Solvent-Free Route to Adipic Acid

Mechanistic Insights into the Conversion of Cyclohexene to Adipic Acid by H_2O_2 in the Presence of a TAPO-5 Catalyst[**]

Sang-Ok Lee, Robert Raja, Kenneth D. M. Harris, John Meurig Thomas,[*] Brian F. G. Johnson, and Gopinathan Sankar

The current, widely used and environmentally harmful industrial method of producing adipic acid (**2**) first entails the oxidation of cyclohexane by nitric acid (with extensive liberation of the greenhouse gas N_2O) to a mixture of cyclohexanol and cyclohexanone.[1,2] This mixture is then rather inefficiently converted to adipic acid (and some other products) by using a homogeneous cobalt-containing catalyst. Research into alternative, more benign methods of producing **2** is therefore called for; and we have previously reported how appropriately designed Co^{III}- or Mn^{III}-containing microporous aluminophosphate catalysts offer a means of yielding **2** in air, in a solvent-free fashion either from cyclohexane[3] or from *n*-hexane.[4] Since cyclohexene (**1**) is nowadays readily produced by catalytic partial hydrogenation of benzene,[5,6] there is interest in using aqueous H_2O_2 as an oxidant[7–10] to produce **2** and **4** with the aid of a suitable catalyst. Sato et al.[11] used a peroxytungstate (Na_2WO_4) in the presence of a phase-transfer catalyst ($CH_3(n\text{-}C_8H_{17})HSO_4$) to convert **1** to **2**; and Deng et al.,[12] employing a similar overall approach, replaced the harmful phase-transfer catalyst with a peroxytungstate–organic complex prepared in situ (such as $[W(O)(O_2)L_2]^{2-}$, where L_2 is an organic acid with multifunctional groups).

We here report another direct, environmentally benign method involving aqueous H_2O_2 and a molecular sieve catalyst based on TAPO-5 (Figure 1; titanium framework-substituted aluminophosphate number 5 in the IZA classification, see Experimental Section), which greatly facilitates recycling and the separation of products, and which requires no organic solvent.[13] Our TAPO-5 catalyst is bifunctional in that it possesses both Brønsted acidity (signified by its ability to catalyze the dehydration of methanol to dimethyl ether) and the ability to release nascent oxygen from H_2O_2. (Whilst the conversion of cyclohexene to adipic acid by H_2O_2 is a step in the right direction, it does suffer from the disadvantage of requiring four molecules of H_2O_2 per molecule of alkene converted. Ideally, it would be better if O_2 were used, as an oxidant with the right catalyst, and it is our belief that discovering such a catalyst will be facilitated by mechanistic studies of the kind we describe below).

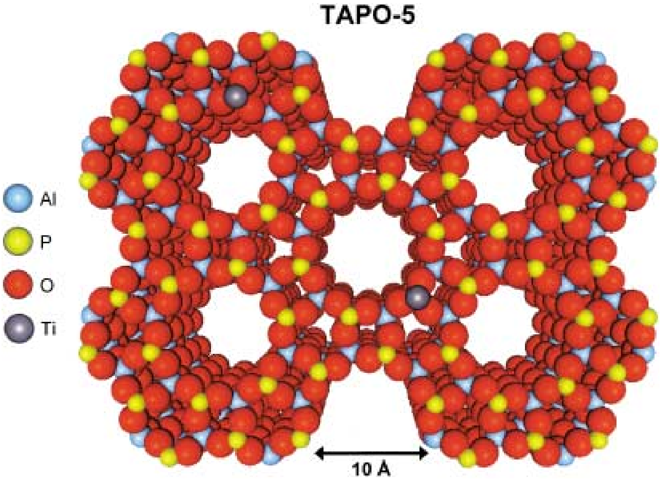

Figure 1. The structure of TAPO-5.

From the results of our parallel ^{13}C and ^{1}H NMR and GC-MS analyses conducted during the course of the catalytic conversion of **1** to **2** in the presence of TAPO-5, and from additional analytical measurements starting with certain intermediates (notably **3** and **4**) we conclude that the mechanistic pathway from **1** to **2** is as shown in Scheme 1. This conclusion is further confirmed by the fact that there is essentially no change in the concentration of the diols and of the other products when the catalyst is filtered off after 24 h. This further proves that there is no significant leaching of the Ti center during catalysis, as otherwise there would be appreciable changes with time in the concentration of the diols and other products as a result of a homogeneously catalyzed reaction made possible by the leached titanium. When, however, the filtered TAPO-5 catalyst is reused, its activity is seen to be significantly diminished. (There could well be ways, which we shall explore, for reactivating the filtered catalyst).

Importantly, we found that the *cis*-diol (*cis*-**4**), but not the *trans*-diol (*trans*-**4**), is formed by a free radical mechanism. The *cis*-diol is also seen to react significantly more readily than its *trans* analogue.

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[*] Prof. Sir J. M. Thomas, G. Sankar
The Royal Institution of Great Britain
Davy Faraday Research Laboratory
21 Albemarle Street, London W1S 4BS (UK)
and
Department of Materials Science and Metallurgy
New Museums Site
Pembroke Street, Cambridge CB2 3QZ (UK)
Fax: (+44) 1223-334-567
E-mail: jmt@ri.ac.uk
Dr. S.-O. Lee, Dr. R. Raja, Prof. B. F. G. Johnson
Department of Chemistry
University of Cambridge
Lensfield Road, Cambridge CB2 1EW (UK)
Fax: (+44) 1223-336-017
Prof. K. D. M. Harris
School of Chemical Sciences
University of Birmingham
Edgbaston, Birmingham B15 2TT (UK)

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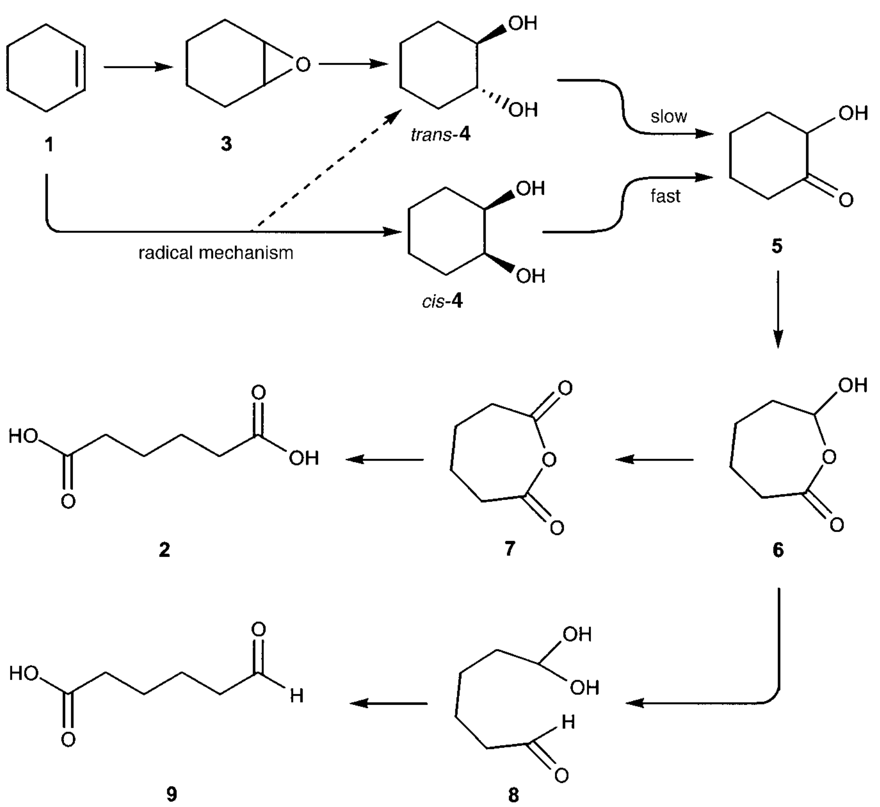

Scheme 1. Mechanistic pathway for the oxidation of cyclohexene (**1**) to adipic acid (**2**).

The performance, including turnover numbers (TONs), of TAPO-5 in the conversion of **1** to **2** is shown in Figure 2 and Table 1. Note that the conversion of **1** reaches essentially 100% at 72 h, and that the selectivity towards adipic acid increases steadily throughout the course of reaction, attaining about 30% at 72 h. GC-MS provided unambiguous evidence for the production of relatively small amounts of cyclohexene oxide (**3**), which are detectable at the early stages (ca. 10 min) of the reaction. ^{13}C NMR measurements showed that the concentration of **4** reaches a maximum at about 24 h and that the concentrations of **5, 6**, and **7** reach maxima at about 48 h, whereas those of **2, 8**, and **9** continue to increase even at 72 h. A separate experiment (Table 2), discussed below, involving **3** as a starting reagent (in place of **1**), confirmed the rapidity of its catalytic conversion under our (mild) reaction conditions.

1,2-Cyclohexanediol (**4**) has two stereoisomers (*trans* and *cis*), and our recorded ^{13}C NMR spectra yield a ratio of *cis*/*trans* of 0.4 at 5 h, which subsequently decreases to 0.1 (at 12 h), then to 0.05 (48 h), and zero at 72 h. The fact that both stereoisomers are formed prompts two questions: 1) are they each produced by the same mechanism, and 2) what are their relative reactivities insofar as producing **2** is concerned?

The second of these questions is readily answered by using authentic (pure) samples of either the *cis*-diol or the *trans*-diol as starting reagents (Table 3); it is evident that, in each case, reaction proceeds smoothly to **2** by the same sequence (shown in Scheme 1). The faster reaction of the *cis*-diol compared with the *trans*-diol can provide an explanation for the fact that, in the reaction starting from **1**, the relative amount of *cis*-diol is lower throughout the course of reaction. (It is difficult to ascertain whether the *cis*- and *trans*-diols are produced in comparable amounts from **1** given that their subsequent rates of reaction are substantially different). The reasons for the faster reaction of the *cis*-diol are not yet clear. But it could devolve upon the subtleties of conformation. Thus, the *cis*-diol has two energetically equivalent conformations (axial–equatorial and equatorial–axial).

Table 1: Conversion and selectivity, determined from GC-MS analysis, for the reaction of cyclohexene and aqueous H_2O_2 in TAPO-5 (see Experimental Section for reaction conditions and Scheme 1 for identity of products).

Time [h]	Conversion [%]	TON	Selectivity [%] 4	5	6	7	8	9	others	2
5	6.1	18.9	53.1	21.5	16.4	4.7	0	0	4.3	0
12	17.3	53.6	58.2	15.7	9.4	6.8	2.3	0	5.3	3
24	49.5	153.5	66.4	3.7	2.8	2.9	3.1	1.3	6.7	13.1
48	99.1	307.2	55.2	3.2	3.4	3.5	3.3	2.5	7.8	21.1
72	100	310	30	2.9	3.4	3.2	9.2	7.5	13.5	30.3

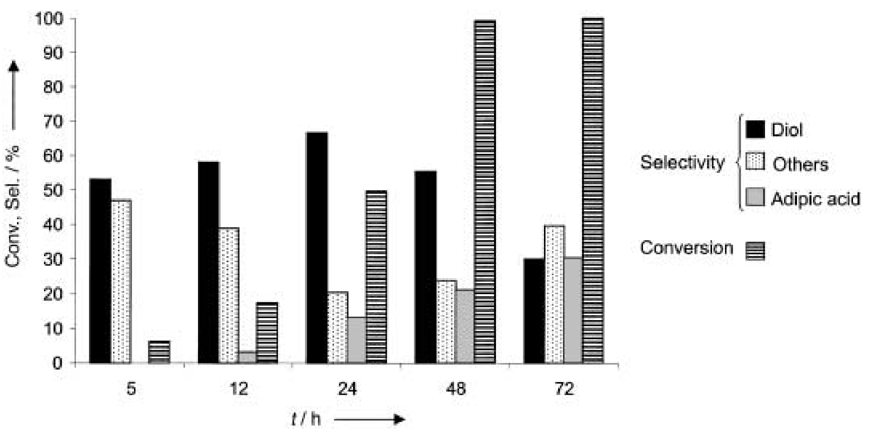

Figure 2. Conversion and selectivity for the reaction of cyclohexene (**1**) and aqueous H_2O_2 in TAPO-5 (see also Table 1).

Table 2: Conversion and selectivity, determined from GC-MS analysis, for the reaction using **3** as the starting reagent (see Experimental Section for reaction conditions and Scheme 1 for identity of products).

Time	Conversion [%]	TON	Selectivity [%] **4**	**5**	**6**	**7**	**8**	**9**	others	**2**
10 min	99.9	309.7	82.9	5.6	3.7	2.3	0	0	5.5	0
24 h	100	310	36.7	2.9	3.3	3.1	2.3	4.3	7.6	39.8
48 h	100	310	8.2	3.2	3.4	3.4	11.4	13.7	17.9	38.8

Table 3: Conversion and selectivity, determined from GC-MS analysis, for the separate reactions using *trans*-1,2-cyclohexanediol and *cis*-1,2-cyclohexanediol as the starting reagent (see Experimental Section for reaction conditions and Scheme 1 for identity of products).

Reagent	Time [h]	Conversion [%]	TON	Selectivity [%] **5**	**6**	**7**	**8**	**9**	others	**2**
trans-diol	6	10.2	31.6	9.4	4.7	4.1	2.3	4.1	4.1	71.3
	12	31.2	96.7	3.8	3.2	3.7	5.6	7.9	8.3	67.5
	24	71.5	221.7	3.2	3.4	3.4	8.7	10.3	12.8	58.2
cis-diol	6	30.8	95.5	4.3	3.6	3.2	3.8	6.4	8.7	70
	12	73.2	226.9	3.7	3.3	3.6	6.4	8.3	9.1	65.7
	24	100	310	0	1.8	3.4	11.6	17.1	21.3	44.8

The two conformations of the *trans*-diol (axial–axial and equatorial–equatorial), on the other hand, are of different energy, and for the isolated molecule it is the equatorial–equatorial conformation that is of lower energy. If this conformation of the *trans*-diol also predominates inside the pores of the TAPO-5 catalyst, the faster reaction of the *cis*-diol may be related to the presence of an axial substituent, which is more readily displaced than an equatorial substituent in a reaction that proceeds by nucleophilic substitution.

In answering the first question raised above, we note that in the reaction carried out using the epoxide **3** as a starting reactant only the *trans*-diol is produced. This is indeed the expected product from the acid-catalyzed ring opening of the epoxide by nucleophilic substitution—in this case one of the OH groups of the *trans*-diol would derive from the nucleophile. Clearly, the *cis*-diol must be generated by a different mechanism, one that does not proceed via cyclohexene oxide (**3**). To explore the possibility that this reaction is radical based, we took cyclohexene as the starting reagent but in the presence of a free radical scavenger (hydroquinone).[14,15] In this reaction only the *trans*-diol is formed. The radical scavenger evidently suppresses all production of the *cis*-diol, the production of which from **1** under normal conditions therefore occurs by a free-radical mechanism. With the epoxide **3** as the starting reagent, both in the presence or in the absence of hydroquinone scavenger, the products were the same in each case, showing that the conversion of **3** to the *trans*-diol does not proceed by a radical mechanism.

To assess whether subsequent stages of the overall reaction of cyclohexene (from **4** onwards, Scheme 1) also involve participation of free radicals, separate experiments were carried out using either the *cis*-diol or the *trans*-diol as starting reagents in the presence of the radical scavenger. The fact that reaction proceeds in the same manner as in the absence of the scavenger proves that the formation of **2** from both the *cis* and *trans* diols (**4**) does not involve a radical mechanism.

Finally, a control experiment was carried out in which **1** and aqueous H_2O_2, but with no TAPO-5 catalyst, were allowed to react under conditions identical to those of the catalytic reaction. Very small amounts of the *cis*-diol and *trans*-diol were produced, but no further reaction ensued even after 24 h. The TAPO-5 catalyst is clearly implicated in all the stages shown in Scheme 1.

In summary, we have shown that a TAPO-5 molecular sieve catalyst is effective in the production of adipic acid from cyclohexene in the absence of an organic solvent, and have gained insights into the intermediates and the mechanism of the overall reaction by means of NMR and GC-MS analyses. Although the yield of adipic acid is not as high as in other, recently evolved[3,4,11,12,16] methods of synthesis, we have uncovered mechanistic details not hitherto detected, and, in particular, established the key importance of the stereochemistry of the 1,2-cyclohexanediol in the progress of the reaction. The task now is first, to pursue methods, especially those that promote radical participation, which increase the proportion of the *cis*-diol in the initial stages of the reaction, and, second, to design other transition-metal-ion-substituted aluminophosphate catalysts that will convert cyclohexene (**1**) in air to adipic acid (**2**). There is at least one open-structure catalyst that we have already identified that effects such a conversion at low temperatures, in a solvent-free fashion.

Experimental Section

The reagents for TAPO-5 synthesis were 85 % H_3PO_4 (Aldrich), aluminium hydroxide hydrate (Aldrich), titanium(diisopropoxide)-bis(2,4-pentanedionate) (75 %, Aldrich), and tetraethylammonium hydroxide (TEAOH 35 %, Aldrich). The reactant gel was prepared according to the following procedure. Aluminum hydroxide hydrate and a solution of titanium(diisopropoxide)bis(2,4-pentanedionate) in 2-propanol were added to a solution of phosphoric acid in water, and the mixture was stirred until homogeneous. A solution of TEAOH was then added slowly with vigorous stirring to obtain a gel with empirical composition 1.0 Al:1.48 P:0.02 Ti:0.8 TEAOH:40 H_2O. The gel was sealed in a teflon-lined stainless steel autoclave and heated at 175 °C under autogeneous pressure for 2 h. The solid product was isolated by filtration, washed with deionized water and dried in air (90 °C). The as-prepared product was calcined at 550 °C, first in nitrogen for 1 h and then in dry oxygen for 10 h. The material was characterized by powder X-ray diffraction to confirm the AFI structure. Prior to use in the catalytic reaction, the material was dehydrated at 110 °C under vacuum for 1 h.

The catalytic reactions were carried out in the batch mode using a glass vessel fitted with a condenser circulating chilled water. The vessel was heated in an oil bath to 80 °C. The substrate (cyclohexene, cyclohexene oxide, *cis*-1,2-cyclohexanediol or *trans*-1,2-cyclohexanediol, ca. 0.062 mol), H_2O_2 (30 g, 0.22 mol; 25 % in aqueous solution) and catalyst (0.5 g of TAPO-5) were introduced into the glass vessel and the contents were stirred using a magnetic stirrer. Small aliquots of reaction medium (both aqueous and organic) were removed periodically, and subsequently analyzed by gas chromatography

(Varian model 3400 CX) employing a HP-1 capillary column (25 m × 0.32 mm) and a flame ionization detector. The identity of the products was further confirmed by using GC-MS (VG Prospec mass spectrometer equipped with a Fisons 8000 series gas chromatograph employing a 25 m DB5 capillary column). Solution-state ^1H and ^{13}C NMR recorded at 400.14 MHz and 100.61 MHz, respectively, on a Bruker AMX 400 spectrometer.

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