JOC The Journal of Organic Chemistry

NOTE

pubs.acs.org/joc

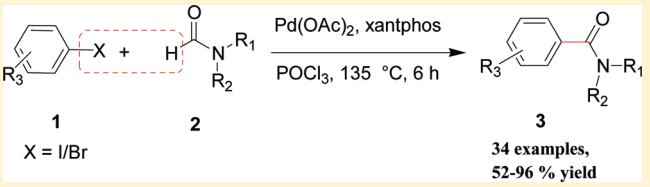
Palladium-Catalyzed Carbon-Monoxide-Free Aminocarbonylation of Aryl Halides Using N-Substituted Formamides as an Amide Source

Dinesh N. Sawant, Yogesh S. Wagh, Kushal D. Bhatte, and Bhalchandra M. Bhanage*

Department of Chemistry, Institute of Chemical Technology, N. Parekh Marg, Matunga, Mumbai-400019, India

Supporting Information

ABSTRACT: A carbon-monoxide-free aminocarbonylation of various N-substituted formamides with aryl iodides and aryl bromides using palladium acetate and Xantphos is described. The developed methodology is applicable for a wide range of formamides and aryl halides containing different functional groups furnishing good to excellent yield of the corresponding products. N-substituted formamides are used as an amide source wherein a Vilsmeier-type intermediate plays a major role, thus eliminating the need of toxic carbon monoxide gas.



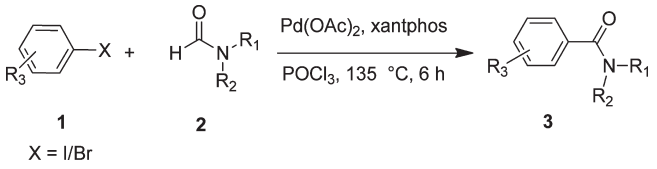
Amides are very important functional groups in the synthesis of numerous organic molecules, biologically active compounds, and natural products.[1] In 1974, Heck reported the first palladium-catalyzed aminocarbonylation reaction, that is, reaction between aryl, heterocyclic, and alkenyl halides with primary or secondary amines and carbon monoxide (CO) for amide synthesis.[2] After the first report, various protocols for aminocarbonylation were developed using CO as a source of the carbonyl group.[3] However, CO is a highly lethal gas, with a main concern of its handling, storage, and transport. Also, the reaction setup requires high-pressure reactors such as autoclaves, specialized gas handling procedures, stainless steel tanks, and cylinders for safety transportation, which restricts the utility of CO in the carbonylation reactions. Therefore, the development of newer CO-free methods for the synthesis of amides is of significant interest among organic chemists.[4] In recent years, many efforts have surged in this direction, and various carbon monoxide alternatives for amide synthesis, such as metal carbonyls like $Mo(CO)_6$,[5] $Ni(CO)_4$,[6] and $W(CO)_6$,[7] were intensively investigated, while other sources like carbamoylsilane,[8] carbamoylstannanes,[9] formamide,[10] and DMF[11] are attractive potential alternatives for toxic CO gas. In comparison with organic material, inorganic metal carbonyl and their derivatives are highly toxic and relatively much more expensive and most of these protocols require specialized microwave equipment. The use of carbamoylsilane and carbamoylstannane is limited to the synthesis of *N*,*N*-dimethyl-substituted amide derivatives, and these compounds are commercially not available. In addition to this, carbamoylstannane is prepared via carbonylation−stannylation of lithium amides, which is thermally unstable and toxic, hence limiting its application.

In literature, few reports exist on aminocarbonylation using DMF as either a source of carbon monoxide or an amide. Hallberg et al. employed DMF as a carbon monoxide source,[12] where, in presence of a strong base and imidazole, DMF decompose to CO, which reacts with amine and aryl halide, providing corresponding aminocarbonylated product. However, the use of microwave, in situ CO generation, and high reaction temperature in the range of 180−190 °C restricts its applications. Hiyama et al. were the first to use DMF as an amide source using $Pd_2(dba)_3$ as catalyst and $POCl_3$ a key additive in acidic conditions.[13] This involved a Vilsmeier-type intermediate playing a vital role in the reaction, but protocol was specifically limited to aryl iodides and DMF only. Lee et al. reported a $Ni(OAc)_2 \cdot 4H_2O$/phosphite catalytic system for aminocarbonylation using DMF as an amide source in basic conditions using NaOMe or KOMe as base; further they extended the same protocol for other formamides.[14] However, this protocol was not applicable for aryl halides containing different functional groups. Especially, most of the aryl iodides do not provide satisfactory yield and undergo dehalogenation. Similarly, the yields for amides other than *N*-methyl formamide and *N*-cyclohexylformamide are quite low, and amides like diethylformamide, diisopropyl formamide, formamide, *etc.* did not produce any product.

Recently, we reported a heterogeneous protocol using Pd/C and phosphoryl chloride for CO-free aminocarbonylation.[15] However, the heterogeneous catalyst results in lowering the yield of product and required 24 h for completion of the reaction, and scope the is limited to aryl iodides and DMF only. Considering the limitations of the reported protocols, we herein report $Pd(OAc)_2$/Xantphos as a new catalytic system for CO-free aminocarbonylation. Present protocol is applicable for all types of formamide derivatives, aryl iodides, as well as aryl bromides, providing good to excellent yield of desired products. The developed methodology tolerated a wide range of functional groups with an additional advantage of lower reaction time and higher yields as compared to earlier protocols. While exploring a cyanide-free protocol for cyanation reaction using formamide, we observed that the same reaction conditions are applicable for CO-free aminocarbonylation (Scheme 1).[16]

Received: April 11, 2011
Published: May 27, 2011

Scheme 1. CO-Free Aminocarbonylation of Aryl Halides Using N-Substituted Formamides as an Amide Source



1 2 3

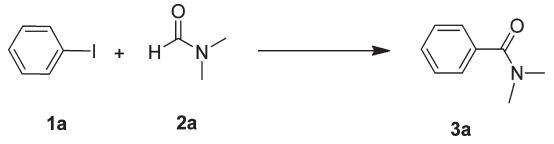
X = I/Br

Table 1. Test Experiment for CO-Free Amniocarbonylation of Iodobenzene (1a) with DMF (2a)[a]

entry	$Pd(OAc)_2$	Xantphos	$POCl_3$	yield (%)[b]
1	−	−	+	0
2	−	+	+	0
3	+	−	+	18
4	+	+	−	0
5	+	+	+	93

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (10 mL/mmol), $Pd(OAc)_2$ (5 mol %), Xantphos (10 mol %), $POCl_3$ (2.0 mmol), 140 °C, 24 h under nitrogen atmosphere. [b] GC yield.

Table 2. Screening of Metal Precursors and Ligands[a]



1a 2a 3a

entry	ligand	Pd catalyst	yield (%)[b]
1	Xantphos[c]	$Pd(OAC)_2$	93
2	DPPF[d]	$Pd(OAC)_2$	81
3	DPPM[e]	$Pd(OAC)_2$	0
4	DPPE[f]	$Pd(OAC)_2$	0
5	DPPP[g]	$Pd(OAC)_2$	0
6	DPPB[h]	$Pd(OAC)_2$	0
7	Xantphos	$PdCl_2$	91
8	Xantphos	$Pd(acac)_2$	71
9	Xantphos	$CuCl_2$	0
10	Xantphos	$Cu(OAC)_2$	0
11	Xantphos	$NiCl_2$	0
12	Xantphos	$Ni(OAC)_2$	0

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (10 mL/mmol), catalyst (5 mol %), ligand (10 mol %), $POCl_3$ (2.0 mmol), 140 °C, 24 h under nitrogen atmosphere. [b] GC yield. [c] Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene. [d] DPPF = 1,1-bis(diphenylphosphino)ferrocene. [e] DPPM = 1,1-bis(diphenylphosphino)methane. [f] DPPE = 1,1-bis(diphenylphosphino)ethane. [g] DPPP = 1,1-bis(diphenylphosphino)propane. [h] DPPB = 1,1-bis(diphenylphosphino)butane.

Initially, the coupling of DMF with iodobenzene was chosen as a model reaction and $Pd(OAc)_2$/Xantphos as a catalytic system for optimization of reaction parameters. Test experiments showed that $Pd(OAc)_2$, Xantphos, and $POCl_3$ are essential to obtain a higher yield of desired product (Table 1).

Observing the importance of ligand in reaction, we screened various phosphine bidentate ligands (Table 2), and it was observed that bite angle might play a major role. Only Xantphos and DPPF afforded 93 and 81% yield, respectively (Table 2, entries 1 and 2), while other ligands such as DPPM DPPE, DPPP, and DPPB exhibited no activity (Table 2, entries 3−6). Therefore, with Xantphos as the choice of ligand, we studied the effect of different metal precursors. It was observed that $PdCl_2$ and $Pd(OAc)_2$ provided similar yield of product (Table 2, entries 1 and 7). Hence, $Pd(OAc)_2$ was selected for further study as it is quite economical in comparison to $PdCl_2$, while other metal precursors such as copper and nickel were unable to catalyze the reaction (Table 2, entries 9−12).

Table 3. Optimization of CO-Free Aminocarbonylation of Aryl Halides Using N-Substituted Formamides[a]

entry	Pd/L	mol %	$POCl_3$ (mmol)	DMF (mL)	time (h)	yield (%)[b]
effect of time						
1	1:2	5	2	10	24	93
2	1:2	5	2	10	18	93
3	1:2	5	2	10	6	92
4	1:2	5	2	10	4	72
effect of catalyst loading						
5	1:2	4	2	10	6	91
6	1:2	3	2	10	6	92
7	1:2	2	2	10	6	73
8	1:2	1	2	10	6	38
effect of metal to ligand ratio						
9	1:1.5	3	2	10	6	82
10	1:1	3	2	10	6	70
influence of $POCl_3$ concentration						
11	1:2	3	2.5	10	6	93
12	1:2	3	1.5	10	6	78
influence of DMF concentration						
13	1:2	3	2	8	6	92
14	1:2	3	2	6	6	91
15	1:2	3	2	5	6	92
16	1:2	3	3	3	6	84
17	1:2	3	2	1	6	45

[a] Reaction conditions: **1a** (1.0 mmol), **2a**, $Pd(OAC)_2$, Xantphos, $POCl_3$, 140 °C, under nitrogen atmosphere. [b] GC yield.

Furthermore, we examined the influence of various reaction parameters like time, catalyst loading, Lewis acids, effect of solvents, and temperature (Table 3). To our surprise, during the study, we observed completion of reaction within 6 h with optimum yield of 92% (Table 3, entry 3). When the reaction was carried out with 3 mol % of $Pd(OAc)_2$ and 6 mol % of Xantphos, similar yields were obtained (Table 3, entry 6), while reducing the catalyst loading further results in lower yields. The reduction in the amount of Xantphos resulted in reduced yield of product (Table 3, entries 9 and 10), indicating that a 1:2 ratio of $Pd(OAc)_2$ to Xantphos is essential for higher yields (Table 3, entry 6). In order to replace $POCl_3$, we screened various other Lewis acids such as PCl_3, $SOCl_2$, $FeCl_3$, BF_3:OEt_2, etc. (refer to Supporting Information, Table S1). Among the examined Lewis acids, only PCl_3 provided low yield of product, while use of other Lewis acids was futile. It was observed that an increase of $POCl_3$

dx.doi.org/10.1021/jo200754v |J. Org. Chem. 2011, 76, 5489–5494

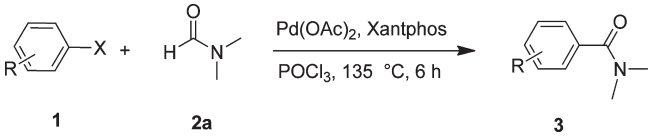
Table 4. Influence of Temperature[a]

entry	temperature (°C)	yield of **3a** (%)[b]
1	145	93
2	140	92
3	135	92
4	130	80
5	120	75

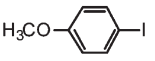
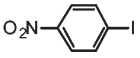
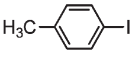
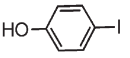
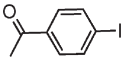
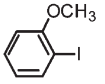
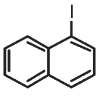
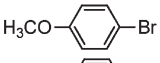
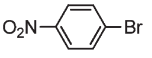
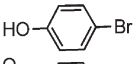
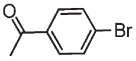
[a] Reaction conditions: **1a** (1.0 mmol), **2a** (5 mL/mmol), $Pd(OAc)_2$ (3 mol %), Xantphos (6 mol %), $POCl_3$ (2.0 mmol), 6 h, under nitrogen atmosphere. [b] GC yield.

concentration led to a slight increase in yield of product, while a decrease in $POCl_3$ concentration gave lower yield, addressing 2 mmol of $POCl_3$ as an optimized concentration (Table 3, entries 6, 11, and 12). Effect of DMF was also studied, which revealed that 5 mL of DMF is essential for best results while lowering the amount of DMF from 5 to 1 mL results in lower yield (Table 3, entries 13−17). In order to reduce the amount of DMF further, we screened various cosolvents, such as toluene, xylene, DMSO, NMP, 1,4-dioxane, ethylene glycol, etc., along with DMF, but all attempts were unsuccessful (see Supporting Information, Table S2). The temperature study shows that 135 °C is the optimum

Table 5. Scope of CO-Free Aminocarbonylation of Aryl Iodides and Aryl Bromides[a]



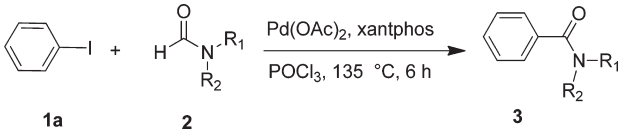
1 2a 3

Entry	Aryl halides	Product	Yield [%][b]
1		**3a**	93
2		**3b**	92
3		**3c**	96
4		**3d**	94
5		**3e**	88
6		**3f**	93
7		**3g**	78
8		**3h**	85
9		**3a**	14
10		**3a**	72[c]
11		**3b**	76[c]
12		**3c**	74[c]
13		**3e**	69[c]
14		**3f**	73[c]
15		**3g**	67[c]
16		**3h**	64[c]

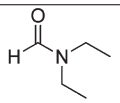
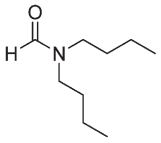
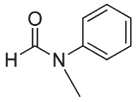
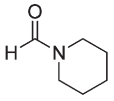
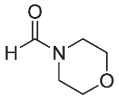
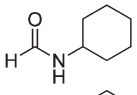
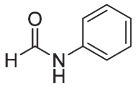
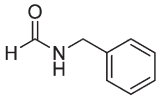
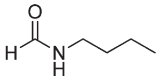
[a] Reaction conditions: **1** (1.0 mmol), **2a** (5 mL/mmol), $Pd(OAc)_2$ (3 mol %), Xantphos (6 mol %), $POCl_3$ (2.0 mmol), 135 °C, 6 h under nitrogen atmosphere. [b] Isolated yield. [c] **1** (1.0 mmol), **2a** (5 mL/mmol), $Pd(OAc)_2$ (5 mol %), Xantphos (10 mol %), $POCl_3$ (2.0 mmol), 165 °C, 24 h under nitrogen atmosphere.

dx.doi.org/10.1021/jo200754v |J. Org. Chem. 2011, 76, 5489–5494

Table 6. Scope of N-Substituted Formamides for CO-Free Amniocarbonylation[a]

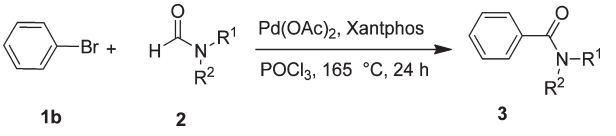


1a 2 3

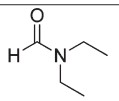
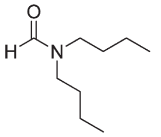
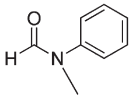
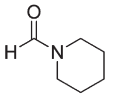
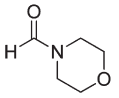
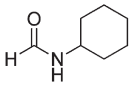
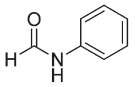
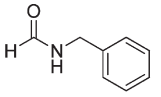
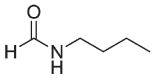
Entry	Formamides	Product	Yield [%][b]
1		**4a**	91
2		**5a**	90
3		**6a**	85
4		**7a**	90
5		**8a**	92
6		**9a**	87
7		**10a**	82
8		**11a**	88
9		**12a**	81

[a] Reaction conditions: iodobenzene (1.0 mmol), **2** (5 mL/mmol), $Pd(OAc)_2$ (3 mol %), Xantphos (6 mol %), $POCl_3$ (2.0 mmol), 135 °C, 6 h under nitrogen atmosphere. [b] Isolated yield.

Table 7. Scope of N-Substituted Formamides for CO-Free Amniocarbonylation[a]



1b 2 3

Entry	Formamides	Product	Yield [%][b]
1		**4a**	72
2		**5a**	71
3		**6a**	52
4		**7a**	79
5		**8a**	73
6		**9a**	63
7		**10a**	59
8		**11a**	68
9		**12a**	70

[a] Bromobenzene (1.0 mmol), **2** (5 mL/mmol), $Pd(OAc)_2$ (5 mol %), Xantphos (10 mol %), $POCl_3$ (2.0 mmol), 165 °C, 24 h under nitrogen atmosphere. [b] Isolated yield.

temperature to obtain a higher yield of desired products (Table 4).

Thus, the optimized reaction conditions are **1a** (1 mmol), $POCl_3$ (2 mmol), $Pd(OAc)_2$ (3 mol %), and Xantphos (6 mol %), in 5 mL/mmol of DMF at 135 °C, for a time period of 6 h.

In order to study the potential and general applicability of developed methodology, various aryl iodides containing different functional groups were investigated (Table 5). We observed that electron-donating as well as electron-withdrawing groups provided remarkable yield of products. A variety of functional groups including methoxy, trifluoromethyl, nitro, hydroxyl, and carbonyl were well-tolerated (Table 5, entries 1−6), whereas *ortho* substituents furnished moderate yield (Table 5, entry 7) as this might be due to steric hindrance. Similarly, 1-iodonaphthalene also exhibited moderate yield of desired product (Table 5, entry 8). Next, we attempted to widen the scope of our methodology for aryl bromides and found that aryl bromides were well-tolerated but with decreased yields (Table 5, entry 9). By increasing catalyst loading and improving reaction conditions, we achieved moderate yields (Table 5, entry 10). The catalyst exhibited remarkable activity where a variety of functional groups, such as OCH_3, NO_2, OH, and carbonyl, on the aryl bromide were well-tolerated, furnishing good yield of expected products (Table 5, entries 11−14). Whereas *ortho* substitution on aryl bromides leads to a decrease in yield (Table 5, entry 15), sterically hindered 1-iodonaphthalene provided a good yield of product (Table 5, entry 16).

The main goal behind exploring the protocol was to widen the scope of various N-substituted formamides for CO-free aminocarbonylation. In context, we screened a range of formamides and observed that all kinds of formamides provided excellent yield of products with iodobenzene (Table 6). The *N*,*N*-disubstituted sterically hindered formamides such as *N*,*N*-diethylformamide, *N*,*N*-dibutyl formamide, and *N*-methyl-*N*-phenylformamide reacted smoothly, furnishing excellent yields (Table 6, entries 1−3). Second, we screened cyclic formamides such as

dx.doi.org/10.1021/jo200754v |*J. Org. Chem.* 2011, 76, 5489–5494

1-formylpiperidine and 4-formylmorpholine that provided the highest yield of desired products (Table 6, entries 4 and 5). In the case of N-monosubstituted formamide, it was observed that *N*-hexylformamide and *N*-phenylformamide gave moderate yield (Table 6, entries 6 and 7), while *N*-butylformamide and *N*-benzylformamide offered an appreciable yield of desired product (Table 6, entries 8 and 9).

To expand the scope of aryl bromides, coupling of various formamides with bromobenzene was carried out. The *N*,*N*-disubstituted sterically hindered formamides are well-tolerated, giving moderate yield (Table 7, entries 1−3), while cyclic formamides were found to react smoothly, providing the highest yield of products (Table 7, entries 4 and 5). The N-monosubstituted formamides were also successfully applied to this system (Table 7, entries 6−9). It is noteworthy to mention that no N-arylated product in any case of N-monosubstituted or unsubstituted formamide was obtained.

In summary, we developed a new protocol for CO-free aminocarbonylation wherein all types of N-substituted formamides can be coupled with aryl iodides as well as aryl bromides, providing an excellent yield of desired products. Lower reaction time adds an additional credit to the present study. In general, all kinds of functional groups were very well-tolerated, offering higher yields. Furthermore, neither the reaction required external toxic CO gas nor there was formation of in situ CO as it involved a Vilsmeier-type intermediate utilizing formamides used as amide source instead of a toxic CO source. This advancement in CO-free aminocarbonylation reaction thus is appealing because the developed protocol will prove to be an attractive alternative to the reported methods for aminocarbonylation reactions.

EXPERIMENTAL SECTION

General: All products are well-known compounds. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as internal standard. *J* (coupling constant) values were reported in hertz. Splitting patterns of proton are described as s (singlet), d (doublet), t (triplet), and m (multiplet). GC analysis was carried out on a gas chromatograph equipped with a flame ionization detector using a fused capillary column. All products obtained and discussed in this work have been previously reported and characterized by suitable technique.

General Experimental Procedure for Aminocarbonylation of DMF with Aryl Iodides: A mixture of iodobenzene (1 mmol), $Pd(OAc)_2$ (3 mol %), and Xantphos (6 mol %) in DMF (5 mL/mmol) was placed in a 25 mL two-necked round-bottom flask equipped with a condenser at room temperature under nitrogen atmosphere. Then $POCl_3$ (2 mmol) was added to the reaction mixture and was placed in an oil bath and magnetically stirred at 135 °C for 6 h under complete nitrogen atmosphere. After completion, the reaction mixture was cooled to room temperature and was poured into a saturated solution of $NaHCO_3$ (50 mL). The product was extracted with ethyl acetate (4 × 20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to afford the crude product which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate combination) to afford the pure product. The product was confirmed by GC−MS and ^{1}H and ^{13}C NMR spectroscopic analysis.

General Experimental Procedure for Aminocarbonylation of DMF with Aryl Bromides. A mixture of bromobenzene (1 mmol), $Pd(OAc)_2$ (5 mol %), and Xantphos (10 mol %) in DMF (5 mL/mmol) was placed in a 25 mL two-necked round-bottom flask equipped with a condenser at room temperature under nitrogen. Then $POCl_3$ (2 mmol) was added to the reaction mixture and was placed in and oil bath and magnetically stirred at 165 °C for 24 h under complete nitrogen atmosphere. After completion, the reaction mixture was cooled to room temperature and was poured into a saturated solution of $NaHCO_3$ (50 mL). The product was extracted with ethyl acetate (4 × 20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to afford the crude product which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate combination) to afford the pure product. The product was confirmed by GC−MS and ^{1}H and ^{13}C NMR spectroscopic analysis.

3a:[13] GC−MS *m*/*z* (% relative intensity) 149 (M^+, 19), 148 (47), 105 (100), 77 (77), 51 (27); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (s, 3H), 3.11 (s, 3H), 7.40 (br s, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.4, 39.7, 127.1, 128.4, 129.6, 136.4, 171.8.

3b:[12] GC−MS *m*/*z* (% relative intensity) 179 (M^+, 18), 178 (24), 136 (9), 135 (100), 107 (16), 92 (13), 77 (23), 64 (9), 63 (5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.0 (br s, 6H), 3.83 (s, 3H), 6.69−6.92 (m, 2H), 7.39−7.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.3, 39.6, 55.1, 113.3, 128.1, 128.8, 160.3, 171.3.

3c:[15] GC−MS *m*/*z* (% relative intensity) 194 (M^+, 39), 193 (100), 177 (12), 150 (86), 147 (19), 120 (33), 104 (66), 92 (35), 76 (50), 50 (20), 44 (11); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (s, 3H), 3.14 (s, 3H), 7.58−7.62 (m, 2H), 8.26−8.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.3, 39.2, 123.7, 128.0, 142.4, 148.2, 169.2.

3d:[12] GC−MS *m*/*z* (% relative intensity) 163 (M^+, 29), 162 (28), 148 (9), 119 (100), 118 (10), 91 (72), 65 (26).

3e:[17] GC−MS *m*/*z* (% relative intensity) 165 (M^+, 19), 164 (33), 121 (100), 93 (27), 65 (27), 44 (28).

3f:[18] GC−MS *m*/*z* (% relative intensity) 191 (M^+, 37), 190 (45), 148 (11), 147 (100), 119 (25), 104 (9), 91 (24), 76 (15), 43 (20).

3g:[12] GC−MS *m*/*z* (% relative intensity): 179 (M^+, 18), 178 (24), 136 (9), 135 (100), 107 (16), 92 (13), 77 (23), 64 (9), 63 (5).

3h:[12] GC−MS *m*/*z* (% relative intensity) 199 (M^+, 41), 198 (18), 156 (13), 155 (100), 128 (11), 127 (83), 126 (15), 77 (11).

4a:[19] GC−MS *m*/*z* (% relative intensity) 177 (M^+, 14), 176 (36), 105 (100), 77 (43), 51 (10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19−1.31 (br d, 6H), 3.33 (br s, 2H), 3.62 (br s, 2H), 7.44−7.46 (m, 5H); IR (neat) 2973, 2935, 2875, 1631, 1456, 1382, 1287, 1220, 1097, 1027, 942, 872, 786, 705, 628 cm^{-1}.

5a:[20] GC−MS *m*/*z* (% relative intensity) 233 (8), 232 (7), 190 (13), 105 (100), 77 (28); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.71 (br s, 3H), 0.92−1.07 (br d, 5H), 1.40 (br s, 4H), 1.60 (br s, 2H), 3.14 (br s, 2H), 3.44 (br s, 2H), 7.28−7.29 (m, 5H); IR (neat) 2932, 2958, 2872, 1635, 1578, 1495, 1465, 1423, 1377, 1297, 1265, 1192, 1102, 956, 922, 786, 731, 700, 651 cm^{-1}.

6a:[21] GC−MS *m*/*z* (% relative intensity) 211 (26), 118 (5), 105 (100), 77 (59), 51 (13); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (s, 3H), 7.21−7.48 (m, 10H); IR (neat) 3060, 2936, 1640, 1595, 1494, 1446, 1419, 1366, 1302, 1176, 1106, 1076, 1026, 922, 791, 769, 724, 701, 654, 579 cm^{-1}.

7a:[7] GC−MS *m*/*z* (% relative intensity) 190 (3), 189 (30), 188 (100), 106 (9), 105 (99), 77 (60), 51 (13); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.73−1.80 (br d, 6H), 3.52 (br s, 2H), 3.80 (br s, 2H), 7.51 (s, 5H); IR (neat) 3026, 3057, 2998, 2936, 2855, 1630, 1577, 1465, 1431, 1369, 1275, 1110, 1003, 853, 787, 731, 707, 632 cm^{-1}.

8a:[5c] GC−MS *m*/*z* (% relative intensity) 191 (12), 190 (32), 176 (8), 105 (100), 86 (15), 77 (53), 56 (15), 51 (14); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62−3.81 (br s, 8H), 7.53 (br s, 5H); IR (neat) 2979, 2901, 2859, 1626, 1426, 1361, 1300, 1271, 1111, 1073, 1020, 933, 840, 796, 736, 712, 592 cm^{-1}.

9a:[7] GC−MS *m*/*z* (% relative intensity) 203 (M^+, 27), 122 (76), 105 (100), 79 (13), 77 (54); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43−1.60 (m, 5H), 1.79−1.95 (m, 3H), 2.15−2.20 (m, 2H), 4.11−4.15 (br s, 1H), 6.43 (br s, 1H), 7.45−7.66 (m, 3 H), 7.91−7.99 (m, 2H); IR (neat)

dx.doi.org/10.1021/jo200754v |*J. Org. Chem.* 2011, 76, 5489–5494

3329, 3238, 3069, 2929, 2851, 1627, 1534, 1488, 1329, 1151, 1083, 890, 694 cm^{-1}.

10a:[7] GC−MS *m*/*z* (% relative intensity) 197 (M^+, 32), 106 (7), 105 (100), 77 (56), 51 (13); ^1H NMR (300 MHz, $CDCl_3$) δ 7.12−7.18 (m, 1H), 7.33−7.39 (m, 2H), 7.43−7.56 (m, 3 H), 7.64−7.68 (m, 2H), 7.84−7.89 (m, 2H), 8.18 (br s, 1H); IR (neat) 3344, 3054, 1655, 1599, 1531, 1439, 1322, 1261, 1075, 1028, 927, 910, 885, 790, 749, 716, 690, 583, 508 cm^{-1}.

11a:[7] GC−MS *m*/*z* (% relative intensity) 211 (M^+, 11), 210 (70), 209 (26), 106 (27), 105 (100), 91 (10), 77 (63), 51 (15); ^1H NMR (300 MHz, $CDCl_3$) δ 4.60 (m, 2H), 6.85 (br s, 1H), 7.32−7.51 (m, 8H), 7.78−7.81 (m, 2H); IR (neat) 3327, 3059, 1640, 1542, 1418, 1314, 1259, 1185, 1057, 990, 727, 693, 667 cm^{-1}.

12a:[7] GC−MS *m*/*z* (% relative intensity) 177 (M^+, 9), 176 (2), 135 (24), 134 (17), 105 (100), 77 (41), 51 (12); ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 3H), 1.32−1.42 (m, 2H), 1.51−1.61 (m, 2H), 3.37−3.43 (m, 2H), 6.80 (br s, 1H), 7.33−7.47 (m, 3H), 7.76−7.79 (m, 2H).

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^1H and ^{13}C NMR of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Phone: + 91-22 3361 1111/2222. Fax: +91-22 2414 5614. E-mail: bm.bhanage@ictmumbai.edu.in, bhalchandra_bhanage@yahoo.com.

■ ACKNOWLEDGMENT

The authors are grateful to the University Grant Commission, India, for financial support under UGC SAP program, Green Technology Centre of Institute of Chemical Technology, India.

■ REFERENCES

(1) (a) Li, J.; Xu, F.; Zhang, Y.; Shen, Q. *J. Org. Chem.* **2009**, *74*, 2575–2577. (b) Luszczki, J. J.; Swiader, M. J.; Swiader, K.; Paruszewski, R.; Turski, W. A.; Czuczwar, S. J. *Fund. Clin. Pharmacol.* **2008**, *22*, 69–74. (c) Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Kantam, M. L. *Eur. J. Org. Chem.* **2008**, 3619–3622. (d) Vora, H. U.; Rovis, T. *J. Am. Chem. Soc.* **2007**, *129*, 13796–13797. (e) Bode, J. W.; Sohn, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 13798–13799. (f) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, 790–792. (g) Malawska, B. *Curr. Top. Med. Chem.* **2005**, *5*, 69–85. (h) Kobayashi, I.; Muraoka, H.; Hasegawa, M.; Saika, T.; Nishida, M.; Kawamura, M.; Ando, R. J. *Antimicrob. Chemother.* **2002**, *50*, 129–132.

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

(3) (a) WU, X.-F.; Neumann, H.; Beller, M. *Chem. Asian J.* **2010**, *5*, 2168–2172. (b) Tambade, P. J.; Patil, Y. P.; Bhanage, B. M. *Appl. Organomet. Chem.* **2009**, *23*, 235–240. (c) Brennführer, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114–4133. (d) Tambade, P. J.; Patil, Y. P.; Bhanushali, M. J.; Bhanage, B. M. *Synthesis* **2008**, *15*, 2347–2352. (e) Martinelli, J. R.; Watson, D. A.; Freckmann, D. M. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7102. (f) Martinelli, J. R.; Clark, T. P.; Watson, D. A.; Munday, R. H.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8460–8463. (g) Skoda-Földes, R.; Takács, E.; Horváth, J.; Tuba, Z.; Kollar, L. *Green Chem.* **2003**, *5*, 643–645.

(4) For reviews: (a) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Buriol, L.; Machado, P. *Chem. Rev.* **2009**, *109*, 4140–4182. (b) Morimsoto, T.; Kakiuchi, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 5580–5588.

(5) (a) Wieckowska, A.; Fransson, R.; Odell, L. R.; Larhed, M. *J. Org. Chem.* **2011**, *76*, 978–981. (b) Ren, W.; Yamane, M. *J. Org. Chem.* **2010**, *75*, 8410–8415. (c) Roberts, B.; Liptrot, D.; Alcaraz, L.; Luker, T.; Stocks, M. J. *Org. Lett.* **2010**, *12*, 4280–4283. (d) Ren, E.; Yamane, M. *J. Org. Chem.* **2010**, *75*, 3017–3020. (e) Letavic, M. A.; Ly, K. S. *Tetrahedron Lett.* **2007**, *48*, 2339–2343. (f) Wannberg, J.; Dallinger, D.; Kappe, C. O.; Larhed, M. *J. Comb. Chem.* **2005**, *7*, 574–583. (g) Wannberg, J.; Kaiser, N. K.; Vrang, L.; Samuelsson, B.; Larhed, M.; Hallberg, A. *J. Comb. Chem.* **2005**, *7*, 611–617. (h) Wu, X.; Rönn, R.; Gossas, T.; Larhed, M. *J. Org. Chem.* **2005**, *70*, 3094–3098. (i) Yamazaki, K.; Kondo, Y. *J. Comb. Chem.* **2004**, *6*, 121–125. (j) Wannberg, J.; Larhed, M. *J. Org. Chem.* **2003**, *68*, 5750–5753. (k) Kaiser, N. K.; Hallberg, A.; Larhed, M. *J. Comb. Chem.* **2002**, *4*, 109–111.

(6) Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* **1969**, *91*, 1233–1234.

(7) Ren, W.; Yamane, M. *J. Org. Chem.* **2009**, *74*, 8332–8335.

(8) (a) Cunico, R. F.; Pandey, R. K. *J. Org. Chem.* **2005**, *70*, 9048–9050. (b) Cunico, R. F.; Maity, B. C. *Org. Lett.* **2003**, *5*, 4947–4949. (c) Cunico, R. F.; Maity, B. C. *Org. Lett.* **2002**, *4*, 4357–4359.

(9) Lindsay, C. M.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 569–573.

(10) Wan, Y.; Alterman, M.; Larhed, M.; Hallberg, A. *J. Comb. Chem.* **2003**, *5*, 82–84.

(11) Muzart, J. *Tetrahedron* **2009**, *65*, 8313–8323.

(12) DMF as CO source: Wan, Y.; Alterman, M.; Larhed, M.; Hallbeg, A. *J. Org. Chem.* **2002**, *67*, 6232–6235.

(13) DMF as amide source in acidic condition: Hosoi, K.; Nozaki, K.; Hiyama, T. *Org. Lett.* **2002**, *4*, 2849–2851.

(14) DMF as amide source in basic condition: (a) Ju, J.; Jeong, M.; Moon, J.; Jung, H. M.; Lee, S. *Org. Lett.* **2007**, *9*, 4615–4618. (b) Jo, Y.; Ju, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2009**, *74*, 6358–6361.

(15) Tambade, P. J.; Patil, Y. P.; Bhanushali, M. J.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 2221–2224.

(16) Sawant, D. N.; Wagh, Y. W.; Tambade, P. J.; Bhatte, K. D.; Bhanage, B. M. *Adv. Synth. Catal.* **2011**, *353*, 781–787.

(17) Eckardt, R.; Carstens, E.; Fiedler, W. *Pharmazie* **1975**, *30*, 633–637.

(18) Karimi, F.; Langström, B. *Eur. J. Org. Chem.* **2003**, *11*, 2132–2137.

(19) Hans, J. J.; Driver, R. W.; Burke, S. D. *J. Org. Chem.* **2000**, *65*, 2114–2121.

(20) Li, Y.; Zhao, Y.; Xu, Y. *Tetrahedron Lett.* **2010**, *51*, 1434–1436.

(21) Ozawa, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1985**, *107*, 3235–3245.