



High production of adamantane oxygenates in propionic acid using VO(acac)₂ and Eu(OTf)₃ with O₂

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ABSTRACT

VO(acac)₂ with 1 atm O₂ catalysed the oxidation of adamantane to adamantanone, adamantanols and its esters in propionic acid at 353–393 K. Propionic acid was a more suitable solvent for the oxidation than acetic, butyric, valeric, or hexanoic acids. The maximum yield of oxygenates was 65% (3300 TON) in 360 min. Adamantane solubilities and chemical stabilities of carboxylic acid were important for the oxidation; however, the coordination of carboxylic anions with the vanadium catalyst strongly affected the oxidation activity. The oxidation rate of adamantane was enhanced 3.8 times by the addition of the Eu(OTf)₃ co-catalyst. The product selectivity for various oxidations of alkane and UV–vis spectroscopic studies of V species indicated that an active species was electrophilic vanadium peroxide species coordinated propionic anion and OTf.

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1. Introduction

Adamantane oxygenates are essential components of photore-sists used in ArF excimer laser lithography and medicines for Parkinson's disease and Alzheimer's dementia [1–3]. They are also useful in anticancer and antiviral treatment. They are mainly manufactured by the sulphuric acid oxidation using a large amount of pitch and SO₂ [4], bromination of adamantane with Br₂, and hydrolysis of bromoadamantanes to adamantane oxygenates and equimolar HBr [5]. A new synthesis method catalysed by *N*-hydroxy imide was recently developed by Daisel Co. [6,7]; however, conventional methods offer the advantages of being economical. Therefore, development of a new environment friendly method for the oxidation of adamantane is important.

Over the last few decades, various catalytic oxidation systems [6–41] using H₂O₂ [8–23] and a gaseous mixture of O₂ and H₂ [24–30] have been reported. The most attractive and economical oxidant is O₂. The ideal catalytic oxidation system would be air without any reducing agents under mild conditions. Several oxidation catalysts used under mild conditions have been reported, e.g., ruthenium complex [31–35], polyoxometalate [32–37], V/montmorillonite catalysts [38] and *N*-hydroxy imide [6,7]. We recently reported the VO(acac)₂ catalyst for

adamantane oxidation with O₂ (≤ 1 atm) in acetic acid [42,43]. The highest turnover rate of 87 h⁻¹ achieved in our previous work was much higher than other studies; e.g., 4.9 h⁻¹ for the [WZnRu₂(OH)(H₂O)}(ZnW₉O₃₄)₂]¹¹⁻ catalyst [32], 2.4 h⁻¹ for the H₅PV₂Mo₁₀O₄₀ catalyst [37], 2.2 h⁻¹ for the NHPI-Co(acac)₂ catalyst [6] and 1.6 h⁻¹ for the V-montmorillonite catalyst [38]. Our oxidation system with VO(acac)₂ catalyst afforded higher productivity of adamantane oxygenates. We describe details of the effects of acidic solvents and strong acid additives on the oxidation of adamantane and the catalysis of vanadium in this paper.

2. Experimental

Oxidation procedures—Oxidation of adamantane was performed in a Pyrex flask (100 mL) using a condenser, gas-introduction tube and thermocouple. The VO(acac)₂ catalyst (0.5 mM) was dissolved in a mixture of adamantane (0.47 M) and propionic acid (EtCO₂H, 10 mL) in the flask. The temperature of the flask was controlled by an oil bath and the actual reaction temperature was monitored using the thermocouple. Oxidation was performed for 360 min by stirring using a magnetic-spin bar and bubbling O₂ (10 mL min⁻¹) into the solution. Products in the gas phase were analysed using a gas chromatograph (GC, Shimadzu GC-8A, TCD-detector) with a Porapak Q packed column (40 × 2 m) at every hour. After the oxidation, the reaction solution was neutralised using NaOH (aq.), and the products were extracted with a CH₂Cl₂/*n*-C₇H₁₆ or 1-C₄H₉OH/*n*-C₇H₁₆ mixture. The extracted reaction mixture was analysed using a GC (Shimadzu GC-14A, FID-detector) and a gas-chromatograph

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mass-spectrograph (GC–MS, Shimadzu QP-2000A) with a HR-20M capillary column (0.250 × 25 m) using an external standard of naphthalene.

The major product was 1-adamantanol with 2 mol% detected as carboxylic acid 1-adamantyl esters in the oxidation of adamantane. The mixture of the two products was indicated as 1-AdOX. Other products were 2-adamantanol and its acetate (2-AdOX), 2-adamantanone (2-AdO), 1,3-adamantanediol and its acetates (1,3-AdOX), and CO₂ from EtCO₂H solvent. Minor products were 5-hydroxy-2-adamantanone and 1,4-adamantanediol.

If peroxide products are produced in the reaction mixture, we cannot depend on GC analysis data. Peroxide products selectively convert to each alcohol by reduction with Ph₃P. We can confirm the formation of peroxide products by comparing samples before and after adding Ph₃P [15,39–41]. This peroxide test using Ph₃P was conducted for important samples of the adamantane and other alkane oxidations in this study. We confirmed that there was no formation of peroxide products when we compared and discussed the selectivity of the products.

To obtain information on the reactivity of active species, the following oxidation parameters were used in this study.

3°-selectivity—The ratio of the sum of 3°-oxygenated product yields per the sum of mono-oxygenated product yields was defined as the 3°-selectivity (Eq. (1)).

$$3^\circ\text{-selectivity} = \frac{1\text{-AdOX}}{1\text{-AdOX} + 2\text{-AdO} + 2\text{-AdOX}} \quad (1)$$

A/K parameter—The ratio of alcohol (CyOH) to ketone (CyO) in the oxidation of cyclohexane was defined as the A/K parameter (Eq. (2)).

$$A/K = \frac{(\text{CyOH} + \text{CyOAc})}{\text{CyO}} \quad (2)$$

KIE parameter—The kinetic isotope effect was calculated from the sum of quantities of oxygenated cy-C₆H₁₂ and the sum of quantities of oxygenated cy-C₆D₁₂ (Eq. (3)).

$$\text{KIE} = \frac{(\text{sum of oxygenated cy-C}_6\text{H}_{12})}{(\text{sum of oxygenated cy-C}_6\text{D}_{12})} \quad (3)$$

RC parameter—The parameter for retention of the configuration of the tertiary C–H bond for the oxidation of *cis*- and *trans*-1,2-dimethylcyclohexane was defined as follows. The RC parameter was calculated from yields of *cis*- and *trans*-1,2-dimethyl cyclohexan-1-ol (Me₂Cy-1-OH).

$$\text{RC} = \frac{(\text{yield of } cis\text{-Me}_2\text{Cy-1-OH}) - (\text{yield of } trans\text{-Me}_2\text{Cy-1-OH})}{(\text{yield of } cis\text{-Me}_2\text{Cy-1-OH}) + (\text{yield of } trans\text{-Me}_2\text{Cy-1-OH})} \quad (4)$$

Spectroscopic studies—UV–vis spectroscopy studies were conducted for reaction mixtures under near oxidation conditions at 365 K by JASCO V-650.

Agents—VO(acac)₂ and 1,2-dimethylcyclohexane were obtained from Tokyo Chemical Industry; acetic acid, propionic acid (EtCO₂H), cyclohexane, adamantane and AIBN (2,2'-azobis(isobutyronitrile)) were obtained from Wako Pure Chemical Industries; cyclohexane-d₁₂ (99.5% deuterium) was obtained from Cambridge Isotope Laboratories; and Eu(OTf)₃ and O₂ (99.99%) were obtained from Aldrich and Taiyo Nippon Sanso, respectively. All agents were of special grade and were used without further purification.

3. Results and discussion

3.1. Effects of carboxylic acid on the oxidation of adamantane using VO(acac)₂

We recently reported the oxidation of adamantane using the VO(acac)₂ catalyst with O₂ in AcOH [42,43]. The formation rate of products increased with the concentration of adamantane in AcOH until 0.89 M. The highest turnover number (TON), which is based on V for the adamantane oxygenates was 560 at 0.89 M over 360 min; however, the maximum yield of 34% for the sum of the adamantane oxygenates was obtained at 0.47 M. White deposition of adamantane on the walls of the flask and tube was observed at 0.89 M of adamantane, which was close to the saturation concentration in AcOH. A near-saturation concentration of adamantane is not favourable for effective oxidation because of the deposition of adamantane. Thus, a high solubility of adamantane in carboxylic acid (solvent) is important. The boiling point of carboxylic acid may also be important in controlling the concentration of O₂ under the reaction conditions. A higher carboxylic acid solvent is a candidate to obtain a higher solubility of adamantane and boiling point. Table 1 shows adamantane solubilities at 298 K and the boiling points of propionic, butyric, valeric, hexanoic, and acetic acids, and the results of the adamantane oxidation (0.47 mM) with 1 atm O₂ at 373 K.

The order of the solubilities of adamantane and boiling points are hexanoic acid > valeric acid > butyric acid > propionic acid > acetic acid. Their pK_a values are similar, i.e., 4.8. The order of the yield of the sum of the adamantane oxygenates was propionic acid (21% yield) > acetic acid (10%), butyric acid (10%) > valeric acid (5.0%) > hexanoic acid (4.3%). This fact indicated that the solubility of adamantane may be important for the oxidation but carboxylic acid should directly affect the catalytic activity of VO(acac)₂. However, the 3°-selectivity defined by Eq. (1) did not differ widely among the acids and ranged from 78 to 82%. Carboxylic acids may function as a ligand of the vanadium active species and enhance the catalytic activity. When the 3°-selectivity value of 79% in propionic acid was recalculated to a reactivity of 2° and 3° C–H bonds, which are defined by the oxygenate yield per number of C–H bonds, the reactivity was 2°:3° = 1:11. The 3° C–H bond was 11 times more reactive than the 2° C–H bond. The active vanadium species may be electrophilic because the electron density of the 3° C–H bond is

Table 1
Oxidation of adamantane with 1 atm O₂ using the VO(acac)₂ catalyst in carboxylic acids

Run	Solvents (acids)	b.p. (K)	Solubility ^a (mM)	Product yields (mM)					CO ₂ (mmol)	3° sel (%)
				1-AdOX ^b	2-AdO	2-AdOX ^b	1,3-AdOX ^b	Total		
1	CH ₃ CO ₂ H	390	46	37.5	5.81	4.92	1.08	49.4	0.155	78
2	C ₂ H ₅ CO ₂ H	414	170	72.9	9.18	10.7	3.41	96.2	0.613	79
3	C ₃ H ₇ CO ₂ H	435	210	35.8	4.33	4.96	1.55	46.7	0.436	79
4	C ₄ H ₉ CO ₂ H	458	240	18.9	2.43	1.82	0.56	23.7	0.520	82
5	C ₅ H ₁₁ CO ₂ H	475	280	15.7	2.41	1.56	0.71	20.4	0.741	80

T = 373 K, 6 h, VO(acac)₂ 5 μmol (0.47 mM), adamantane 5 mmol (0.47 M), carboxylic acid 10 mL, P(O₂) 1 atm.

^a Solubilities of adamantane at 293 K.

^b AdOX is sum of adamantanol and its esters.

Table 2
Oxidation of adamantane with O₂ using various complexes in propionic acid

Run	Catalyst	Product yields (mM)					CO ₂ (mmol)	3° sel. (%)
		1-AdOX ^a	2-AdO	2-AdOX ^a	1,3-AdOX ^a	Total		
2	VO(acac) ₂	72.9	9.18	10.7	3.41	96.2	0.613	79
6	Co(acac) ₃	41.1	4.46	4.92	0.71	51.1	0.195	81
7	Mn(acac) ₂ ·2H ₂ O	40.1	3.86	4.91	0.41	49.6	0.175	82
8	Fe(acac) ₃	9.25	0.94	1.08	n.d. ^b	11.3	0.0325	82
9	None	3.87	0.21	0.48	n.d. ^b	4.55	0.0088	85

T = 373 K, 6 h, catalyst 5 μmol (0.47 mM), adamantane 5 mmol (0.47 M), EtCO₂H 10 mL, P(O₂) 1 atm.

^a AdOX is sum of adamantanol and its esters.

^b Not detected.

higher than that of the 2° C–H bond. The reactivities of 2° and 3° C–H bonds in other carboxylic acids were 1:10 (AcOH), 1:12 (butyric acid), 1:13 (valeric acid) and 1:12 (hexanoic acid). The electrophilicities of the active vanadium species in each carboxylic acid were similar, but their oxidation activities differed significantly.

The higher carboxylic acids, valeric acid and hexanoic acid, showed lower oxidation activities of adamantane as mentioned above, whereas the CO₂ yield relatively increased. This indicated that the competitive oxidation of adamantane and higher carboxylic acids proceeded with the active vanadium species. The chemical stability of carboxylic acids is important for oxidation. As a result, propionic acid (EtCO₂H) has a higher solubility of adamantane, good ligand nature and higher chemical stability for oxidation. Therefore, we chose EtCO₂H as the solvent for oxidation.

To study the catalysis of VO(acac)₂ in EtCO₂H, the auto-oxidation activity for adamantane was determined by promoters under the same conditions. Co(acac)₃, Mn(acac)₂·2H₂O and Fe(acac)₃ showed oxidation activities of 11, 10 and 2.4%, respectively, as shown in Table 2. The yield of the blank test without using a catalyst was 0.97%. These oxidation activities were lower than those when the VO(acac)₂ catalyst was used. The 3°-selectivity of 79% using the VO(acac)₂ catalyst was slightly lower than that of 81% using Co, 82% using Mn and 85% of the blank test. The difference in the product selectivity between the VO(acac)₂ catalyst and the promoters was small, but a significant difference in the oxidation activity was observed.

3.2. Effects of reaction conditions

Fig. 1a shows the dependence of the formation rates of products for the adamantane oxidation (0.47 mM) in EtCO₂H on reaction temperatures. Each formation rate increased exponentially from 353 to 393 K. The major product was 1-AdOX, and the product distributions were similar at all reaction temperatures. The sum of product yields was 54% (640 TON) at 393 K. The oxidation rate of adamantane (r , mol L⁻¹ h⁻¹) increased exponentially with the reaction temperature (T). A plot of $\ln r$ against $1/T$ is shown in Fig. 1b, which shows good linearity. The apparent activation energy for the oxidation of adamantane in EtCO₂H was 100 kJ mol⁻¹ which is greater than that of 76 kJ mol⁻¹ in AcOH [42]. These values indicate that the rate-determining step in the oxidation using vanadium catalyst in EtCO₂H and AcOH is the dissociation of a C–H bond of adamantane; however, the active species in the two acids may be not the same since different activation energies were observed. The 3°-selectivity decreased slightly from 79% at 353 K to 74% at 393 K. The same distribution of products was obtained at each reaction temperature after the peroxide test.

Fig. 2a shows time courses for the adamantane oxidation (0.47 M) in EtCO₂H at 393 K. The quantity of oxygenates increased smoothly with reaction time, except for that of 1,3-AdOX. The increase in the quantity of 1,3-AdOX accelerated with reaction time.

Successive oxidation of 1-AdOX to 1,3-AdOX was confirmed by the oxidation of 1-AdOX. The 3°-selectivity decreased slightly from 77 to 74% during the oxidation, due to the successive oxidation of 1-AdOX. A small decrease in the 3°-selectivity, as shown in Fig. 1, may also be due to the successive oxidation of 1-AdOX. Fig. 2b shows a plot of $\ln(1 - X)$ against reaction time (X : conversion of adamantane). The plot in Fig. 2b shows good linearity; therefore, the oxidation rate of adamantane depended on first-order of adamantane concentration ($k = 0.276$ h⁻¹ at 393 K).

Table 3 shows the effects of the adamantane concentration on oxidation activity in EtCO₂H at 393 K. The sum of product yields increased with the concentration and the highest product concentration of 1.04 M (3300 TON, 65% yield) was obtained at 1.59 M adamantane. This productivity for the oxidation was much better than that of 0.23 M (560 TON, 26% yield) in AcOH [42]. The higher adamantane solubility of EtCO₂H improved the productivity of adamantane oxygenates. The 3°-selectivity was 76% and it did not depend on the adamantane concentration. As mentioned above, EtCO₂H was suitable for the oxidation of adamantane using the VO(acac)₂ catalyst with O₂.

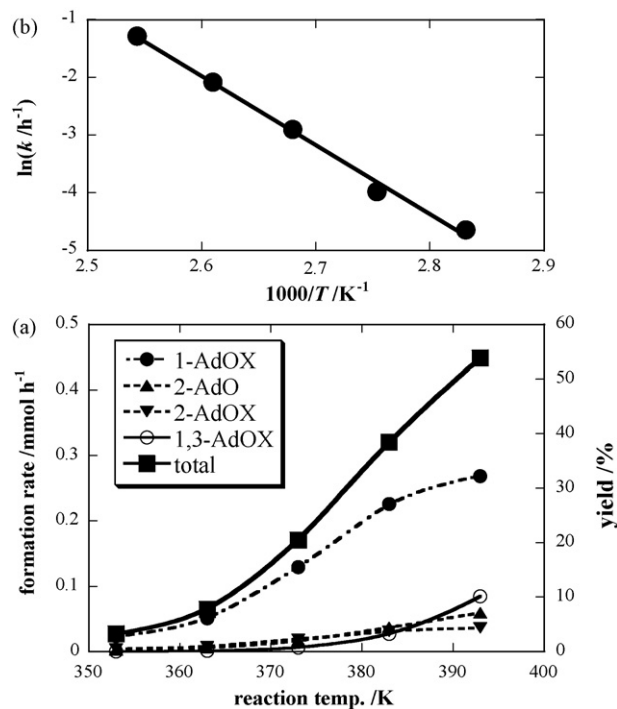


Fig. 1. (a) Temperature dependence of the oxidation rate of adamantane with O₂ using the VO(acac)₂ catalyst. (b) The Arrhenius plot of $\ln(k)$ against T^{-1} . T = 353–393 K, 6 h, VO(acac)₂ 5 μmol (0.47 mM), EtCO₂H 10 mL, adamantane 5 mmol (0.47 M), P(O₂) 1 atm.

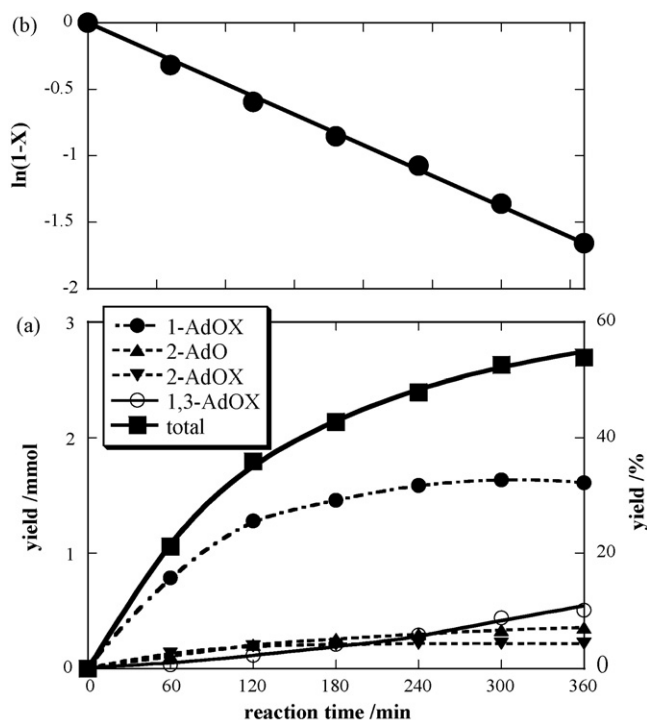


Fig. 2. (a) Time courses of the oxidation of adamantane. (b) A $\ln(1-X)$ plot against reaction time, where X is conversion of adamantane. $T=393$ K, $\text{VO}(\text{acac})_2$ $5 \mu\text{mol}$ (0.47 mM), adamantane 5 mmol (0.47 M), EtCO_2H 10 mL, $P(\text{O}_2)$ 1 atm.

3.3. Activation of V catalyst by $\text{Eu}(\text{OTf})_3$

As described in Section 3.1, the vanadium active species may have electrophilicity. Thus, an increase in oxidation activity is expected by increasing the electrophilicity of the active species. We have examined the addition of Lewis acid of $\text{Eu}(\text{OTf})_3$ (0 – 9.4 mM) to the mixture of $\text{VO}(\text{acac})_2$ (0.47 mM), adamantane (0.47 M) and EtCO_2H (10 mL).

Table 4 shows the effects of the $\text{Eu}(\text{OTf})_3$ addition on the adamantane oxidation at 373 K. Run 2 is the standard result of oxidation using the $\text{VO}(\text{acac})_2$ catalyst without $\text{Eu}(\text{OTf})_3$. The catalytic activity of $\text{Eu}(\text{OTf})_3$ without the $\text{VO}(\text{acac})_2$ catalyst was very low for oxidation (run 13), which was as inactive as the blank test (run 9 in Table 2). Adding $\text{Eu}(\text{OTf})_3$ of 0.47 mM enhanced the total yield of adamantane oxygenates (run 14) 1.5 times. $\text{Eu}(\text{OTf})_3$ functions as a co-catalyst of the $\text{VO}(\text{acac})_2$ catalyst for the adamantane oxidation. The selectivity to esters in 1-, 2-, and 1,3-AdOX increased by the addition of $\text{Eu}(\text{OTf})_3$. The esterification of adamantanol and EtCO_2H was catalysed by $\text{Eu}(\text{OTf})_3$. The distribution of products did not change for adamantane oxidation using $\text{VO}(\text{acac})_2$ and $\text{Eu}(\text{OTf})_3$ in EtCO_2H before and after the peroxide test.

When the quantity of $\text{Eu}(\text{OTf})_3$ addition increased to 0.94 (run 15), 4.7 (run 16) and 9.4 mM (run 17), the yield of adamantane oxy-

Table 3
Effects of concentration of adamantane on the oxidation using the $\text{VO}(\text{acac})_2$ catalyst

Run	Adamantane (M)	Products yields (mM)					CO_2 (mmol)	3° sel. (%)
		1-AdOX ^a	2-AdO	2-AdOX ^a	1,3-AdOX ^a	Total		
10	0.47	151	33.4	20.4	47.7	253	3.14	74
11	0.89	291	62.4	22.9	129	505	3.83	77
12	1.59	581	120	67.1	274	1040	4.36	76

$T=393$ K, 6 h, $\text{VO}(\text{acac})_2$ $5 \mu\text{mol}$, adamantane 5 – 20 mmol, EtCO_2H 10 mL, $P(\text{O}_2)$ 1 atm.

^a AdOX is sum of adamantanol and its esters.

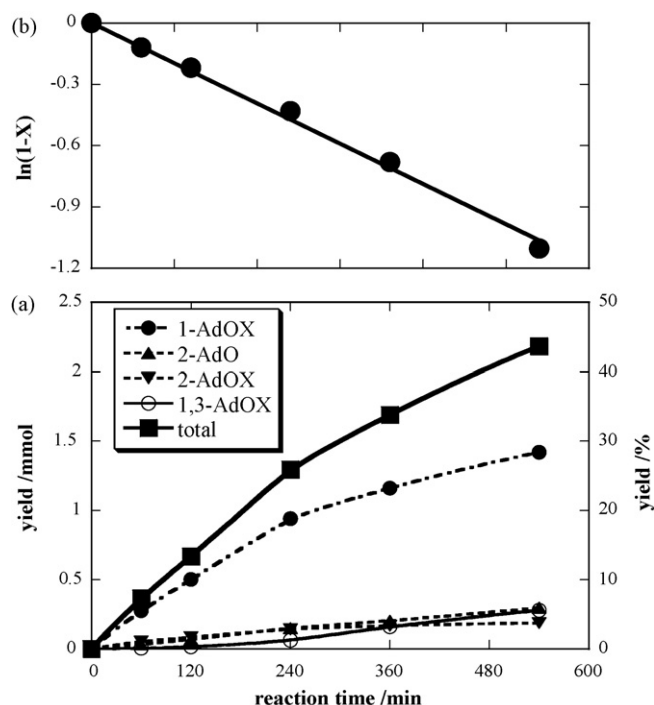


Fig. 3. (a) Time courses of the oxidation of adamantane using the $\text{VO}(\text{acac})_2$ catalyst and the $\text{Eu}(\text{OTf})_3$ co-catalyst. (b) A $\ln(1-X)$ plot against reaction time, where X is conversion of adamantane. $T=373$ K, $\text{VO}(\text{acac})_2$ $5 \mu\text{mol}$ (0.47 mM), $\text{Eu}(\text{OTf})_3$ $10 \mu\text{mol}$ (0.94 mM), adamantane 5 mmol (0.47 M), EtCO_2H 10 mL, $P(\text{O}_2)$ 1 atm.

genates and the selectivity to esters slightly increased. However, excess addition of $\text{Eu}(\text{OTf})_3$ was not effective for oxidation. The 3° -selectivity apparently decreased with the $\text{Eu}(\text{OTf})_3$ addition. It was confirmed that 1,3-AdOX was produced by successive oxidation of 1-AdOX. Therefore, the 3° -selectivity at early stages of oxidation remained constant with or without the $\text{Eu}(\text{OTf})_3$ addition.

Fig. 3a shows time courses of the adamantane oxidation using the $\text{VO}(\text{acac})_2$ catalyst with the $\text{Eu}(\text{OTf})_3$ co-catalyst in EtCO_2H at 373 K. The sum yield of oxygenated products increased smoothly for 9 h. No induction period was observed. The 3° -selectivity slightly decreased from 77 to 75% with the reaction time. A plot of $\ln(1-X)$ against the reaction time described a linear line (Fig. 3b). The oxidation rate of adamantane depended on the first-order of the adamantane concentration as well as that shown in Fig. 2b. High productivity of the adamantane oxygenates was performed at a lower temperature of 373 K using the $\text{VO}(\text{acac})_2$ catalyst and $\text{Eu}(\text{OTf})_3$ co-catalyst.

3.4. Reactivity of active species

To obtain information regarding the character of V active species and the oxidation mechanisms in EtCO_2H with and without $\text{Eu}(\text{OTf})_3$, reactivities of four oxidation systems were compared

Table 4Effects of the $\text{Eu}(\text{OTf})_3$ addition on the oxidation of adamantane with O_2 using the $\text{VO}(\text{acac})_2$ catalyst in propionic acid at 373 K

Entry	$\text{VO}(\text{acac})_2$ (mM)	$\text{Eu}(\text{OTf})_3$ (mM)	Product yields (mM) (ester select. (%))					CO_2 (mmol)	3° sel. (%)
			1-AdOX ^a	2-AdO	2-AdOX ^a	1,3-AdOX ^a	Total		
2	0.47	0	72.9 (0.6)	9.18	10.7 (27)	3.41 (2.5)	96.2	0.613	79
13	0	0.94	0.66 (64)	0.09	0.16 (19)	n.d. ^b	0.91	0.014	72
14	0.47	0.47	101 (41)	15.2	14.6 (47)	8.53 (50)	139	1.11	77
15	0.47	0.94	109 (54)	19.2	15.7 (49)	14.9 (54)	159	1.47	76
16	0.47	3.8	128 (57)	26.1	19.0 (53)	21.4 (62)	194	2.28	74
17	0.47	9.4	125 (55)	31.0	18.5 (80)	25.9 (73)	200	2.83	72

 $T = 373$ K, 6 h, adamantane 5 mmol (0.47 M), EtCO_2H 10 mL, $P(\text{O}_2) = 1$ atm.^a AdOX is sum of adamantanol and its esters.^b Not detected.

for oxidations of cyclohexane (CyH) and dimethylcyclohexane ($\text{Me}_2\text{-CyH}$), as shown in Table 5. The following four oxidation systems were used; *system 1*: $\text{VO}(\text{acac})_2/\text{EtCO}_2\text{H}$, *system 2*: $\text{VO}(\text{acac})_2\text{-Eu}(\text{OTf})_3/\text{EtCO}_2\text{H}$, *system 3*: $\text{VO}(\text{acac})_2/\text{AcOH}$ and *system 4*: AIBN/ EtCO_2H . The oxidations were accelerated by the $\text{Eu}(\text{OTf})_3$ addition. The reaction time was controlled to decrease the TON to suppress the successive oxidation of products. The peroxide tests were conducted for the four oxidation systems. The distribution of products did not change for the *systems 1–3* before and after the peroxide test. In *system 4*, however, the product distribution changed significantly by the addition of Ph_3P . The initial products were peroxide compounds; therefore, a KIE factor and a RC parameter were calculated using GC analysis data after adding PPh_3 .

A/K parameter—The ratio of the yields of alcohol to ketone (A/K) in the oxidation of cyclohexane (Eq. (2)) is usually one for an auto-oxidation mechanism by the decomposition of hydroperoxide [43–45]; therefore, the A/K value is suitable as an indicator of the auto-oxidation mechanism. The A/K values observed in *systems 1–3* were over 4 and the selectivity to cyclohexanol was high, as shown in the second column. The A/K parameters were obviously different from those of the auto-oxidation.

KIE factor—To obtain information on the rate-determining step in the oxidation of cyclohexane, studies on the kinetic isotope effects (KIE) (Eq. (3)) were performed for the competitive oxidation of cyclohexane and cyclohexane- d_{12} (1:1 mol) at 365 K, as shown at the third column. A fairly large KIE value of 3.9 was obtained for *system 1* which is as large as that of *system 2* (3.8). These KIE values indicate that the rate-determining step is the dissociation of a C–H bond of cyclohexane using the $\text{VO}(\text{acac})_2$ catalyst with and without the $\text{Eu}(\text{OTf})_3$ co-catalyst in EtCO_2H . A small KIE value of 2.8 was obtained in acetic acid (*system 3*) [42,43], which is the same as that observed in stoichiometric oxidation with $\text{VO}(\text{O}_2)(\text{Pic})\cdot 2\text{H}_2\text{O}$ (2.8) [46]. Large KIE values of 7.0 and 7.3 were obtained in the

auto-oxidation by $\text{Co}(\text{acac})_3$ promoter in AcOH [40], and by an AIBN initiator in EtCO_2H (*system 4*), respectively.

RC parameter—Retention of the configuration of the tertiary C–H bond for the oxidation of *cis*-1,2-dimethylcyclohexane (*cis*- Me_2CyH) by Eq. (4) was studied to obtain information on intermediates formed during oxidation. The major products were *cis*- and *trans*-1,2-dimethylcyclohexan-1-ol (*cis*- and *trans*- Me_2CyOH). The minor products were *cis*-1,2-dimethylcyclohexan-3-ol, -4-ol, -3-one, -4-one and *cis*-1-formyl-2-methylcyclohexane. The configurations of the two methyl groups of the minor products were retained completely in EtCO_2H , as well as that in AcOH .

A lower RC value (26%) was obtained for the oxidation of *cis*- Me_2CyH by the $\text{VO}(\text{acac})_2$ catalyst in EtCO_2H (*system 1*) than in AcOH (37%). On the other hand, the RC value was 14% for the auto-oxidation by the AIBN initiator in EtCO_2H (*system 4*). Lower RC values (6–14%) were reported in the radical reaction by HO^\bullet [41]. A higher RC value of 33% was obtained for the oxidation using the $\text{VO}(\text{acac})_2$ catalyst with the $\text{Eu}(\text{OTf})_3$ co-catalyst (*system 2*), but its reliability was not high because a side-reaction of dehydration of $\text{Me}_2\text{Cy-1-OH}$ proceeded by a strong Lewis acid of $\text{Eu}(\text{OTf})_3$.

Alkyl radical intermediates should form in *systems 1–4* because the RC values were not high. Stereochemistry on tertiary carbon may be strongly influenced by subsequent addition of a functional group. The rate constant for the disappearance of stereochemistry of the tertiary alkyl radical was to be about 10^9 s^{-1} (first-order kinetics) at 365 K [47]. If the addition of the functional group was slow ($> 10^{-9} \text{ s}$), a lower RC value was observed [41].

The active species on vanadium in *systems 1–3* is differs from that in auto-oxidation, because significant differences in A/K values and KIE values were observed. However, an alkyl radical intermediate species may be produced after the dissociation of a C–H bond of alkane in *systems 1–3*. The slow addition of oxygen species on vanadium to alkyl radical intermediate produced alcohol.

3.5. Spectroscopic studies for V species

Fig. 4 shows *in situ* UV–vis spectra of the reaction mixture of $\text{VO}(\text{acac})_2$ (0.5 mM), cyclohexane (1.85 M) and EtCO_2H using a UV cell with a 10 mm optical length at 365 K. Strong absorption below 300 nm was observed in spectrum (a). This absorption corresponded to the absorption of solutions of 1 mM acetylacetonate and EtCO_2H ($\lambda_{\text{max}} = 274 \text{ nm}$). This indicated that a ligand exchange reaction between acac^- and EtCO_2^- proceeded on $\text{VO}(\text{acac})_2$ in EtCO_2H . Therefore, $\text{VO}(\text{OCOEt})_2$ may be present in the solutions at 365 K. When 1 atm oxygen was introduced in the solution of spectrum (a) for 0.5 h at 365 K, the broad UV absorption of 300–400 nm was observed in spectrum (b). This broad absorption of 300–400 nm disappeared when Ar was introduced in the solution (spectrum (b)) for 0.5 h at 365 K (spectrum (c)). The same broad absorption spectrum appeared with the re-introduction of O_2 . The chemical species giving the broad UV absorption was reversible. This indicates that the

Table 5

Reactivities of vanadium and auto-oxidation systems

Oxidation system	Substrates and parameter		
	Cy- C_6H_{12}	Cy- $\text{C}_6\text{H}_{12}/$ Cy- C_6D_{12} ^a	<i>cis</i> - $\text{Me}_2\text{-CyH}$ ^b
	A/K	$k_{\text{H}}/k_{\text{D}}$	RC
$\text{VO}(\text{acac})_2/\text{propionic acid}$ ^c	4.0	3.9	26%
$\text{VO}(\text{acac})_2\text{-Eu}(\text{OTf})_3/\text{propionic acid}$ ^d	4.9	3.8	(33%) ^f
$\text{VO}(\text{acac})_2/\text{acetic acid}$ [43] ^e	5.2	2.8	37%
AIBN/ <i>propionic acid</i> ^e	–	7.3	14%

 $T = 365$ K, substrate 20 vol%, solvent 80 vol%.^a 1: 1 (mol) mixture of cyclohexane and cyclohexane- d_{12} .^b *cis*-1,2-dimethylcyclohexane.^c $\text{VO}(\text{acac})_2$ 0.5 mM.^d $\text{VO}(\text{acac})_2$ 0.5 mM, $\text{Eu}(\text{OTf})_3$ 1 mM.^e AIBN 1 mM. Product yields were obtained after reduction with PPh_3 .^f A part of 1,2-dimethylcyclohexan-1-ol was dehydrated by $\text{Eu}(\text{OTf})_3$.

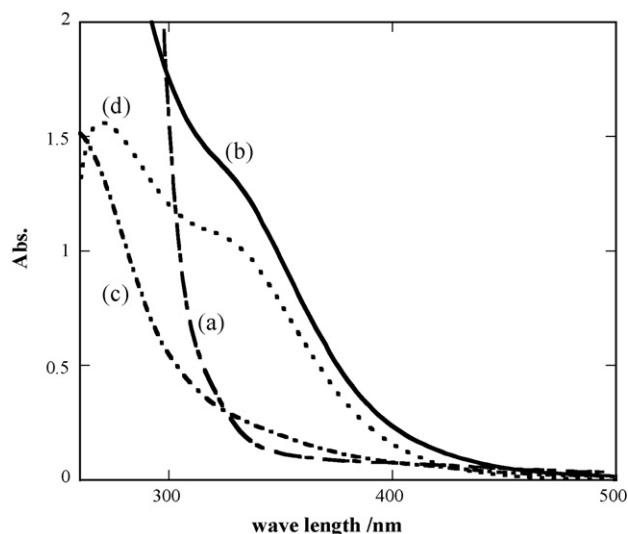


Fig. 4. UV-vis spectra of the reaction mixture (a) before and (b) after oxidation 1 h, (c) after Ar purge for 0.25 h, and (d) difference of (b) and (c). $T=365$ K, $\text{VO}(\text{acac})_2$ $5 \mu\text{mol}$ (0.47 mM), EtCO_2H 10 mL, adamantane 5 mmol (0.47 M), (a) and (c) $P(\text{Ar})$ 1 atm, (b) $P(\text{O}_2)$ 1 atm.

chemical species giving the broad UV absorption of 300–400 nm may be an active oxygen species for the oxidation. A broad UV absorption of 300–400 nm is also observed for the oxidation mixture catalysed by $\text{VO}(\text{acac})_2$ in AcOH [43]. Very similar species may be produced in both oxidation systems.

Spectrum (d) is a differential spectrum of spectrums (b) and (c). Two absorption peaks of 270 and 320 nm appear. UV absorption of 320 nm was reported for charge transfer absorption from a peroxide ligand to a vanadium centre (LMCT) [48].

Fig. 5 shows a UV-vis spectra of the solutions of $\text{VO}(\text{acac})_2$ (0.5 mM), $\text{Eu}(\text{OTf})_3$ (1 mM), cyclohexane (1.8 M) and EtCO_2H . A shoulder peak of UV absorption at 316 nm was observed in spectrum (e) for the solution at 365 K, but a similar shoulder absorption peak was not observed in Fig. 4 (spectrum (a)). In a separate experiment, no UV absorption around 316 nm was confirmed for a solution of acetylacetonate (1 mM), $\text{Eu}(\text{OTf})_3$ (1 mM), cyclohexane (1.8 M) and EtCO_2H . Therefore, ^-OTf may coordinate with the

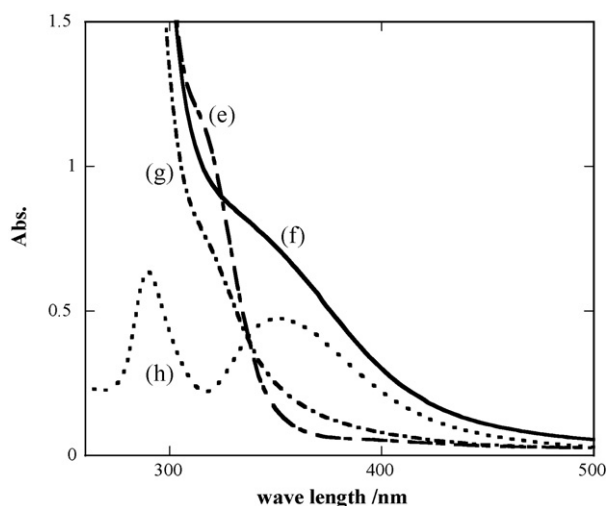


Fig. 5. UV-vis spectra of the reaction mixture (a) before and (b) after oxidation 0.5 h, (c) after Ar purge for 0.25 h, and (d) difference of (b) and (c). $T=365$ K, $\text{VO}(\text{acac})_2$ $5 \mu\text{mol}$ (0.47 mM), $\text{Eu}(\text{OTf})_3$ $10 \mu\text{mol}$ (0.94 mM), EtCO_2H 10 mL, adamantane 5 mmol (0.47 M), (a) and (c) $P(\text{Ar})$ 1 atm, (b) $P(\text{O}_2)$ 1 atm.

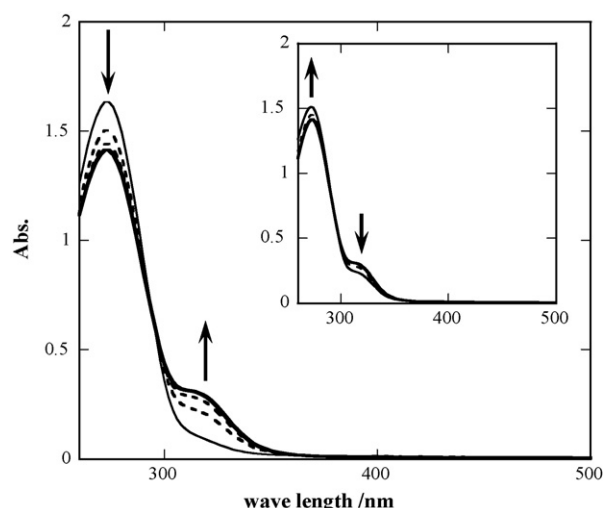


Fig. 6. Effects of the $\text{Eu}(\text{OTf})_3$ addition on UV-vis spectra in $\text{VO}(\text{acac})_2/\text{EtCO}_2\text{H}$ solution. $\text{VO}(\text{acac})_2$ 0.5 mM. $\text{Eu}(\text{OTf})_3$: 0 (sharp line), 0.5 (dotted line), 1 (dotted line) and 2 mM (bold line). Inset: $\text{Eu}(\text{OTf})_3$ 2 (bold line), 5 (dotted line) and 10 mM (sharp line). Optical length: 2 mm.

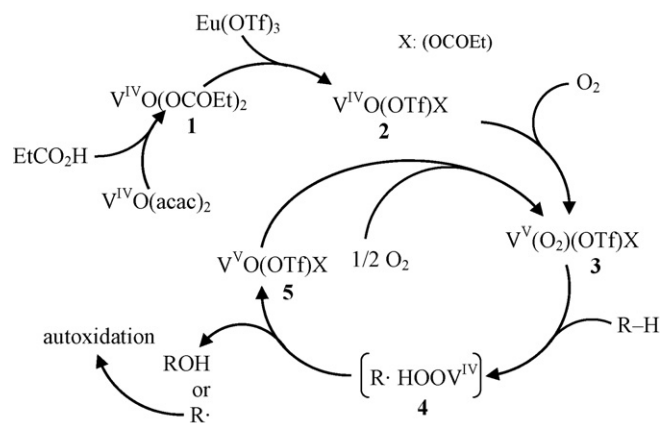
vanadium species in the solution of $\text{VO}(\text{acac})_2$, $\text{Eu}(\text{OTf})_3$, cyclohexane and EtCO_2H (system 2). To obtain information about the species at 316 nm, the effect of the quantity of $\text{Eu}(\text{OTf})_3$ added to the solutions of $\text{VO}(\text{acac})_2$ 0.5 mM and EtCO_2H was measured on the absorption at 316 nm, as shown in Fig. 6. UV absorption at 316 nm increased with increasing quantities of $\text{Eu}(\text{OTf})_3$ from 0.5 to 2 mM and that at 274 nm decreased. Thus, an isosbestic point was observed at 295 nm. When the quantity of $\text{Eu}(\text{OTf})_3$ addition increased >2 mM, reverse changes of UV absorptions at 316 and 274 nm were observed (inset of Fig. 6). UV absorption at 316 nm decreased with increasing quantities of $\text{Eu}(\text{OTf})_3 >2$ mM and that at 274 nm increased. This complicated observation can be explained as follows: (i) A ligand exchange between $\text{VO}(\text{OCOEt})_2$ and $\text{Eu}(\text{OTf})_3$ proceeds, and $\text{VO}(\text{OCOEt})(\text{OTf})$ forms by the addition of $\text{Eu}(\text{OTf})_3 <2$ mM. (ii) A second ligand exchange between $\text{VO}(\text{OCOEt})(\text{OTf})$ and $\text{Eu}(\text{OTf})_3$ proceeds, and $\text{VO}(\text{OTf})_2$ forms at a higher concentration of $\text{Eu}(\text{OTf})_3 >2$ mM. In other words, distribution of vanadium species depends on the quantity of $\text{Eu}(\text{OTf})_3$ added and $\text{VO}(\text{OCOEt})_2$ and $\text{VO}(\text{OTf})(\text{OCOEt})$ are presence in the reaction mixture at 1 mM $\text{Eu}(\text{OTf})_3$.

A spectrum (f) was analysed for the solution in O_2 after oxidation for 0.5 h and a broad UV absorption of 300–400 nm appeared. This broad UV absorption disappeared by passing Ar, as shown in spectrum (g). These observations of the UV spectra are similar to those for the $\text{VO}(\text{acac})_2/\text{EtCO}_2\text{H}$ system (Fig. 4). Spectrum (h) provides a differential spectra of the spectrums (f) and (g) in Fig. 5. Two UV absorption peaks appear at longer wavelengths than those for the $\text{VO}(\text{acac})_2/\text{EtCO}_2\text{H}$ system (Fig. 4, spectrum (d)).

If the UV absorption peak at 320 nm in spectrum (d) of Fig. 4 was the LMCT absorption of the peroxide V species, as described above, the UV absorption peak at 340 nm in spectrum (h) of Fig. 5 may be the LMCT absorption of peroxide V species in the $\text{VO}(\text{acac})_2\text{-Eu}(\text{OTf})_3/\text{EtCO}_2\text{H}$ system. This shift of UV absorption from 320 to 340 nm should indicate a decrease in the electron density of vanadium by coordination of ^-OTf .

3.6. Reaction scheme

A reaction scheme for the oxidation of adamantane (alkane) in the $\text{VO}(\text{acac})_2\text{-Eu}(\text{OTf})_3/\text{EtCO}_2\text{H}$ system was proposed in Scheme 1.



Scheme 1.

The starting form of $V^{IV}O(acac)_2$ is converted to $V^{IV}O(OCOEt)_2$ (**1**) by a ligand exchange reaction with $EtCO_2H$, and then the **1** species forms $V^{IV}O(OTf)(OCOEt)$ (**2**) though the ligand exchange with $Eu(OTf)_3$. The **2** species may be oxidised with O_2 to a peroxide species of $V^V(O_2)(OTf)X$ (**3**). This **3** species shows UV absorption of spectrum (d), but the actual form of the **3** species has not been identified. The **3** species attacks the C–H bonds of adamantane and dissociates a C–H bond, forming an alkyl radical intermediate (R^\bullet HOOV (**4**)). The **4** intermediate species produces alcohol and $V^VO(OTf)X$ (**5**) through a rebound-like mechanism. The actual form of the **5** species has not been identified. The dissociation process is the rate-determining step during the oxidation because the significant KIE value was observed. An electron withdrawing ligand of $-OTf$ may accelerate oxidation activity of peroxide on vanadium in the **3** species. The reaction rate between the hydroxyl group and alkyl radical intermediate is not fast, therefore the RC values were not high.

Oxidation using vanadium catalysts and H_2O_2 has been studied very well [13–15,39–41,47]. The formation of HO^\bullet as the active species and of alkyl hydroperoxide (ROOH) as the primary product and the reaction mechanisms were discussed in this work. The selective conversion of ROOH to alcohol by reduction with Ph_3P was also discussed. Therefore we accounted the formation of peroxide compounds in our $VO(acac)_2-Eu(OTf)_3/EtCO_2H$ system with O_2 by the peroxide testing using Ph_3P . We confirmed that there was no difference in product distribution before and after adding Ph_3P , and there was no formation of the peroxide products in the reaction mixture.

In the chemistry of vanadium catalysts, H_2O_2 and O_2 , H_2O_2 reduces $V(V)$ to $V(IV)$. The $V(IV)$ species activates H_2O_2 , and HO^\bullet is produced. HO^\bullet attacks a C–H bond of alkane, and alkyl radical (R^\bullet) forms by abstraction of H^\bullet . Then, an alkyl radical reacts with O_2 and peroxides are produced (Eq. (5)). An important function is that H_2O_2 works as both reductant and oxidant in the oxidation using the vanadium catalyst, H_2O_2 and O_2 [13–15,39–41,47]. In our $VO(acac)_2-Eu(OTf)_3/EtCO_2H$ system, we use O_2 and no reductant is used. It is impossible to reduce $V(V)$ catalyst to $V(IV)$ during the oxidation. Therefore, HO^\bullet may not be involved in our oxidation mechanism and the alkyl peroxide formation by Eq. (5) is not involved in our major oxidation scheme.



We consider that the major oxidation scheme of the $VO(acac)_2-Eu(OTf)_3/EtCO_2H$ system is the hydroxylation of alkanes with the **3** peroxide species through a rebound-like mechanism, because the selectivity for various oxidations differed from that of auto-

oxidation, as discussed in Table 5. However, a part of the alkyl radical intermediate may leak from the inner (**4** species) to the outer sphere, and auto-oxidation may proceed simultaneously. The function of the $Eu(OTf)_3$ co-catalyst is to reserve $-OTf$ for the V catalyst and acid catalyst for the esterification of adamantanol.

4. Conclusion

Oxidation of adamantane with O_2 was efficiently catalysed by the $VO(acac)_2$ in propionic acid under mild conditions. The product formation rate was accelerated by the addition of the $Eu(OTf)_3$ co-catalyst. The actual active form of vanadium species under oxidation has not been clarified; however, it was suggested by UV–vis spectroscopic studies that peroxide vanadium species coordinated propionic acid and $-OTf$.

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