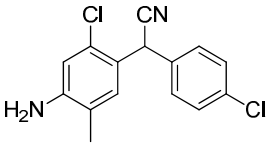
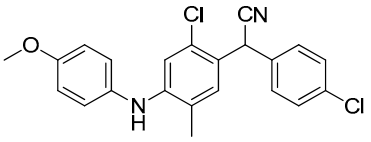
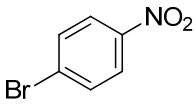
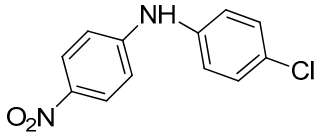
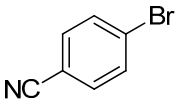
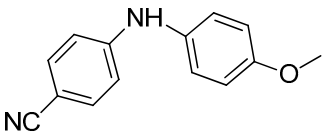


Figure 2. Various classes of ligands used in this study.

With the reaction conditions established we tried to investigate the scope of the new protocol on different substituted aromatic bromo compounds by treating with various amines (Table 3). We found that electron donating para-substituted on aromatic halo partner was tolerated well to give corresponding products in good to excellent yields (entries **1**, **2**, **3** and **5**), but with ortho-substituted and electron-withdrawing group bearing aromatic bromo compounds observed a loss in yield (entries **4**, **6** and **7**) with no improvement in the reaction conversion on prolonged reaction.

Table 3. Various substrates and reagents used to optimization of arylamination reaction.

Entry	Aromatic Halo Compounds	Amine	Product [a] and Yield (%)
1	 **4 a**	 **2 a**	 **5 a [a] (81)**
2	**4 a**	 **2 r**	 **5 b (80)**
3	 **4 b**	 **2 s**	 **5 c (79)**
4	 **4 c**	**2 a**	 **5 d[a] (61)**
5	**4 b**	 **2 p**	 **5 e(78)**
6	 **4 d**	**2 a**	 **5 f [a] (59)**
7		**2 a**	 **5 g[a] (58)**

[a] Reported compounds.

All novel compounds exhibited spectral properties consistent with the assigned structures and were fully characterized by their spectroscopic data (mass, elemental, ^{1}H and ^{13}C NMR analysis). It was found that the use of a catalyst PS-Co(BBZN)Cl_2, in combination with some ligands provided a robust catalytic system. On the basis of previous mechanistic studies in cobalt-catalyzed C−N bond formation reactions, it was possible to propose a mechanism for the conversion of 3-(adamantan-1-yl)-N-(4-chlorophenyl)-4-methoxyaniline (**3 a**) as shown in Figure 3 [32–34].

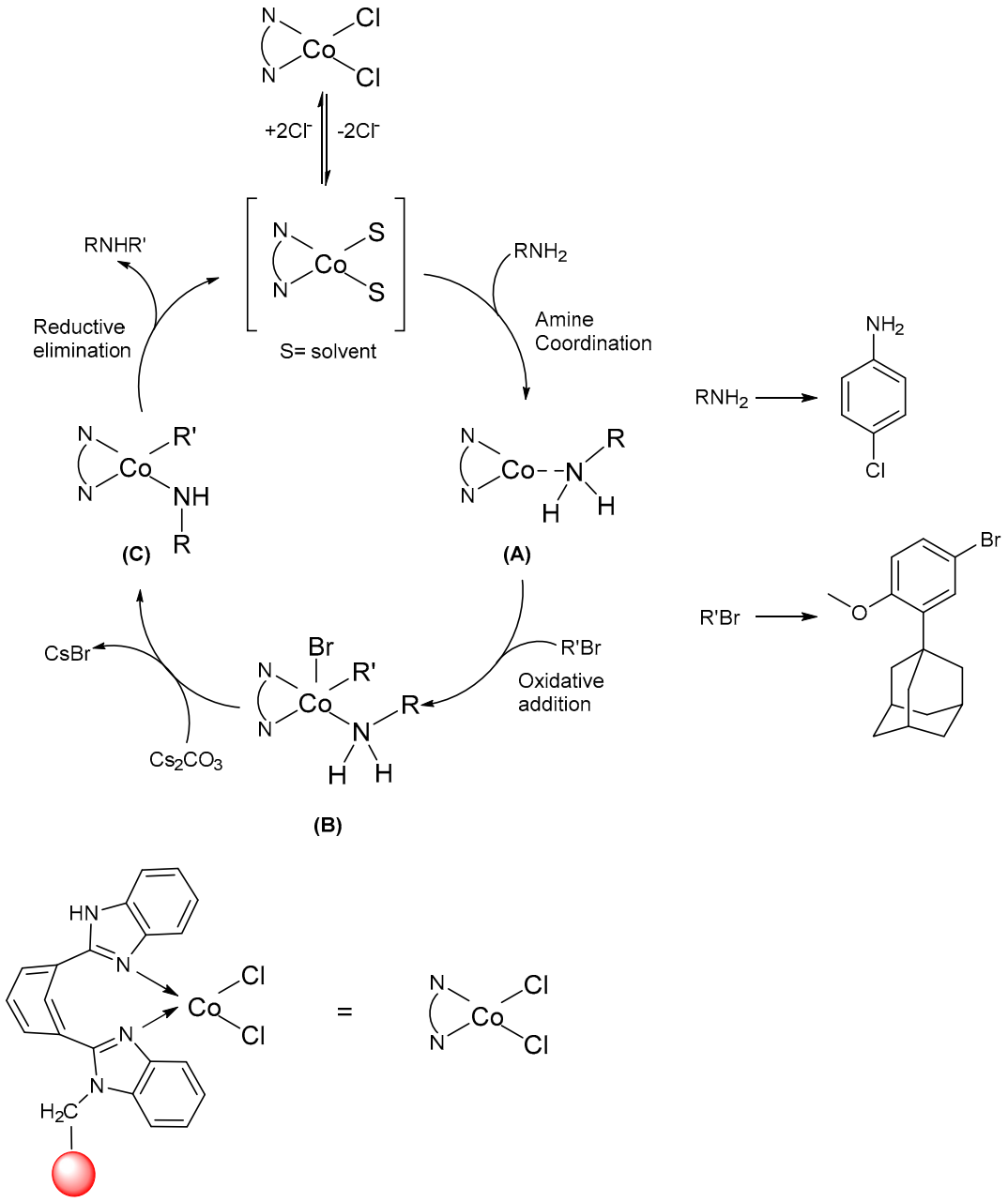


Figure 3. Plausible mechanism for the generation of arylamines using PS-Co(BBZN)Cl_2 as a catalyst.

Initially, the catalyst makes a complex with amine to form a catalyst-amine complex **A**, which undergoes an oxidative addition reaction with 1-(5-bromo-2-methoxyphenyl)adamantane and complex **B** formation occurs. Complex **B** reacts with cesium carbonate base and undergoes metathesis step, which gave complex **C**. Finally, the reductive elimination reaction complex **C** takes place and thereby catalyst regeneration and the desired product formation occur in the last step (Figure 3).

Further, we performed density-functional theory calculations using dispersion corrected CAM-B3 LYP functional and 6–31+G method [35]. All electron basis set as implemented in the Gaussian 09 package [36]. The minima nature of the structures has been confirmed based on computed real harmonic vibrational analysis at the same level of theory. Gibbs free energy calculations for four intermediate cobalt complexes were chosen for our mechanistic elucidation. Initially $CoCl_2$ makes the coordination complex with the ligand and reacts with aromatic amine and forms Co-NH bond quickly

[intermediate (**a**); ΔE = −6.03 kcal/mole], which in turn gets stabilized by releasing HCl and attains a lower energy intermediate with a ΔE of −9.62 kcal/mole. Alkyl bromide adds to the intermediate (**b**) quickly and attains still lower energy of ΔE of −17.18 kcal/mole where the bindentate ligand detachment takes place and immediate loss of HCl takes place and again attains lowest energy intermediate (**d**) of ΔE = −19.62 kcal/mole, which gives the product immediately. The optimized geometries and the energy profile diagram of intermediates (**a**–**d**) are shown in Figures 4 and 5, respectively. On the basis of lower Gibbs free energy of intermediates across (**a**) to (**d**), we can conclude that the reaction occurs naturally upon cobalt chloride coordination complex formation occurring with the bidentate ligands.

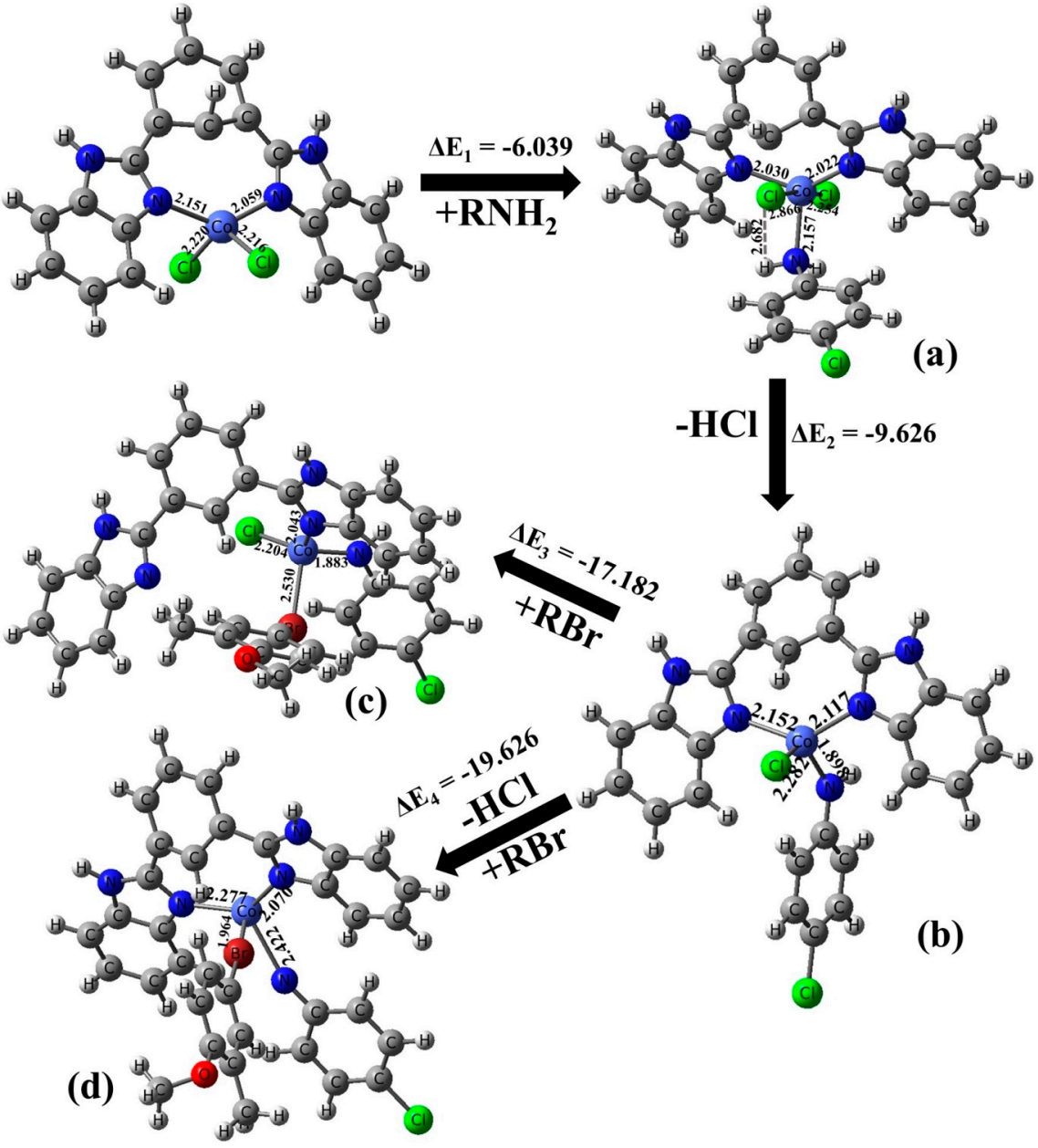


Figure 4. Computed intermediate structures (**a**–**d**) and reaction path. Energy difference ΔE are given in kcal/mole.

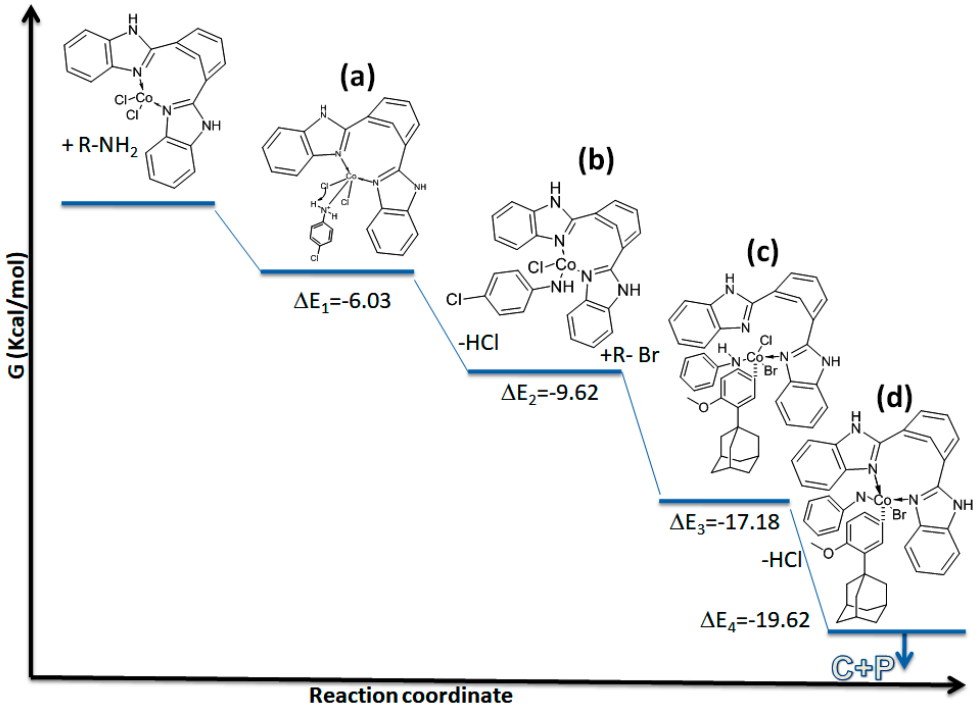
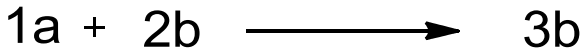


Figure 5. Energy profile diagram or arylamination reaction. C= catalyst; P = product.

2.2. Recyclability of the Catalyst

Further, the superiority of PS-Co(BBZN)Cl_2 catalyst was its recyclability, which was investigated by using the compound **1 a** and **2 b** as a model reaction. After each run, the catalyst was filtered off and washed with water followed by methanol, it was then dried in an oven at 120 °C for 15 min and used directly for the next reaction. The results were summarized (Table 4). We recorded that the catalyst could be used thrice and isolated yields achieved were above 70%.

Table 4. The recycling of the catalyst [a].



Run	1	2	3
Yield [b] (%)	86	81	75

[a] Reaction conditions—1 a (1 mmol), 2 b (1 mmol), BINAP (15 mol%), (PS-Co (BBZN)Cl_2) (12 mol%), CS_2 CO_3 (3 mmol), 1,4-dioxane (5 mL), N_2 atmosphere 10 h, 100 °C. [b] Isolated yield.

3. Materials and Methods

3.1. Procedure for the Synthesis of PS-Co(BBZN)Cl_2 Complex

3.1.1. Preparation of BBZN Functionalized Polymer Support

The chloromethylated polystyrene beads cross-linked with 6.5% divinylbenzene were first washed with a mixture of THF and water in the ratio 4:1 using Soxhlet extractor for 48 h. The beads were then vacuum dried. The chloromethylated polystyrene beads (3 g) were allowed to swell in DMF solution of BBZN ligand (5.2 g) was added to the above suspension followed by the addition of triethylamine (12 mL) in ethylacetate (105 mL) and was heated at 60 °C for 45 h in a water bath. It was cooled to room temperature, filtered, and washed with DMF. The beads were then Soxhlet extracted with ethanol to remove any unreacted BBZN and dried in an oven at 60 °C overnight.

3.1.2. Preparation of PS-Co(BBZN)Cl_2 Complex

The functionalized beads (1.0 g) were allowed to swell in 50 mL acetonitrile and toluene mixture in the ratio 1:1 for 1 h. Then the solvent was decanted. To this, 1.426 g of $CoCl_2$.6 H_2 O dissolved in methanol (100 mL) was added at intervals (4 times) and heated at 60 °C for 48 h. It was filtered, washed with alcohol and Soxhlet extracted to remove any unreacted $CoCl_2$.6 H_2 O. It was filtered and dried in an oven at 60 °C for 10 h and vacuum dried.

3.2. General Procedure for (PS-Co(BBZN)Cl_2) Complex Catalyzed C−N Bond-Formation Reaction

A dried Schlenk tube was charged with substrate **1 a** (320 mg, 1 mmol), **2 a** (127.6 mg, 1 mmol), BINAP (48 mg, 15 mol%), (PS-Co(BBZN)Cl_2](38 mg, 12 mol%). The tube was evacuated and backfilled with N_2, and Cs_2 CO_3 (975 mg, 3 mmol) followed by reagent grade 1, 4-dioxane (5 mL). The reaction mixture was heated to 100 °C for 10 h. After completion of reaction the mass was cooled to room temperature, filtered off the catalyst, the solvent quenched with water and diluted with ethyl acetate (10 mL). The layers were separated, and the aqueous layer was extracted with (5 mL) ethyl acetate. The combined organic layer was washed with water (10 mL), dried over anhydrous sodium sulphate and the solvent was removed in vacuum. The crude product was purified using silica gel column chromatography.

3.2.1. 3-(Adamantan-1-yl)-N-(4-chlorophenyl)-4-methoxyaniline (**3 a**)

Pale Yellow colored solid; mp 140–142 °C: ^{1}H NMR (400 MHz,$CDCl_3$) 7.14–7.12 (d, J = 8.0 Hz, 2 H), 6.95–6.91 (m, 2 H), 6.81–6.78 (m, 3 H), 5.46 (s, 1 H), 3.80 (s, 3 H), 2.05 (m, 9 H), 1.74 (m, 6 H); ^{13}C NMR (100 MHz,CDCl3) 155.0, 144.2, 139.9, 134.8, 129.2, 123.6, 120.6, 119.1, 116.4, 112.6, 55.4, 40.6, 37.1, 29.1; LCMS (MM : ES + APCI) 368.4 $(M + H)^+$; Anal.Calcd for C_{23} H_{26} ClNO: C, 75.08; H, 7.12; N, 3.81. Found: C, 75.01; H, 7.15; N, 3.88.

3.2.2. 3-(Adamantan-1-yl)-4-methoxy-N-(4-methoxyphenyl)aniline (**3 b**)

Brown colored solid; mp 117–119 °C: ^{1}H NMR (400 MHz,$CDCl_3$) 7.48–7.46 (d, J = 8.0 Hz, 2 H), 7.24 (m, 1 H), 6.88–6.86 (d, J = 8.0 Hz, 2 H), 6.72–6.70 (d, J = 8.0 Hz, 2 H), 5.39 (s, 1 H), 3.89 (s, 3 H), 3.83 (s, 3 H), 2.06–2.03 (m, 9 H), 1.75 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) 153.8, 142.2, 138.9, 130.4, 128.2, 122.5, 118.1, 115.5, 111.8, 55.0, 53.7, 40.3, 36.96, 28.9; LCMS (MM : ES + APCI) 364.4 $(M + H)^+$; Anal.Calcd for C_{24} H_{29} NO_2: C, 79.30; H, 8.04; N, 3.85. Found: C, 79.26; H, 8.11; N, 3.79.

3.2.3. 3-(Adamantan-1-yl)-4-methoxy-N-(4-(trifluoromethyl)phenyl)aniline (**3 c**)

Off-white colored solid; mp 124–126 °C: ^{1}H NMR (400 MHz,$CDCl_3$) 7.64–7.61 (m, 2 H), 7.45–7.39 (m, 3 H), 7.24 (s, 1 H), 6.96–6.94 (d, J = 8.0 Hz, 1 H), 5.36 (s, 1 H), 3.87 (s, 3 H), 2.13–2.04 (m, 9 H), 1.77 (m, 6 H); ^{13}C NMR (100 MHz,$CDCl_3$) 159.1, 145.1, 139.1, 131.8, 127.0, 125.7 (JCF = 25.7 Hz), 112.1, 55.2, 40.6, 37.2 (JCF = 7.6 Hz), 29.7, 29.1; LCMS (MM : ES + APCI) 402.2 $(M + H)^+$; Anal.Calcd for C_{24} H_{26} F_3 NO: C, 71.80; H, 6.53; N, 3.49. Found: C, 71.76; H, 6.59; N, 3.41.

3.2.4. 3-((3-(Adamantan-1-yl)-4-methoxyphenyl)amino)phenol (**3 d**)

Off-white colored solid; mp 98–100 °C; ^{1}H NMR (400 MHz,CDCl3) 7.43 (s, 1 H), 7.08 (s, 1 H), 6.99–6.96 (m, 4 H), 6.84–6.82 (d, J = 8.0 Hz, 1 H), 5.62 (s, 1 H), 4.80(s, 1 H), 3.82 (s, 3 H), 2.05 (m, 9 H), 1.74 (m, 6 H); ^{13}C NMR (100 MHz,CDCl3) 159.2, 154.3, 146.2, 139.9, 129.7, 121.3, 119.9, 117.7, 115.3, 112.6, 111.2, 55.4, 40.6, 37.1, 29.1; HRMS Calcd 372.1934 Found: 372.1938 $(M + H)^+$; Anal.Calcd for C_{24} H_{29} NO_2: C, 79.30; H, 8.04; N, 3.85. Found: C, 79.26; H, 8.11; N, 3.79.

3.2.5. 3-(Adamantan-1-yl)-N-(2-fluorophenyl)-4-methoxyaniline (**3 e**)

Yellow colored solid; mp 106–108 °C: ^{1}H NMR (400 MHz, $CDCl_3$) 7.10–7.06 (m, 1 H), 6.98–6.96 (dd, J1 = 2.7 Hz, J2 = 2.2 Hz, 2 H), 6.84–6.83 (d, J = 4.0 Hz, 1 H), 6.81 (s, 1 H), 5.50 (s, 1 H), 3.81 (s, 3 H), 2.05 (m, 9 H), 1.75 (m, 6 H); ^{13}C NMR (100 MHz,$CDCl_3$) 158.4, 155.4, 147.1, 139.9, 134.1, 130.3, 121.5,

120.0, 118.8, 114.6, 112.8 (JCF = 53.4 Hz), 55.4, 40.5, 37.2, 29.0; LCMS (MM : ES + APCI) 352.4 $(M + H)^+$; Anal.Calcd for C_{23} H_{26} FNO: C, 78.60; H, 7.46; N, 3.99. Found: C, 78.71; H, 7.39; N, 3.91.

3.2.6. 3-(Adamantan-1-yl)-4-methoxy-N-(p-tolyl)aniline (**3 f**)

Off-white colored solid; mp 108–110 °C: ^{1}H NMR (400 MHz,$CDCl_3$) 7.03–7.01 (d, J = 8.0 Hz, 2 H), 6.95–6.89 (dd, J1 = 4.0 Hz, J2 = 4.0 Hz, 2 H), 6.85–6.83 (d, J = 8.0 Hz, 2 H), 6.80–6.78(d, J = 8.0 Hz, 1 H), 5.39 (s, 1 H), 3.80 (s, 3 H), 2.26 (s, 3 H), 2.05 (m, 9 H), 1.74 (m, 6 H); ^{13}C NMR (100 MHz,$CDCl_3$) 154.2, 142.6, 139.7, 129.8, 128.9, 119.4, 117.6, 116.3, 112.7, 55.5, 40.6, 37.1, 37.0, 29.1, 20.6; LCMS (MM : ES + APCI) 348.4 $(M + H)^+$; Anal. Calcd for C_{24} H_{29} NO: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.90; H, 8.46; N, 3.99.

3.2.7. N-(3-Adamantan-1-yl)-4-methoxyphenyl)pyridin-3-amine (**3 g**)

Pale yellow colored solid; mp 103–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.42–8.41 (d, J = 4.0 Hz, 1 H), 7.47–7.43 (m, 2 H), 7.29–7.27 (m, 2 H), 7.23–7.22 (m, 2 H), 5.58 (s, 1 H), 3.85 (s, 3 H), 2.14–207 (m, 9 H), 1.79–1.73 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) 161.9, 153.0, 143.7, 136.1, 126.8, 125.9, 124.0, 123.0, 121.9, 117.6, 115.1, 56.1, 40.8, 38.0, 28.6; LCMS (MM : ES + APCI) 335.4 $(M + H)^+$; Anal. Calcd for C_{22} H_{26} N_2 O: C, 79.00; H, 7.84; N, 8.38. Found: C, 79.08; H, 7.79; N, 8.33.

3.2.8. N-(3-Adamantan-1-yl)-4-methoxyphenyl)-5-methylpyridin-2-amine (**3 h**)

Off-white colored solid; mp 101–102 °C: ^{1}H NMR (400 MHz, $CDCl_3$); 8.42 (s, 1 H), 7.53–7.47 (m, 3 H), 7.03–7.01 (d, J = 8.0 Hz, 2 H), 5.60 (s, 1 H), 3.83 (s, 3 H), 2.30 (s, 3 H), 2.09 (m, 9 H), 1.78 (m, 6 H); ^{13}C NMR (100 MHz, CDCl3) 160.2, 155.2, 145.0, 139.2, 128.9, 126.4, 121.4, 119.5, 117.4, 115.7, 54.8, 39.9, 36.4, 27.5, 27.0, 21.9; HRMS Calcd: 371.2094; Found: 371.2098 $(M + H)^+$; Anal. Calcd for C_{23} H_{28} N_2 O: C, 79.27; H, 8.10; N, 8.04. Found: C, 79.32; H, 7.99; N, 8.09.

3.2.9. N-(3-Adamantan-1-yl)-4-methoxyphenyl)naphthalen-1-amine (**3 i**)

Pale yellow colored solid; mp 105–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.09–8.07 (d, J = 8.0 Hz, 1 H), 8.03–8.01 (d, J = 8.0 Hz, 1 H), 7.96–7.94 (d, J= 8 Hz, 1 H), 7.60–7.28 (m, 6 H), 5.51 (s, 1 H), 3.83 (s, 3 H), 2.13–2.05 (m, 9 H), 1.76–1.73 (m, 6 H); ^{13}C NMR (100 MHz,$CDCl_3$) 153.9, 145.7, 138.3, 133.9, 132.7, 131.9, 128.7, 128.3, 128.2, 127.1, 126.9, 126.3, 125.9, 125.5, 111.4, 55.2, 40.4, 37.2, 29.2; LCMS (MM : ES + APCI) 384.4 $(M + H)^+$; Anal.Calcd for C_{27} H_{29} NO: C, 84.55; H, 7.62; N, 3.65. Found: C, 84.61; H, 7.59; N, 3.69.

3.2.10. N-(3-Adamantan-1-yl)-4-methoxyphenyl)-1 H-inden-2-amine (**3 j**)

Pale yellow colored solid; mp 116–118 °C: ^{1}H NMR (400 MHz, $CDCl_3$) 7.64–7.61 (m, 2 H), 7.45–7.39 (m, 3 H), 6.96–7.94 (d, J = 8 Hz, 2 H), 6.19 (s, 1 H), 5.34 (s, 1 H), 3.83 (s, 3 H), 3.29 (s, 2 H), 2.13–2.07 (m, 9 H), 1.77 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) 154.0, 144.4, 138.9, 132.0, 130.0, 126.0, 125.9, 120.1, 119.9, 115.5, 104.4, 55.4, 44.3, 40.8, 37.3, 29.7, 29.2; LCMS (MM : ES + APCI) 372.2 $(M + H)^+$ Anal.Calcd for C_{27} H_{29} NO: C, 84.06; H, 7.87; N, 3.77. Found: C, 84.11; H, 7.94; N, 3.72.

3.2.11. 4.((3-(Adamantan-1-yl)-4-methoxyphenyl)amino)phenyl)(piperidin-1-yl)methanone (**3 k**)

Off-white colored solid; mp 121–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.65–7.62 (m, 2 H), 7.45–7.39 (m, 3 H), 6.97–6.95 (d, J = 8.0 Hz, 1 H), 5.37 (s, 1 H), 3.87 (s, 3 H), 3.47–3.39 (m, 4 H), 2.14–2.13 (m, 9 H), 2.08–2.04 (m, 3 H), 1.78 (m, 6 H), 1.45 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.4, 155.2, 145.6, 138.9, 131.8, 127.0, 125.8, 125.6, 112.5, 55.5, 46.2, 40.5, 37.2, 37.1, 29.7, 29.1, 24.4; LCMS (MM : ES + APCI) 445.2 $(M + H)^+$; Anal.Calcd for C_{29} H_{36} N_2 O_2: C 78.34; H 8.16; N 6.30; Found: C 78.39; H 8.10; N 6.24.

3.2.12. 2.(4-((3-Adamantan-1-yl)-4-methoxyphenyl)amino)-2-chloro-5-methylphenyl)-2-(4-chlorophenyl)acetonitrile (**3 l**)

Yellow colored solid; mp 129–132 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.62–7.51 (m, 3 H), 7.32–7.26 (m, 2 H), 6.84–6.81 (d, J = 12.0 Hz, 2 H), 6.35–6.25 (m, 2 H), 5.66 (s, 1 H), 5.27 (s, 1 H), 3.82 (s, 3 H), 2.16–1.66

(m, 18 H); ^{13}C NMR (75 MHz,$CDCl_3$) 156.0, 1139.8, 136.6, 133.3, 126.8, 125.8, 125.6, 123.3, 121.7, 117.6, 55.3, 42.5, 41.6, 41.1, 40.9, 36.9, 36.5, 36.1, 35.6, 28.5, 27.9, 18.13; HRMS Calcd: 553.1784; Found: 553.1892 $(M + H)^+$; Anal.Calcd for C_{32} H_{32} Cl_2 N_2 O: C 72.31; H 6.07; N 5.27; Found: C 72.39; H 6.01; N 5.24.

Off-white colored solid; mp 118–120 °C; 3-(adamantan-1-yl)-4-methoxy-N-(o-tolyl)aniline (**3 m**): ^{1}H NMR (400 MHz, CDCl3) 7.40 (s, 1 H), 7.36 (d, 1 H), 7.17–7.10 (m, 4 H), 6.94 (d, 1 H), 5.37 (s, 1 H), 3.87 (s, 3 H), 2.41 (s, 3 H), 2.14 (m, 6 H), 2.06 (m, 3 H), 1.77 (m, 6 H); HRMS Calcd 370.214. Found: 370.212 $(M + H)^+$.

6-Chloro-N-(p-tolyl)-9 H-fluoren-2-amine (**5 b**)

Yellow colored solid; mp 131–132 °C ^{1}H NMR (400 MHz, DMSO-d_6); 8.10 (s, 1 H), 8.05–8.03 (d, J = 8 Hz, 1 H), 7.76 (s, 1 H), 7.53–7.51 (d, J = 8.0 Hz, 1 H), 7.38–7.21 (m, 4 H), 7.16–7.12 (m, 2 H), 5.36 (s, 1 H), 4,37 (s, 2 H), 2.39 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6); 140.7, 140.5, 137.8, 135.5, 129.1, 127.8, 127.5, 127.0, 125.4, 123.2, 121.4, 119.9, 112.1, 110.6, 41.20, 23.5; HRMS Calcd 328.0863; Found: 328.0866 $(M + Na)^+$; Anal.Calcd for C_{20} H_{16} ClN: C, 78.55; H, 5.27; N, 4.58; Found: C, 78.58; H, 5.21; N, 4.55.

N-(4-Methoxyphenyl)benzo[d]isoxazol-3-amine (**5 c**)

White colored solid; mp 98–100 °C: ^{1}H NMR (400 MHz, DMSO-d_6); 8.44–8.42 (d, J = 8.0 Hz, 1 H), 8.08–8.06 (d, J = 8.0 Hz, 1 H), 8.02–8.00 (d, J = 8.0 Hz, 1 H), 7.95–7.91 (m, J = 8.0 Hz, 2 H), 7.71–7.67 (m, 1 H), 7.26–7.24 (d, J = 8.0 Hz, 2 H), 5.32 (s, 1 H), 3.88 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6); 164.1, 159.7, 152.0, 147.4, 132.2, 127.2,125.6, 123.4, 121.7, 118.9, 114.4, 113.8, 55.2; HRMS Calcd 263.0791; Found: 263.0794 $(M + Na^+)$; Anal.Calcd for C_{14} H_{12} N_2 O_2: C, 69.99; H, 5.03; N, 11.66; Found: C, 70.05; H, 5.08; N, 11.59.

2-(2-Chloro-4-((4-methoxyphenyl)amino)-5-methylphenyl)-2-(4-chlorophenyl)acetonitrile (**5 e**)

Off-white colored solid; mp 111–112 °C: ^{1}H NMR (400 MHz, DMSO-d_6); 7.57–7.53 (m, 3 H), 7.51–7.42 (m, 3 H), 7.35–7.31 (m, 2 H), 7.08–7.02 (m, 2 H), 5.72 (s, 1 H), 5.32 (s, 1 H), 3.83 (s, 3 H), 2.13 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-d_6); 152.0, 149.8, 141.1, 140.0, 137.1, 132.4, 132.3, 132.1, 129.1, 128.6, 123.1, 120.8, 116.1, 54.99, 36.6, 17.9; HRMS Calcd 419.0688; Found: 419.0692 $(M + Na^+)$; Anal.Calcd for C_{22} H_{18} Cl_2 N_2 O: C, 66.51; H, 4.57; N, 7.05; Found: C, 66.59; H, 4.52; N, 7.11.

4. Conclusions

In conclusion, we prepared PS-Co (BBZN)Cl_2 catalyst and used it for the C−N bond formation reaction. A series of adamantyl-tethered-amino biphenylic compounds were synthesized by new protocol. Our synthetic methodology is much improved compared to existing methodologies as the catalyst is effective, inexpensive and recyclable.

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4344/10/11/1315/s1, SI-01: Experiment Section, SI-02: Spectral characterization Co(BBZN)Cl_2, SI-03 to14: Spectral characterization of compounds 4 a-4 l.

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Conflicts of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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