

CERIUM CATALYZED SELECTIVE OXIDATION OF SECONDARY ALCOHOLS  
IN THE PRESENCE OF PRIMARY ONES

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*Abstract: The combination of  $(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$ - $\text{NaBrO}_3$  or  $\text{Ce}(\text{SO}_4)_2 \cdot 2\text{H}_2\text{SO}_4$ - $\text{NaBrO}_3$  has been found to be effective for the title selective oxidation.*

Although cerium(IV) ion oxidation of organic compounds has been widely studied,<sup>1</sup> application of cerium(IV) ammonium nitrate (CAN) oxidation of alcohols to organic synthesis has been limited because of the large quantities of reagents required and the lack of generality of the reaction.<sup>2</sup> Here we wish to report that under CAN catalysis  $\text{NaBrO}_3$  oxidizes prosaic secondary alcohols<sup>7</sup> into ketones in excellent yields and certain diols are thus converted into the expected keto alcohols with high selectivity.

To a suspension of  $\text{NaBrO}_3$  (0.30 g, 2.0 mmol) in aq. acetonitrile ( $\text{CH}_3\text{CN}/\text{H}_2\text{O} = 7/3$  v/v, 12 ml) cyclododecanol (0.37 g, 2.0 mmol) and CAN (0.11 g, 0.2 mmol) were added. The mixture was heated at reflux for 30 min. The resulting yellow suspension was diluted with ether (20 ml), then washed with sat.  $\text{NaHCO}_3$  and brine. After ether extraction (10 mlx2), the combined organic layer was dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was purified by preparative TLC (AcOEt-hexane, 1:10) to yield cyclododecanone (0.36 g, 98%).


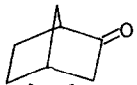

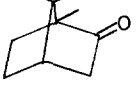
Variations in catalysts and oxidants have been examined with cyclododecanol as the substrate. Cerium(IV) ammonium nitrate and cerium(IV) sulfate<sup>8</sup> were equally active as catalyst, while cerium(III) chloride and cerium(IV) oxide were inactive. Sodium bromate was far superior to other oxidants tried.<sup>9</sup> Although the longer reaction period was required, the amount of cerium(IV) and  $\text{NaBrO}_3$  could be reduced from 0.1 mol and 1.0 mol to 0.035 mol and 0.35 mol, respectively, per 1.0 mol of cyclododecanol without decrease of the yield of cyclododecanone.

As shown in Table 1, wide variety of secondary alcohols could be easily oxidized to ketones. Primary alcohol, however, was recovered practically unchanged. On treatment of 1-dodecanol (1.0 mmol) with cerium(IV) sulfate<sup>10</sup> (0.035 mmol) and  $\text{NaBrO}_3$  (0.35 mmol) in aq.  $\text{CH}_3\text{CN}$  at reflux for 30 min<sup>11</sup> dodecanal was obtained in only 2% yield along with 92% recovery of starting alcohol. Olefinic moiety even in the remote position from hydroxyl group

Table 1. Oxidation of Secondary Alcohols

$$\text{RR}'\text{CHOH} \xrightarrow[\text{NaBrO}_3 \text{ (2.0 mmol), aq. CH}_3\text{CN, 80}^\circ\text{C}]{(\text{NH}_4)_2\text{Ce(NO}_3)_6 \text{ (0.2 mmol)}} \text{RR}'\text{CO}$$

(2.0 mmol)

Run	Alcohol	Reaction Time (h)	Product	Yield(%) <sup>a</sup>
1	4-Dodecanol	0.8	4-Dodecanone	94
2	Cyclododecanol	0.2	Cyclododecanone	98
3	4- <i>t</i> -Butylcyclohexanol	0.5	4- <i>t</i> -Butylcyclohexanone	86
4	PhCH(OH)C(O)Ph	4.5	PhC(O)C(O)Ph	66 (9)
5		0.3		82 <sup>b</sup>
6		1.0		77 <sup>b</sup>
7	<i>l</i> -Menthol	0.3	<i>l</i> -Menthone	82 <sup>c</sup>
8	3 $\beta$ -Cholestanol	0.8	3-Cholestanone	97 <sup>d</sup>
9	11-Dodecen-2-ol	7.0	11-Dodecen-2-one	3 (71)

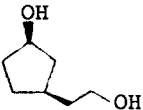
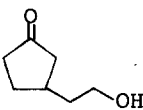
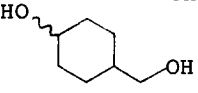
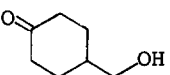

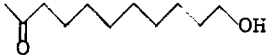
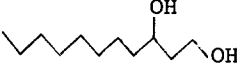
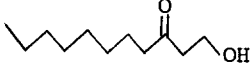
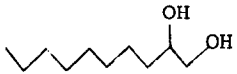
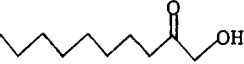
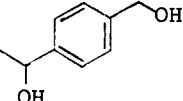
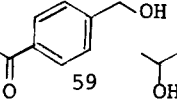
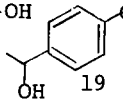
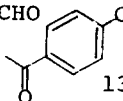
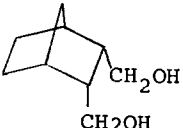
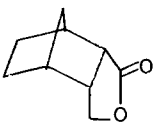
<sup>a</sup>Isolated yields unless otherwise stated. The figures in parentheses indicate the yields of recovered, unreacted alcohols. <sup>b</sup>Glpc yields using an internal standard. <sup>c</sup>Contaminated by less than 1% of *iso*-menthone. <sup>d</sup>Because of solubility problem, CH<sub>3</sub>CN/H<sub>2</sub>O/ClCH<sub>2</sub>CH<sub>2</sub>Cl = 2:1:1 system was used as solvent.

interrupts the oxidation (run 9).<sup>12</sup> It is worth noting that the oxidation proceeds smoothly even with the substrates undergoing C-C bond fission upon treatment with stoichiometric amount of CAN (run 4, 5, and 6).<sup>6,13</sup>

It was anticipated that the treatment of primary, secondary diols with this technique would afford hydroxy ketones arising from selective oxidation at the secondary carbon.<sup>14,15</sup> This was indeed the case as demonstrated by the reactions summarized in Table 2. The selectivity was excellent except the case of 1-*p*-hydroxymethylphenylethanol. In this particular substrate, the secondary hydroxyl group reacts only three times the rate of primary one.

The system is also effective for the oxidation of a primary, primary 1,4-diol. For instance, treatment of 2,3-dihydroxymethylbicyclo[2.2.1]-heptane with CAN-NaBrO<sub>3</sub> provided  $\gamma$ -lactone in good yield. The reaction proceeded *via* lactol.<sup>16</sup>

Table 2. Selective Oxidation of Diols<sup>a</sup>

Alcohol (1.0 mmol)	Ce Salt (x10 <sup>-2</sup> mmol)	NaBrO <sub>3</sub> (mmol)	Reaction Time (h)	Product	Yield <sup>b</sup> (%)
	CAN (10)	1.0	0.5		89
	CAN (10)	1.0	0.25		83
	CS <sup>c</sup> (3.5)	1.0	2.0		86
	CS <sup>c</sup> (8)	0.8	19.0		88
	CS <sup>c</sup> (20)	2.0	24.0		50
	CAN (3.5)	0.35	1.5		59
1-Dodecanol <sup>d</sup>	CS <sup>c</sup> (4.0)	0.40	1.0		19
4-Dodecanol					13
				Dodecanal	<u>3</u>
				4-Dodecanone	<u>98</u>
l-Menthol <sup>d</sup>	CAN (3.5)	0.45	1.0	l-Menthone	<u>37</u>
Cyclododecanol				Cyclododecanone	<u>83</u>
	CAN (10)	1.0	6.5		87

<sup>a</sup>Reactions were performed on 1.0 mmol scale in aq. CH<sub>3</sub>CN at 80°C.

<sup>b</sup>Isolated yields unless otherwise specified. The underlined figures refer to the yields determined by glpc relative to an internal standard.

<sup>c</sup>Cerium(IV) sulfate. <sup>d</sup>Two hydroxy compounds (1.0 mmol each) were employed.

## References and Notes

1. T-L. Ho, *Synthesis*, 1973, 347 and references cited therein.
2. Stoichiometric CAN oxidation of benzylic alcohols<sup>3</sup> and cyclopropylcarbinols<sup>4</sup> affords the carbonyl compounds, whereas 1,2-diarylethanol<sup>5</sup> and *exo*- and *endo*-bicyclo[2.2.1]heptan-2-ol<sup>6</sup> do not react in the expected way. The former substrates have been cleaved into benzaldehydes, while the latter into 3- and 4-cyclopentenacetaldehydes as

major products.

3. W. S. Trahanovsky, L. B. Young, and G. L. Brown, *J. Org. Chem.*, 32, 3865 (1967).
4. L. B. Young and W. S. Trahanovsky, *ibid.*, 32, 2349 (1967).
5. P. M. Nave and W. S. Trahanovsky, *J. Am. Chem. Soc.*, 90, 4755 (1968).
6. W. S. Trahanovsky, P. J. Flash, and L. M. Smith, *ibid.*, 91, 5068 (1969).
7. The CAN-NaBrO<sub>3</sub> system has been reported to effect the oxidation of benzylic alcohols briefly. T-L. Ho, *Synthesis*, 1978, 936. See also T-L. Ho, *Synth. Commun.*, 9, 237 (1979).
8. H. L. Hintz and D. C. Johnson, *J. Org. Chem.*, 32, 556 (1967).
9. Several oxidants were examined for the oxidation of cyclododecanol in aq. CH<sub>3</sub>CN in the presence of 10 mol% CAN. The results are given in order of oxidant, reaction conditions, and % yield of cyclododecanone: <sup>t</sup>BuOOH, 15 h at 80°C, 13%; 30% H<sub>2</sub>O<sub>2</sub>, 5 h at 80°C, 7%; N-methylmorpholine-N-oxide, 5.5 h at 80°C, 0%.
10. The use of CAN instead of cerium(IV) sulfate under the same reaction conditions resulted in formation of dodecanoic acid in 30% yield in addition to recovered 1-dodecanol (60%). CAN was, however, as effective as cerium(IV) sulfate for the selective oxidation of primary, secondary diols (Table 2). Treatment of a mixture of 1-dodecanol and 4-dodecanol (1.0 mol each) with CAN (0.1 mol) and NaBrO<sub>3</sub> (1.0 mol) gave 4-dodecanone in 98% yield together with recovered 1-dodecanol (95%).
11. Under the same reaction conditions, cyclododecanol was converted into cyclododecanone in 95% yield.
12. Allylic alcohol such as 2-cycloocten-1-ol was not easily oxidized and provided the corresponding enone in 9% yield contaminated by unidentified products after 1 h at reflux (45% of starting alcohol remained).
13. Benzoin splits into benzaldehyde and benzoic acid. T-L. Ho, *Synthesis*, 1972, 560.
14. (a) Y. Ueno and M. Okawara, *Tetrahedron Lett.*, 1976, 4597. (b) M. E. Jung and L. M. Speltz, *J. Am. Chem. Soc.*, 98, 7882 (1976); M. E. Jung and R. W. Brown, *Tetrahedron Lett.*, 1978, 2771. (c) G. H. Posner, R. B. Perfetti, and A. W. Runquist, *ibid.*, 1976, 3499. (d) M. A. Neirabeyeh, J. C. Ziegler, and B. Gross, *Synthesis*, 1976, 811.
15. For the preferential oxidation of primary over secondary hydroxyls, see H. Tomioka, K. Takai, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 22, 1605 (1981).
16. Financial support by the Ministry of Education, Science, and Culture, Japanese Government (Grant-in-Aid #56306043) is acknowledged.

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