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Nickel (II)-Catalyzed efficient aminocarbonylation of unreactive alkanes with formanilides—Exploiting the deformylation behavior of imides

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ABSTRACT

Challenging functionalization of $C(sp^3)$-H has recently attracted much attention of organic chemists. In this paper, we developed a $Ni(acac)_2$-catalyzed activation of unreactive alkanes with formanilides in the presence of carbon monoxide to furnish moderate to excellent yields of amides. This is the first example of aminocarbonylation of inert alkanes using nickel-based catalyst, and formanilides is disclosed to be an interesting amine source owing to the peculiar deformylation nature of imide intermediates.

1. Introduction

A tremendous growth in transition-metal-catalyzed C–H activation has been witnessed over recent decades.[1] Functionalization of C–H bonds represents a powerful, valuable, straightforward strategy for the construction of complex organic frameworks relative to pharmaceuticals and natural products, etc.[2] In comparison with the well-developed $C(sp^2)$-H activation, synthetically useful $C(sp^3)$-H activation started rather late because of the inert nature of alkanes and the selectivity issue in the reaction.[3] Group-assisting methodology has been exploited to improve the reactivity and selectivity of alkanes in order to achieve the controllable functionalization.[4] In spite of the most recent progress in straight-functionalization of directing-group-free alkanes, $C(sp^3)$-H activation has still been a challenging issue pursued by synthetic chemists.[5] On the other hand, the first-row transition metals have acted as positive alternatives to the second- and third-row metals in many organic reactions. In the case of VIII elements, different valence of Fe, Co, Ni, have presented comparable performance in some reactions[6] that catalyzed by Ru, Rh, Pd, Ir, and Pt.[7] And lately, nickel-based catalyst has been reported for the activation of some inert sp^3 carbon-hydrogen bonds.[8]

Promoted by those pioneering progress in sp^3 C–H activation, we have developed a Ni-catalyzed carbonylation of unreactive alkanes with formanilides in carbon monoxide to acquire high yields of amide products. Herein, we wish to describe the results of this study.

2. Results and discussion

We initiated the activation reaction with cyclohexane (**1a**, also as the solvent) and aniline as the model substrates for catalyst-screening (Table 1). Most reactions gave N, N$^{/}$-diphenylurea as the main product, wherein, Cu-catalytic procedures just leaded to inseparable mixtures (Table 1, Entries 1–15). To our pleasure, $Co(acac)_2$ and $Ni(acac)_2$ also exhibited certain activation on the transformation even without assistance of auxiliary ligands (Table 1, Entries 11–15). Replacing aniline with its hydrochloride, urea formation was partly controlled, but the yield of **3aa** was still unsatisfactory (Table 1, Entry 16). Without the catalyst, the activation of cyclohexane didn't take place but urea was generated by the interaction between aniline and CO in the presence of DTBP (Table 1, Entry 17).

Hindered by the serious urea formation between aniline and CO, we had to turn to other amine sources to improve the selectivity.

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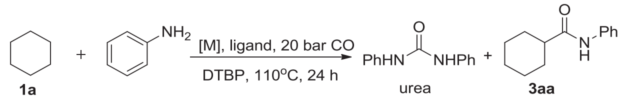
Table 1
The initial exploration into activation of cyclohexane with aniline for catalyst-screening[a].



Entry	Metal	Ligand	3aa Yield(%)[b]
1	$CoCl_2$	1,10-phen	trace
2	$CoCl_2$	PPh_3	trace
3	$NiCl_2$	1,10-phen	Trace
4	$NiCl_2$	PPh_3	Trace
5	$Co(OAc)_2$	1,10-phen	Trace
6	CuCl	1,10-phen	Trace
7	CuI	1,10-phen	Trace
8	$Cu(OAc)_2$	1,10-phen	Trace
9	$FeCl_3$	1,10-phen	0
10	$Fe(acac)_2$	1,10-phen	13
11	$Co(acac)_2$	1,10-phen	31
12	$Co(acac)_2$	PPh_3	34
13	$Ni(acac)_2$	1,10-phen	39
14	$Ni(acac)_2$	PPh_3	40
15	$Ni(acac)_2$	–	42
16[c]	$Ni(acac)_2$	–	47
17	–	–	0

acac = acetylacetonate. DTBP = di-*tert*-butylperoxide. 1,10-phen = 1,10-phenanthroline.

[a] Reaction conditions unless otherwise stated: **1a** (20 mL), **2a** (10 mmol), metal (10% mol), ligand (20% mol), DTBP (12 mmol), CO (20 bar), time 24 h.

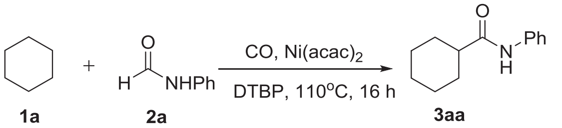
[b] Isolated yields, Urea was obtained as the main product.

[c] Aniline hydrochloride was utilized instead of **2a**.

Formanilide, which can be looked as the integrity of CO and aniline, seemed a desirable substrate due to its weakened nucleophilicity. Hence a new round of probe into the reaction of formanilide (**2a**) was started using $Ni(acac)_2$ as the catalyst.

The first reaction between **1a** and **2a** was conducted under 20 bar nitrogen pressure at 110 °C only giving trace of **3aa** without urea generation (Table 2, Entry 1). Surprisingly, an excellent yield of **3aa** (90%) was obtained while the reaction underwent under 20 bar of carbon monoxide (Table 2, Entry 2). Noteworthy, the requirement of carbon monoxide disclosed clearly that a deformylation behavior should be involved in the process. Then, condition-optimization was performed concerning mainly the pressure and the charging amounts of catalyst but leading to no better results (Table 2, Entries 3 and 4). Benzene was checked as an auxiliary solvent giving a comparably satisfactory result (Table 2, Entry 5), from which it can also be seen that sp^2 C–H bond be steady enough to the catalytic conditions. Acetonitrile was an unfavorable solvent for this conversion (Table 2, Entry 6). To confirm the effect in this transformation, control experiments were carried out as shown in Entries 7–9 (Table 2). Without the catalyst and additional solvents, DTBP was also able to generate a little quantity of urea in no more than 10% yield but with no **3aa** observed (Table 2, Entry 7). Dichloroethane, which was reported by Lei and coworkers as a facilitating solvent for metal-free carbonylation of cyclohexane,[9] was confirmed to be some helpful to the reaction in the absence

Table 2
Condition optimization for the Ni-catalyzed reaction of **1a** and **2a** in CO[a].



Entry	Catalyst loading	Auxiliary solvent	Pressure	3aa Yield(%)[b]
1	10 mol%	–	20 bar N_2	trace
2	10 mol%	–	20 bar CO	90
3	10 mol%	–	10 bar CO	85
4	5 mol%	–	20 bar CO	80
5	10 mol%	benzene[c]	20 bar CO	87
6	10 mol%	acetonitrile[c]	20 bar CO	44
7	–	–	20 bar CO	0
8[d]	–	$ClCH_2CH_2Cl$[c]	60 bar CO	<10%
9	10 mol%	$ClCH_2CH_2Cl$[c]	20 bar CO	88

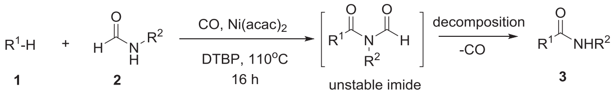
[a] Reaction conditions (unless otherwise stated): **1a** (20 mL), **2a** (10 mmol), CO, catalyst (10 mol%), DTBP (12 mmol), 110 °C, 16 h.

[b] Isolated yield.

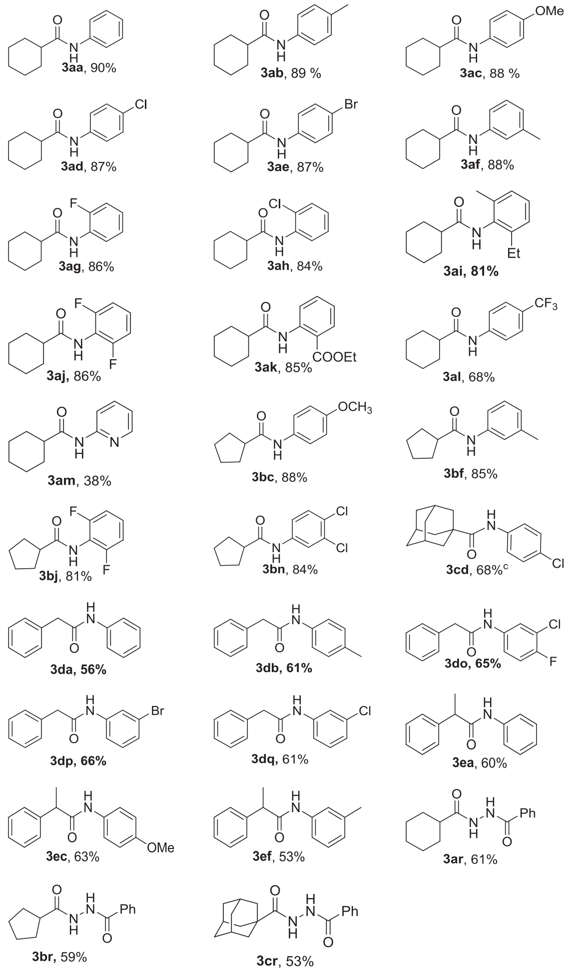
[c] Solvent (20 mL), **1a** (10 mmol).

[d] The reaction was conducted under the conditions according to the literature.[9]

Table 3
Ni-catalyzed carbonylation of alkanes with formanilides[a].



3, yield[b]



[a] Reaction conditions (unless specially illustrated): **1** (20 mL), **2** (10 mmol), CO, $Ni(acac)_2$ (10 mol%), DTBP (12 mmol), 110 °C, 16 h.

[b] Isolated yield.

[c] adamantane (**3c**, 10 mmol), dichloroethane solvent (20 mL).