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ARTICLE

Synthesis of Formamides Containing Unsaturated Groups by N-Formylation of Amines using CO_2 with H_2

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Formamides have wide applications in industry and have been synthesized using CO_2 as carbon source and H_2 as reducing agent. However, previous systems required noble catalyst and high temperature to achieve high efficiency, and the substrate scope was mostly limited to saturated amines. Selective N-formylation of amines containing unsaturated groups using CO_2 and H_2 is challenging because the efficient catalysts for the N-formylation are usually very active for hydrogenation of the unsaturated groups. Herein, we firstly achieved the selectively and efficiently N-formylation of amines containing unsaturated groups using CO_2 and H_2 using $Cu(OAc)_2$-4-dimethylaminopyridine (DMAP) catalytic system. The substrates were converted to the desired formamides, while the unsaturated groups, such as carbonyl group, C=C bond, C≡N bond and ester group remained. The main reason for the excellent selectivity of the $Cu(OAc)_2$-DMAP catalytic system was that it was very active for the N-formylation reaction, but was not active for hydrogenation of the unsaturated groups.

Introduction

CO_2 is an abundant and cheap C1 resource. Conversion of CO_2 into value-added chemicals is an important approach for human being to participate in global carbon cycle.[1-7] Catalytic chemical reduction is one of the most efficient routes. Some value-added chemicals have been synthesized by chemical reduction of CO_2.[8-18]

Formamides are a class of chemicals with widespread applications in industry as solvents and raw materials for synthesis of other chemicals.[19-20] Various routes and feedstocks have been used to synthesize formamides,[21-36] and using CO_2 as a carbon resource and H_2 as the reducing reagent is ideal route.[22] Various saturated amines have been prepared using CO_2 and H_2 as feedstocks.[37-38] Ding and his co-workers reported the N-formylation of a series saturated amines with H_2 and CO_2 catalyzed by ruthenium based homogeneous catalyst at 120 °C.[39] Shi et al. found that heterogeneous catalyst palladium was also active for this kind of reactions at 130 °C.[40] Various saturated formamides have also been synthesized using organosilanes as the reducing reagent and CO_2 as carbon resource.[25-36]

The formamides containing unsaturated group are more desirable in many cases because unsaturated group can be easily further functionalized to produce useful compounds.[41-42] So far, the formamides with unsaturated functional group are generally synthesized by using CO, formic acid or methylformate as the carbon resources.[44-45] It is interesting to produce this kind of formamides using CO_2 to replace these carbon resources. Recently, Kobayashi and his co-workers reported the N-formylation of amines containing unsaturated group using CO_2 as the carbon resource and Ph_2SiH_2 as the reducing agent, and a chelating bis(NHC) rhodium complexes (NHC=N-heterocyclic carbene) was used as the catalysts.[46]

It is well known that hydrogen is commonly used reducing agent because it is abundant, economic, non-toxic, and the only byproduct is H_2O. N-formylation of amine derivatives containing unsaturated group using CO_2 and H_2, in which the unsaturated group remains unreacted, is highly desirable, but is challenging. One of the main reasons is that CO_2 is thermodynamically very stable and kinetically inert in typical organic syntheses. So the direct reaction between H_2 and CO_2 usually requires hash reaction conditions, at which the unsaturated group, such as carbonyl group, C=C bond, C≡N bond and ester group, is easily hydrogenated.

In this work, we discovered that Cu-DMAP (**1a**) catalytic system could catalyze this kind of reactions very effectively, and the unsaturated groups (e.g. carbonyl group, C=C bond, C ≡N bond and ester group) could be remained. As far as we known, this is the first work for the synthesis of formamides containing unsaturated groups by N-formylation of amines using CO_2 with H_2.

Results

Compared to precious metal catalysts, abundant and in-expensive first-row transition metals, especially Cu, Ni, and Co,

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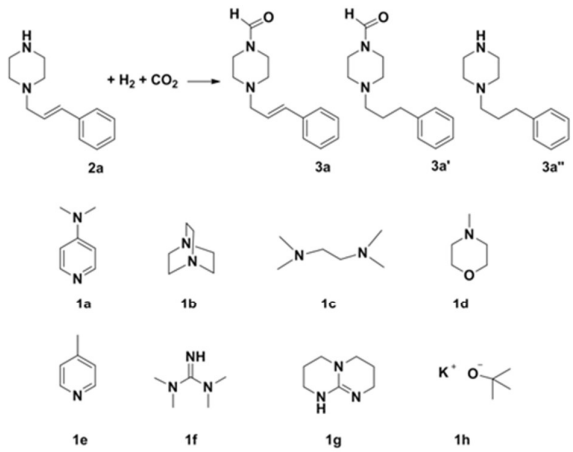
are advantageous for large-scale chemical processes. DMAP is a useful nucleophilic catalyst for a variety of reactions.[43] We studied the performances of copper salts for the N-formylation reaction of 1-cinnamylpiperazine (**2a**) with or without additives. $Cu(OAc)_2$ only afforded 20% yield of **3a** in the absence of additive (Table 1, entry 1). DMAP (**1a**) was the best additive among those tested and $Cu(OAC)_2$-DMAP catalytic system could afford 91% yield of **3a** in 6 h (Table 1, entry 2). DABCO (**1b**, 1,4-diazabicyclo[2.2.2]octane) and N,N,N',N'-tetramethyl-1,2-diaminopropane (**1c**) were also effective for promoting the reaction and the yields of **3a** were 46% and 38%, respectively (Table 1, entries 3 and 4). The promoting effect of 4-methylmorpholine (**1d**) was poor, and the yield of **3a** was only 28% (Table1, entry 5). 4-Methylpyridine(**1e**), tetramethylguanidine (**1f**) and TBD (**1g**, 1,5,7-triazabicyclo[4.4.0]dec-5-ene) suppressed the reaction and afforded yields of **3a** below 20% (Table 1, entries 6-8). Inorganic base potassium isopropoxide (**1h**) completely suppressed the reaction (Table 1, entry 9). The other metal complexes also exhibited high selectivity for the N-formylation reaction, while the activity was very low at the reaction conditions (Table 1, entries 10-14). Furthermore, the counterions of the copper salts containing oxygen led to higher activity (Table 1, entries 2 and 10-12). $Cu(OAc)_2$-DMAP was the most active and selective catalytic system, and the yield of the desired product could be as high as 99% at the optimized condition (Table 1, entry 15). The higher activity of $Cu(OAc)_2$ attribute to the basicity of OAC^- and it maybe help to activate H_2 by the interaction of oxygen of OAC^- with H_2. And the reaction mechanism would be discussed below. In addition, the yield of the product was very low when only DMAP (**1a**) was used without metal catalyst (Table 1, entry 16). It can be known from Entries 1, 15, 16 that $Cu(OAc)_2$ and DMAP had excellent synergistic effect for the reaction. No formic acid was detected without amines that indicated that the N-formylation reaction catalyzed by $Cu(OAc)_2$-DMAP didn't involve the hydrogenation of CO_2 to formic acid (Table 1, entry 17) and this result is consistent with the result reported in the literature[47]. The reaction can't occur without $Cu(OAc)_2$ and DMAP (Table 1, entry 18). The composition of the gas after reaction was also checked and only CO_2 and H_2 were detected. We also studied the effects of temperature and solvents on the reaction using $Cu(OAc)_2$-DMAP catalytic system for the N-formylation reaction of 1-cinnamylpiperazine (**2a**), and the results were listed in Table S1. The yields of the desired product increased with increasing temperature in the range of 70 °C and 90 °C. Toluene THF was the most effective among the solvents checked.

Table 1. Catalyst screening for the N-formylation of 1-cinnamylpiperazine.[a]



Entry	Metal precursor	Additive	Yield (%)[b]	Selectivity (%)[c]
1	$Cu(OAc)_2$	None	20	>99
2	$Cu(OAc)_2$	**1a**	91	>99
3	$Cu(OAc)_2$	**1b**	46	>99
4	$Cu(OAc)_2$	**1c**	38	>99
5	$Cu(OAc)_2$	**1d**	28	>99
6	$Cu(OAc)_2$	**1e**	13	>99
7	$Cu(OAc)_2$	**1f**	19	>99
8	$Cu(OAc)_2$	**1g**	6	>99
9	$Cu(OAc)_2$	**1h**	0	/
10	$CuSO_4$	**1a**	57	>99
11	$Cu(NO_3)_2$	**1a**	17	>99
12	$CuCl_2$	**1a**	3	>99
13	$Ni(OAc)_2$	**1a**	19	>99
14	$Co(OAc)_2$	**1a**	21	>99
15	$Cu(OAc)_2$[d]	**1a**	99	>99
16	None	**1a**	3	>99
17	$Cu(OAc)_2$[e]	**1a**	/	/
18	None	**None**	0	/
19	$Cu(OAc)_2$[f]	**1a**	7	>99

[a] Reaction conditions: 1-cinnamylpiperazine 1 mmol, $P_{CO2} = P_{H2} = 40$ atm, metal precursor 10 mol% based on substrate, additive 2 mmol, THF 1.5 mL, 90 °C, 6 h. [b] Yield of **3a** was determined by GC. [c] Selectivity of **3a** was determined by GC. [d] 9 h. [e] Without amines. [f] 4 MPa CO_2 were added firstly, and the solution stirred 1h. Then discharge the CO_2, while adding hydrogen 4 MPa and stirred 6 hours.

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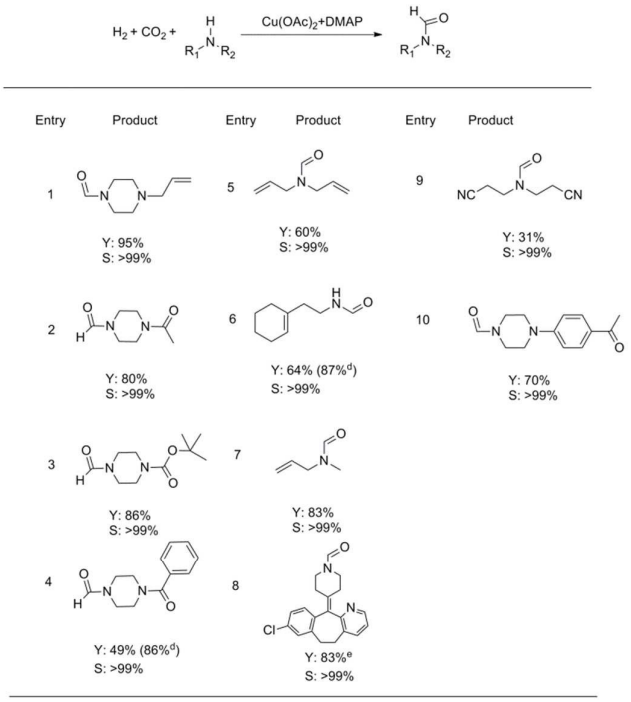
Table 2. Cu catalyzed N-formylation of amines containing unsaturated group using CO_2 and H_2.[a,b,c]

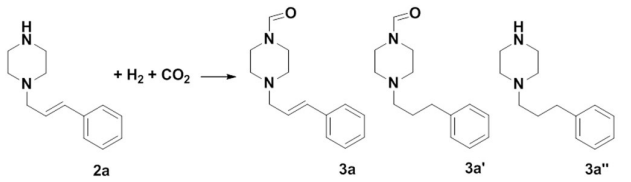


[a] Reaction conditions: amine 1 mmol, $P_{CO2} = P_{H2}$ = 40 atm, $Cu(OAc)_2$ 10 mol% based on substrate, DMAP 2 mmol, THF (1.5 mL), 90 °C, 12 h. [b] Yield was determined by GC. [c] Selectivity was determined by GC. [d] 20 h. [e] Yield was determined by ^{1}H NMR.

The results above indicate that $Cu(OAc)_2$ and DMAP (**1a**) is an excellent combination for the N-formylation of 1-cinnamylpiperazine. We further explored the formylation of various amines with different unsaturated groups to examine the versatility of the catalytic system using H_2 as a reductant in THF, and the results are listed in Table 2. The N-formylation reaction proceeded smoothly to selectively afford the corresponding formamides in good to excellent yields, and C=C bond, carbonyl group and ester group could be remained. $Cu(OAc)_2$-DMAP catalytic system was effective for piperazine derivatives. The yield of 4-allylpiperazine-1-carbaldehyde could reach 95% in 12 h (Table 2, entry 1). The yield of 1-formyl-4-acetylpiperazine and 1-Boc-4-formylpiperazine were all above 80% (Table 2, entries 2 and 3). 86% yield of 4-benzoyl-1-piperazinecarboxaldehyde was obtained when the reaction time prolonged to 20 h (Table 2, entry 4). The reactivity of chain secondary amines that contains C=C bond was lower than piperazine derivatives with C=C bond (Table 1, entries 1 and 5-7). The yield of N,N-diallylformamide, N-(2-cyclohex-1-enyl-ethyl)-formamide and N-methyl-N-allyl-formamide were 60%, 64% and 83% in 12 h, respectively (Table 1, entries 5-7), while 87% yield of N-(2-cyclohex-1-enyl-ethyl)-formamide was obtained when the reaction time was prolonged to 20 h (Table 2, entry 6). The yield of N-formyl desloratadine was 83% (Table 2, entry 8). The yield of N,N-bis-(2-cyano-ethyl)-formamide was 31% in 12 h (Table 2, entry 9). The yield of 4-(4-acetylphenyl)piperazine-1-carbaldehyde was above 70% (Table 2, entries 10).

The above results indicate that $Cu(OAc)_2$-DMAP catalytic system was highly selective and efficient for the N-formylation of various amines with unsaturated groups using H_2 and CO_2. The efficiency and selectivity of the commonly used catalysts for the N-formylation reaction of saturated amines[40, 48-50] were also tested using the N-formylation reaction of 1-cinnamylpiperazine (**2a**) (Table 3). The conversion of **2a** could reach 99% at 90 °C in 6 h, but almost no desired product **3a** was detected over Pd/Al_2O_3 (Table 3, entry 1). The similar result was obtained over Pd/C catalyst. When $PdCl_2$ was used as the catalyst, the conversion of **2a** was 94%, while the selectivity for **3a** was only 3% (Table 3, entry 3). For all the Pd based catalysts checked, other byproducts such as n-proplbenzene, piperazine that were from the cleavage of C-N bond were detected (Table 3, entries 1-3). The performance of the Ru complexes were also investigated (Table 3, entries 4-6). The conversion of **2a** was 95%, and the selectivity of **3a**, **3a'** and **3a''** was only 11%, 13% and 11% respectively over $[(C_6H_5)_3P]_3Ru(CO)(Cl)H$ and 65% selectivity of the byproducts from the cleavage of C-N bond was detected (Table 3, entry 4). At the same reaction condition, the conversion of **2a** was 75% over $Ru_3(CO)_{12}$ and the selectivity of **3a** was 33% (Table 3, entry 5). Similarly, the conversion and selectivity of **3a** over $RhCl_3$ were low (Table 3, entry 7). All the results above indicate that the noble metal based catalysts, which are commonly used in the N-formylation reaction of saturated amines had very poor selectivity for the N-formylation of the amine containing C=C bond.

Table 3 The N-formylation of 1-cinnamylpiperazine (**2a**) over different catalysts



Entry	catalyst	Conversion (%)	Selectivity (%)			
			3a	3a'	3a''	others[a]
1	Pd/Al_2O_3	>99	trace	36	48	16
2	Pd/C	>99	0	47	36	17
3	$PdCl_2$	94	3	22	50	25
4	$[(C_6H_5)_3P]_3Ru(CO)(Cl)H$	95	11	13	11	65
5	$Ru_3(CO)_{12}$	75	33	7	7	53
6	$RhCl_3$	77	42	trace	trace	58

Reaction conditions: **2a** 1 mmol, $P_{CO2}=P_{H2}$=40 atm, catalyst 10 mol%, THF 1.5 mL, 90 °C, 6 h. Conversion and selectivity was determined by GC, [a] the product from the cleavage of C-N bond.

The most interesting part of this work is that $Cu(OAc)_2$-DMAP catalytic system was very selective and effective for the

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N-formylation reactions of various amines with unsaturated bond. To investigate the reason for this interesting phenomenon, we studied its catalytic activity for hydrogenation of a series of compounds containing different unsaturated bonds and the results are shown in Figure 1. The catalytic system was not active for the hydrogenation of the unsaturated bonds (-C≡N, C=C, C=O), which can explain reasonably the high selectivity of $Cu(OAc)_2$-DMAP catalytic system for the N-formylation reactions. We also used $PdCl_2$ as the catalyst for hydrogenation of these substrates. (Figure 1) We found that these substrates converted to the corresponding saturated compounds, which can explain the low selectivity of noble metal catalytic system for the N-formylation reactions.

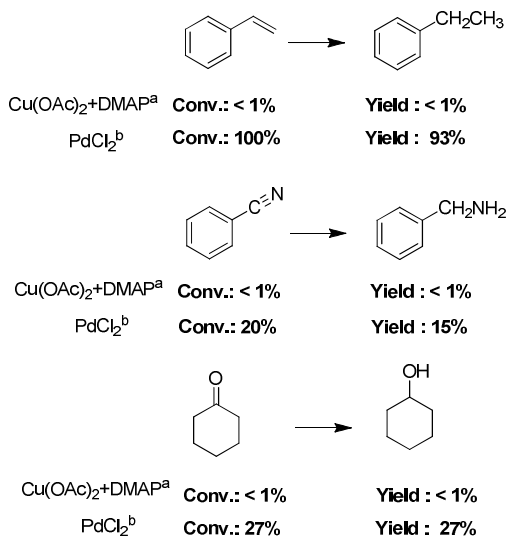
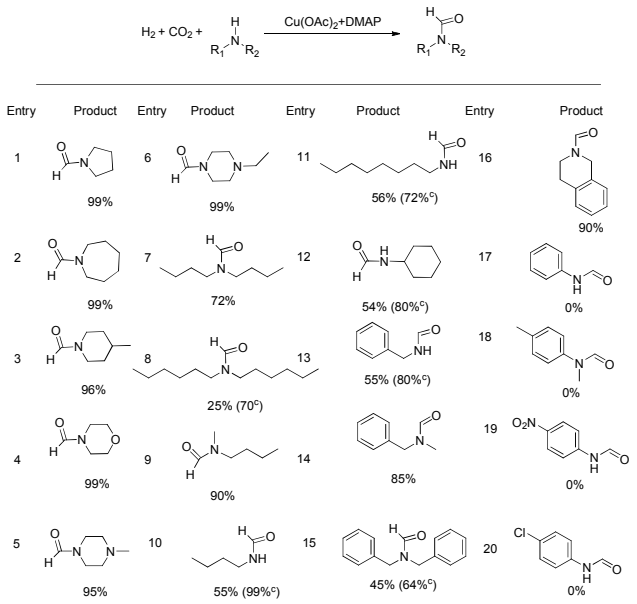


Figure1. Hydrogenation of the compounds containing various unsaturated bonds with different catalysts. Reaction conditions: a reactant 1 mmol, $P_{CO2} = P_{H2}$ = 40 atm, $Cu(OAc)_2$ 10 mol% based on substrate, DMAP 2 mmol, THF 1.5 mL, 90 °C, 6 h. b reactant 1 mmol, $P_{CO2} = P_{H2}$ = 40 atm, $PdCl_2$ 10 mol% based on substrate, THF 1.5 mL, 90 °C, 6 h. Conversion of the reactant was determined by GC.

Noble metal based catalysts are commonly used in the N-formylation reaction of saturated amines.[37-40, 48-50] In this work, we also studied the catalytic performance of the $Cu(OAc)_2$-DMAP catalytic system for the N-formylation reaction of typical saturated amines , and the results are provided in Table 4. It can be known that the catalytic system was also very effective for the N-formylation of saturated amines. The excellent activity of $Cu(OAc)_2$-DMAP system results from synergistic effect of $Cu(OAc)_2$ and DMAP for N-formylation reactions, as discussed above (Table 1, Entries 1, 15, 16). However, the $Cu(OAC)_2$-DMAP catalytic system

Table 4. Cu catalyzed N-formylation of amines without unsaturated group using H_2 and CO_2.[a,b]



[a] Reaction conditions: amine 1 mmol, PCO2 = PH2 = 40 atm, $Cu(OAc)_2$ 10 mol% based on substrate, DMAP 2 mmol, THF 1.5 mL, 90 °C, 12 h. [b] Yield was determined by GC. [c] 20 h.

To study the reaction mechanism, control experiment was performed. (Table 1, entry 19) Firstly the reaction of 1-cinnamylpiperazine and 4 MPa CO_2 was allowed to proceed for 1 h in the presence of $Cu(OAc)_2$-DMAP. The CO_2 was removed and 4 MPa H_2 was added and stirred for 6 h, and the product **3a** was also produced, which indicated that CO_2 and 1-cinnamylpiperazine or DMAP can form the salt[51] and the salt further reacted with hydrogen to the final product.

It has been reported that oxygen-containing ligands may help to activate hydrogen.[53] Similarly, we got a transition state for OAc^- assisted hydrogen cracking through calculation.[52](Figure S1 in SI) On the basis of the experimental results, the possible reaction mechanism was proposed for the reaction over $Cu(OAc)_2$-DMAP catalytic system (Figure 2). Amines can react with CO_2 to form internal salt very easily.[51] Next, the cleavage of H−H bond accompanied with the formation of C-H bond and O-H bond. And finally H_2O was lost and got the final product. In order to further illustrate the role of DMAP, the reaction solutions with and without DMAP at 50 °C were examined using UV-Vis spectroscopy and the spectra were shown in Fig. 3. The absorption peak of copper acetate appears at 696 nm(a). Without DMAP, the absorption peak was observed at around 579 nm, which are characteristic of coordinate of copper and amine (b). For the reaction solution with DMAP, the peak shifts to 667 nm indicated the coordination of copper and DMAP (c).

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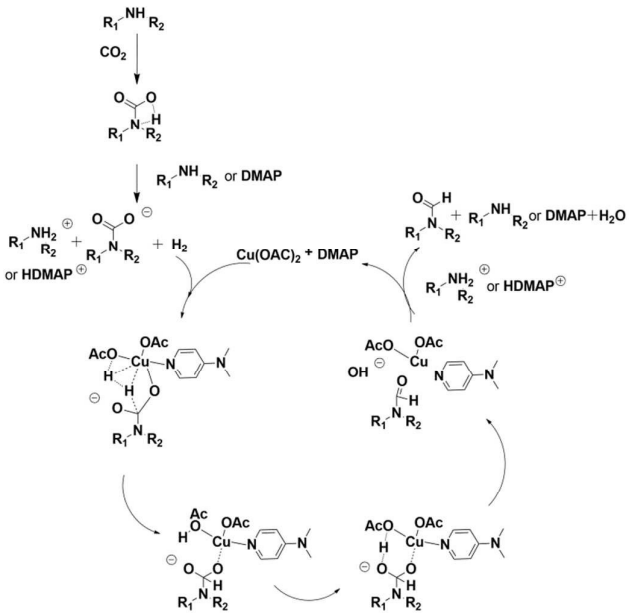

Figure 2.The possible reaction mechanism for the N-formylation using H_2 and CO_2.

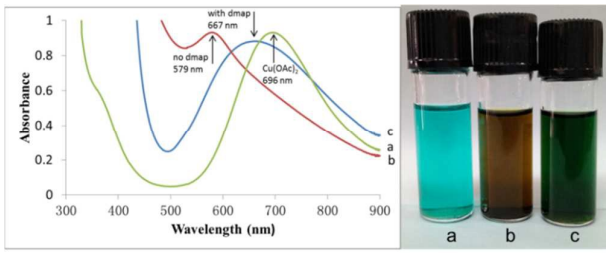

Figure 3. UV-Vis absorption spectra of reaction solution without DMAP (a), with DMAP (b) and $Cu(OAc)_2$. Reaction conditions: 1-cinnamylpiperazine 1 mmol, P_{CO2} = P_{H2} = 40 atm, $Cu(OAc)_2$ 10 mol% based on substrate, DMAP 2 mmol, THF 1.5 mL, 50 °C, 6 h.

Conclusions

In summary, $Cu(OAc)_2$-DMAP catalytic system are very selective and active for the N-formylation reactions of amines containing unsaturated groups using H_2 and CO_2. The unsaturated groups in the substrates, including carbonyl group, C=C bond and ester group, are all stable under the reaction condition. High yields of the desired formamides can be obtained with selectivity of >99%. However, the selectivity of the desired product over Pd, Ru and Rh based catalysts, which are commonly used for the N-formylation reactions of saturated amines, is very low because the catalysts are also very active for the hydrogenation of the unsaturated bonds. We believe that the highly selective, active, and cheaper catalytic system has great potential of application for producing formamides with unsaturated groups.

Acknowledgements

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Synthesis of Formamides Containing Unsaturated Groups by N-Formylation of Amines using CO_2 with H_2

Hangyu Liu, Qingqing Mei, Qingling Xu*, Jinliang Song, Huizhen Liu* and Buxing Han*

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1. Experimental section

Chemicals

4-dimethylaminopyridine, DBACO, TMG, potassium tert-butoxide, 4-methylpyridine, 4-methylmorpholine, tetramethylethylenediamine, $PdCl_2$, Chloroform-d, 3,3'-IMinodipropionitrile, 4'-piperazinoacetophenone, 1-allylpiperazine, diallylamine, 1-acetylpiperazine, 2-(1-cyclohexenyl)ethylamine, 1-Boc-piperazine, N-allylmethylamine, 1-benzoylpiperazine, 1,2,3,4-tetrahydroisoquinoline, benzonitrile, α-Al_2O_3, 1-phenyl-1-propyne, pyrrolidine, N-ethylpiperazine, butylamine, dibutylamine, 4-methylpiperidine, dihexylamine, n-octylamine, cyclohexylamine, morpholine, 1-methylpiperazine, cyclohexene, styrene, n-decane and tetrahydrofuran were purchased from J&K Scientific Ltd. $Cu(OAc)_2$, 1,5,7-triazabicyclo[4.4.0]dec-5-ene, $RhCl_3$, desloratadine, benzylamine, dibenzylamine, hexamethyleneimine, N-methylbutylamine and N-methylbenzylamine was provided by Energy Chemical. Trans-1-cinnamylpiperazine, Pd/C, carbonylchlorohydridotris(triphenylphosphine)ruthenium(II) and $Ru_3(CO)_{12}$ purchased from alfa aesar. $CuSO_4$•$5H_2O$, $Cu(NO_3)_2$•$3H_2O$, $CuCl_2$•$2H_2O$, $Ni(OAc)_2$•$4H_2O$, $Co(OAc)_2$•$4H_2O$, nitrobenzene, cyclohexanone and sodium tetrahydroborate was provided by Sinopharm Chemical Reagent Co., Ltd. The CO_2 (99.99%), H_2 (99.99%) and N_2 (99.99%) were provided by Beijing Analytical Instrument Company.

Characterization

^1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance III HD 400 MHz NMR spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C) at ambient temperature in $CDCl_3$. GC/MS analysis was conducted on Agilent 7890B GC+ 5977 MSD. Sample analysis was operated on an Agilent 6820 gas chromatography equipped with a flame ionization detector (FID) and a HP-5 capillary column (30 m × 0.25 mm × 0.25 μm), Agilent Technologies Singapore (Sales) Pte Ltd., Singapore.

N-Formylation of amines using H_2 and CO_2

The reaction was carried out in a Teflon-lined stainless-steel reactor of 10 mL in capacity with a magnetic stirrer. The pressure was determined by a pressure transducer (FOXBORO/ICT, Model 93), which could be accurate to ±0.025 MPa. In a typical experiment, 0.1 mmol of $Cu(OAc)_2$ and 2 mmol of 4-dimethylaminopyridine (DMAP) were loaded into the reactor. 1 mmol of substrate and 1.5 mL solvent (e.g. THF) were added. The reactor was sealed and purged with H_2 to remove the air at ambient temperature. The reactor was placed in an air bath at desired temperature. H_2 of 40 atm was added, and then CO_2 was charged until the total pressure reached 80 atm, and then the stirrer was started at 500 rpm. After reaction the reactor was placed in ice water and the gas was released. The reaction mixture was analyzed by GC-MS and GC with decane as an internal standard, or purified by flash column

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chromatography on silica gel to afford the desired product was characterized by ^{1}H NMR and ^{13}C NMR.

Prepare of Pd/Al_2O_3

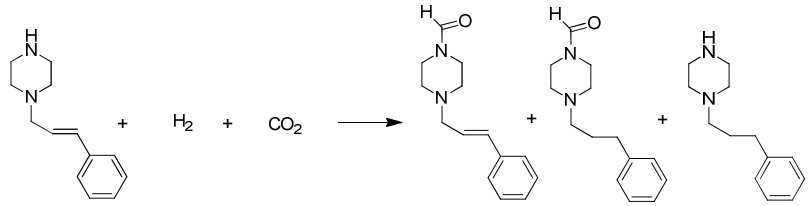
Suitable amount of H_2PdCl_4 (8 mg) were added into 50 mL distilled water and 400 mg α-Al_2O_3 was added to the solution under stirring. A freshly prepared solution of $NaBH_4$ (0.1 M, 20 mL) was then added under stirring to form a dark solution. After the mixture was further stirred for 3 h at 30 ^{o}C, it was centrifuged and washed by water, dried at 120 ^{o}C for 4 h and calcined at 350 ^{o}C for 4 h in air. A grey solid sample was obtained.[s1]

Compution

The geometrical optimizations TS were performed at the 6-31G* level. All calculations were performed with the Gaussian 09 programs. Frequencies were calculated at the same level to confirm each stationary point to be either a minimum (no imaginary frequency) or a saddle point (unique imaginary frequency).

2. Optimization of reaction conditions

Table S1 Optimization of condition for the catalytic N-formylation reaction of 1-cinnamylpiperazine[a]



2a 3a 3a' 3a''

Entry	T (^{o}C)	Solvent	$Cu(OAc)_2$ (mol%)[b]	DMAP (equiv)[b]	Yield (%)[c]
1	70	THF	10	2	2
2	80	THF	10	2	51
3	90	THF	10	2	91
4	90	water	10	2	0
5	90	toluene	10	2	85
6	90	cyclohexane	10	2	61
7	90	acetonitrile	10	2	53
8	90	1,4-dioxane	10	2	83

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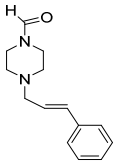
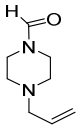
9	90	ethanol	10	2	3
10	90	THF	5	2	67
11	90	THF	2	2	33
12	90	THF	10	1	25
13	90	THF	10	0.5	16

[a]Reaction conditions: trans-1-cinnamylpiperazine (1 mmol), P_{CO2}=P_{H2}= 40 atm, solvent (1.5 mL), 6 h. [b]The amount based on the substrate, [c]Yield of **3a** was determined by GC.

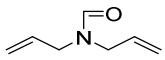
3. Characterization data for the N-formylation products



4-cinnamylpiperazine-1-carbaldehyde: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (s, 1H), 7.38-7.21 (m, 5H), 6.56-6.51 (m, 1H), 6.27-6.20 (m, 1H), 3.59-3.56 (t, J =5.1 Hz, 2H), 3.40-3.37 (t, J =5.1 Hz, 2H), 3.18-3.16 (m, 2H), 2.51-2.45 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ160.52, 136.47, 133.33, 128.42, 127.49, 126.15, 125.65, 60.70, 53.28, 52.17 45.44, 39.77.



4-allylpiperazine-1-carbaldehyde: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (s, 1H), 5.89-5.79 (m, 1H), 5.23-5.17 (m, 2H), 3.59-3.56 (t, J =5.1 Hz, 2H), 3.40-3.38 (t, J =5.1 Hz, 2H), 3.04-3.01 (t, J =5.5 Hz, 2H), 2.47-2.44 (t, J = 5.1 Hz, 2H), 2.43-2.41 (t, J = 5.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ160.67, 134.35, 118.45, 61.53, 53.33, 52.20, 45.60, 39.93.



N,N-diallylcarboxamide:^{1}H NMR ($CDCl_3$,400 MHz) δ 8.13 (s, 1H), 5.79-5.66 (m, 2H), 5.26-5.14 (m, 4H), 3.95-3.94 (m, 2H), 3.83-3.81 (m, 2H). ^{13}C NMR ($CDCl_3$,100 MHz) δ162.51, 133.10, 132.12, 118.55, 118.08, 58.44, 49.25, 44.32.

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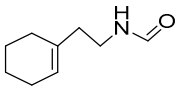
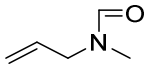
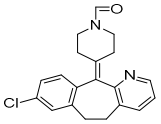


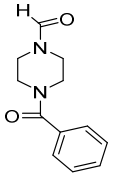
N-(2-cyclohex-1-enyl-ethyl)-formamide:^{1}H NMR ($CDCl_3$,400 MHz) δ 8.16 (s, 0.79H), 8.06-7.97 (m, 0.21H), 5.49 (s, 1.72H), 5.30 (s, 0.24H), 3.40-3.27 (m, 2H),2.17-2.13 (s, 2H), 2.01-2.00 (s, 2H), 1.93-1.91 (m, 2H), 1.66-1.52 (m, 4H). ^{13}C NMR ($CDCl_3$,100 MHz) δ164.35, 161.07, 134.23, 133.20, 124.63, 123.64, 37.35, 35.72, 28.00, 27.75, 25.12, 25.08, 22.69, 22.66, 22.22, 22.15.



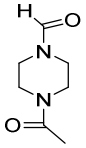
N-methyl-N-allyl-formamide: ^{1}H NMR ($CDCl_3$,400 MHz) δ 8.08 (s, 1H), 5.79-5.69 (m, 1H), 5.30-5.18 (m, 2H), 3.96-3.94 (d, J= 6.0Hz, 1H), 3.84-3.82(d, J= 5.7Hz, 1H), 2.91(s, 1H), 2.84 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ162.67, 132.87, 131.86, 118.45, 118.06, 51.98, 46.61, 33.96, 29.45.



N-formyl desloratadine: ^{1}H NMR ($CDCl_3$,400 MHz) δ8.39-8.36 (m, 1H), 8.06 (s, 1H), 7.42 (s, 1H),7.16-7.0 (m, 4H),3.35-3.20 (m, 2H),3.1-3.0 (m, 2H),2.9-2.6 (m, 4H),2.3-2.4 (m, 4H).



4-benzoyl-1-piperazinecarboxaldehyde: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.08 (s, 1H), 7.41 (m, 5H), 3.73-3.40 (m, 8H).^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.24, 159.82, 134.03, 128.87, 127.43, 125.85, 44.20, 38.69.



1-formyl-4-acetylpiperazine: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (s, 1H), 3.63-3.36 (m, 8H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ168.542, 160.37, 160.29, 46.13, 44.99, 44.89, 44.47, 41.23, 40.07, 39.37, 20.70.

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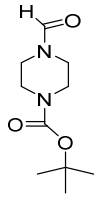
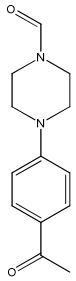
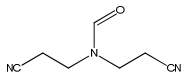


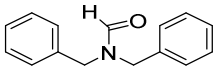
1-Boc-4-formylpiperazine: ^{1}HNMR ($CDCl_3$, 400 MHz) δ8.08 (s, 1H), 3.53-3.35 (m, 8 H), 1.48 (s, 9H). ^{13}C NMR ($CDCl_3$,100 MHz) δ160.69, 154.20, 80.25, 45.24, 39.75, 28.17.



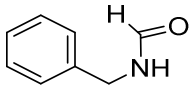
4-(4-acetylphenyl)piperazine-1-carbaldehyde: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (s, 1H), 7.84 (d, J = 8.70 Hz, 2H), 6.86 (d, J =8.70 Hz, 2H), 3.64 (t, J = 5.04 Hz, 2H), 3.49 (t, J = 5.52, 2H), 3.30 (dt, J = 17.06, 5.21 Hz, 4H), 2.48 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.91, 160.55, 153.40, 129.99, 127.80, 113.85, 48.01, 46.77, 44.56, 39.16, 25.84.



N,N-bis-(2-cyano-ethyl)-formamide: ^{1}HNMR ($CDCl_3$, 400 MHz) δ8.23 (s, 1H), 3.72-3.66 (m, 4 H), 2.78-2.68 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ163.07, 117.90, 117.39, 44.33, 43.66, 15.96.



N,N-dibenzylformamide:^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.54 (s, 1H), 7.43-7.26 (m, 10H), 4.51 (s, 2H), 4.33 (s, 2H). ^{13}C NMR (CDCl3, 100 MHz) δ 161.24, 134.60, 134.31, 127.27, 127.08, 126.73, 126.62, 126.17, 125.99,48.51, 42.93.



N-benzylformamide: ^{1}H NMR (400 MHz, $CDCl_3$)δ8.23 (s, 1H), 8.15 (d, J = 11.9 Hz, 1H), 7.21-7.40 (m, 5H), 6.07 (s, 1H), 4.46 (d, J = 5.9 Hz, 2H), 4.39 (d, J = 6.5 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 161.07, 160.83 , 137.71, 128.8, 128.6, 127.6, 127.5, 127.0, 45.7, 41.9

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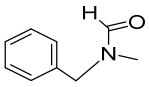
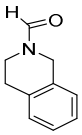
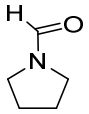


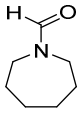
N-benzyl-N-methylformamide: ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.29-8.16 (m, 1H), 7.39-7.19 (m, 5H), 4.51-4.37 (m, 2H), 2.82-2.76 (m, 3H).^{13}C NMR (100 MHz,$CDCl_3$) δ 161.55, 161.40, 135.02,134.84, 127.68, 127.50, 127.40, 126.98, 126.82, 126.40, 126.31, 52.12, 46.44, 32.83, 28.15.



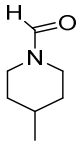
3,4-dihydro-2(1H)-isoquinolinecarbaldehyde: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.21 and 8.16 (m,1H), 7.16-7.08 (d,J=30.8 Hz, 4H), 4.63-4.48(m,2H), 3.73-3.59 (m, 2H), 2.85 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ160.83, 160.33, 133.55, 132.86, 131.58, 130.96, 128.32, 128.18, 126.25, 125.87, 125.75, 125.69, 125.16, 46.43, 42.38, 41.44, 37.16, 28.90, 27.13.



N-formylpyrrolidine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H),3.46-3.38 (d, J = 30.2 Hz,4H), 2.00-1.88 (m, 4H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 159.97, 45.19, 42.28, 24.10, 23.42.



1-(formyl)-hexahydro-1H-azepine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 3.41-3.33 (d, J = 31.3 Hz, 4H), 1.68 (s, 4H), 1.53 (s, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 161.49, 46.36, 42.05, 28.99, 26.72, 25.64, 25.59.



4-methyl-1-formylpiperidine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 4.33-4.30 (m, 1H),3.57-3.54 (m, 1H), 3.01 (s, 1H),2.59 (s, 1H), 1.65-1.62 (m, 3H), 1.18-1.03 (m, 2H), 0.93 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ159.41, 44.78, 38.54, 33.42, 32.03, 29.93, 20.44.

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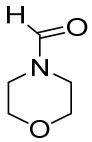
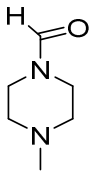
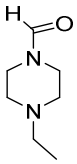


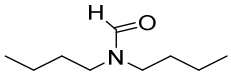
N-formylmorpholine: ^{1}H NMR (400 MHz, $CDCl_3$) δ8.05 (s, 1H), 3.70-3.68 (t, J = 4.9 Hz, 2H), 3.66-3.64 (t, J = 4.9 Hz, 2H), 3.57-3.54 (t, J = 4.9Hz, 2H), 3.43-3.40 (t, J = 4.9 Hz, 2H).^{13}C NMR (100 MHz,$CDCl_3$) δ 160.31, 66.68, 65.84,45.22, 40.02.



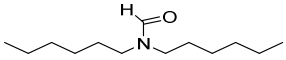
4-formyl-1-methylpiperazine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 3.54 (s, 2H), 3.36 (s, 2H), 2.44 – 2.35 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.90, 52.43, 51.47, 44.84, 43.72, 39.17.



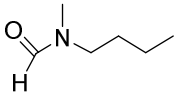
4-ethyl-1-formylpiperazine: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 3.52 (s, 2H), 3.36 (s, 2H), 2.39-2.35 (m, 6H), 1.06 (m, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 159.24, 51.77, 50.77, 50.58, 44.12, 38.45, 10.57.



N,N-dibutylformamide: ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.04 (s, 1H)3.29-3.27 (t, J = 5.8 Hz, 2H), 3.20-3.18 (t, J = 5.8 Hz, 2H),1.51 (s, 4H),1.32-1.29 (m, 4H), 0.94-0.92 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ161.76, 46.26, 40.94, 29.85, 28.52, 19.26, 18.74, 12.93, 12.77.



N,N-dihexylformamide:^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 3.28 (t, J=6.4 Hz, 2H), 3.18 (t, J=6.9 Hz, 2H), 1.52 (s, 4H), 1.29 (s, 12H), 0.89 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 47.4, 42.1, 31.5, 31.4, 28.6, 27.3, 26.6, 26.1, 22.6, 22.5, 14.0, 14.0.



N-butyl-N-methylformamide: ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.03 (s, 1H),3.33-3.29(t,

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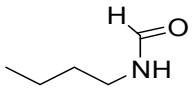
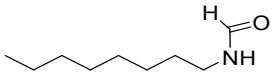
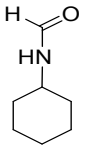
J = 6.0 Hz, 0.55H), 3.23-3.19 (t, J = 6.0 Hz,1.22H),2.91 (s, 1.0H), 2.83 (s, 2H), 1.52-1.50(m,2H), 1.29-1.26 (m, 2H), 0.94-0.91 (t, J = 5.8 Hz, 3H).^{13}C NMR (100 MHz,$CDCl_3$) δ161.71, 161.58, 48.38, 42.95, 33.65, 29.17, 27.88, 18.62, 17.87, 12.97, 12.81.



N-butylformamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-7.91 (m, 1H), 5.78 (s, 1H), 3.44-3.07 (m, 2H), 1.59-1.45 (m, 2H), 1.43-1.28 (m, 2H), 0.94 (m, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 160.77, 46.17, 39.94, 34.71, 33.27, 31.36, 21.72.



N-octylformamide:^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-7.91 (m, 1H), 5.53 (d, J = 149.5 Hz, 1H), 3.25 (m, 2H), 1.49 (m, 2H), 1.29 (d, J = 10.8 Hz, 9H), 0.88 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.57, 161.13, 77.35, 77.03, 76.71, 41.75, 38.20, 31.70, 31.65, 31.24, 29.52, 28.88, 28.78, 26.79, 26.34, 22.54, 14.01.



N-cyclohexylformamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09(s, 1H),5.54 (br, 1H), 5.89-5.29 (m, 1H), 3.96-2.75 (m, 1H), 1.99-1.85 (m, 2H), 1.80-1.57 (m, 3H), 1.44 -1.25 (m, 3H), 1.24-1.09 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.50, 160.26, 50.93, 47.09, 34.71, 33.05, 25.43, 25.04, 24.73.

4. Cartesian coordinate and energy of transition state at the B3LYP /6-31G* level

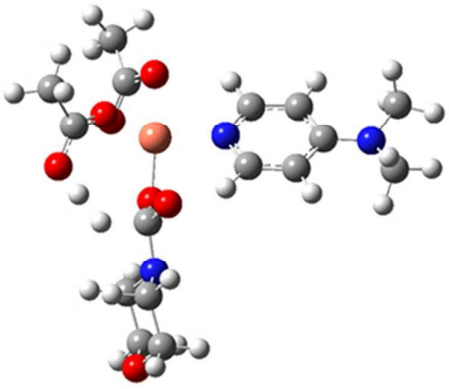


Figure S1. transition state for OAc- assisted hydrogen cracking

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transition state:

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29		-0.000001973	0.000001992	0.000001368
2	6		0.000000099	-0.000000167	-0.000000197
3	6		0.000000135	-0.000000061	0.000000133
4	6		0.000000000	-0.000000759	-0.000001612
5	1		0.000000181	-0.000000981	-0.000001339
6	6		0.000000058	-0.000000270	-0.000000846
7	1		0.000000015	0.000000237	0.000000720
8	6		-0.000000012	-0.000001221	-0.000002099
9	1		-0.000000004	-0.000000963	-0.000002182
10	1		-0.000000042	-0.000000183	-0.000000838
11	7		0.000000407	-0.000000615	-0.000001081
12	7		0.000000170	0.000000338	-0.000000856
13	6		-0.000000324	-0.000001761	-0.000004655
14	1		-0.000000610	-0.000000791	-0.000003318
15	1		-0.000000352	-0.000001494	-0.000004350
16	1		0.000000693	-0.000001890	-0.000003232
17	6		-0.000000338	-0.000000788	-0.000002581
18	1		-0.000000306	-0.000000312	-0.000002360
19	1		0.000000130	-0.000000903	-0.000002261
20	1		-0.000000222	-0.000000717	-0.000002808
21	8		-0.000000090	0.000000809	0.000004730
22	8		0.000001619	-0.000000227	0.000002118
23	6		-0.000000292	-0.000001767	0.000002708
24	6		-0.000000951	0.000001360	0.000003388
25	8		-0.000000487	-0.000001105	0.000000449
26	8		0.000000759	0.000001016	0.000001940
27	6		0.000001677	-0.000001432	0.000003548
28	1		0.000001739	-0.000002061	0.000003233
29	1		0.000001679	-0.000001587	0.000003629
30	1		0.000001467	-0.000001405	0.000003882
31	6		-0.000000211	0.000001208	0.000002519
32	1		0.000001133	0.000000214	0.000004657
33	1		0.000000402	0.000001723	0.000002472
34	1		-0.000000606	0.000002043	0.000004299
35	8		0.000000231	0.000000408	-0.000001457
36	6		-0.000002127	-0.000000186	-0.000000551
37	8		0.000001384	-0.000002630	-0.000000449
38	6		-0.000000679	0.000001421	-0.000000399

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39	6	0.000000250	-0.000000334	-0.000000501
40	6	-0.000000903	0.000001866	-0.000001095
41	1	-0.000000593	0.000001367	0.000000549
42	6	-0.000000353	0.000000298	-0.000001671
43	1	0.000000130	-0.000000626	-0.000001057
44	1	-0.000001199	0.000001993	-0.000001693
45	1	-0.000000393	0.000000046	-0.000001898
46	7	-0.000002332	0.000001254	0.000000585
47	8	-0.000000836	0.000001411	-0.000001379
48	1	-0.000001306	0.000002587	-0.000000780
49	1	-0.000000854	0.000001973	0.000000083
50	1	-0.000000025	-0.000000200	-0.000000260
51	1	-0.000000610	0.000000440	-0.000002246
52	1	-0.000001034	-0.000003186	0.000003684
53	1	0.000005707	0.000004617	0.000001354

SCF- Energy:B3LYP (PCM, THF)/6-31G* = -2956.149565 (a.u.)

5. Full citation of Gaussian program (Reference 44 details)

Gaussian 09, Revision A.1, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

6. References

S1. X. J. Cui, Y. Zhang, Y. Q. Deng and F. Shi, *Chem. Commun.*, 2014, **50**, 189-191.

S2. M. Cossi, G. Scalmani, N. Rega, V. Barone, *J. Chem. Phys.*, 2002, **117**, 43-54.