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Copper(II) catalyzed reaction of gaseous alkanes with amine *N*-oxides

Yuki Taniguchi [a,*], Tsugio Kitamura [a], Yuzo Fujiwara [a,*], Shiro Horie [b], Ken Takaki [b]

[a] *Department of Chemical Science and Technology, Faculty of Engineering, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812, Fukuoka, Japan*

[b] *Department of Applied Chemistry, Faculty of Engineering, Hiroshima University, Kagamiyama, Higashi-Hiroshima 739, Higashi-Hiroshima, Japan*

Abstract

Transition metal salts such as copper acetates catalyze the reaction of gaseous alkanes with *N,N*-dialkylmethylamine *N*-oxides in trifluoroacetic acid (TFA) to afford *N,N*-dialkylaminomethylated alkanes in good yields. Aminomethylation reaction of propane with trimethylamine *N*-oxide gave *N,N*-dimethylisobutylamine as a single regioisomer together with isopropyl trifluoroacetate. Ethane reacts with trimethylamine *N*-oxide affording *N,N*-dimethylpropylamine as a sole product. From the reaction of methane, methyl trifluoroacetate was obtained exclusively.

Keywords: Aminomethylation; Amine *N*-oxide; Copper acetate; Alkane; C–H Activation

1. Introduction

Activation and functionalization of inactive C–H bonds of gaseous alkanes have attracted a great attention recently, in connection with resources for energy and chemicals production [1]. Unreactive C–H bonds of saturated hydrocarbons can be also activated by transition metal complexes. We have reported that the $Pd(OAc)_2/Cu(OAc)_2/K_2S_2O_8$/trifluoroacetic acid (TFA) system can cause the carboxylation of alkanes such as cyclohexane, propane, ethane, and methane to give the corresponding alkanoic acids in high yields [2]. These reactions serve as novel C–C bond forming reactions *via* the alkane C–H bond activation by transition metal complexes. Although carbon–oxygen bond forming reactions to afford ketones, alcohols and esters from hydrocarbons by using various oxidants have been extensively studied [1,3,4], little is known on C–C bond forming reactions [5]. Aminomethylation of olefins with *sec*-amines catalyzed by transition metal catalysts such as niobium and tungsten has been reported [6]. The rhodium catalyzed reaction of olefins with CO, water, and amines has been known to cause aminomethylation of olefins [7]. However the corresponding reaction of alkanes is very rare. Recently, the mercury-photosensitized amination of alkanes has been reported by Crabtree et al. and a trace amount of aminomethylated product was obtained as a by-product [8]. In

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[*] Corresponding authors.

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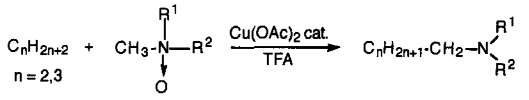
continuing studies on exploring synthetic reactions *via* thermal activation of alkane C–H bonds by transition metals, we have found that trimethylamine *N*-oxides react with gaseous alkanes in the presence of a catalytic amount of $Cu(OAc)_2$ giving the corresponding aminomethylated products. Herein we describe a novel reaction of methylamine *N*-oxides with gaseous alkanes such as ethane and propane in the presence of a catalytic amount of $Cu(OAc)_2$ to afford *N,N*-dialkylaminomethylated alkanes (Eq. (1)) [9].

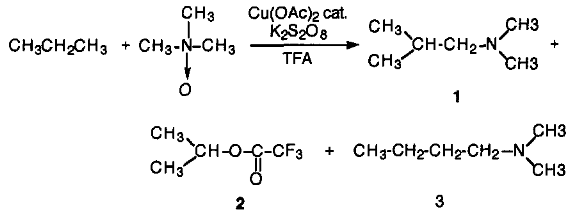


$$C_nH_{2n+2} + CH_3\text{-}\overset{R^1}{\underset{O}{N}}\text{-}R^2 \xrightarrow[\text{TFA}]{Cu(OAc)_2\text{ cat.}} C_nH_{2n+1}\text{-}CH_2\text{-}N(R^1)(R^2) \quad n = 2,3$$

(1)

2. Reaction of propane

We investigated the reaction of propane with trimethylamine *N*-oxide using transition metal catalysts in trifluoroacetic acid (TFA), and found that the $Cu(OAc)_2$ catalyst system gives high yields of *N,N*-dimethylisobutylamine (**1**) together with isopropyl trifluoroacetate (**2**) (Eq. (2)).



(2)

Table 1 summarizes the results of the reactions of propane (10 atm in an autoclave; 41 mmol) with anhydrous trimethylamine *N*-oxide (5 mmol) and $K_2S_2O_8$ (9 mmol) in TFA (5 mL) using various copper and palladium salts (0.05 mmol) under the conditions of 150°C for 20h. As is apparent from the table, the $Cu(OAc)_2/K_2S_2O_8$/TFA system gave the highest yield of aminomethylated product **1**.

Table 1
Effect of catalysts for aminomethylation of propane [a]

Run	Catalyst (mmol)	Product and yield (%) [b]			
		1		**2**	
1	none		(3.0) [c]		(7.3)
2	$Cu(OAc)_2$ (0.05)	1020	(10.2)	3140	(31.4)
3	$Cu(OAc)_2$ (0.1)	420	(4.2)	960	(9.6)
4	$Cu(OAc)_2$ (0.5)	40	(0.4)	98	(1.0)
5	$Cu(OAc)_2$ (1.0)	29	(0.3)	70	(0.7)
6	$Pd(OAc)_2$ (0.05)	360	(3.6)	440	(4.4)
7	$Pd(OAc)_2/Cu(OAc)_2$ (0.05 each)	920	(9.2)	300	(3.0)
8	$CuCl_2$ (0.05)	540	(5.4)	1500	(15.0)
9	CuCl (0.05)	520	(5.2)	800	(8.0)
10	$CuSO_4$ (0.05)	720	(7.2)	1860	(18.6)
11	Cu powder (0.05)	900	(9.0)	1140	(11.4)

[a] Conditions: C_3H_8 (10 atm), $(CH_3)_3N(O)$ (5 mmol), TFA (5 mL), $K_2S_2O_8$ (9 mmol), 150°C, 20 h.
[b] ^{1}H-NMR yield based on catalyst. Numbers in parentheses are the yields based on $(CH_3)_3N(O)$.
[c] *N,N*-Dimethylbutylamine (**3**) was also formed in 3.0% yield.

The reaction proceeded catalytically to give *N,N*-dimethylisobutylamine (**1**) and isopropyl trifluoroacetate (**2**) along with large amounts of trimethylamine. In this copper-catalyzed reaction of propane with trimethylamine *N*-oxide, *N,N*-dimethylbutylamine (**3**) was not obtained. In the absence of copper salt, the products **1**, **2**, and **3** were formed in 3.0, 7.3, and 3% yields based on trimethylamine *N*-oxide, respectively (run 1). Of the catalysts we tested, $Cu(OAc)_2$ was the best giving **1** and **2** in 1020 and 3140% yields based on Cu, respectively (run 2). When the amount of $Cu(OAc)_2$ was increased from 0.05 mmol to 1.0 mmol, the yields of **1** and **2** decreased to 29 and 70% yields based on Cu, respectively (run 5). $Pd(OAc)_2$ alone and $Cu(OAc)_2/Pd(OAc)_2$ mixed catalysts have lower catalytic activity.

Since it became apparent that $Cu(OAc)_2$ catalyst gave the best result, we further investigated the reaction of propane using various additives (Table 2). Addition of a small amount of $K_2S_2O_8$ (1 mmol) gave the best result for the yields of **1** (1400% on Cu) and **2** (520% on Cu) (run 3). Although the role of $K_2S_2O_8$ for aminomethylation is unknown, $K_2S_2O_8$ was not necessary for the esterification of propane (run

Table 2
Effect of additives for aminomethylation of propane [a]

Run	Additive (mmol)	Product and yield (%) [b]			
		1		**2**	
1	none	740	(7.4)	6200	(62.0)
2	$K_2S_2O_8$ (0.5)	860	(8.6)	580	(5.8)
3	$K_2S_2O_8$ (1.0)	1400	(14.0)	520	(5.2)
4	$K_2S_2O_8$ (3.0)	1320	(13.2)	1440	(14.4)
5	$K_2S_2O_8$ (5.0)	1060	(10.6)	1020	(10.2)
6	$K_2S_2O_8$ (7.0)	1160	(11.6)	1280	(12.8)
7	$K_2S_2O_8$ (9.0)	1020	(10.2)	3140	(31.4)
8	$KHSO_4$ (1.0)	1100	(11.0)	940	(9.4)
9	K_2SO_4 (1.0)	740	(7.4)	640	(6.4)
10	$(NH_4)_2S_2O_8$ (9.0)	800	(8.0)	620	(6.2)
11	PhCOOO^{t}Bu (9.0)	76	(0.8)	700	(7.0)
12	^{t}BuOOH (9.0)	0	(0)	0	(0)

[a] Conditions: C_3H_8 (10 atm), $(CH_3)_3N(O)$ (5 mmol), $Cu(OAc)_2$ (0.05 mmol), TFA (5 mL), 150°C, 20 h.

[b] ^{1}H-NMR yield based on catalyst. Numbers in parentheses are the yields based on $(CH_3)_3N(O)$.

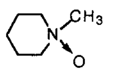
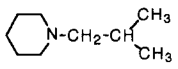
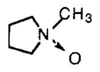
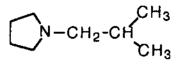
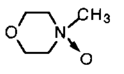
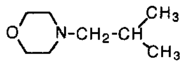
1). In the absence of $K_2S_2O_8$ the yield of **2** went up to 62% based on trimethylamine *N*-oxide, but the yield of **1** was very low. The similar ester formations from gaseous alkanes are reported by Sen et al. [3a–3b] and Moiseev et al. [3c]. The solvent effect was also examined to find that the uses of formic, acetic, and hydrochloric acids resulted in no reaction. Trifluoroacetic acid (TFA) was the best solvent for the reaction of propane. From these results, the best reaction conditions were determined to be 150°C for 20h under 10 atm C_3H_8 for the aminomethylation of propane.

In addition to trimethylamine *N*-oxide, other tertiary methylamine *N*-oxides such as *N*-methylpiperidine, *N*-methylpyrrolidine, and *N*-methylmorpholine *N*-oxides reacted with propane to afford the corresponding *N*-isobutyl-piperidine, -pyrrolidine, and -morpholine (Table 3). As described above, aminomethylation reaction of propane with methylamine *N*-oxides gave isobutylamines exclusively, which is consistent with the bond dissociation energy of propane C–H bonds and the greater stability of isopropyl radical with respect to n-propyl radical [10]. The aminomethylation occurred exclusively on the *N*-methyl group of amine *N*-oxides.

3. Reaction of ethane

Ethane also reacted with trimethylamine *N*-oxide giving *N*,*N*-dimethylpropylamine (**4**) exclusively. The representative results are shown in Table 4. In the case of aminomethylation of ethane, an addition of $K_2S_2O_8$ was ineffective (runs 2–4). The reaction conditions of 10 atm pressure of ethane and the reaction temperature at 150°C gave the best result affording propylamine **4** in 1460% yield based on Cu (14.6%

Table 3
Aminomethylation of propane [a]

Amine *N*-Oxide	Product	Yield (%)[b)]
		660
		180
		28

[a] Conditions: C_3H_8 (10 atm), $R_2N(O)CH_3$, (5 mmol), $Cu(OAc)_2$ (0.05 mmol), $K_2S_2O_8$ (1 mmol), TFA (5 mL), 150°C, 20 h.

[b] GC yields based on Cu.

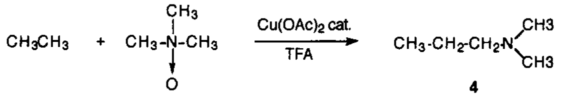
Table 4
Aminomethylation of ethane [a]

Run	Pressure (atm)	Temperature (°C)	Additive (mmol)	Yield of **4** (%) [b]
1	30	150	–	340
2	30	150	$K_2S_2O_8$ (1.0)	340
3	30	150	$K_2S_2O_8$ (3.0)	220
4	30	150	$K_2S_2O_8$ (9.0)	220
5	1	150	–	160
6	5	150	–	380
7	10	150	–	1460
8	20	150	–	600
9	10	80	–	0
10	10	120	–	0
11	10	180	–	880

[a] Conditions: $(CH_3)_3N(O)$ (5 mmol), $Cu(OAc)_2$ (0.05 mmol), TFA (5 mL), 20 h.

[b] ^{1}H-NMR yield based on catalyst.

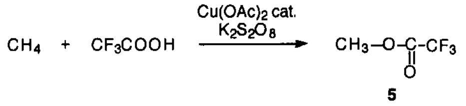
on amine *N*-oxide) (run 7). Similar reaction of ethane with *N*-methylpiperidine *N*-oxide gave *N*-propylpiperidine in 340% yield.



$$CH_3CH_3 + CH_3\text{-}\overset{CH_3}{\underset{O}{N}}\text{-}CH_3 \xrightarrow[TFA]{Cu(OAc)_2\ cat.} CH_3\text{-}CH_2\text{-}CH_2N(CH_3)_2 \quad \mathbf{4} \qquad (3)$$

4. Reaction of methane

Methane is the least reactive alkane, but one of the most abundant, and so selective conversion to useful chemical products is very valuable [1]. However, it is difficult to achieve because of its low reactivity. We tried the reaction of methane (40 atm) with trimethylamine *N*-oxide (10.0 mmol) and $K_2S_2O_8$ (9 mmol) in the presence of $Cu(OAc)_2$ (0.05 mmol) in TFA (5 mL) at 150°C for 20 h. From the reaction, methyl trifluoroacetate (**5**) was obtained in 2200% yield besed on $Cu(OAc)_2$ as a sole product without the formation of *N,N*-dimethyethylamine. Since methyl trifluoroacetate (**5**) was obtained in 2600% yield even in the absence of trimethylamine *N*-oxide, amine *N*-oxide is not necessary for the esterification of methane (Eq. (4)).



$$CH_4 + CF_3COOH \xrightarrow{\substack{Cu(OAc)_2\ cat.\\ K_2S_2O_8}} CH_3\text{–}O\text{–}\underset{O}{\underset{\|}{C}}\text{–}CF_3 \quad \mathbf{5} \qquad (4)$$

5. Conclusion

In summary, it was found that copper catalysts can promote the aminomethylation of alkanes with *tert*-amine *N*-oxides. The reactions shown in this article provided a potentially useful tool for alkane conversion to important chemicals because of high turnover numbers of the catalysts and high selectivities of the products.

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