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One-step catalytic cyclohexane oxidation to adipic acid using molecular oxygen

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Using combination of Mn–Co transition metal species with *N*-hydroxyphthalimide as a catalyst for one-step oxidation of cyclohexane with molecular oxygen in acetic acid at 353 K can give more than 95% selectivity towards oxygenated products with adipic acid as a major product at a high conversion (ca. 78%). A turnover number of 74 for this partial oxidation are also recorded.

KEY WORDS: adipic acid; one-step oxidation; catalyst; cyclohexane oxidation; *N*-hydroxyphthalimide; radical; selectivity.

1. Introduction

A considerable research effort has been made to develop efficient methods for oxidation of unactivated C–H bonds of alkanes because of the importance of the substrates in view of both industrial and synthetic aspects [1–7]. Catalytic oxidation of alkanes has been explored using different oxidants [8], and those reactions with molecular oxygen under mild conditions [9] are especially rewarding due to its cheap availability and production of H_2O as the main harmless by-product. However, the oxidation of cyclohexane turns out to be the least efficient of all major industrial processes [10]. At present, the industrial oxidation of cyclohexane to adipic acid undergoes a two-step process. The first step involves oxidation of cyclohexane to cyclohexanone and cyclohexanol at around 423 K and 1–2 MPa pressure using either a soluble cobalt catalyst or no catalyst, in the liquid phase, in which the total cyclohexane conversion is less than 4%. Under such low conversion the selectivity towards cyclohexanol and cyclohexanone (KA oil) can be optimized at 70–85% without much over-oxidation of the products [11–13]. The second step involves oxidation of the KA oil to adipic acid *via* the use of nitric acid as a mild oxidant. The side product produced from this step includes nitrous oxide (N_2O), which shows a global warming effect of 300 times higher than carbon dioxide. Research is on going to improve reaction selectivity of this two-step process. For example, addition of boric acid to the oxidation mixture proved to be effective, which allowed approximately 10% conversion of cyclohexane with 90% selectivity for KA oil [14]. Murahashi *et al.* reported the oxidation of cyclohexane over iron powder and observed 11% conversion with 95% selectivity to KA oil [15]. However, finding a one-step method for manufacturing adipic acid from cyclohexane without producing NOx is the most urgent issue from the viewpoint of green chemistry. There have been some interesting work led by Thomas and co-workers in using molecular sieve catalysts with active site isolation for the direct oxidation of cyclohexane to adipic acid in gas phase (solvent free) [16,17]. In a similar line of research, Moden *et al.* have claimed the selective nature of MnAPO-5 catalysts for the cyclohexane oxidation [18].

Considering the key challenge in the cyclohexane oxidation to adipic acid from reaction mechanistic aspects, it may require a catalytic system to activate C–H of the molecule probably *via* generation of alkyl radicals, followed by a specific breakage of one C–C bond to cause ring opening before further oxidations of both terminal ends to the acid functionality. However, product and reaction intermediates containing C–H and C–C bonds will be equally susceptible for attack by the same catalyst system at a high level of conversion. There have been some attempts to initially generate cyclohexanyl radical in the presence of radical initiator by thermal process. However, this auto-oxidation procedure requires harsh reaction conditions with the reactions being carried out under high temperatures [19]. Under such conditions both the homolytic cleavages of C–H and C–C bonds will take place leading to a poor selectivity to adipic acid. Until now, there has been no satisfactory general method for homolytic cleavage of the carbon-hydrogen bond of alkanes under mild conditions to selectively produce carbon radicals. In order to accomplish this, a new method for the generation of carbon radicals under mild conditions is required. Such a method may become an indispensable tool for organic synthesis. Recently, researchers found that phthalimide *N*-oxyl (PINO) radical, generated from *N*-hydroxyphthalimide (NHPI) [20], abstracts a hydrogen atom from

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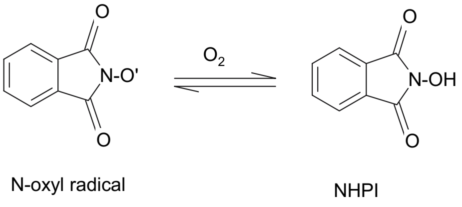
the carbon–hydrogen bond of various hydrocarbons including alkanes, alcohols, ethers, acetals, and aldehydes under mild conditions, and forms the corresponding carbon radical with high selectivity and high catalytic efficiency. *N*-hydroxyphthalimide has been named a "Carbon Radical Producing Catalyst" (hereafter CRPC). The NHPI enables production of oxygen-containing compounds, such as ketones and carboxylic acids, from alkanes. This NHPI also facilitates the addition of functional groups to alkanes, resulting in nitroalkanes, alkyl sulfonic acids, and oxyalkylates under mild conditions with high selectivity, both of which were difficult to accomplish previously. It is noted that a preliminary study from Iwahama *et al.* [21] on the oxidation of cyclohexane using CRPC has recently been carried out. *N*-oxyl radical is thought to be the key active species during the oxidation of cyclohexane to cyclohexanone and adipic acid in the presence of NHPI (see Scheme 1) [21]. Thus, the presence of catalyst species such as Co(II) or Mn(II) species may assist the smooth generation of *N*-oxyl radical from NHPI and molecular oxygen and promote the redox degradation of the resulting cyclohexyl hydroperoxide, which will be eventually converted into adipic acid.

This short paper is to carry out a preliminary study on the one-step conversion of cyclohexane to adipic acid using NHPI as a radical catalyst in the presence of a small amount of a transition metal. It is found that the mixture of NHPI and Co/Mn species as a catalyst shows the best catalytic performance under our conditions. The catalyzed reaction gives >95% selectivity to partially oxidized di-acid products (adipic acid (C6); glutaric acid (C5) and succinic acid (C4)) in liquid phase at *ca.*78% conversion. The optimized selectivity towards the adipic acid for this one-step catalytic oxidation is of about 65%.

2. Experimental



Scheme. 1 A possible involvement of *N*-oxyl radical from NHPI during cyclohexane oxidation in the presence of O2 and Mn(II)/Co(II).

Typically, the liquid phase oxidation of cyclohexane was conducted as follows: First, manganese(II) acetylacetonate and cobalt(II) acetate tetrahydrate were added into a 300 mL Parr autoclave pressure reactor. *N*-hydroxyphthalimide was then added as the radical catalyst followed by adding a known amount of acetic acid as solvent with cyclohexane pre-dissolved in it. Finally, the autoclave reactor was closed and pure oxygen was charged at room temperature. The high-pressure reactor was heated up to a desired temperature. The reaction was allowed to react for 8 h excluding the time for the reactor to reach the desired reaction temperature. After reaction the reactor was then cooled down to −60 (C in a dry-ice/acetone bath prior to connecting the gas outlet of the reactor to a two stage solvent trap containing dichloromethane (DCM) (Fisher, 99+%), followed by releasing the pressure to these vessels. Later, methanol (Fisher, 99+%) was used to wash the ice-like reaction mixture from the reactor. All solution was transferred into an ice cooled 250 mL volumetric flask *via* an anhydrous $MgSO_4$ filter. In order to wash any remaining product the reactor was washed twice with 20 mL methanol at 85 (C. All of the solutions after the washing were finally collected in the 250 mL volumetric flask. This methanol solution was then marked as Solution A-1 for cyclohexane analysis with GC-MS with toluene as the external standard.

To analyze this solution for any oxygenate products, the volume of Solution A-1 was reduced to minimum by rotary evaporator with water bath set at 50 (C. Then, 40 mL methanol, 10 mL water and a catalytic amount of concentrated sulphuric acid were added to the resulting mixture, and the solution was stirred at 65 (C for 15 h in order to complete the esterification process (this step is necessary to determine the high boiling acid products by GC-MS, for example, methanol reacts with adipic acid to give dimethyladipate ester). After that, certain amount of sodium hydrogen carbonate was added to the esterification solution until there was no more gas bubble coming out from the solution. Then, rotary evaporator was used to reduce the volume of the reaction mixture with water bath set at 40 (C, where most of the water contented should be remained as two solution layers appeared after methanol was removed. The solution was then transferred into a 250 mL separation flask with 30 mL of diethyl ether added to extract any oil soluble products. The upper layer, which was the diethyl ether solution, was transferred into an ice cooled 250 mL volumetric flasks (Solution A-2) via a filter containing 1 g of anhydrous $MgSO_4$ in order to dry and to filter the solution. The extraction was repeated for another four times. The last extraction was conducted with the same manner as the previous extractions except a known amount of sodium chloride (NaCl) was used to saturate the aqueous layer in order to reduce the solubility of any remaining organic oxygenates from the aqueous layer. Identification and quantification of oxygenates obtained after the reaction were then conducted with GC-MS. 10 mL Solution A-2 and 0.3 mL 0.030 M toluene/methanol were transferred into a 25 mL volumetric flask and made up to 25 mL with diethyl ether (Solution D-1). Different oxygenates could then be identified from their mass spectra. The concentration of a number of the mainly observed oxygenates were determined according to previously obtained calibration curves, where toluene was used as the external standard.

3. Results and discussion

The quantity of reactants, reaction time and temperature used are summarized in Table 1. According to the above analytical conditions, the total cyclohexane conversions and the conversions to oxygenate were determined and are also summarized in Table 2. It is noted that acetic acid appeared to be essential for the liquid phase oxidation of cyclohexane as the absence of acetic acid in Trial 10 produced a poor cyclohexane conversion. It seems that acetic acid plays a main role in bringing the cyclohexane, NHPI and the catalyst (tradition metal salts) into a single phase to facilitate the catalysis. Thus, in the presence of acetic acid all reactants can be mixed and reacted in a homogeneous phase.

By comparing Trial 1 and Trial 2 with different cyclohexane to O_2 molar ratios where the O_2 was increased from 1:2.7 to 1:5.3, there appeared no significant change in terms of the total cyclohexane conversion and the selectivity towards the oxygenates. Apart from that, there was also no observable change in their TONs. Also, by comparing Trial 6 and Trial 7 with different cyclohexane to O_2 molar ratios where the O_2 content was increased from 1:5.3 to 1:7.1, there was also no significant change in terms of selectivity towards the oxygenates and the TONs. It is generally known that oxygen solubility is low in organic solvents despite a high pressure of di-oxygen applied. Thus, these findings could suggest that there might have been limited oxygen availability in the acetic acid. The amount of dissolved oxygen (20 bars) remained unchanged in the reaction medium, which might have limited the rate of oxidation despite the change of the alkane concentration.

N-hydroxyphthalimide was used as a radical catalyst in this series of trials. The NHPI used in Trial 2, Trial 3 and Trial 4 was decreased from 10% in Trial 2 to 5% in Trial 3 then to 1% in Trial 4. (The % of NHPI used was with respect to the total number of moles of cyclohexane added in the trial). It is interesting to note that the decrease of NHPI produced a decrease in the total conversion of cyclohexane. However, it is more interesting to observe that there was an increase in the selectivity towards oxygenates when the use of NHPI was decreased. By comparing the conversion of cyclohexane to all oxygenates with the overall conversion of cyclohexane in each case, there was apparently a major carbon lost during the oxidation due to the over-usage of the radical catalyst. It is interesting to find that the more radical catalyst we placed in the reactor, the higher the chance for oxygenates to undergo further oxidations, leading to a higher conversion but associated with a poorer selectivity. This observation clearly implies that the selectivity towards oxygenates of this catalytic oxidation reaction can be optimized by primarily varying the concentration of the radical catalyst used.

As seen from Trials 3, 5 and 6, the use of Mn–Co in Trial 6 produced a 100% cyclohexane conversion, which indicated that Mn–Co works as a better catalyst pair in terms of catalytic activity. Mn was not as good as Mn–Co but better than Co alone in terms of catalytic activity. It is noted that the catalytic oxidation of cyclohexane with Mn as a catalyst in Trial 3 gave a total conversion of cyclohexane of 73% and 28.8% of which were oxygenates which contained 15.2% of dimethyl succinate, 19.6% of dimethyl glutarate and 65.2% of dimethyl adipate. Also, the reaction encountered a carbon loss of 71.2%. The main reason for the carbon lost could due to the further oxidation of cyclohexane to volatile products such as carbon monoxide, carbon dioxide and probably to carbonaceous residue, which, unfortunately, cannot be detected by the current analytical protocols.

In order to obtain the best total cyclohexane conversion and the best selectivity towards oxygenates

Table 1
A table summarized all the oxidation reactions conducted in this study

Trial	Acetic acid (mL)	C_6H_{12} mL	O_2 bar	C_6H_{12}:O_2 molar ratio	Catalyst [d] (%)	NHPI [d] (%)	Temperature (K)	Time (h)
1[b]	20	5	20	1:2.7	Mn 1	10	373	8
2[c]	20	5	20	1:5.3	Mn 1	10	373	8
3[c]	20	5	20	1:5.3	Mn 1	5	373	8
4[c]	20	5	20	1:5.3	Mn 1	1	373	8
5[c]	20	5	20	1:5.3	Co 1	5	373	8
6[c]	20	5	20	1:5.3	Mn–Co 1	5	373	8
7[a]	5	1.25	20	1:7.1	Mn–Co 1	5	373	8
8[a]	5	1.25	20	1:7.1	Mn–Co 1	5	353	8
9[a]	5	1.25	20	1:7.1	Mn–Co 1	5	343	8
10[a]	0	1.25	20	1:7.1	Mn–Co 1	5	353	8

[a] 100 mL reactor used;
[b] 150 mL reactor used;
[c] 300 mL reactor used;
[d] % with respect to the total number of mole of cyclohexane added.

Table 2
A table listed all catalytic performances according to conditions in Table 1

Trial	Conversion to Oxygenates/%	TON/h^{-1}[a]	Total cyclohexane conversion/%	Selectivity to Oxygenates/%
1	12.4	12.1	58	21.3
Products	Dimethyl succinate (20.3%); Dimethyl glutarate (20.8%); Dimethyl adipate (58.9%)			
2	13	12.7	64	20.3
Products	Dimethyl succinate (20.6%); Dimethyl glutarate (23.2%); Dimethyl adipate (56.2%)			
3	21	20.6	73	28.8
Products	Dimethyl succinate (15.2%); Dimethyl glutarate (19.6%); Dimethyl adipate (65.2%)			
4	9.7	9.7	23	42.2
Products	Methyl hydracrylate (2.3%); Cyclohexanol (2.7%); Butyrolactone (7.7%); Dimethyl succinate (9.8%); Dimethyl glutarate (15.5%); Dimethyl adipate (62.0%)			
5	1.3	1.3	58	2.2
Products	Methyl hydracrylate (10.5%); Cyclohexanol (7.3%); Dimethyl succinate (14.0%); Dimethyl glutarate (19.7%); Dimethyl adipate (48.5%)			
6	12	11.6	100	12.0
Products	Methyl hydracrylate (8.5%); Cyclohexanol (8.9%); Butyrolactone (5.1%); Methyl-4-hydroxybutanoate (4.9%); Dimethyl succinate (8.2%); Dimethyl glutarate (12.9%); Dimethyl adipate (51.6%)			
7	11	16.6	100	11
Products	Methyl hydracrylate (3.3%); Cyclohexanol (1.6%); Butyrolactone (2.7%); Dimethyl succinate (7.6%); Dimethyl glutarate (15.2%); Dimethyl adipate (69.5%)			
8	74	74.2	78	94.9
Products	Methyl hydracrylate (1.2%); Cyclohexanol (2.2%); Butyrolactone (0.6%); Dimethyl succinate (9.4%); Dimethyl glutarate (18.6%); Dimethyl adipate (68.0%)			
9	Trace	–	5	–
Products	Dimethyl adipate (Trace)			
10	0.8	0.8	7	11.4
Products	Cyclohexanol (33.1%); Cyclohexanone (34.7%); 1, 1-Dimethoxycyclohexane (14.3%) Dimethyl adipate (17.9%)			

[a] TON = [(Total number of mole of oxygenates produced) / (Total number of mole of metal ion)].

with a minimum carbon lost, the temperature of the reaction was altered from 373 K in Trial 7 to 343 K in Trial 9. It was evident that a good carbon balance was obtained in Trial 8 where the total cyclohexane conversion was 78% with 74% of the starting cyclohexane converted to oxygenate. Therefore, a carbon balance (selectivity towards oxygenates) of 95% was obtained. It was noted that amongst the 74% cyclohexane conversion to oxygenates, 68% of that was the dimethyl adipate. Thus, there was a 50% conversion of cyclohexane to adipic acid in a single step oxidation, which represented the best result from this present study.

4. Conclusion

To summarize this new preliminary study, we have shown that the combination of Mn(II) and Co(II) is an efficient catalyst for the one-step aerobic oxidation of cyclohexane to adipic acid, displaying a much higher activity than Co(II) and Mn(II) alone. On the other hand, Co–Mn is the best catalyst in term of selectivity towards oxygenates under the conditions studied. Also we observed in this study there is a direct proportional relationship between the cyclohexane conversion and the amount of catalyst initiator "NHPI". However, regarding selectivity towards oxygenates the relationship becomes the opposite. Equally, the same trends were found with respect to the temperature effect. These reflect the major challenge of selective oxidation of organic molecules where higher substrate conversion will associate with lower selectivity due to the problems of 'over-oxidation' of the products. Bearing in mind that the main goal of "green chemistry" is to achieve both high conversion and high selectivity for cyclohexane with producing fewer harmful products to the environment, thus the present preliminary result showing more than 50% yield of adipic acid from the single-step aerial oxidation of cyclohexane using NHPI/transition metal ion without using nitric acid represents a promising new direction.

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References

[1] D.H.R. Barton, N. Ozbalik, in: *Activation, Functionalization of Alkanes*, ed. C.L. Hill. (John Wiley, New York, 1989) pp. 281.

[2] D.H.R. Barton, S.D. Beviere, W. Chavasiri, E. Csuhai, D. Doller and W.G. Liu, J. Am. Chem. Soc. 114 (1992) 2147.

[3] D.H.R. Barton and W. Chavasiri, Tetrahedron 50 (1994) 19.

[4] U. Schuchardt, W.A. Carvalho and E.V. Spinac, Syn. Lett. 713 (1993).

[5] E.V. Spinace, H.O. Pastore and U. Schuchardt, J. Catal. 157 (1995) 631.

[6] U. Schuchardt, R. Pereira, C.E.Z. Kraembuhl, M. Rufo and R. Buffon, Appl. Catal A 131 (1995) 135.

[7] K.W. Lee, S.B. Kim, K.W. Jun and E.K. Shim, New J. Chem 17 (1993) 409.

[8] D.H.R. Barton, Tetrahedron 46 (1990) 3743.

[9] C. Sheu, A. Sohkowiak, S. Jeon and D.T. Sawyer, J. Am. Chem. Soc. 112 (1990) 879.

[10] KV. Ingold, Aldrichimica Acta 22 (1989) 69.

[11] N. Sawatari, T. Yokota, S. Sakaguchi and Y. Ishii, J. Org. Chem. 66 (2001) 7889.

[12] L. Simandi, *Catalytic Activation of Dioxygen by Metal Complexes* (Kluwer Academic Publisher, Netherlands, 1992).

[13] G.W. Parshall and S.D. Ittel, *Homogeneous Catalysis* (Wiley, New York, 1992).

[14] S. Ciborowski, in: *Studies in Surface Science and Catalysis*, ed. L. I. Simandi. (Elsevier, Amsterdam, 1991).

[15] S.I. Murahashi, Y. Oda and T. Naota, J. Am. Chem. Soc. 114 (1992) 7913.

[16] J.M. Thomas, R. Raja, G. Sankar, B.F. Johnson, D. Lewis, Chemistry (Weinheim an der Bergstrasse, Germany, 2001) 7:2973.

[17] J.M. Thomas, R. Raja, G. Sankar, R.G. Bell, Accounts of chemical research 34, (2001), 191 and references therein.

[18] B. Moden, B.Z. Zhan, J. Dakka, J.G. Santiesteban and E. Iglesia, J. Catal. 239 (2006) 390.

[19] A.K. Suresh, M. Sharma and T. Sridhar, Ind. Eng. Chem. Res. 39 (2000) 3958.

[20] Y. Ishii, J. Mol. Catal. A-Chem. 117 (1997) 123.

[21] T. Iwahama, K. Syojyo, S. Sakaguchi and Y. Ishii, Org. Process Res. Dev. 2 (1998) 255.