

Cobalt-Catalyzed Unstrained C-N Bond Activation: the Synthesis of Tertiary Amides by Carbonylation of Tertiary Amines

Yizhu Lei, Rui Zhang, and Guangxing Li

Abstract—This work describes a highly efficient unstrained C-N bonds activation approach for synthesis of tertiary amides via catalytic carbonylation of tertiary amines using a $\text{NaCo}(\text{CO})_4/\text{AlCl}_3/\text{Me}_4\text{NI}$ catalyst system. Under relatively mild reaction conditions, moderate to excellent yields of amides were obtained using 3.0 mol% cobalt dosages. This work also proposed a plausible mechanism.

Keywords—Carbonylation, Tertiary amides, C-N bonds.

I. INTRODUCTION

THE amide is one of the most important functional groups in chemistry. It plays a major role in the elaboration and composition of biological and chemical systems and polymer compounds [1]. While amide bond formation remains a fundamental reaction in organic chemistry [2], amides are usually prepared by coupling of carboxylic acids and amines by the use of either a coupling reagent or by prior conversion of the carboxylic acid into a derivative [3]. However, these methods are suffering from relatively high raw material costs, poor atom economy and poor step economy. Over the past few years, chemists have made great efforts to develop suitable and environmentally friendly processes, and alternative procedures include the Staudinger ligation [4], aminocarbonylation of aryl halides [5]-[8], oxidative amidation of aldehydes or alcohols [9], [10], and carbonylation of tertiary amines [11]. For synthesis of secondary amides, among all alternative methods, carbonylation of corresponding tertiary amines has attracted extensive interest due to the 100% atom efficiency and the easy availability and low cost of raw material. However, the carbon-nitrogen bond (C-N bond) is strong in organic molecules. Therefore, transformations via C-N bond cleavage are usually difficult, and high reaction temperature and CO pressure are generally required [12]. Therefore, finding a mild conditions and highly efficient catalytic system for carbonylation of tertiary amines is imperative. Recently, we

introduced Lewis acid and $(\text{CH}_3)_4\text{NI}$ as the promoters in cobalt-catalyzed carbonylation of trimethylamine reaction, and both the promoters showed good promoting effect [13]. However, carbonylation of other tertiary amines by cobalt catalyst has never been reported.

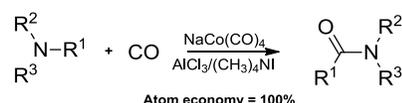


Fig. 1 Carbonylation of tertiary amine to tertiary amide.

Herein, we report a direct and efficient approach for synthesizing tertiary amides via the carbonylation of tertiary amines using inexpensive $\text{Na}[\text{Co}(\text{CO})_4]$ as a catalyst with the aid of $(\text{CH}_3)_4\text{NI}$ and AlCl_3 (Fig. 1). Under relatively mild reaction conditions, moderate to excellent yields of desired amides were obtained by using only 3 mol% of the catalyst. This process represents a promising route for the synthesis of tertiary amides because of the use of easy available sources, the high atom economy (100 %) and its environmental friendliness.

II. EXPERIMENTAL

A. Reagents

All reagents and solvents were analytical grade reagents and used without further purification unless noted. CO with a purity of 99.99% was purchased from the local manufacturer.

B. Catalyst Preparation

$\text{NaCo}(\text{CO})_4$ was prepared in a 250 mL stainless steel autoclave. Generally, CoCl_2 (1 mmol), Na_2SO_3 (1 mmol), Zn powder (1.3 mmol) and 25 mL of N-methyl pyrrolidone (NMP) were charged into the reactor. After purging four times with CO, the autoclave was pressurized with CO to 2.0 MPa at room temperature. The reaction was performed at 55 °C for 3 h. After the reaction, the reactor was cooled to room temperature and carefully depressurized. Then a light purple NMP solution of $\text{NaCo}(\text{CO})_4$ was collected and afforded to catalysis experiments.

C. Catalytic Experiments

The catalytic reactions were carried out in a 250 mL stainless steel autoclave. In a typical experiment, the prepared NMP solution of $\text{NaCo}(\text{CO})_4$, $(\text{CH}_3)_4\text{NI}$, AlCl_3 and tertiary amine

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was charged into the reactor. After purging four times with CO, the autoclave was pressurized with CO to 4 MPa and heated at 220 °C for 6-13 h. During the reaction, CO was added to maintain a total pressure of 5.5 MPa. After completion of the reaction, autoclave was cooled by ice water and depressurized to atmospheric pressure. Then the liquid mixture was analyzed qualitatively by GC and GC-MS

III. RESULTS AND DISCUSSION

A. Effect of the Temperature and Pressure

To continue optimizing the reaction condition of cobalt-catalyzed carbonylation of trimethylamine [13], herein, we initially studied the effect of reaction temperature on the cobalt-catalyzed carbonylation of trimethylamine over a wide reaction temperature ranging from 180 to 230 °C. The results were shown in Table I (entries 1-5), it was demonstrated that the conversion of trimethylamine was strongly affected by temperature. At 180 °C, the trimethylamine conversion is very low due to the slow reaction rate at a low reaction temperature. By rising the temperature to above 220 °C, there is a significant increase in the trimethylamine conversion. Further increasing the temperature from 220 to 230 °C, the reaction was almost finished in 4 h.

The influence of total pressure on the carbonylation of trimethylamine was tested (Table I, entries 6-8). The results show that there is a significant relationship between the conversion of trimethylamine and CO pressure. Since the pressure varied from 2.0 to 4.0 MPa, the trimethylamine conversion increased notably from 23% to 96.7%. Although a higher pressure favors the rate of the reaction, a lower pressure around 4.0 MPa was also sufficient to conduct the synthesis of DMAc. Hence, we chose 4.0 MPa as the suitable pressure in the carbonylation of trimethylamine.

TABLE I
EFFECT OF THE TEMPERATURE AND PRESSURE

Entry	T (°C)	P _{CO} (MPa)	Yield _{DMAc} (%)
1	180	4	22.4
2	200	4	62.6
3	210	4	80.0
4	220	4	92.3
5 ^a	230	4	90.5
6	220	3	88.2
7	220	2	80.8
8	220	1	31.5

Reaction conditions: NaCo(CO)₄ (1 mmol), (CH₃)₄Ni (3 mmol), AlCl₃ (6 mmol), trimethylamine (34 mmol), NMP (50 mL), 220 °C, 6 h, stirring speed: 500 rpm.

^aReaction time (4 h).

With these results in hand, we next demonstrate the general applicability of this catalytic system for the carbonylation of other tertiary amine. As shown in Table II, the value of the methodology is proven by the carbonylation of various commercially available tertiary amines. Trialkylamines, trimethylamine and dimethylethylamine, gave corresponding amides in moderate to excellent yields. As an example of

arylamines, dimethylaniline also gave N-methyl-N-phenyl-acetamide in 91.3% yield. Alicyclic tertiary amines, such as N-methylpyrrolidine, N-methylpiperidine and 4-methylmorpholine, reacted with CO to afford the corresponding amides in moderate to excellent yields (Table II, entries 4-6).

TABLE II
CARBONYLATION OF TERTIARY AMINES

Entry	Reactants	Time (h)	T (°C)	Products	Yield (%)
1		6	220		94.0
2		6	220		68.7
3		13	230		91.3
4		8	230		81.2
5		8	230		90.1
6		8	230		63.3

Reaction conditions: Sub./Cat.=(34 molar ratio), solvent NMP 50 mL, NaCo(CO)₄ 1 mmol, (CH₃)₄Ni:AlCl₃:NaCo(CO)₄ = 3:6:1 (molar ratio), CO 4 MPa, stirring speed 500 rpm.

B. Proposed Mechanism

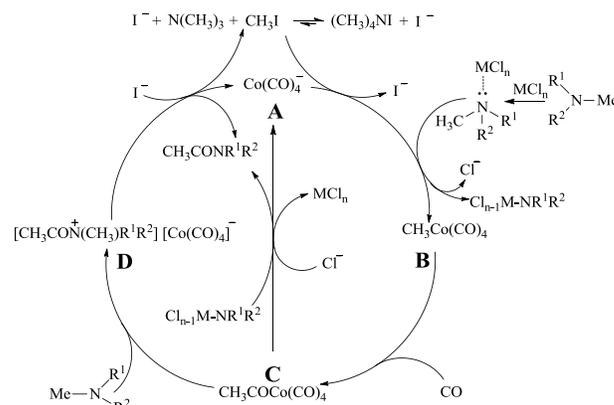


Fig. 2 Proposed mechanism of DMAc formation by carbonylation of tertiary amine.

Based on the above result and taking into account of the results published about Co-catalyzed carbonylation of trimethylamine [13], we proposed a reaction mechanism for carbonylation of tertiary amine catalyzed by cobalt carbonyl complexes in Fig. 2. Initially, the nucleophilic attack of the species A either on the activated C–N bond in AlCl₃ adduct of tertiary amine or on the generated MeI leads to the 18e tetracarbonyl intermediate B [14]. Subsequent insertion of CO to Co–C bonds affords intermediate C. Then, the active species C could react readily with tertiary amine to form the unstable quaternary ammonium salt, as the reported active acetyl iodide [15], [16]. Immediately, the desired product was formed with release of methyl halide by decomposition of unstable species D. Moreover, we believed that the desired product could be also obtained by the reaction of AlCl₂-NR¹R² and species C.

Although $\text{AlCl}_2\text{-NR}^1\text{R}^2$ is thermally quite stable [17], the active metal–nitrogen bond may make it more active than trimethylamine.

IV. CONCLUSION

In summary, a novel cobalt catalytic system for direct synthesis of tertiary amides by carbonylation of tertiary amines has been developed. This process represents a promising route for the synthesis of tertiary amides because of the use of easy available sources, the high atom economy (100 %) and its environmental friendliness.

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REFERENCES

- [1] C. L. Allen, J. M. J. Williams, "Metal-catalysed approaches to amide bond formation," *Chem. Soc. Rev.*, vol. 40, pp. 3405–3415, Mar. 2011.
- [2] E. Valeur, M. Bradley, "Amide bond formation: beyond the myth of coupling reagents," *Chem. Soc. Rev.*, vol. 38, pp. 606–631, Dec. 2008.
- [3] S. Roy, S. Roy, G.W. Gribble, "Metal-catalyzed amidation," *Tetrahedron*, vol. 68, pp. 9867–9923, Dec. 2012.
- [4] M. Köhn, R. Breinbauer, "The Staudinger ligation—a gift to chemical biology," *Angew. Chem., Int. Ed.*, vol. 43, pp. 3106–3116, May 2004.
- [5] J. R. Martinelli, T. P. Clark, D. A. Watson, R. H. Munday, S. L. Buchwald, "Palladium-catalyzed aminocarbonylation of aryl chlorides at atmospheric pressure: The dual role of sodium phenoxide," *Angew. Chem., Int. Ed.*, vol. 46, pp. 8460–8463, Nov. 2007.
- [6] A. Mansour, T. Kehat M. Portnoy, "Dendritic effects in catalysis by Pd complexes of bidentate phosphines on a dendronized support: Heck vs. carbonylation reactions," *Org. Biomol. Chem.*, vol. 6, pp. 3382–3387, Jul. 2008.
- [7] Y. Zhu, C. Li, A. O. Biying, M. Sudarmadji, A. Chen, D. T. Tuan, A. M. Seayad, "Stabilized well-dispersed Pd(0) nanoparticles for aminocarbonylation of aryl halides," *Dalton Trans.*, vol. 40, pp. 9320–9325, Jul. 2011.
- [8] T. T. Dang, Y. Zhu, S. C. Ghosh, A. Chen, C. L. L. Chai, A. M. Seayad, "Atmospheric pressure aminocarbonylation of aryl iodides using palladium nanoparticles supported on MOF-5," *Chem. Commun.*, vol. 48, pp. 1805–1807, Dec. 2012.
- [9] J. W. W. Chang, P. W. H. Chan, "Highly efficient ruthenium(II) porphyrin catalyzed amidation of aldehydes," *Angew. Chem., Int. Ed.*, vol. 47, pp. 1138–1140, Jan. 2008.
- [10] J.-F. Soulé, H. Miyamura, S. Kobayashi, "Powerful amide synthesis from alcohols and amines under aerobic conditions catalyzed by gold or gold/iron, -nickel or -cobalt nanoparticles," *J. Am. Chem. Soc.*, vol. 133, pp. 18550–18553, Oct. 2011.
- [11] H. Mei, W. Han, J. Hu, S. Xiao, Y. Lei, R. Zhang, W. Mo, G. Li, "Palladium-catalyzed unstrained $\text{C}(\text{sp}^3)\text{-N}$ bond activation: the synthesis of *N,N*-dimethylacetamide by carbonylation of trimethylamine," *Appl. Organomet. Chem.*, vol. 27, pp. 177–183, Mar. 2013.
- [12] P. Roose, "Process for preparing secondary amides by carbonylation of a corresponding tertiary amine," WO Patent 2010057874 A1, 2010.
- [13] Y. Lei, R. Zhang, W. Han, H. Mei, Y. Gu, B. Xiao, G. Li, "Promotion effects of Lewis acid/ $(\text{CH}_3)_3\text{NI}$ on $[\text{Co}(\text{CO})_4]^-$ -catalyzed C–N bond activation in the carbonylation of trimethylamine," *Catal. Commun.*, vol. 38, pp. 45–49, Aug. 2011.
- [14] C. M. Thomas, G. Süss-Fink, "Ligand effects in the rhodium-catalyzed carbonylation of methanol," *Coord. Chem. Rev.*, vol. 243, pp. 125–142, Aug. 2003.
- [15] M. G. Voronkov, I. P. Tsyrendorzhiyeva, V. I. Rakhlin, "Acyl iodides in organic synthesis: XI. unusual NC bond cleavage in tertiary amines," *Russian Journal of Organic Chemistry*, vol. 44, pp. 481–484, Mar. 2008.
- [16] M. G. Voronkov, N. N. Vlasova, O. Yu. Grigor'eva, L. I. Belousova, A. V. Vlasov, "Acyl iodides in organic synthesis. reactions of acetyl iodide with urea, thiourea, and their *N, N*-disubstituted derivatives," *Russian Journal of Organic Chemistry*, vol. 45, pp. 486–490, Oct. 2009.
- [17] J.K. Ruff, "The preparation and reactions of dialkylamino derivatives of aluminum," *J. Am. Chem. Soc.*, vol. 83, pp. 2835–2839, Jul. 1961.