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EXCELLENT SYNTHESIS OF ADIPIC ACID

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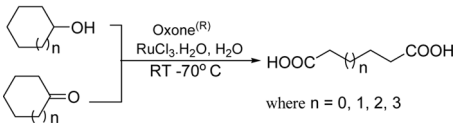
GRAPHICAL ABSTRACT



Abstract *A simple, straightforward, and environmentally benign protocol for the synthesis of adipic acid from oxidation of cyclohexanone with Oxone® in the presence of 0.5 mol% $RuCl_3 \cdot nH_2O$ is reported. The reaction completes within a very short time even at room temperature. The generality of the method is shown successfully for synthesis of other C-5 to C-8 dicarboxylic acids.*

Keywords Adipic acid; oxidation; Oxone; ruthenium chloride; water

The industrial application of adipic acid in the production of Nylon-6 along with increased environmental concerns associated with the traditional method of using nitric acid[1] as oxidant for oxidation of cyclohexanone or a cyclohexanone/cyclohexanol mixture have led to the development of a number of methods for its synthesis. There are only a few methods that carry all the traits to justify themselves as environmentally and industrially benign. Use of oxidizing agents such as $KMnO_4$,[2,3] CrO_3,[4] or KO_2[5] lack the desired ingredients to attract industry because of tedious purification process from their deoxygenated counterparts, while use of oxygen as the oxidizing agent in the presence of the catalyst uses hexamethyldisilazane (HMPA) or acetic acid as solvent. Recently, Sato et al.[6] reported the use of 30% hydrogen peroxide as oxidizing agent in the presence of a catalytic amount of tungstic acid for the synthesis of adipic acid from cyclohexanol/cyclohexanone. Although easy separation technique, easily available or by-product-free reagent system, and good conversion are the keys to judge its efficacy, use of high temperature (at 90 °C) for about 20 h left further scope for better energy- and time-efficient protocols.

Use of Oxone®, a potassium triple salt with potassium monopersulfate as an oxidizing agent, is finding a lot of applications in oxidation of boron, nitrogen,

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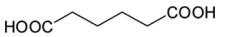
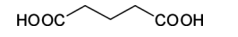
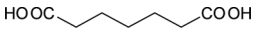
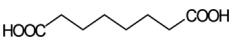
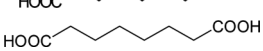
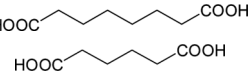
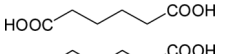
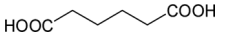
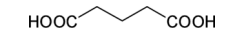
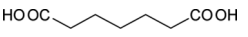
sulfur, and phosphorus compounds.[7] It has already been demonstrated that Oxone is very useful for epoxidation of olefins, oxidation of aldehydes to carboxylic acids and esters, oxidative cyclization, and cleavage of olefins. Being a water-soluble and nonhazardous solid reagent, its application is further bolstered by a recent surge of consciousness for design and development of reaction protocols using environmentally benign reagents and solvent. In continuation of our recent interest in Oxone-mediated epoxidation of olefins[8] coupled with the versatility of Oxone as powerful oxidizing source, we wanted to explore the applicability of Oxone for the synthesis of adipic acid.

Initially, we tried to oxidize cyclohexanone dissolved in acetonitrile by heating with an aqueous solution of Oxone at 60 °C. Unfortunately, formation of the desired adipic acid was not observed even after 36 h. This finding led us to believe that Oxone, by itself, may not be robust enough to accomplish this oxidation, but we decided to look for a catalyst that can change the reactivity profile of Oxone. Because Ru catalysts, such as RuO_2 and RuO_4, are known oxidizing agents,[9] we decided to use $RuCl_3 \cdot nH_2O$ as catalyst for the conversion. A literature survey revealed that a similar oxidizing system has already been developed by Bressan et al., consisting of water-soluble metal sulfophthalocyanines and Oxone to oxidize cyclohexanone to adipic acid.[10] We reasoned that instead of $RuCl_3 \cdot nH_2O$-derived complexes, if $RuCl_3 \cdot nH_2O$ can be used directly, it may lead to the development of a more user-friendly protocol. To that effect, when the aforesaid reaction was carried out in the presence of 1 mol% $RuCl_3 \cdot nH_2O$, we could observe the complete conversion of cyclohexanone to adipic acid within 4 h. Here, we encountered a problem in purification of the product, because the sulfate derivatives of Oxone also gave solid precipitates upon cooling. Finally, it was averted by diluting the reaction mixture with ethanol and cooling the mixture at 5–10 °C overnight. The solid sulfates were filtered off, and the filtrate was cooled to 0 °C to get the solid adipic acid in absolutely pure form. Following our successful attempt to purify adipic acid, we tried the same reaction in the absence of acetonitrile only to find that the reaction works well here, too. It is interesting to note that reaction in water takes less time (2 h) than in an acetonitrile–water mixture (4 h).

In our effort to optimize the amount of Oxone required for the reaction, we observed that use of 2 equiv. of Oxone generated adipic acid in 62% yield only, whereas use of 3 equiv. of Oxone gave 83% yield. Optimum conversion was found by using 4 equiv. of Oxone to obtain the purified product in 98% yield. The optimum amount of the catalyst, $RuCl_3 \cdot H_2O$, was determined by keeping the ratio of cyclohexanone and Oxone (1:4) constant and varying the amount of the catalyst. It was observed that 0.5 mol% of the catalyst is optimum and an increase of catalyst ratio up to 1 mol% affected neither the yield nor the reaction time. Use of 0.1 mol% of the catalyst led to increase in the reaction time (4 h) but gave a similar yield. Increase in reaction temperature up to 70 °C had only a little effect on the rate of the reaction: the reaction underwent completion within 1.5 h at 70 °C as compared 2 h at 25 °C.[11] Having optimized the aforementioned parameters, we extended the applicability of our method to synthesize C-5 to C-8 dicarboxylic acids from their corresponding cyclic ketones. When the reaction was carried out with cyclic alcohols, it was observed that reaction is very slow at RT and the percentage of yield also gets adversely affected. Increasing the reaction temperature to 70 °C considerably reduces the reaction time as well as enhances the yields. Our results are summarized in Table 1.

It has been observed that reactions of cyclohexanone and cyclopentanone with Oxone–$RuCl_3 \cdot H_2O$ reagent system undergo completion within a very short reaction

Table 1. Oxidation of cyclic ketones and alcohols via Scheme 1[a,b]

Entry	Substrate	Time (h)	Yield	Product
1	Cyclohexanone	2[c]	98	
2	Cyclopentanone	5[c]	90	
3	Cycloheptanone	7[c]	75	
4	Cyclooctanone	16[c]	49	
5	Cyclooctanone	6[d]	81	
6	Cyclohexanol	20[c]	73	
7	Cyclohexanol	6[d]	92	
8	Cyclopentanol	8[d]	95	
9	Cycloheptanol	8[d]	78	
10	Cyclooctanol	8[d]	89	
11	Octan-3-one	10[d]	—	No reaction

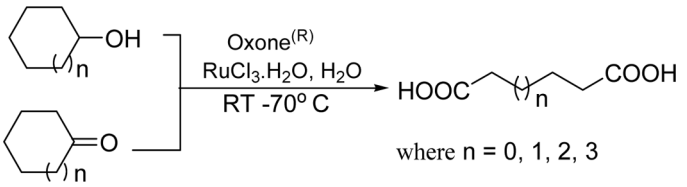
[a]Ratio of ketone Oxone $RuCl_3 \cdot nH_2O = 1{:}4{:}0.005$.
[b]Ratio of alcohol Oxone $RuCl_3 \cdot nH_2O = 1{:}5{:}0.005$.
[c]Reaction was carried out at RT.
[d]At 70 °C.

time at room temperature to give their corresponding dicarboxylic acids. In contrast, cyclooctanone reacts relatively slowly and does not give complete conversion of the starting material at room temperature even after 16 h. At elevated temperature (70 °C), cyclooctanone gave 81% yield of the corresponding dicarboxylic acid after 6 h. Comparatively lower yield of the reaction with no starting material left may be due to the formation of smaller dicarboxylic acids as the side products. When cyclohexanol (entry 6) was treated with 5 equiv. of Oxone in the presence of 0.5 mol% $RuCl_3 \cdot H_2O$ at room temperature, it took 20 h for complete consumption of cyclohexanone and gave adipic acid in 73% yields. The reaction time was drastically reduced to 6 h to give the product in 92% yield (entry 7) when the reactions were carried out at 70 °C. It has also been observed that irrespective of ring sizes, all the cyclic alcohols (entries 7–10) gave the optimum yield at 70 °C within 6–8 h of reaction time. When the reaction was carried out for octan-3-one, the starting material remained intact even after heating for 10 h at 70 °C.

In conclusion, we have developed an easy and straightforward method for synthesis of adipic acid from cyclohexanone at ambient temperature within 2 h, which is far superior to existing methods in terms of reaction time and temperature. Nevertheless, the method demonstrates synthesis of adipic acid without using any harmful solvent in the entire process. The method was successfully applied for synthesis of other C-5 to C-8 dicarboxylic acids from their cycloalkanone and cycloalkanol counterparts just by varying the temperature and reaction time.

TYPICAL PROCEDURE

An aqueous solution of Oxone (24.6 g, 40 mmol) in water (15 mL) was added to cyclohexanone (0.98 g, 10 mmol) and $RuCl_3 \cdot nH_2O$ (0.011 g, 0.05 mmol) and allowed



Scheme 1. Synthesis of C5–C8 dicarboxylic acids.

to stir at room temperature, while monitoring the progress of the reaction by thin-layer chromatography (TLC). After 2 h, the reaction mixture was diluted with ethanol (15 mL) and kept at 0–5 °C overnight. The mixure was then filtered, and the residue was washed with ethanol (3×30 mL). The combined ethanol–water solution was then kept at 0–5 °C overnight to get colorless precipitates, which upon drying gave solid adipic acid in 98% yield (1.431 g, 9.8 mmol). Mp 151–153 °C (lit.[7] 151–154 °C). IR (KBr): 1685, 2500–3100 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): 1.74 (m, 4H), 2.42 (m, 4H), 5.34 (s, 2H); $^{13}CNMR$ (100 MHz, CD_3OD): 176.90, 34.21, 25.21; MS (m/z): 128, 100, 87, 73, 69, 60, 43, 41; Elemental analysis for $C_6H_{10}O_4$ (%) calcd: C, 49.31; H, 6.90. Found: C, 49.38; H, 6.73.

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