

# Efficient Oxidation of Adamantanes by Sodium Nitrite with Molecular Oxygen in Trifluoroacetic Acid

Osamu Onomura,<sup>a</sup> Yutaka Yamamoto,<sup>a</sup> Noriaki Moriyama,<sup>a</sup> Fumiaki Iwasaki<sup>b</sup> and Yoshihiro Matsumura\*<sup>a</sup>

<sup>a</sup>Graduate School of Biomedical Sciences, Nagasaki University, 1-14 Bunkyo-machi, Nagasaki 852-8521, Japan”

<sup>b</sup>Tsukuba Research Lab., Tokuyama Co. Ltd., 40 Wadai, Tsukuba 300-4247, Japan”

Fax: +81-95-819-2476

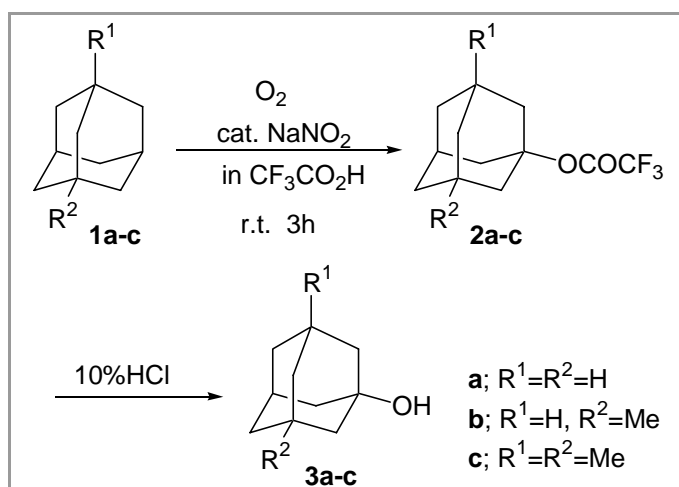
E-mail: matumura@net.nagasaki-u.ac.jp

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**Abstract:** Oxidation of adamantanes by oxygen was effectively achieved by use of sodium nitrite as a catalyst in trifluoroacetic acid (TFA) to give 1-adamantyl trifluoroacetates, from which adamantanol were obtained in good yields. A catalytic amount of sodium nitrite was essential and TFA was the best solvent among solvents examined for this oxidation.

**Key words:** Alcohols, Hydrocarbons, Oxidations, Oxygen, Radical Reactions.

Oxidation of adamantane (**1a**) to 1-adamantanol (**3a**) has continued to attract much interest because of a versatility of **3a** in material sciences.<sup>1</sup> Among a variety of methods for the transformation of **1a** to **3a** or its derivatives,<sup>2</sup> use of oxygen as an oxidant is worthwhile from both economical and mechanistic viewpoints; iron(III)/aldehyde/O<sub>2</sub>,<sup>3</sup> iron(II)/H<sub>2</sub>S/O<sub>2</sub>,<sup>4</sup> NHPI/O<sub>2</sub>,<sup>5</sup> TiO<sub>2</sub>/hv/O<sub>2</sub>,<sup>6</sup> electrochemical reduction/Tl(III)/porphyrin/O<sub>2</sub>,<sup>7</sup> Ru(III)-polyoxometalate/O<sub>2</sub>,<sup>8</sup> and V(IV)-polyoxometalate/O<sub>2</sub>.<sup>9</sup> However, those reported methods give **3a** in low yields and require some metal ion or organic halide catalyst under drastic conditions. We report herein an efficient method for oxidation of adamantanes **1a-c** to 1-adamantanol **3a-c** using a catalytic amount of easily available sodium nitrite (NaNO<sub>2</sub>) with molecular oxygen (Scheme 1).



Scheme 1

A typical condition of our method is as follows; a solution of **1a** in TFA containing 0.2 equiv of NaNO<sub>2</sub> was stirred at r.t. under an oxygen atmosphere. Since the organic extract of the reaction was a mixture of 1-adamantyl trifluoroacetate (**2a**) and a few % of **3a**, it was then treated with an aqueous 1N HCl solution overnight followed by extraction with CH<sub>2</sub>Cl<sub>2</sub> to afford **3a** in 96% yield without contamination of **2a**. Similar reaction of methyl-substituted adamantanes **1b,c** with oxygen afforded methyl-substituted adamantanol **3b,c** in good yields. Those results were shown in Table 1 (Entries 3-5).

In order to give some insight into the reaction mechanism, oxidation of **1a-c** was carried out under a variety of reaction conditions (Entries 1, 2, 6-17 in Table 1).

The results indicated that three kinds of factors were critical for the oxidation of **1a-c** to **3a-c**. First one is the effect of NaNO<sub>2</sub> as a catalyst on the yield of **3a**. That is, the absence of NaNO<sub>2</sub> didn't cause any oxidation of **1a** (Entry 1) but only 1mol% of NaNO<sub>2</sub> was enough for the completion of the oxidation of **1a** (Entry 2). NOBF<sub>4</sub><sup>10</sup> was usable in placement of NaNO<sub>2</sub> (Entry 6), whereas NaNO<sub>3</sub> didn't cause any oxidation of **1a** (Entry 7).

The second one was an oxygen effect. The reactions in Entries 1-7 were carried out under an oxygen atmosphere (1 atm) or an aerobic condition where satisfactory results were obtained when NaNO<sub>2</sub> was used as a catalyst (Entries 2-5, 8). However, the yield of **3a** was narrowly 10% under a nitrogen atmosphere even if 0.2 equiv of NaNO<sub>2</sub> was used (Entry 9). Another noticeable point was that the yields of **3a** were dependent on the amount of NaNO<sub>2</sub> (46% for 1 equiv of NaNO<sub>2</sub>; Entry 10, and 92% for 2 equiv of NaNO<sub>2</sub>; Entry 11).

The third one was a solvent effect. AcOH and MsOH were not suitable to the oxidation (Entries 12,13) but a prolonged reaction time gave **3a** in a satisfactory yield in the latter solvent (Entry 14). Chlorodifluoroacetic acid was a usable solvent for this oxidation (Entry 16), while difluoroacetic acid was not (Entry 15). The use of concd sulfuric acid resulted in a formation of a mixture of **3a** and 2-adamantanone in low yields (Entry 17).<sup>1a</sup>

Table 1 Oxidation of Adamantane **1a-c**<sup>a</sup>

Entry	Substrate	Catalyst	(equiv)	Solvent	Atmosphere	Time (h)	Product <b>3a-c</b>	Yield (%) <sup>b</sup>
1	<b>1a</b>	-	( - )	TFA	O <sub>2</sub>	24	<b>3a</b>	0
2	<b>1a</b>	NaNO <sub>2</sub>	(0.01)	TFA	O <sub>2</sub>	3	<b>3a</b>	92
3	<b>1a</b>	NaNO <sub>2</sub>	(0.2 )	TFA	O <sub>2</sub>	3	<b>3a</b>	96
4	<b>1b</b>	NaNO <sub>2</sub>	(0.2 )	TFA	O <sub>2</sub>	3	<b>3b</b>	96
5	<b>1c</b>	NaNO <sub>2</sub>	(0.2 )	TFA	O <sub>2</sub>	3	<b>3c</b>	96
6	<b>1a</b>	NOBF <sub>4</sub>	(0.2 )	TFA	O <sub>2</sub>	3	<b>3a</b>	91
7	<b>1a</b>	NaNO <sub>3</sub>	(1.0 )	TFA	O <sub>2</sub>	3	<b>3a</b>	0
8	<b>1a</b>	NaNO <sub>2</sub>	(0.2 )	TFA	air	3	<b>3a</b>	92
9	<b>1a</b>	NaNO <sub>2</sub>	(0.2 )	TFA	N <sub>2</sub>	3	<b>3a</b>	10
10	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	TFA	N <sub>2</sub>	3	<b>3a</b>	46
11	<b>1a</b>	NaNO <sub>2</sub>	(2.0 )	TFA	N <sub>2</sub>	3	<b>3a</b>	92
12	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	AcOH	O <sub>2</sub>	24	<b>3a</b>	0
13	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	MsOH	O <sub>2</sub>	3	<b>3a</b>	7
14	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	MsOH	O <sub>2</sub>	72	<b>3a</b>	89
15	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	HCF <sub>2</sub> CO <sub>2</sub> H	O <sub>2</sub>	24	<b>3a</b>	15
16	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	ClCF <sub>2</sub> CO <sub>2</sub> H	O <sub>2</sub>	3	<b>3a</b>	93
17	<b>1a</b>	NaNO <sub>2</sub>	(1.0 )	concd H <sub>2</sub> SO <sub>4</sub>	O <sub>2</sub>	24	<b>3a</b>	31 <sup>c</sup>

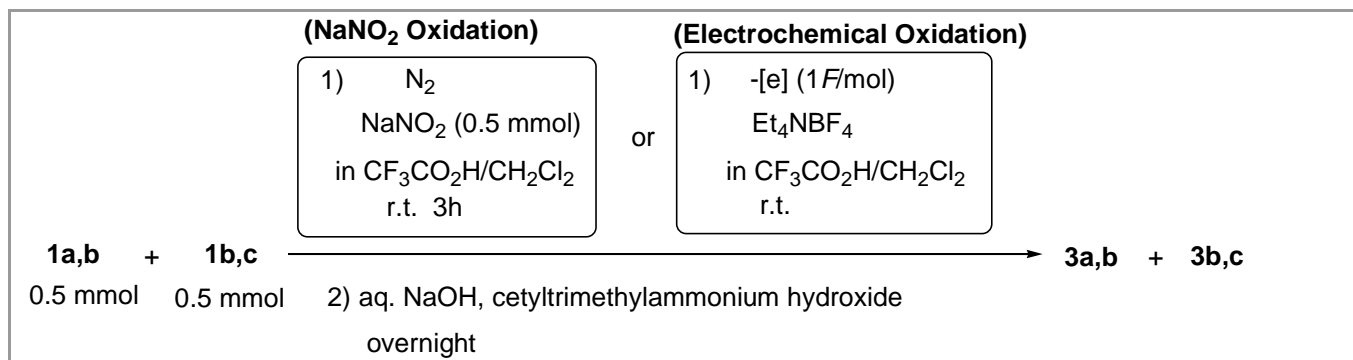
<sup>a</sup> The reaction was carried out by stirring a solution of substrate (1 mmol) and a catalyst in a solvent (5 mL) at r.t. under an atmosphere described in the Table.

<sup>b</sup> Isolated yield after treatment of the reaction mixture with 1N HCl (10 mL) overnight.

<sup>c</sup> In addition, 2-adamantanone (18%) was isolated as a byproduct.

Further information for the mechanism was speculated on the basis of the ratios of the oxidation products in competitive oxidation reactions between **1a**, **1b**, and **1c** by NaNO<sub>2</sub> and by electrochemical method,<sup>2m</sup> which has been known to initiate the oxidation of **1a** with electron transfer (Scheme 2). The results are summarized in Table 2, in which the ratios of products **3a-c** almost depended

on the number of bridgehead hydrogens of **1a-c** in the competitive oxidation reactions by O<sub>2</sub>/NaNO<sub>2</sub> (Entries 1-3), whereas the competitive oxidation reactions between **1a-c** by electrochemical method afforded **3a-c** with 1.1-1.3 ratio of products **3a-c**, which were not dependent on the number of bridgehead hydrogens of **1a-c** (Entries 4-6).



**Scheme 2** Competitive oxidation reaction between **1a-c** by NaNO<sub>2</sub> and by electrochemical method

An involvement of radical species in those oxidation reactions was then examined by adding TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) as a radical scavenger<sup>11</sup> to a solution for oxidation of **1a**. In the oxidation of **1a** by O<sub>2</sub>/NaNO<sub>2</sub>, as an amount of TEMPO increased, the yield of product **3a** decreased (Scheme 3), while in the electrochemical oxidation of **1a** addition of 0.2-1.0 equiv of TEMPO didn't show any effect to the reaction (Scheme 4).

On the basis of those results, we propose that NO works as a hydrogen abstractor from **1a** to afford adamantyl radical as an intermediate (Scheme 5)<sup>12</sup> since it has been

reported that active species from NaNO<sub>2</sub> in TFA for aromatic nitration include NO as shown in Scheme 6,<sup>13</sup> and NO has been known to oxidize dihydropyridine with a hydrogen abstraction mechanism.<sup>14</sup> This proposed mechanism can be supported by the facts that the competitive reactions between **1a-c** depended on the number of bridgehead hydrogens of **1a-c**, and that 1 equiv of TEMPO completely retarded the oxidation of **1a** by O<sub>2</sub>/NaNO<sub>2</sub>. On the other hand, electrochemical oxidation of **1a** was not affected by TEMPO since it proceeded with electron transfer mechanism.

NO may also work to oxidize adamantyl radical to adamantyl cation and it can be regenerated by oxygen

since 2 equiv of NaNO<sub>2</sub> was necessary to complete the oxidation of **1a** under a nitrogen atmosphere.

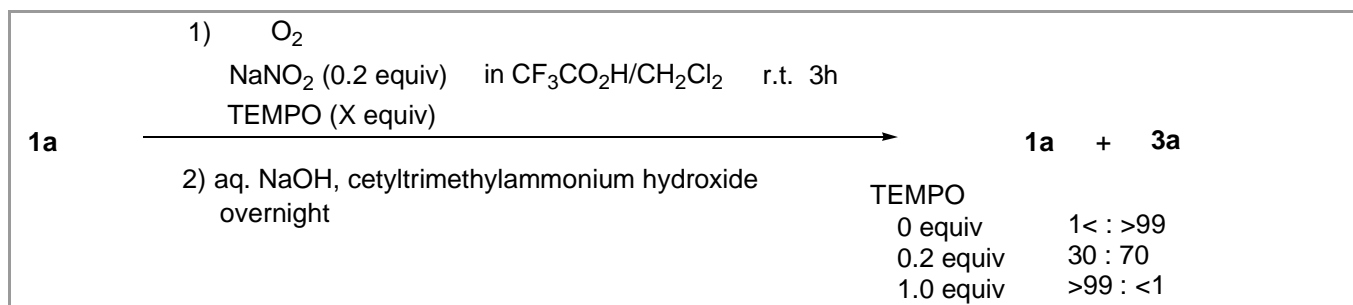
**Table 2** Competitive Reactions between **1a,b,c** by NaNO<sub>2</sub><sup>a</sup> and Electrochemical Oxidation<sup>b</sup>

Entry	Substrate <b>1a,b</b> (R <sup>1</sup> ,R <sup>2</sup> )/ <b>1b,c</b> (R <sup>1</sup> ,R <sup>2</sup> )	Number of Bridgehead Hydrogen (Ratio)	Oxidation Method	Product <sup>c</sup>	Ratio of Product <b>3a,b</b> / <b>3b,c</b>
1	<b>1a</b> (R <sup>1</sup> =R <sup>2</sup> =H)/ <b>1b</b> (R <sup>1</sup> =H, R <sup>2</sup> =Me)	4/3 (1.3)	NaNO <sub>2</sub>	<b>3a/3b</b>	1.4
2	<b>1a</b> (R <sup>1</sup> =R <sup>2</sup> =H)/ <b>1c</b> (R <sup>1</sup> =R <sup>2</sup> =Me)	4/2 (2.0)	NaNO <sub>2</sub>	<b>3a/3c</b>	2.2
3	<b>1b</b> (R <sup>1</sup> =H, R <sup>2</sup> =Me) / <b>1c</b> (R <sup>1</sup> =R <sup>2</sup> =Me)	3/2 (1.5)	NaNO <sub>2</sub>	<b>3b/3c</b>	1.5
4	<b>1a</b> (R <sup>1</sup> =R <sup>2</sup> =H)/ <b>1b</b> (R <sup>1</sup> =H, R <sup>2</sup> =Me)	4/3 (1.3)	Electrochemical Oxidation	<b>3a/3b</b>	1.1
5	<b>1a</b> (R <sup>1</sup> =R <sup>2</sup> =H)/ <b>1c</b> (R <sup>1</sup> =R <sup>2</sup> =Me)	4/2 (2.0)	Electrochemical Oxidation	<b>3a/3c</b>	1.3
6	<b>1b</b> (R <sup>1</sup> =H, R <sup>2</sup> =Me) / <b>1c</b> (R <sup>1</sup> =R <sup>2</sup> =Me)	3/2 (1.5)	Electrochemical Oxidation	<b>3b/3c</b>	1.1

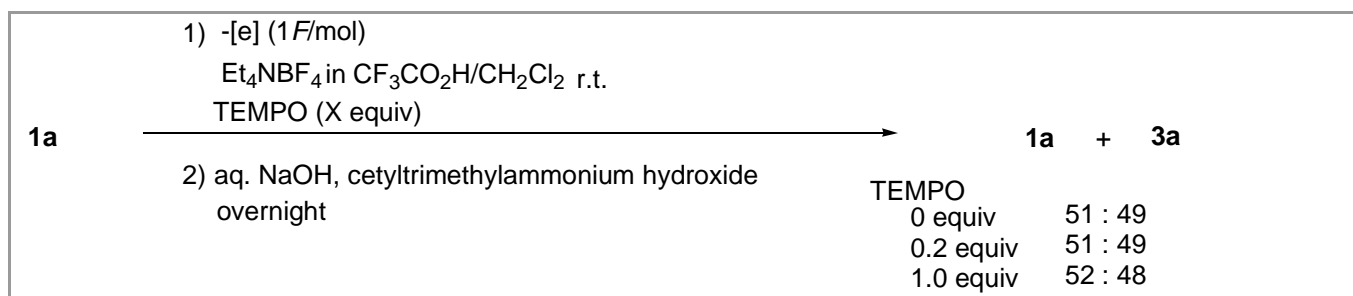
<sup>a</sup> The reaction was carried out by stirring a solution of substrates (each 0.5 mmol) and NaNO<sub>2</sub> (0.5 mmol) in a mixture of TFA (5 mL) and dichloromethane (3 mL) at r.t. under a nitrogen atmosphere for 3h.

<sup>b</sup> 1F/mol of electricity was passed through a solution of substrates (each 0.5 mmol) and Et<sub>4</sub>NBF<sub>4</sub> (1.0 mmol) in a mixture of TFA (5 mL) and dichloromethane (5 mL).

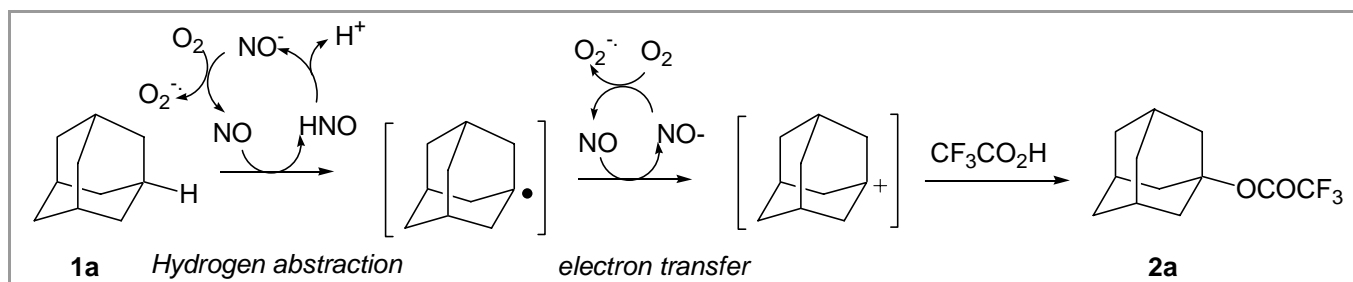
<sup>c</sup> Isolated yield after treatment of the reaction mixture with 10% NaOH (10 mL) and cetyltrimethylammonium hydroxide (0.2 mL) overnight.



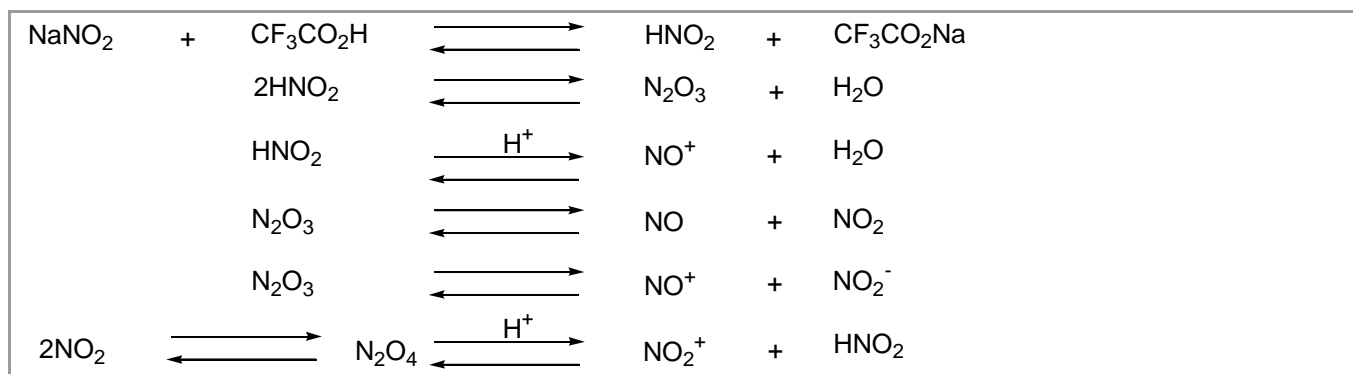
**Scheme 3** Influence of TEMPO on the O<sub>2</sub>/NaNO<sub>2</sub> oxidation of **1a**



**Scheme 4** Influence of TEMPO on electrochemical oxidation of **1a**



**Scheme 5** Plausible reaction mechanism for oxidation of **1a** by O<sub>2</sub>/NaNO<sub>2</sub>



**Scheme 6** Active species generated from  $\text{NaNO}_2$  in TFA

The method presented herein is very promising from a practical viewpoint for oxidation of adamantanes since the reaction conditions are mild, the yields of **3a-c** are high, sodium nitrite is an economically available reagent, and most of TFA can be recovered,<sup>15</sup> though the solvent effect can not be explained at present. Further application of this method to other organic compounds than adamantanes is now under investigation.

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