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Stable and Reusable Binaphthyl-Supported Palladium Catalyst for Aminocarbonylation of Aryl Iodides

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Abstract: A binaphthyl-supported Pd nanoparticles (Pd-BNP)-catalyzed aminocarbonylation of aryl iodides in the presence of carbon monoxide and amines for the synthesis of amides has been developed. This methodology provides an efficient route for the synthesis of a COX-2 enzyme inhibitor having anti-inflammatory activity.

Keywords: aminocarbonylation; binaphthyl-supported palladium catalyst; carboxylic amides; carbon monoxide insertion; reusable catalyst

The amide bond constitutes one of the most essential parts in organic synthesis and has a specific role in chemical and pharmaceutical industries.[1] The amide bond is the main chemical bond linkage in peptides and proteins as well. Various important marketed drugs such as diltiazem,[1e] atorvastatin, and itopride have an amide bond in their backbone (Figure 1).[2] Recently, applications of amide group-containing molecules have increased in the areas of pharmaceuticals, agrochemicals, polymers and materials.[3,4] This has served to stimulate efforts towards the development of a more economic and catalytic methods for amide synthesis.

Traditionally, amides are synthesized from acid chlorides and amines or by condensation of carboxylic acids with amines using coupling reagents.[5] Later on, several methods using alcohols or aldehydes under oxidative amidation conditions have been developed for amide synthesis.[6]

Aminocarbonylation of alkyl or aryl halides is an efficient alternative method for amide synthesis, in which the required intermediate carbonyl moiety can be accessed *in situ*, in one step, from the readily available feedstock carbon monoxide and aryl halides. Heck and co-workers have opened a new platform for amide synthesis, since then the use of carbon monoxide as an *in situ* source of generating the carbonyl moiety has increased using homogeneous palladium catalysts.[7,8] On the other hand, transition metal nanoparticles as catalyst have attracted great interest because of their unique properties, such as small particle size, high surface area, higher interaction with the substrate, increased reactivity and selectivity, easy purification and easy separation.[9]

Recently, we have developed an easily reusable form of Pd nanoparticles (Pd-BNP) stabilized by a binaphthyl backbone through Pd–$C_{(sp^2)}$ sigma bonds for the synthesis of polysubstituted olefins, benzonitriles and for different types of carbon-carbon bond forming reactions.[10] In order to contribute to the existing few reports on the usage of heterogeneous catalysts for aminocarbonylation,[11,12] and to explore the developed Pd-BNP catalyst for the same, we herein, report the usage of easily reusable Pd nanopartcles (Pd-BNP) as catalyst for the synthesis of amides from easily available carbon monoxide, aryl iodides and amines through aminocarbonylation (Scheme 1).[13]

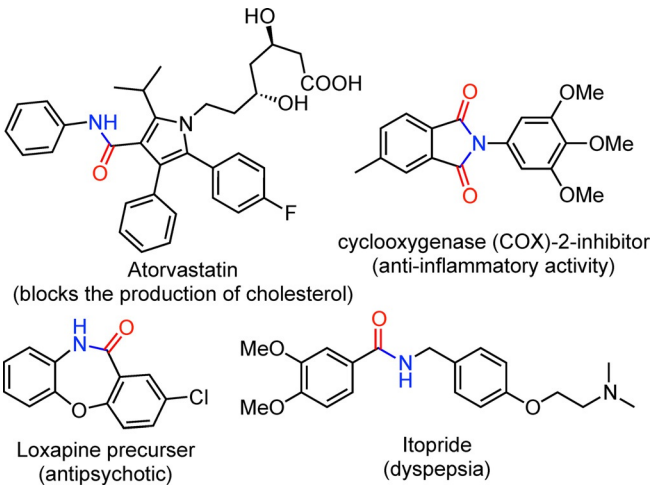
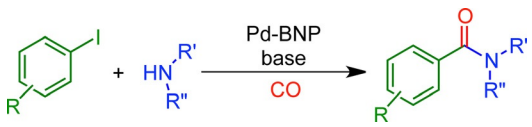


Figure 1. Representative examples of amide bond-containing biologically active molecules.



Scheme 1. Aminocarbonylation of aryl iodide using Pd-BNP catalyst.

The initial study was carried out using 4-iodotoluene **1a** and 4-methoxyaniline **2a** as model substrates with 2 equiv. of K_2CO_3 in the presence of 2 mol% of Pd-BNP at 110 °C in dry toluene in the presence of CO. To our delight, the reaction was completed within 24 h and afforded a 74% yield of the corresponding amide *N*-(4-methoxyphenyl)-4-methylbenzamide **3a** as product (Table 1, entry 1).

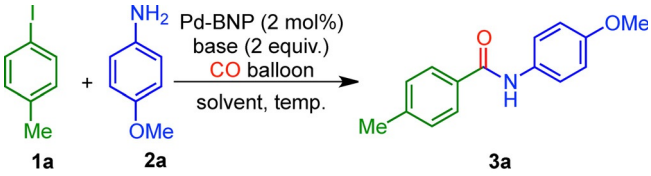
To improve the efficiency of this Pd-BNP-catalyzed aminocarbonylaion, various bases, such as NEt_3, Na_2CO_3, 1,4-diazabicyclo[2.2.2]octane (DABCO) etc. were screened. As expected, product **3a** was isolated in 95% yield by employing DABCO as base at 110 °C within 16 h (entry 4) and the results are summarized in Table 1.

To improve the efficiency of this reaction, several solvents were screened. Solvents other than toluene such as THF, dioxane, methanol and water gave inferior results (entries 6–9). The yield of **3a** was reduced when the reaction temperature was lower than 110 °C (entry 10). We also screened different equivalents of amine **2a** and DABCO used (entry 11–15). It was found that 2 equiv. of **2a** and 2 equiv. of DABCO were necessary for the completion of this transformation (entry 4).When 2 mol% of Pd/C were used as catalyst instead of Pd-BNP, a 45% yield of product **3a** was isolated (entry 19).

Using the optimized reaction conditions, the scope of the Pd-BNP-catalyzed aminocarbonylation for the synthesis of amides **3** was investigated using various substituted aryl iodides **1** with amines **2** and the results are summarized in Table 2.

It was observed that when any electron-donating group is present in the aromatic ring of either aryl iodides or aromatic amines, the reaction worked better and good to excellent yields of the amides were isolated (**3a–3g** and **3n–3s**) than when electron-withdrawing groups were present in either of the two aromatic rings (**3h–3k** and **3t**). In the case of aliphatic secondary amines such as piperidine and morpholine, the reactions were very slow and low yields of the corresponding amide were isolated (**3u** and **3v**). Primary amines such as phenylethylamine, benzylamine, propylamine and *n*-butylamine also provided moderate yields of the corresponding products **(3w–3z)**. Also, when any *ortho*-substitution was present in the aromatic ring of either aryl iodide or amines, no product formation was observed. With substituents such as acetyl and amide groups present in the *para*-position

Table 1. Optimization of the reaction conditions for the aminocarbonylation.[a]



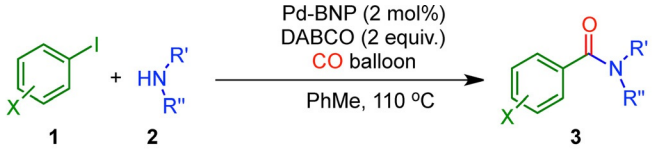
1a **2a** **3a**

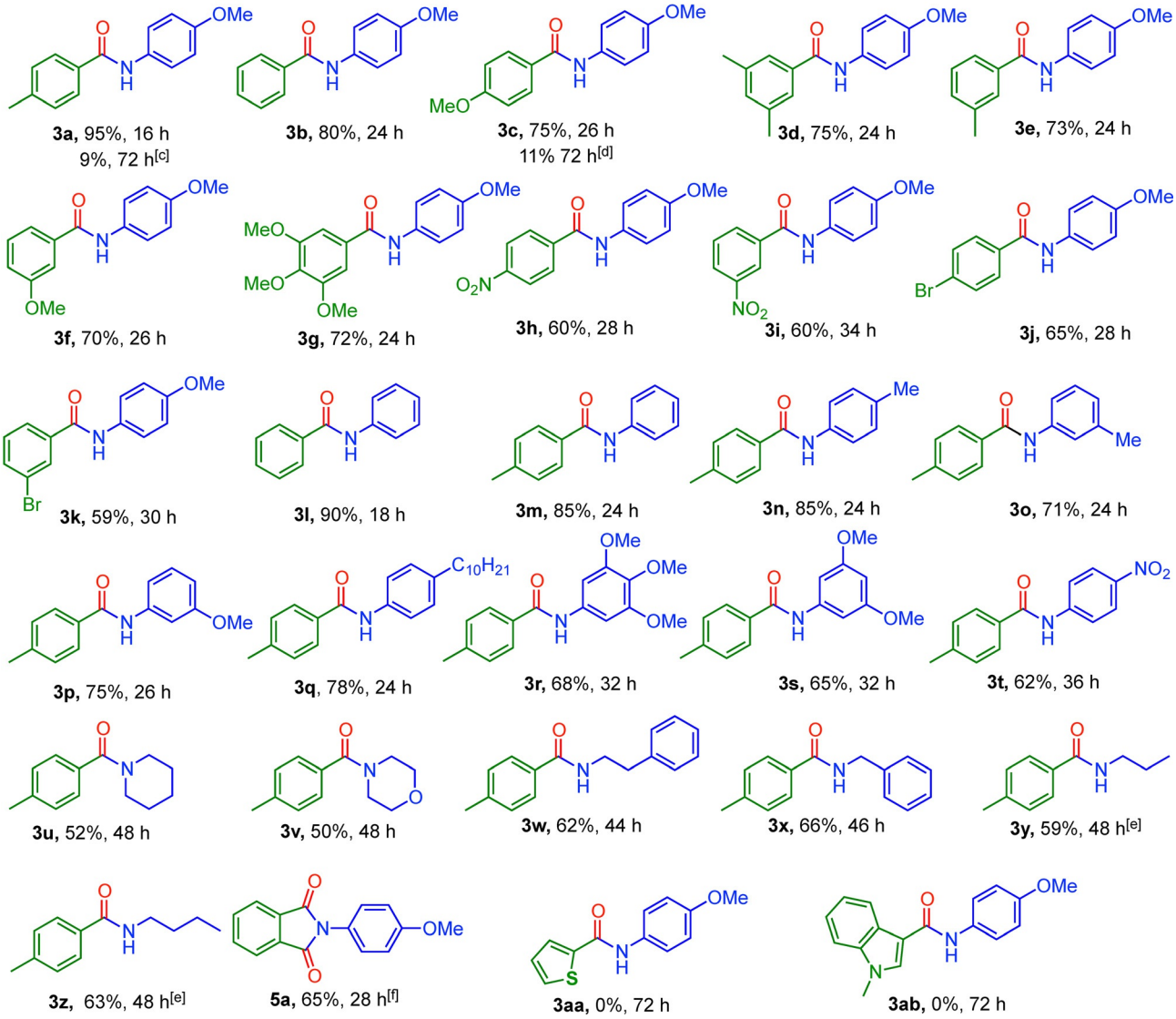
Entry	Base	Solvent	Temp. [°C]	Time [h]	Yield [%][b]
1	K_2CO_3	PhMe	110	24	74
2	Na_2CO_3	PhMe	110	24	54
3	NEt_3	PhMe	110	24	50
4	DABCO	PhMe	110	16	95
5	KOAc	PhMe	110	28	53
6	DABCO	THF	65	24	35
7	DABCO	1,4-dioxane	100	24	30
8	DABCO	MeOH	80	32	nr[c]
9	DABCO	H_2O	100	48	nr[c]
10	DABCO	PhMe	100	24	60
11	DABCO	PhMe	110	24	56[d]
12	DABCO	PhMe	110	20	76[e]
13	DABCO	PhMe	110	26	56[f]
14	DABCO	PhMe	110	20	75[g]
15	DABCO	PhMe	110	12	95[h]
16	DABCO	PhMe	110	24	65[i]
17	DABCO	PhMe	110	48	nr[c][j]
18	-	PhMe	110	24	nr[c][k]
19	DABCO	PhMe	110	24	45[l]

[a] *Reaction conditions:* 0.5 mmol of **1a**, 1.0 mmol of **2a**, 2 mol% of Pd-BNP (10.6 mg, 10 wt% by ICP-OES analysis) and 4 mL of solvent.
[b] Isolated yield.
[c] nr = no reaction.
[d] 1 equiv. of **2a**.
[e] 1.5 equiv. of **2a**.
[f] 1 equiv. of DABCO.
[g] 1.5 equiv. of DABCO.
[h] 3 equiv. of DABCO.
[i] 1 mol% of Pd-BNP.
[j] In the absence of Pd-BNP.
[k] In the absence of DABCO.
[l] 2 mol% of Pd/C used.

of anilines, formation of the corresponding amide did not take place even a trace amount. Heteroaryl iodides such as 2-iodothiophene and 3-iodo-1-methyl-1*H*-indole were unreactive under the standard reaction condition **(3aa–3ab)**. The less reactive aryl bromides such as 4-bromotoluene and 4-bromoanisole had given poor yields, 9% and 11%, respectively, and aryl chlorides 4-chlorotoluene and 4-chloroanisole were also remain unreactive under the optimized condition employed. When 1,2-diiodobenzene was used with 4-methoxyaniline **2a**, double carbonylation took place and the *N*-substituted phthalimide 2-(4-methox-

Table 2. Substrate scope for aminocarbonylation using the Pd-BNP catalyst.[a,b]





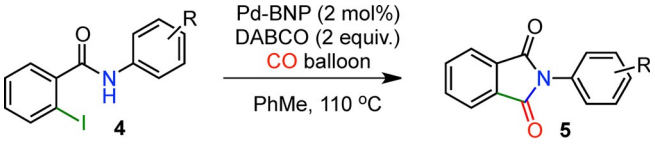
[a] *Reaction conditions:* 0.5 mmol of **1**, 1.0 mmol of **2**, 4 mL of PhMe.
[b] Isolated yield.
[c] 4-Bromotoluene as aryl halide.
[d] 4-Bromoanisole as aryl halide.
[e] Reaction carried out in a Schlenk pressure tube.
[f] 1,2-Diiodobenzene as the aryl iodide.

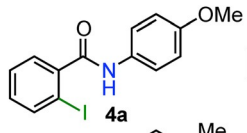
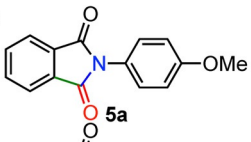
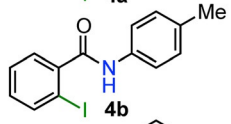
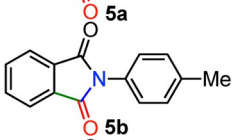
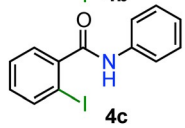
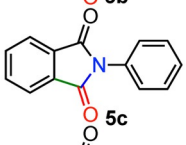
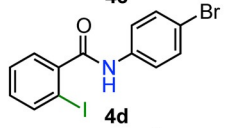
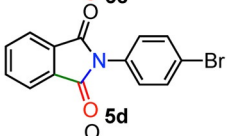
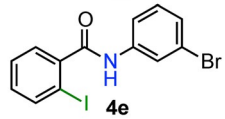
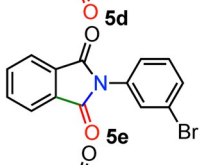
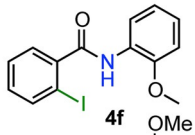
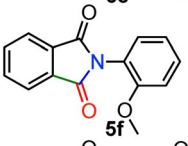
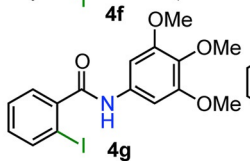
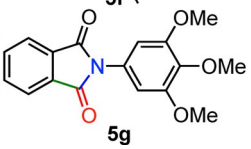
yphenyl)isoindoline-1,3-dione **5a** was isolated in 65% yield.[14]

After successfully completing the intermolecular aminocarbonylation, the intramolecular aminocarbonylation under the optimized reaction using 2-iodo-*N*-(4-methoxyphenyl)benzamide **4a** was carried out. Reaction completed within 24 h and 90% yield of the corresponding amide 2-(4-methoxyphenyl)isoindoline-1,3-dione **5a**[15] was isolated (Table 3, entry 1).

In order to explore the scope of the Pd-BNP catalyst, intramolecular aminocarbonylation was carried out using various 2-iodo-*N*-arylbenzamides **4** under

Table 3. Substrate scope for intramolecular aminocarbonylation using Pd-BNP catalyst.[a]



Entry	Substrate	Product	Time [h]	Yield [%][b]
1	 **4a**	 **5a**	24	90
2	 **4b**	 **5b**	24	91
3	 **4c**	 **5c**	24	88
4	 **4d**	 **5d**	26	90
5	 **4e**	 **5e**	26	83
6	 **4f**	 **5f**	36	56
7	 **4g**	 **5g**	28	67

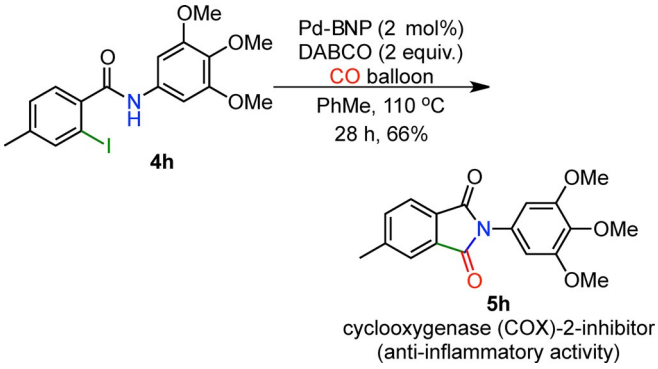
[a] *Reaction conditions:* 0.5 mmol of **4**, 4 mL of PhMe.
[b] Isolated yield.

the optimized reaction condition, which provided *N*-substituted isoindoline-1,3-dione derivatives **5** in excellent yield (Table 3).

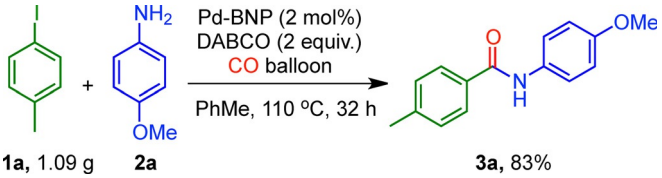
To check the applicability of Pd-BNP catalyst, we also have synthesized a cyclooxygenase (COX-2) inhibitor, 5-methyl-2-(3,4,5-trimethoxyphenyl)isoindoline-1,3-dione **5h**, having a half maximal inhibitory concentration of $IC_{50} = 0.4\ \mu M$ (Scheme 2).[2b] Cyclooxygenase inhibitors are known to have anti-inflammatory activity and help to relieve pain.[16]

A gram scale experiment was performed by employing 1.09 g (5 mmol) of **1a** under the optimized reaction conditions to show the reliability of this synthetic protocol. Aminocarbonylation proceeded smoothly to afford **3a** in 83% yield (Scheme 3).

To check the recyclability and reusability of the Pd-BNP catalyst, the reaction was carried out using 4-iodotoluene **1a** and 4-methoxyaniline **2a** with 2 mol% of Pd-BNP under the optimized reaction conditions and the result is summarized in Figure 2.



Scheme 2. Synthesis of a COX-2 inhibitor using Pd-BNP.



Scheme 3. Gram scale synthesis of amide **3a**.

We have recovered the catalyst for up to five cycles and in all cycles, the Pd-BNP was quantitively recovered. It is important to mention that in all the five cycles, the recovered Pd-BNP catalyst gave more than 90% of isolated yield of product. TEM analysis of the recovered catalyst after the fifth cycle showed that there was hardly any change in particle size of the Pd-BNP catalyst (Figure 3).[17]

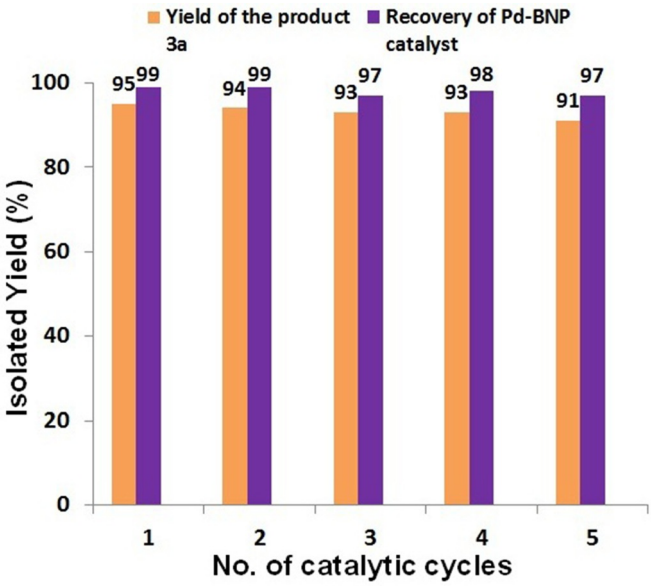


Figure 2. Recycling of the Pd-BNP catalyst.

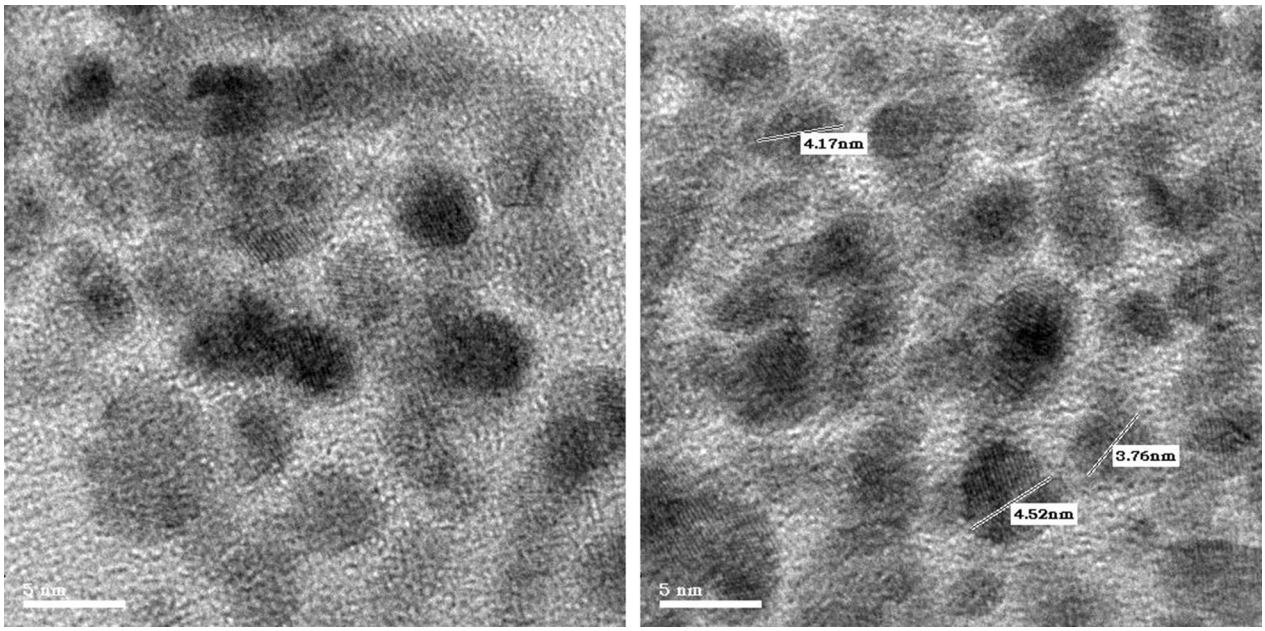


Figure 3. HR-TEM images of Pd-BNP catalyst before (*left*) and after the fifth catalytic cycle (*right*).

We carried out the aminocarbonylation reaction under optimized condition using 20 equiv. of mercury, complete inhibition of the reaction was observed; even on allowing the reaction to proceed for up to 48 h. This experiment suggests that the catalyst is heterogeneous in nature. A leaching experiment was also performed using the hot filtration test in which Pd-BNP catalyst was separated from the reaction mixture. The reaction was carried out under the optimized condition. After 2 h, the reaction mixture was centrifuged; filtered and Pd-BNP catalyst was removed. A 9% yield of **3a** was obtained and yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. The Pd-BNP-free mother liquor (filtrate) was than further used to carry out the aminocarbonylation reaction under the similar conditions for 24 h. There progress of reaction was observed and a 25% yield of **3a** was obtained by ^{1}H NMR. ICP-OES analysis of a liquid aliquot withdrawn from the reaction mixture after 2 h of the aminocarbonylation reaction showed that a minimal of 0.034 ppm (0.21 wt%) of Pd was present in the solution, which could be reason for the progress of the reaction after separating the catalyst from the reaction mixture.

In conclusion, an efficient, cost-effective binaphthyl-supported palladium (Pd-BNP) catalyst for the aminocarbonylation of aryl iodides using carbon monoxide and amines for the synthesis of amides has been developed. The scope of the reaction has been studied with regard to various aryl iodides and amines to yield the corresponding amides in good yields. The Pd-BNP catalyst was also successfully utilized for the intramolecular aminocarbonylation and yielded various substituted isoindoline-1,3-dione derivatives in excellent yield. This methodology provides an efficient way for the synthesis of a COX-2 enzyme inhibitor having anti-inflammatory activity. The catalyst has been recovered and reused up to five times without any loss in particle size and reactivity.

Experimental Section

Typical Experimental Procedure for Aminocarbonylation (3)

Aryl iodide (0.5 mmol), amine (1 mmol), Pd-BNP catalyst (10.6 mg, 2 mol%) and DABCO (2 equiv.) were charged in an oven-dried reaction tube equipped with magnetic pellet and capped with septum. The reaction tube was evacuated and freshly distilled toluene (4 mL) was added. The reaction tube was refilled with CO using a balloon and stirred at 110 °C until completion of the reaction as monitored by TLC. The reaction mixture was then allowed to cool to room temperature. Then the solvent was completely evaporated on a rotary evaporator and the residue extracted with ethyl acetate (3 × 10 mL). The organic phase was dried over Na_2SO_4 and concentrated under vacuum. The resulting reaction mixture was purified by column chromatography on silica gel (hexanes:ethyl acetate) to get amide product **3**.

Typical Experimental Procedure for Intramolecular Aminocarbonylation (5)

2-Iodo-*N*-arylbenzamide **4** (0.5 mmol), Pd-BNP catalyst (10.6 mg, 2 mol%) and DABCO (2 equiv.) was charged in an oven-dried reaction tube equipped with magnetic pellet and capped with septum. The reaction tube was evacuated and freshly distilled toluene (4 mL) was added. The reaction

tube was refilled with CO using a balloon and the mixture stirred at 110 °C until completion as monitored by TLC. The reaction mixture was then allowed to cool to room temperature. Then the solvent was completely evaporated on a rotary evaporator and the residue extracted with ethyl acetate (3 × 10 mL). Then the organic phase was dried over Na_2SO_4 and concentrated under vacuum. The resulting reaction mixture was purified by column chromatography on silica gel (hexanes: ethyl acetate) to get intramolecular aminocarbonylated product, *N*-substituted isoindoline-1,3-dione **5**.

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References

[1] a) K. Kumar, A. Zapf, D. Michalik, A. Tillack, T. Heinrich, H. Boettcher, M. Arlt, M. Beller, *Org. Lett.* **2004**, *6*, 7–10; b) C. A. G. N. Montalbetti, V. Falque, *Tetrahedron* **2005**, *61*, 10827–10852; c) E. Valeur, M. Bradley, *Chem. Soc. Rev.* **2009**, *38*, 606–631; d) V. S. Ananthanarayanan, S. Tetreault, A. Saint-Jean, *J. Med. Chem.* **1993**, *36*, 1324–1332; e) S. Kapur, R. Zipursky, G. Remington, C. Jones, G. McKay, S. Houle, *Am. J. Psychiatry* **1997**, *154*, 1525–1529; f) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes, J. S. Moore, *Chem. Rev.* **2001**, *101*, 3893–4011.

[2] a) A. Graul, J. Castaner, *Drugs Future* **1997**, *22*, 956–968; b) A. A. M. Abdel-Aziz, K. E. H. El Tahir, Y. A. Asiri, *Eur. J. Med. Chem.* **2011**, *46*, 1648–1655; c) Y. Iwanaga, N. Miyashita, T. Saito, K. Morikawa, Z. Itoh, *Jpn. J. Pharmacol.* **1996**, *71*, 129–137; d) T. J. Deming, *Prog. Polym. Sci.* **2007**, *32*, 858–875; e) K. Engstroem, E. V. Johnston, O. Verho, K. P. J. Gustafson, M. Shakeri, C.-W. Tai, J.-E. Baeckvall, *Angew. Chem.* **2013**, *125*, 14256–14260; *Angew. Chem. Int. Ed.* **2013**, *52*, 14006–14010.

[3] a) D.-Y. Hu, Q.-Q. Wan, S. Yang, B.-A. Song, P. S. Bhadury, L.-H. Jin, K. Yan, F. Liu, Z. Chen, W. Xue, *J. Agric. Food Chem.* **2008**, *56*, 998–1001; b) V. R. Pattabiraman, J. W. Bode, *Nature* **2011**, *480*, 471–479.

[4] a) S.-Y. Han, Y.-A. Kim, *Tetrahedron* **2004**, *60*, 2447–2467; b) H. Lundberg, F. Tinnis, N. Selander, H. Adolfsson, *Chem. Soc. Rev.* **2014**, *43*, 2714–2742; c) S. D. Roughley, A. M. Jordan, *J. Med. Chem.* **2011**, *54*, 3451–3479.

[5] a) L. J. Goossen, D. M. Ohlmann, P. P. Lange, *Synthesis* **2009**, 160–164; b) S. Ghosh, A. Bhaumik, J. Mondal, A. Mallik, S. Sengupta, C. Mukhopadhyay, *Green Chem.* **2012**, *14*, 3220–3229; c) D. J. C. Constable, P. J. Dunn, J. D. Hayler, G. R. Humphrey, J. L. Leazer Jr, R. J. Linderman, K. Lorenz, J. Manley, B. A. Pearlman, A. Wells, A. Zaks, T. Y. Zhang, *Green Chem.* **2007**, *9*, 411–420; d) A. El-Faham, F. Albericio, *Chem. Rev.* **2011**, *111*, 6557–6602.

[6] a) S. Muthaiah, S. C. Ghosh, J.-E. Jee, C. Chen, J. Zhang, S. H. Hong, *J. Org. Chem.* **2010**, *75*, 3002–3006; b) L. U. Nordstrom, H. Vogt, R. Madsen, *J. Am. Chem. Soc.* **2008**, *130*, 17672–17673; c) C. Gunanathan, Y. Ben-David, D. Milstein, *Science* **2007**, *317*, 790–792; d) J.-F. Soule, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.* **2011**, *133*, 18550–18553.

[7] a) A. Schoenberg, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3327–3331; b) A. Schoenberg, I. Bartoletti, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3318–3326.

[8] For selected reviews and examples: a) C. Csajagi, B. Borcsek, K. Niesz, I. Kovacs, Z. Szekelyhidi, Z. Bajko, L. Uerge, F. Darvas, *Org. Lett.* **2008**, *10*, 1589–1592; b) W. Magerlein, A. F. Indolese, M. Beller, *Angew. Chem.* **2001**, *113*, 2940–2943; *Angew. Chem. Int. Ed.* **2001**, *40*, 2856–2859; c) C. L. Allen, J. M. J. Williams, *Chem. Soc. Rev.* **2011**, *40*, 3405–3415; d) A. Brennfuehrer, H. Neumann, M. Beller, *Angew. Chem.* **2009**, *121*, 4176–4196; *Angew. Chem. Int. Ed.* **2009**, *48*, 4114–4133; e) S. T. Gadge, B. M. Bhanage, *RSC Adv.* **2014**, *4*, 10367–10389; f) W. Fang, H. Zhu, Q. Deng, S. Liu, X. Liu, Y. Shen, T. Tu, *Synthesis* **2014**, *46*, 1689–1708; g) S. Roy, S. Roy, G. W. Gribble, *Tetrahedron* **2012**, *68*, 9867–9923; h) Y. Ben-David, M. Portnoy, D. Milstein, *J. Am. Chem. Soc.* **1989**, *111*, 8742–8744; i) W. Mägerlein, A. F. Indolese, M. Beller, *Angew. Chem.* **2001**, *113*, 2940–2943; *Angew. Chem. Int. Ed.* **2001**, *40*, 2856–2859; j) E. R. Murphy, J. R. Martinelli, N. Zaborenko, S. L. Buchwald, K. F. Jensen, *Angew. Chem.* **2007**, *119*, 1764–1767; *Angew. Chem. Int. Ed.* **2007**, *46*, 1734–1737; k) J. R. Martinelli, D. A. Watson, D. M. M. Freckmann, T. E. Barder, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 7102–7107; l) V. de La Fuente, C. Godard, C. Claver, S. Castillon, *Adv. Synth. Catal.* **2012**, *354*, 1971–1979; m) P. G. Alsabeh, M. Stradiotto, H. Neumann, M. Beller, *Adv. Synth. Catal.* **2012**, *354*, 3065–3070; n) W. Fang, Q. Deng, M. Xu, T. Tu, *Org. Lett.* **2013**, *15*, 3678–3681; o) C. E. Garrett, K. Prasad, *Adv. Synth. Catal.* **2004**, *346*, 889–900; p) H.-U. Blaser, A. Indolese, F. Naud, U. Nettekoven, A. Schnyder, *Adv. Synth. Catal.* **2004**, *346*, 1583–1598; q) X.-F. Wu, H. Neumann, M. Beller, *Chem. Eur. J.* **2010**, *16*, 9750–9753; r) C. F. J. Barnard, *Organometallics* **2008**, *27*, 5402–5422.

[9] a) O. Verho, A. Nagendiran, E. V. Johnston, C.-w. Tai, J.-E. Baeckvall, *ChemCatChem* **2013**, *5*, 612–618; b) U. Drechsler, B. Erdogan, V. M. Rotello, *Chem. Eur. J.* **2004**, *10*, 5570–5579; c) K. G. Thomas, P. V. Kamat, *Acc. Chem. Res.* **2003**, *36*, 888–898; d) R. Shenhar, V. M. Rotello, *Acc. Chem. Res.* **2003**, *36*, 549–561.

[10] a) D. Ganapathy, G. Sekar, *Org. Lett.* **2014**, *16*, 3856–3859; b) D. Ganapathy, S. S. Kotha, G. Sekar, *Tetrahedron Lett.* **2015**, *56*, 175–178; c) D. Ganapathy, G. Sekar, *Catal. Commun.* **2013**, *39*, 50–54.

[11] a) F. Tinnis, O. Verho, K. P. J. Gustafson, C.-W. Tai, J.-E. Baeckvall, H. Adolfsson, *Chem. Eur. J.* **2014**, *20*, 5885–5889; b) T. T. Dang, Y. Zhu, J. S. Y. Ngiam, S. C. Ghosh, A. Chen, A. M. Seayad, *ACS Catal.* **2013**, *3*, 1406–1410; c) M. V. Khedkar, T. Sasaki, B. M. Bhanage, *ACS Catal.* **2013**, *3*, 287–293; d) A. O. Biying, K. T. Yuanting, N. S. Hosmane, Z. Yinghuai, *J. Organomet. Chem.* **2013**, *747*, 184–188; e) T. T. Dang, Y. Zhu, S. C. Ghosh, A. Chen, C. L. L. Chai, A. M. Seayad, *Chem.*

Commun. **2012**, *48*, 1805–1807; f) Z. S. Qureshi, S. A. Revankar, M. V. Khedkar, B. M. Bhanage, *Catal. Today* **2012**, *198*, 148–153; g) M. V. Khedkar, S. R. Khan, D. N. Sawant, D. B. Bagal, B. M. Bhanage, *Adv. Synth. Catal.* **2011**, *353*, 3415–3422; h) Y. Zhu, L. Chuanzhao, A. O. Biying, M. Sudarmadji, A. Chen, D. T. Tuan, A. M. Seayad, *Dalton Trans.* **2011**, *40*, 9320–9325; i) J. Salvadori, E. Balducci, S. Zaza, E. Petricci, M. Taddei, *J. Org. Chem.* **2010**, *75*, 1841–1847; j) C. Csajagi, B. Borcsek, K. Niesz, I. Kovacs, Z. Szekelyhidi, Z. Bajko, L. Uerge, F. Darvas, *Org. Lett.* **2008**, *10*, 1589–1592.

[12] a) B. Urban, M. Papp, D. Sranko, R. Skoda-Foldes, *J. Mol. Catal. A: Chem.* **2015**, *397*, 150–157; b) H. Mei, J. Hu, S. Xiao, Y. Lei, G. Li, *Appl. Catal. A* **2014**, *475*, 40–47; c) Y. Zhang, H. Sun, W. Zhang, Z. Gao, P. Yang, J. Gu, *Appl. Catal. A* **2015**, *496*, 9–16; d) M. Papp, B. Urban, E. Drotar, R. Skoda-Foeldes, *Green Process. Synth.* **2015**, *4*, 103–115; e) E. Calcio Gaudino, D. Carnaroglio, K. Martina, G. Palmisano, A. Penoni, G. Cravotto, *Org. Process Res. Dev.* **2015**, *19*, 499–505.

[13] The binaphthyl-supported palladium catalyst (Pd-BNP) was prepared using our previously reported procedure. The catalyst displays various properties such as air and moisture stability, is easy to store, shelf stable, highly active and reusable.

[14] A ^{1}H NMR study after completion of the reaction showed 72% conversion and 28% of 1,2 diiodobenzene remaining unreacted under the optimized reaction condition. Even when, the amount of amine **2a** was increased from 2 to 4 or 6 equivalents; complete conversion or formation of **4a** or any other spot such as N^1,N^2-bis(4-methoxyphenyl)phthalamide, was not observed.

[15] Few examples for the synthesis of phthalimides: a) A. V. Iosub, S. S. Stahl, *J. Am. Chem. Soc.* **2015**, *137*, 3454–3457; b) S. P. O. Assis, T. G. Araujo, V. L. M. Sena, M. T. J. A. Catanho, M. N. Ramos, R. M. Srivastava, V. L. M. Lima, *Med. Chem. Res.* **2014**, *23*, 708–716; c) M. V. Khedkar, A. R. Shinde, T. Sasaki, B. M. Bhanage, *J. Mol. Catal. A: Chem.* **2014**, *385*, 91–97; d) M. V. Khedkar, B. M. Bhanage, *Front. Chem. Sci. Eng.* **2013**, *7*, 226–232; e) D. C. Chen, H. Q. Ye, H. Wu, *Catal. Commun.* **2007**, *8*, 1527–1530; f) P. B. Thale, P. N. Borase, G. S. Shankarling, *RSC Adv.* **2014**, *4*, 59454–59461; g) M. V. Khedkar, S. R. Khan, D. N. Sawant, D. B. Bagal, B. M. Bhanage, *Adv. Synth. Catal.* **2011**, *353*, 3415–3422; h) R. Frutos-Pedreno, P. Gonzalez-Herrero, J. Vicente, P. G. Jones, *Organometallics* **2013**, *32*, 4664–4676.

[16] a) K. M. Knights, A. A. Mangoni, J. O. Miners, *Expert Rev. Clin. Pharmacol.* **2010**, *3*, 769–776; b) B. Everts, P. Wahrborg, T. Hedner, *Clin Rheumatol* **2000**, *19*, 331–343; c) T. A. Trappe, S. Z. Liu, *J. Appl. Physiol.* **2013**, *115*, 909–919.

[17] An average size of 4–5 nm for Pd-BNP was observed.

