[Letter]

Nickel(II)-Catalyzed Ethylation of Cycloalkane via Thermal C-H Bond Activation

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Nickel chloride catalyzes the ethylation of cyclohexane with ethylene to give ethylcyclohexane *via* thermal C-H bond activation. This ethylation proceeds catalytically with turnover number 31.

Alkane activation/functionalization under mild conditions is one of the most challenging fields of modern chemistry¹⁾. Recently, we reported the palladium-catalyzed carboxylation of alkanes such as cyclohexane²⁾, propane³⁾,⁴⁾, ethane, and methane⁴⁾.

Alkylation of cycloalkanes with olefins *via* C-H bond activation is very difficult, and drastic reaction conditions are required. Tanaka *et al.* reported the rhodium-catalyzed reaction of cyclooctane with ethylene under severe reaction conditions to give ethylcyclooctane and cyclooctene⁵⁾.

In our continuing work on C-H bond activation, we investigated the reaction of cycloalkanes with ethylene using transition metal complex catalysts. We have found that the reaction of cyclohexane with ethylene (10 atm) gives the corresponding ethylcyclohexane (**1**) in a high turnover of NiCl₂ catalyst under mild reaction conditions (Eq. (1)). We report here these results.

First, we examined the reaction of cyclohexane (5 ml) with ethylene (10 atm) using various transition metals (0.2 mmol) as catalyst and K₂S₂O₈ (9 mmol) as oxidant in trifluoroacetic acid (TFA, 3.3 ml) in a 100-ml stainless steel autoclave with stirring for 20 h at 120 °C. From this reaction, there were obtained ethylcyclohexane (**1**) along with vinyl trifluoroacetate (**2**) derived from the reaction of ethylene with TFA and small amounts of oligomers. The formation of vinyl trifluoroacetate (**2**) by transition metal catalysis is well known⁶⁾. The representative results are summarized in **Table 1**. Other unknown products were also formed in the case of palladium catalysts such as PdCl₂ and Pd(OAc)₂ (Entries 1 and 2, **Table 1**). The best result with Ni(OAc)₂ catalyst was obtained at 10 atm of ethylene pressure and 120 °C of reaction temperature (Entry 7, **Table 1**). Higher ethylene pressure and reaction temperature resulted in the complicate polymerization of ethylene, and the yield of ethylcyclohexane decreased. The catalytic activity under the same reaction conditions (120 °C, 10 atm) has been found to be in the order NiCl₂ > CoCl₂ ~ WCl₆ > NiBr₂ ~ Ni(OAc)₂ ~ NiO > FeCl₂ > MnCl₂ ~ SnCl₂ ~ Co(OAc)₂ ~ Mn(OAc)₂. In particular, the NiCl₂/K₂S₂O₈ system gives both higher yield of

ethylcyclohexane and selectivity (Entry 11, **Table 1**). In addition, the yield of ethylcyclohexane increased from 294 % to 414% (based on Ni) when the temperature of the mixture was elevated quickly to 120 °C by using an oil bath previously heated (quick heating method). As is apparent from **Table 1**, metal chloride catalysts seem to

Table 1 Transition Metal Catalyzed Ethylation of Cyclohexane^a

Entry	Catalyst	Temp, °C	Ethylene Press, atm	Yield, %	
				1 ^b	2 ^c
1	Pd(OAc) ₂	80	20	0.1	. ^d
2	PdCl ₂	80	20	tr ^e	. ^d
3	Ni(OAc) ₂	80	10	33	0.20
4		80	20	9	1.25
5		80	50	1	0.03
6		100	20	79	0.32
7		120	10	160	0.60
8	none	120	20	120	0.64
9		140	20	50	0.44
10		120	10	-	0.43
11		120	10	294(414) ^f	0.14(0.23) ^f
12		120	10	201	0.03
13		120	10	195	0.52
14		120	10	167	0.21
15		120	10	160	0.60
16		120	10	157	0.18
17		120	10	146	0.23
18	SnCl ₂	120	10	140	1.18
19		120	10	139	0.02
20		120	10	134	0.82
21		120	10	127	0.63
22		120	10	125	2.25
23		120	10	122	0.54
24		120	10	120	0.78
25		120	10	71	0.11
26		120	10	68	0.95
27	MnSO ₄	120	10	21	0.33

^aCyclohexane (5 ml), catalyst (0.2 mmol), K₂S₂O₈ (9 mmol), TFA (3.3 ml), 20 h.

^bGC yield based on catalyst. ^cGC yield based on TFA. ^dA large amount of unknown products were formed. ^eTrace amount. ^fQuick heating.

be somewhat effective for the reaction. But the addition of chloride ion sources such as NaCl, KCl, and LiCl to NiCl₂ was not effective. In contrast to metal chloride catalysts, metal sulfates were inactive in this reaction. The

yield of ethylcyclohexane (**1**) increases linearly with reaction time and with the increasing amounts of potassium persulfate ($K_2S_2O_8$), but it decreases with the use of a large excess because of the lower efficiency of stirring. It seems that $K_2S_2O_8$ abstracts $H\cdot$ from cyclohexane to give cyclohexyl radical. Use of other radical initiators such as AIBN, *tert*-butyl perbenzoate and oxidizing agents such as $(NH_4)_2S_2O_8$, OXONE ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) gave inferior results. Trifluoroacetic acid (TFA), a superacid has been found to be the best to accelerate the homolytic radical cleavage of O-O bond of $K_2S_2O_8$ ⁷). Other organic acids such as acetic and formic acids and usual organic solvents such as methanol were inactive.

Then, we examined the effect of the amount of $NiCl_2$ catalyst using the quick heating method. These results were listed in **Table 2**. The turnover number of catalyst increases up to 31 (Entry 4, **Table 2**) when the amount of $NiCl_2$ is decreased to 0.01 mmol, while the yield based on cyclohexane decreases.

Table 2 Effect of the Amount of Nickel Chloride^a

Entry	$NiCl_2$ (mmol)	Yield, %	
		1 ^b	2 ^c
1	0.2	414 (1.7)	0.23
2	0.1	702 (1.4)	0.22
3	0.05	932 (1.1)	0.86
4	0.01	3131 (0.9)	1.91
5	none	-	1.30

^aCyclohexane (5 ml), ethylene (10 atm), $K_2S_2O_8$ (9 mmol), TFA (3.3 ml), 120 °C, 20 h. ^bGC yield based on Ni (on cyclohexane). ^cGC yield based on TFA.

In order to investigate the reaction mechanism, we attempted the reaction with the use of radical scavenger. The ethylation was inhibited by an addition of 4-*tert*-butylcatechol, and no ethylation product was obtained.

Ethylation of adamantane was also investigated. In this reaction, 2-ethyladamantane (**3**) which is derived from ethylation on the secondary carbon of adamantane, was obtained in 178% yield based on Ni together with 1-ethyladamantane (**4**, 40% yield) (Eq.(2)). Use of 0.05 mmol of $NiCl_2$ and 1.0 mmol of $K_2S_2O_8$ gives ethylada-

mantanes (**3** and **4**) in 137 and 35% yields, respectively. These results show that ethylation on the bridge-head carbon (tertiary C) is difficult. On the other hand, palladium(II)-catalyzed carboxylation of adamantane in which electrophilic attack of cationic Pd species on the bridge-head carbon is most favorable, gave 1-

adamantanecarboxylic acid^{2a}). In the present reaction, regiochemistry of the products is the quite opposite to the case of Pd catalyst, showing that the reaction includes radical process.

The mechanism of the nickel-catalyzed ethylation of cyclohexane could be explained as depicted in **Scheme 1**

Scheme 1 Reaction Mechanism

1. K₂S₂O₈ acts as a radical initiator under the acidic media of TFA, and abstracts hydrogen radical (H•) from alkane C-H bond to give a cyclohexyl radical. The cyclohexyl radical generated reacts with nickel(II) catalyst to afford a σ -alkyl nickel(II) complex (A). Then, ethylene insertion followed by solvolysis with TFA yields ethylcyclohexane (1) and nickel(II) catalyst again and thus the catalytic cycle is completed.

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Keywords

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