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Copper-Catalyzed Allylic Oxidation of Cyclohexene with Molecular Oxygen

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Abstract

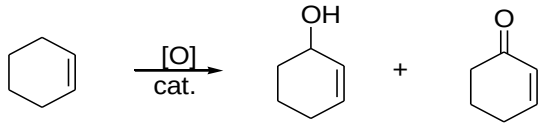
Copper-catalyzed aerobic allylic oxidation of cyclohexene under solvent-free conditions leads to 2-cyclohexenol and 2-cyclohexenone, the important intermediates in chemurgy. This pathway is suitable for industrial production, owing to the high conversion rate and selectivity, the solvent-free conditions, the cheap catalyst and the environment-friendly oxidant and procedure.

Keywords: Catalysis; Copper; Allylic Oxidation; Aerobic Oxidation; Cyclohexene.

1 INTRODUCTION

The allylic oxidation of olefins is one of the most important topics in both academic and industrial researches. In this process, olefins are converted to unsaturated alcohols or ketones while the C=C bond is preserved.[1] The allylic oxidation of cyclohexene is a typical example, since the products 2-cyclohexenol and 2-cyclohexenone are very useful compounds in chemurgy.[2] Up to the present, the catalytic allylic oxidation of cyclohexene has drawn much attention and many effective catalysts have been developed, such as metal nanoparticles,[3-5](Table 1, entries 1-3) metal–organic frameworks,[6](Table 1, entry 4) metal porphyrin complexes [7-9](Table 1, entries 5-7) and non-metal catalysts.[10](Table 1, entry 8) However, some of the above catalysts have resulted in low conversion rates and low selectivity, [6] on the other hand, many of them require organic solvents [3-5, 7-10, 12] and chemical oxidants.[3] Recently, gold has also been found to have strong catalic ability in the allylic oxidation of cyclohexene.[11-13](Table 1, entries 9-11) However, the high price hinders their large scale applications. The ideal catalytic oxidation process suitable for industrial production expected to employ molecular oxygen as the oxidant, simple and abundant catalyst, is carried out in solvent-free conditions.[14] Our group has been trying to achieve this goal in cyclohexene's oxidation for a long time. Recently, the transition metal-catalyzed allylic oxidation of cyclohexene has been investigated by molecular oxygen and it was found that catalyzed by copper, the oxidation of cyclohexene by molecular oxygen led to 2-cyclohexenol and 2-cyclohexenone with high conversion rate and selectivity in solvent-free conditions.(Table 1, entry 12) Herein, our findings were available.

TABLE 1 THE ALLYLIC OXIDATION OF CYCLOHEXENE REPORTED BY RECENT LITERATURES.



1 **2** **3**

Entry	Catalyst	Oxidant	Solvent	Conv. (%)	2+ 3 Select. (%)	Ref.
1	CuO	TBHP	CH_3CN	99	95	3
2	CoO	O_2	*c*-C_6H_{12}	97	80	4
3	CoHAP-γ-Fe_2O_3	H_2O_2	MeCN	88	81	5
4	Cu/Co-MOFs	O_2	-	33	44	6
5	Fe-Por	O_2	MeOH/MeCN	100	99	7
6	Mn-Por	O_2	MeCN	72	67	8
7	Ru-Por	O_2	MeCN	100	94	9

TABLE 1 THE ALLYLIC OXIDATION OF CYCLOHEXENE REPORTED BY RECENT LITERATURES (CONTINUE)

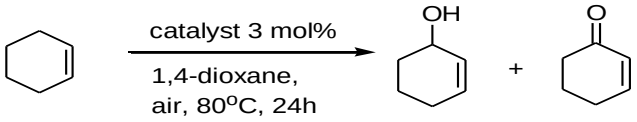
Entry	Catalyst	Oxidant	Solvent	Conv. (%)	2+ 3 Select. (%)	Ref.
8	NHPA + DADCAQ	O2	DMACa	84	69	10
9	Au/SiO_2	H_2O_2	-	68	80	11
10	Au/SBA-15-Py	O_2	toluene	54	57	12
11	Au/La-OMS-2	O_2	-	48	84	13
12	$Cu(OAc)_2{\cdot}H_2O$	O_2	-	66	79	This work

[a] N,N'-dimethylacetamide

2 RESULTS AND DISCUSSION

We initially examined the oxidation of cyclohexene in 1,4-dioxane catalyzed by $Cu(CF_3CO_2)_2$- MnO_2 *bi*-catalysts (Table 2, entry 1). After the mixture was stirred at 80°C in air for 24 hours, the GC analysis indicated that 63% of cyclohexene was converted and both cyclohexenol **2** and cyclohexenone **3** were generated with 11% and 31% selectivity respectively. Further investigations showed that phosphorus ligand would restrain the reaction (Table 2, entry 2) and both $Cu(CF_3CO_2)_2$ and MnO_2 could catalyze the reaction independently (Table 2, entries 3-4). The screenings (Table 2, entries 5-11) demonstrated that $Cu(OAc)_2H_2O$ was the better catalyst and the conversion rate of cyclohexene could reach 79 % with higher selectivity (Table 2, entry 8).

TABLE 2 SCREENING OF CATALYSTS IN 1,4-DIOXANE.[a]



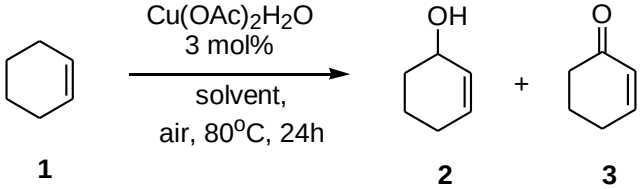
1 **2** **3**

entry	Catalyst (amount/mol%)	Conv. (%)	Select. of 2 (%)	Select. of 3 (%)	Select. of 2+3 (%)
1	$Cu(CF_3CO_2)_2$ (3), MnO_2 (9)	63	11	31	42
2	$Cu(CF_3CO_2)_2$ (3), MnO_2 (9), PPh_3 (12)	2	0	0	0
3	MnO_2 (9)	9	12	50	62
4	$Cu(CF_3CO_2)_2$ (3)	77	8	21	29
5	$Cu(NO_3)_2$ (3)	60	13	50	63
6	$CuBr_2$ (3)	19	27	26	53
7	$CuCl_2$ (3)	64	11	56	67
8	**$Cu(OAc)_2H_2O$ (3)**	**79**	**7**	**61**	**68**
9	$Mn(OAc)_3$(3)	10	28	72	100
10	$Ce(NH_4)_2(NO_3)_6$(3)	64	2	49	51
11	CuO (3)	67	14	32	46

[a] 1 mmol cyclohexene and 2 mL solvent was used; the catalyst amount was based on cyclohexene; The results were detected by GC.

Then, effects of solvents were examined and the reactions were taken in different solvents, such as 1, 4-dioxane, cyclohexane, EtOAc and so on (Table 3, entries 1-7). In terms of the balance of conversion and selectivity, 1, 4-dioxane was the better solvent (Table 3, entry 1). Although the selectivity of **2** and **3** was higher in cyclohexane, the conversion of cyclohexene was very low (Table 3, entry 2). Contrastively, the reaction in CH_3CN had the higher conversion of cyclohexene but the slightly lower selectivity of **2** and **3** (Table 3, entry 5). To enhance the conversion rate of cyclohexene in 1, 4-dioxane, pure O_2 was employed. Although this condition afforded a full conversion of cyclohexene, the selectivity decreased obviously and 1, 2-ethanedioldiformate, an oxydate of solvent, was also observed from GC-MZ (Table 3, entry 8; Scheme 1). Inspired by this result, we carried out the reaction in solvent-free conditions and the total selectivity was roughly satisfied (Table 3, entry 9).

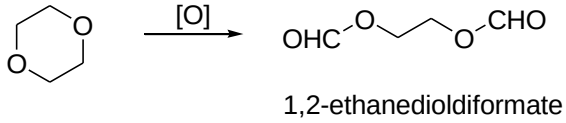
TABLE 3 SCREENING OF SOLVENTS.[a]



1 **2** **3**

Entry	solvent	Conversion (%)	Select. of 2 (%)	Select. of 3 (%)	Select. of 2+3 (%)
1	**1,4-dioxane**	**79**	**7**	**61**	**68**
2	cyclohexane	26	31	49	80
3	EtOAc[b]	58	13	24	37
4	DMSO	82	23	35	58
5	CH_3CN	94	18	49	67
6	DMF	38	35	39	74
7	Benzene[b]	44	24	28	52
8	1,4-dioxane[c]	100	3	46	49
9	-[c, d]	41	28	50	78

[a] 1 mmol cyclohexene, 3 mol % catalyst and 2 mL solvent was used. The results were detected by GC. [b] Reflux. [c] Pure O_2 and [d] 9.5 mmol of cyclohexene were employed.

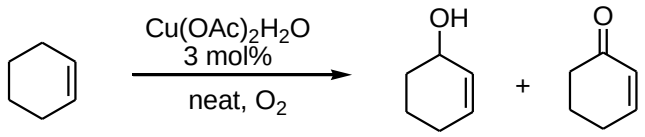


1,2-ethanedioldiformate

SCHEME 1 THE OXIDATION OF 1, 4-DIOXANE.

In industrial production, the reactions in solvent-free conditions could afford higher capacity than those taken in solvents. Therefore, although the conversion rate was lower, the result in table 3, entry 9, would be more effective than any other reactions taken in solvents. In order to gain more improved reaction conditions, further conditional screenings were taken (Table 4). Results in table 4, entries 1-5 showed that the conversion rate of cyclohexene was restrained at high temperature. However, the temperature did not significantly affect the total selectivity of 2 and 3. By comparison of the results in table 4, entries 2, 6 and 7, it was obvious that the reaction time greatly affected the conversion of cyclohexene. The best conditions in table 4 should be the results in entry 2. To examine its reliability in larger scale preparation, the reaction under this condition was also taken in a 10 time larger scale in a 1 L flask charged with O_2 and the product was separated by distillation. Cyclohexene was recovered in 34 % yield (66% conversion rate) while a 2/3 mixture was obtained in 52% yield (79% total selectivity).

TABLE 4 OXIDATION OF CYCLOHEXENE IN A SEALED TUBE WITHOUT SOLVENT.*A*

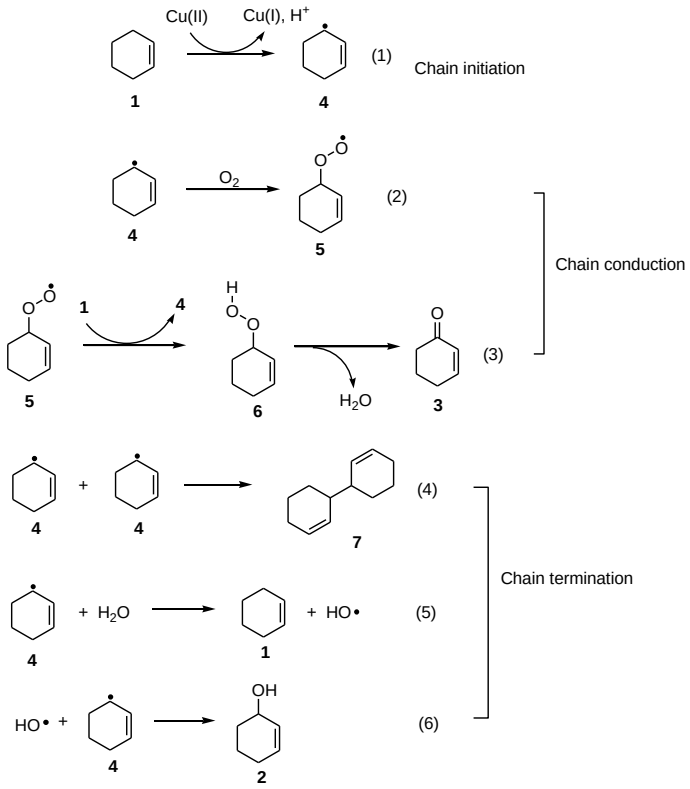


1 **2** **3**

entry	t/°C	t/h	Conv. (%)	Select. of **2** (%)	Select. of **3** (%)	Select. of **2**+**3** (%)
1	40	24	56	34	39	73
2	**60**	**24**	**61**	**30**	**47**	**77**
3	80	24	41	28	50	78
4	100	24	24	33	44	77
5	120	24	17	32	43	75
6	60	6	39	28	45	73
7	60	16	46	32	46	78

[a] 9.5 mmol of cyclohexene and 3 mol% of $Cu(OAc)_2 \cdot H_2O$ were heated in a 100 mL sealed tube charged with O_2; The results were detected by GC.

Based on the literatures [5-21] as well as our previous investigations, [22-23] it was proposed that the reaction underwent through a single-electron-transfer (SET) triggered by free radical mechanism. The SET reaction of Cu (II) [19] with cyclohexene 1 afforded the intermediate 4 and initiated the free radical chain (Scheme 2, *eq.* 1). The oxidation of 4 with O_2 led to the peroxide free radical 5 (Scheme 2, *eq.* 2), which seized hydrogen from 1 to generate the 3-hydroperoxy-1-cyclohexene 6 and regenerate the free radical 4. The dehydration of 6 gave the product cyclohexenone 3 (Scheme 2, *eq*. 3). There are two possible pathways in the chain termination step: (1) the dimerizations of free radical 4 lead to the by-product 7 (Scheme 2, *eq.* 4; This by-product was observed in GC-MZ analysis, further proving the mechanisms we supposed); (2) the hydrogen capture from water lead to the starting material 1 and hydroxyl free radical, which reacted with the free radical 4 to give another product 2 (Scheme 2. *eq.* 5 and 6).



SCHEME 2 PROPOSED MECHANISMS.

3 CONCLUSIONS

In conclusion, copper-catalyzed oxidation of cyclohexene with molecular oxygen afforded the mixture of 2-cyclohexenol and 2-cyclohexenone. In industrial production, the catalyzed dehydrogenation of 2-cyclohexenol easily led to 2-cyclohexenone, useful intermediates in herbicide production. Therefore, this reaction is potentially useful in the production of 2-cyclohexenone. Compared with literatures, our method has the following advantages: (1) The cheap catalyst; (2) The abundant and clean oxidant; (3) The highly atom economic procedure; (4) The solvent-free conditions and the satisfied product selectivity. Our group is now trying to apply this method in larger scale preparation.

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