

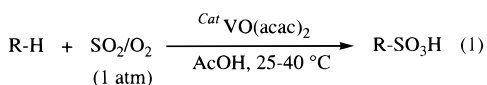
The First Catalytic Sulfoxidation of Saturated Hydrocarbons with SO₂/O₂ by a Vanadium Species

Yasutaka Ishii,* Katsuhisa Matsunaka, and Satoshi Sakaguchi

Department of Applied Chemistry
Faculty of Engineering & High Technology Research Center
Kansai University, Suita, Osaka 564-8680, Japan

Received January 31, 2000

Selective and efficient activation of unreactive C–H bonds in aliphatic hydrocarbons is particularly difficult and is one of the major challenges in chemistry.¹ In contrast to the liquid phase sulfoxidation of aromatic hydrocarbons which has been extensively studied, work on the sulfoxidation of saturated hydrocarbons to alkylsulfonic acids remains at a less satisfactory level. In general, alkylsulfonic acids are prepared by the Strecker synthesis using alkyl halides, preferably alkyl bromides, and an alkali metal or ammonium sulfides,² and by the oxidation of thiols with bromine in the presence of water or hydrogen peroxide combined with acetic acid.³ Until recently, there have been very few studies on the sulfoxidation of saturated hydrocarbons, despite their importance probably because of the difficulty in cleaving the carbon–hydrogen bond. Thus, photo- and peroxide-initiating sulfoxidations, which proceed through a radical process, are usually employed for alkanes such as cyclohexane using a mixture of SO₂ and O₂.^{4a,b} Alkanes are known to react with SO₂/Cl₂ through a radical route under irradiation of light to form the corresponding sulfonyl chlorides.^{4c} However, the efficiency of the sulfoxidation by these methods is insufficient to produce alkylsulfonic acids, and no real progress can be made in the sulfoxidation of alkanes. Therefore, if alkanes can be sulfoxidated catalytically by SO₂/O₂ without irradiation of light or in the absence of peroxide, such a method has enormous synthetic potential and provides a very attractive route to alkylsulfonic acids. However, such sulfoxidation of alkanes via a catalytic process has not been realized so far. We have recently developed the oxidation of alkanes to oxygen-containing compounds with molecular oxygen using *N*-hydroxyphthalimide which serves as the radical catalyst.⁵ In the course of our work, we studied the sulfoxidation of alkanes using SO₂/O₂, and found that vanadium compounds catalyze efficiently the sulfoxidation of alkanes under mild conditions. In this paper, we wish to report the first catalytic sulfoxidation of saturated hydrocarbons by SO₂/O₂ in the presence of a catalytic amount of a vanadium species such as VO(acac)₂ under mild conditions (eq 1).



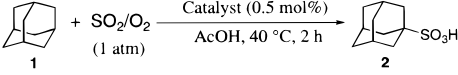
The sulfoxidation of adamantane (**1**) was chosen as a model reaction and allowed to react with a mixture of SO₂ and O₂ under various reaction conditions (Table 1). The reaction of **1** under 1

(1) (a) Hill, C. L. *Activation and Functionalization of Alkanes*; Wiley: New York, 1989. (b) Davies, J. A.; Watson, P. L.; Liebman, J. F.; Greenberg, A. *Selective Hydrocarbon Activation, Principles and Progress*; VCH: Weinheim, 1990. (c) Olah, G. A.; Molnár, A. *Hydrocarbon Chemistry*; Wiley: New York, 1995. (d) Arndtsen, A. B.; Bergman, G. R.; Mobley, A. T.; Peterson, H. T. *Acc. Chem. Res.* **1995**, *28*, 154–162. (e) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879–2932. (f) Dyker, G. *Angew. Chem. Int. Ed.* **1999**, *38*, 1698–1712.

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Table 1. Sulfoxidation of Adamantane (**1**) by SO₂/O₂ Catalyzed by VO(acac)₂^a



run	catalyst	ratio of SO ₂ /O ₂ (atm/atm)	conv. (%)	select. (%)
1	VO(acac) ₂	0.5/0.5	43	98
2	nothing	0.5/0.5	no reaction	
3 ^b	VO(acac) ₂	0.5/0.5	no reaction	
4 ^c	VO(acac) ₂	0.5/0.5	64	81
5	V(acac) ₃	0.5/0.5	50	94
6	VOCl ₃	0.5/0.5	39	85
7	VO(C ₁₇ H ₃₅ COO) ₂	0.5/0.5	56	88
8	VOSO ₄	0.5/0.5	15	n.d.
9	VO(O ⁱ Pr) ₃	0.5/0.5	37	78
10	VO(acac) ₂	0.67/0.33	89	64
11	VOCl ₃	0.67/0.33	80	85
12 ^c	VO(acac) ₂	0.67/0.33	54	98
13	VO(acac) ₂	0.75/0.25	94	27
14 ^c	VO(acac) ₂	0.75/0.25	88	65

^a **1** (2 mmol) was allowed to react under 1 atm of SO₂/O₂ (~2 L) in AcOH (10 mL) in the presence of VO(acac)₂ (0.01 mmol). ^b In the presence of hydroquinone (1 mol%). ^c Reaction condition was 25 °C, 24 h. Conversion (%) was based on the molar ratio of **1** consumed to **1** added. Selectivity (%) was based on the molar ratio of **2** formed to **1** reacted.

atm of a 1:1 mixture of SO₂ and O₂ in the presence of VO(acac)₂ (0.5 mol %) in acetic acid at 40 °C for 2 h produced 1-adamantane sulfonic acid (**2**) in 98% selectivity at 43% conversion of **1**.⁶ The X-ray measurement shows that **2** crystallized as the monohydrate C₁₀H₁₅SO₃·H₂O (**2**·H₂O) (Figure 1).⁷

Although the photosulfoxidation of **1** with SO₂/O₂ in the presence of H₂O₂ at 70 °C for 1 h gives **2**·H₂O (15%),⁸ our sulfoxidation is thought to be the first catalytic method for the synthesis of **2**. Needless to say, no sulfoxidation took place in the absence of VO(acac)₂ (run 2). To reveal the potential of various metal ions on the present sulfoxidation, **1** was allowed to react in the presence of a series of first row transition metal salts, TiO(acac)₂, Cr(acac)₃, Mn(acac)₃, Fe(acac)₃, Co(acac)₂, Ni(OAc)₂, and Cu(OAc)₂ under these conditions. It is interesting to note that no sulfoxidation of **1** was induced by these metal salts other than vanadium ions.⁹ Thus, various vanadium salts were examined. Among the vanadium compounds used, VO(acac)₂ and V(acac)₃ were found to be good catalysts. Surprisingly, the sulfoxidation of **1** was promoted by VO(acac)₂ even at room

(4) (a) Bjellqvist, B. *Acta Chem. Scand.* **1973**, *27*, 3180–3194. (b) Ferguson, R. R.; Crabtree, R. H. *J. Org. Chem.* **1991**, *56*, 5503–5510. (c) Crabtree, R. H.; Habib, A. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol 7., p 14 and references therein.

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
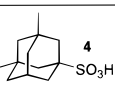

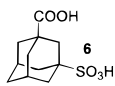

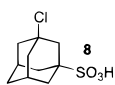

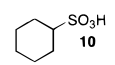

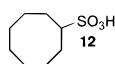
(6) A typical reaction procedure is as follows: A solution (5 mL) of **1** (2 mmol), VO(acac)₂ (3 mg) was placed in a pear-shaped flask equipped with a balloon filled with SO₂ (0.5 atm) and O₂ (0.5 atm). The mixture was stirred at 40 °C for 2 h and then extracted with ethyl acetate. The aqueous layer was concentrated by evaporation, and the solid obtained was recrystallized carefully with ethyl acetate.

(7) The compound **1** crystallized in the orthorhombic space group *P2₁/m* with cell dimensions of *a* = 8.5046(9) Å, *b* = 6.5354(6) Å, and *c* = 10.1605(7) Å; β = 10.037(7)°, *V* = 545.40(9) Å³, and an occupation of *Z* = 2 in cell unit. Data were collected at 23.0 ± 1 °C on an AFC7R Rigaku diffractometer (Cu Kα radiation), to a maximum 2θ = 120.1°, giving 897 unique reflections; the structure was solved by direct methods (SIR88) and refined within full matrix least squares, yielding *R* = 0.072, *R_w* = 0.141 (GOF = 9.76) for 887 unique reflections with *I* > 3.00σ(*I*). Elemental analysis data are as follows: Anal. Calcd for C₁₀H₁₈O₄S: C, 51.26; H, 7.74. Found: C, 51.11, H, 7.55.

(8) Smith, G. W.; Williams, H. D. *J. Org. Chem.* **1961**, *26*, 2207–2212.

(9) A review for the modern synthesis using vanadium species as a catalyst has been reported: Hirao, T. *Chem. Rev.* **1997**, *97*, 2707–2724.

Table 2. Sulfoxidation of Various Alkanes by SO₂/O₂ Catalyzed by VO(acac)₂^a

Run	Substrate	Product	Time (h)	Conv. (%)	Select. (%)
1			5	61	89
2			5	70	93
3			5	56	95
4 ^b	7	8	5	82	91
5			24	46	78
6			24	68	91
7 ^c	Octane 13	C ₈ H ₁₇ -SO ₃ H 14	24	56	83

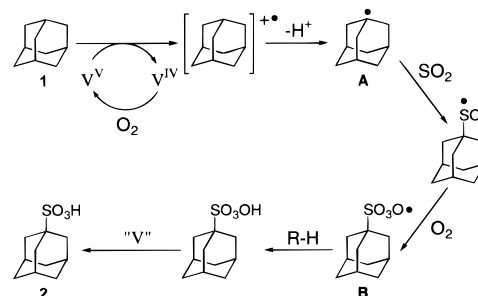
^a The reaction was carried out under the same conditions as run 1 in Table 1. ^b Ratio of SO₂/O₂ was 0.67/0.33 atm. ^c A mixture of 2-, 3-, and 4-octane sulfonic acids. Conversion and selectivity were calculated as the same way as Table 1.

temperature to form **2** in 81% selectivity at 64% conversion after 24 h (run 4). However, when a small amount of hydroquinone was added to the present reaction system, the reaction did not take place at all (run 3). These observations strongly suggest that a radical chain process is involved in the present catalytic sulfoxidation.

When a 2:1 mixture of SO₂ and O₂ was employed for the sulfoxidation of **1**, the reaction was performed in high conversion, but the selectivity to **2** decreased slightly. It is interesting to note that the same reaction at room temperature produced **2** in almost complete selectivity (98%) at 54% conversion (run 12). The sulfoxidation of **1** using a SO₂/O₂ = 3/1 ratio at 40 °C resulted in a considerable amount of undesired byproducts other than **2** (run 13).

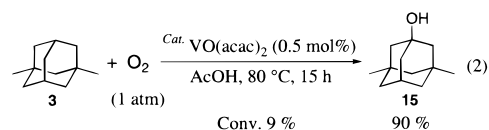
On the basis of these results, several cycloalkanes were allowed to react using a 1:1 mixture of SO₂ and O₂ (SO₂/O₂ = 0.5/0.5 atm) in the presence of VO(acac)₂ (0.5 mol %) under selected reaction conditions (Table 2). 1,3-Dimethyladamantane (**3**) and 1-adamantanecarboxylic acid (**5**) were also subjected to sulfoxidation to form 1,3-dimethyladamantane-5-sulfonic acid (**4**) and 1-carboxyadamantane-3-sulfonic acid (**6**), respectively, in high selectivities. 1-Chloroadamantane (**7**) was also sulfoxidated by the present system to give 1-chloroadamantane-3-sulfonic acid (**8**) (95%) in slightly lower conversion (56%). Thus, the sulfoxidation using a 2:1 mixture of SO₂/O₂ gave **8** in high conversion (82%) and selectivity (91%). Furthermore, cyclohexane (**9**) and cyclooctane (**11**) formed the corresponding sulfonic acids, cyclohexanesulfonic acid (**10**) and cyclooctanesulfonic acid (**12**), respectively. Aliphatic hydrocarbon, octane (**13**), afforded a mixture of 2-, 3-, and 4-octanesulfonic acids (**14**)¹⁰ in 83% at

(10) The octane sulfonic acids formed were difficult to isolate each isomer, and were found to consist of about a 1:1:1 regioisomeric mixture of 2, 3, and 4-octane sulfonic acids by the LC and NMR measurements.

Scheme 1. Possible Reaction Path for V-Catalyzed Sulfoxidation

56% conversion. Unfortunately, methane was not reacted at all under these reaction conditions.¹¹

The sulfoxidation of **1** seems to proceed via the following reaction steps. The sulfoxidation may be initiated by one-electron transfer from adamantane **1** to a V(V) species generated in situ from VO(acac)₂ and O₂ to form an adamantanyl cation radical [A].¹² The resulting [A] is trapped by SO₂ and then O₂ to generate an adamantanylsulfonylperoxy radical [B] which is eventually converted into **3** through the well-known reaction path.¹³ A V(IV) species is reported to undergo the disproportionation to V(V) and V(III) in the oxidative polymerization of diphenyl disulfide by the vanadium ion under dioxygen atmosphere.¹⁴ In addition, α -hydroxycarbonyl compounds are oxidized to α -dicarbonyl compounds by VOCl₃ and VO(acac)₂ under an oxygen atmosphere.¹⁵ In our reaction system, it is reasonable to assume that a V(V) species is generated from VO(acac)₂ under the influence of SO₂/O₂ in the course of the reaction. In fact, adamantane **3** was oxidized to 3,5-dimethyladamantan-1-ol (**15**) in the presence of a catalytic amount of VO(acac)₂ (0.5 mol %) under a dioxygen atmosphere. This shows that an adamantanyl radical derived from **3** is formed and then oxygenated with O₂ to form **15** (Scheme 1 and eq 2).



In conclusion, we have developed the first catalytic sulfoxidation of alkanes by SO₂/O₂ under the influence of VO(acac)₂ under mild conditions. This method provides a novel approach to alkylsulfonic acids which have been difficult to prepare so far.

Acknowledgment. This work was partly supported by Research for the Future program JSPS and Grant-in-Aid for Scientific Research (No. 10450337) from Monbusho.

Supporting Information Available: Experimental details for the general procedure and compound characterization data for all products as well as Figure 1 (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(11) The reaction was carried out using 50 mL-Teflon autoclave. Methane (15 atm) was allowed to react under SO₂ (2.5 atm) and O₂ (2.5 atm) in the presence of VO(acac)₂ (3 mg) in AcOH (5 mL) at 60 °C for 36 h.

(12) The generation of an alkyl radical by the hydrogen atom abstraction from an alkane by V(V) ion has been suggested as an alternative possibility by a reviewer.

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(14) Yamamoto, K.; Tsuchida, E.; Nishide, H.; Jikei, M.; Oyaizu, K. *Macromolecules* **1993**, 26, 3432–3437.

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