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Cerium or Ruthenium Catalyzed Oxidation of Alcohols to Carbonyl Compounds by Means of Sodium Bromate

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Sodium bromate has been found to be effective oxidant for oxidation of alcohols in the presence of cerium or ruthenium compounds in biphase reaction. Selective oxidation of secondary alcohols was performed in the presence of primary ones using cerium(IV) ammonium nitrate (CAN) or cerium(IV) sulfate (CS) as catalyst. For instance, treatment of 1,10-undecanediol with CS/$NaBrO_3$ provided 11-hydroxy-2-undecanone in 82% yield. Ruthenium catalyzed biphase oxidation of alcohols with sodium bromate provided the corresponding aldehydes or ketones in good to excellent yields.

Transition metal catalyzed oxidation of alcohols to carbonyl compounds has been widely studied.1) A variety of oxidants such as *t*-butyl hydroperoxide,2) bis(trimethylsilyl) peroxide,3) chloramine-T4) were employed with many transition metals. In contrast to these procedures with organic oxidants, there are few efficient methods using inorganic oxidants for the oxidation of alcohols because of their insolubility in organic solvents. Here we wish to report two methods which utilize sodium bromate as an oxidant: (1) Cerium(IV) ammonium nitrate catalyzed selective oxidation of secondary alcohols in the presence of primary ones and (2) ruthenium(III) chloride catalyzed oxidation of hydroxyls to carbonyl compounds.

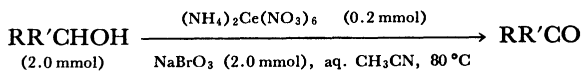
(1) Cerium Catalyzed Selective Oxidation of Secondary Alcohols in the Presence of Primary Ones.5) Although cerium(IV) ion oxidation of organic compounds has been widely studied, application of cerium(IV) ammonium nitrate (CAN) oxidation of alcohols to organic synthesis has been limited because of the large quantities of reagents required and the lack of generality of the reaction.6) Here we wish to report that under CAN catalysis sodium bromate oxidizes secondary alcohols11) into ketones in excellent yields and certain diols are thus converted into the expected keto alcohols with high selectivity.

Treatment of secondary alcohols with a suspension of sodium bromate in aq acetonitrile (CH_3CN:H_2O= 7:3 v/v) at reflux gave the corresponding carbonyl compounds in good to excellent yields. Variations in catalysts and oxidants have been examined with cyclododecanol as the substrate. Cerium(IV) ammonium nitrate and cerium(IV) sulfate12) were equally active as catalyst, while cerium(III) chloride and cerium(IV) oxide were inactive. Sodium bromate was far superior to other oxidants tried. The results for the oxidation of cyclododecanol in aq CH_3CN in the presence of 10 mol% CAN with several oxidants are given in order of oxidant, reaction conditions, and % yield of cyclododecanone: *t*-BuOOH, 15 h at 80 °C, 13%; 30% H_2O_2, 5 h at 80 °C, 7%; *N*-methylmorpholine *N*-oxide, 5.5 h at 80 °C, 0%. Although the longer reaction period was required, the amount of cerium(IV) and sodium bromate could be reduced from 0.1 and 1.0 mol to 0.035 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) sulfate13) (0.035 mmol) and sodium bromate (0.35 mmol) in aq acetonitrile at reflux for 30 min14) dodecanal was obtained in only 2% yield along with 92% recovery of starting alcohol. Olefinic moiety even in the remote position from hydroxyl group interrupts the oxidation (run 9).15) 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).10,16)

It was anticipated that the treatment of primary,

Table 1. Oxidation of Secondary Alcohols

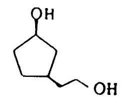
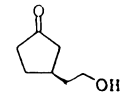
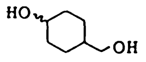
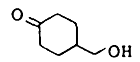
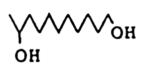
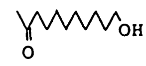
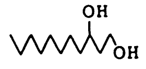
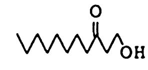
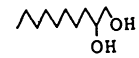
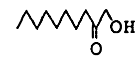
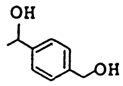
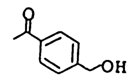
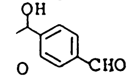
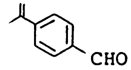
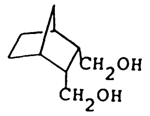
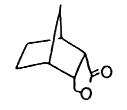


$$\underset{(2.0\,\text{mmol})}{RR'CHOH} \xrightarrow[\text{NaBrO}_3\ (2.0\,\text{mmol}),\ \text{aq. CH}_3\text{CN},\ 80\,^\circ\text{C}]{(NH_4)_2Ce(NO_3)_6\ \ (0.2\,\text{mmol})} RR'CO$$

Run	Alcohol	Reaction Time/h	Product	Yield/%a)
1	4-Dodecanol	0.8	4-Dodecanone	94
2	Cyclododecanol	0.2	Cyclododecanone	98
3	4-*t*-Butyl-cyclohexanol	0.5	4-*t*-Butyl-cyclohexanone	86
4	PhCH(OH)C(O)Ph	4.5	PhC(O)C(O)Ph	66 (9)
5	Norborneol	0.3	Norcamphor	82b)
6	Borneol	1.0	Camphor	77b)
7	*l*-Menthol	0.3	*l*-Menthone	82c)
8	3*β*-Cholestanol	0.8	3-Cholestanone	97d)
9	11-Dodecen-2-ol	7.0	11-Dodecen-2-one	3 (71)

a) Isolated yields unless otherwise stated. The figures in parentheses indicate the yields of recovered, unreacted alcohols. b) Glpc yields using internal standard. c) Contaminated by less than 1% of isomenthone. d) Because of solubility problem, $CH_3CN/H_2O/CH_2ClCH_2Cl=2{:}2{:}1$ system was used as a solvent.

Table 2. Selective Oxidation of Diols[a]

Alcohol 1.0 mmol	Ce Salt $\times 10^{-2}$ mmol	$NaBrO_3$ mmol	Reaction Time/h	Product	Yield[b] %
	CAN (10)	1.0	0.5		89
	CAN (10)	1.0	0.25		83
	CS[c] (3.5)	1.0	2.0		86
	CS[c] (8)	0.8	19.0		88
	CS[c] (20)	2.0	24.0		50
	CAN (3.5)	0.35	1.5		59
					19
					13
1-Dodecanol[d] 4-Dodecanol	CS[c] (3.5)	0.40	1.0	Dodecanal 4-Dodecanone	3 98
l-Menthol[d] Cyclododecanol	CAN (3.5)	0.45	1.0	*l*-Menthone Cyclododecanone	37 83
	CAN (10)	1.0	6.5		87

a) Reactions were performed on 1.0 mmol scale in aq CH_3CN at 80 °C. b) Isolated yields unless otherwise specified. The underlined figures refer to the yields determined by glpc relative to an internal standard. c) Cerium(IV) sulfate. d) Two hydroxy compounds (1.0 mmol each) were employed.

secondary diols with this technique would afford hydroxy ketones arising from selective oxidation at the secondary carbon.[17,18] This was indeed the case as demonstrated by the reactions summarized in Table 2. The selectivity was excellent except the case of 1-[*p*-(hydroxymethyl)phenyl]ethanol. 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-bis(hydroxymethyl)bicyclo[2.2.1]heptane with cerium(IV) ammonium nitrate–sodium bromate provided the corresponding γ-lactone in a good yield. The reaction presumably proceeds via the lactol.

(2) Ruthenium Catalyzed Oxidation of Alcohols to Carbonyl Compounds. In recent years oxidation reactions using ruthenium as a key atom have been extensively developed. Among them, ruthenium complex, $RuCl_2(PPh_3)_3$ proved to be an efficient oxidant for chemoselective oxidation of primary alcohols.[18] Moreover, ruthenium catalyzed reactions with oxidants such as bis(trimethylsilyl) peroxide,[3] amine *N*-oxide,[4] *t*-butyl hydroperoxide,[19] hypervalent iodine compounds,[20] molecular oxygen,[21,22] have been reported. We chose sodium bromate as an oxidant which proved to be an effective and inexpensive oxidant for oxidation of hydroxyl substrates to the corresponding carbonyl compounds.[23]

Secondary alcohols were added to a biphase solution of ruthenium trichloride hydrate and sodium bromate in water and 1,2-dichloroethane ($H_2O:ClCH_2CH_2Cl=1:1$ v/v). The mixture was heated at reflux to yield the corresponding carbonyl compounds in good to excellent yields (Reaction Conditions B). Variations in catalysts and reaction conditions have been examined with cyclododecanol as a substrate. Ruthenium trichloride hydrate, tris(triphenylposhine)ruthenium(II) dichloride, and dodecacarbonyltriruthenium(0) were equally active as catalyst and cyclododecanone was obtained quantitatively with each catalyst. Reaction was accelerated by phase transfer catalyst such as quaternary ammonium salt (Reaction Conditions A). For instance, cyclododecanol was easily oxidized to cyclododecanone even at 25 °C within 30 min (>99% yield), in the presence of tetrabutylammonium bromide. Some representative examples are shown in Table 3.

In contrast, $RuCl_3\cdot nH_2O$ or $RuCl_2(PPh_3)_3$ catalyzed oxidation of primary alcohols resulted in the formation of the desired aldehydes in poor yields along with carboxylic acids and esters. Dodecacarbonyltriruthenium(0) catalyzed reaction (Reaction Conditions D), however, has solved this problem and converted primary alcohols into aldehydes in good yields. In the case of former ruthenium chloride compounds, hydrochloric acid generated during the reaction catalyzes the transformation of the resultant aldehydes into hemiacetals or gem-diols which are oxidized further to esters or carboxylic acids. The use of the buffer solution (pH=10) instead of water prevented these side reactions and provided us with a simple method for the selective formation of aldehydes (Reaction Conditions C).

Table 3. Oxidation of Alcohols with Ruthenium Compounds

Run	Alcohol	Conditions[a]	Reaction Time/h	Yield[b]/%
1	Cyclododecanol	A	0.5	>99
		B	1.0	97
2	4-Dodecanol	A	0.5	98
3	4-*t*-Butyl-cyclohexanol	A	0.5	97
4	*l*-Menthol	A	0.5	93
5	Borneol	A	0.5	98
6	Norborneol	A	0.5	98[c]
7	$PhCH(OH)CH_3$	A	0.5	93
8	11-Dodecen-2-ol	A	1.0	54[d]
		B	7.0	77
9	3*β*-Cholestanol	A	1.5	98
10	Carveol	B	1.5	78
11	2-Cyclohexen-1-ol	B	1.5	69[c]
12	1-Dodecanol	A	1.0	40[e]
		C	1.0	86
		D	1.0	88
13	10-Undecen-1-ol	C	1.2	70
14	2-Dodecen-1-ol	A	2.0	63
		B	2.5	80
15	Cyclohexylmethanol	C	2.5	97[c]
16	Geraniol	C	1.5	78
17	Benzyl alcohol	C	1.5	81

a) Reactions were performed under these conditions A: $RuCl_3\cdot nH_2O$ (5.0 mol%), $n\text{-}Bu_4NBr$ (3.0 mol%), $H_2O/CH_2Cl_2=2$ ml : 2 ml, 25 °C. B: $RuCl_3\cdot nH_2O$ (5.0 mol%), $H_2O/CH_2ClCH_2Cl=2$ ml : 2 ml, 70 °C. C: $RuCl_3\cdot nH_2O$ (5.0 mol%), a buffer solution/$CH_2ClCH_2Cl=2$ ml : 2 ml, 70 °C. The buffer solution (pH 10) is prepared by mixing equal volume of 0.2 M aq Na_2CO_3 and 0.2 M aq $NaHCO_3$. ($M=1\ \text{mol dm}^{-3}$) D: $Ru_3(CO)_{12}$ (5.0 mol%), $H_2O/CH_2ClCH_2Cl=2$ ml: 2 ml, 70 °C. b) Isolated, purified yields unless otherwise noted. c) Glpc yields using an internal standard. d) Transformation of olefin to bromohydrin was observed (23%). e) Dodecanoic acid (20%) and dodecyl dodecanoate (22%) were also obtained.

Experimental

Infrared spectra of neat liquid film samples were determined on a Hitachi grating infrared spectrometer 215, or JASCO IR-810, mass spectra and exact mass on a Hitachi M-80. NMR spectra were recorded on a Varian EM-390, or Varian XL-200 spectrometer using TMS as an internal standard unless otherwise noted. Multiplicity is designed as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Preparative TLC plates were prepared with Merck kiesel-gel PF_{254}. Column chromatography was carried out with silica-gel (Wakogel C-200) at atmospheric pressure.

General Procedure for the Oxidation of Secondary Alcohols with Cerium(IV) Ammonium Nitrate (CAN)/$NaBrO_3$: Cyclododecanol (0.37 g, 2.0 mmol) and catalytic amount of CAN (0.11 g, 0.2 mmol) were added to a suspension of sodium bromate (0.30 g, 2.0 mmol) in aq acetonitrile ($CH_3CN/H_2O=7/3$ v/v, 12 ml). The whole was heated at reflux for 30 min and the resulting yellow suspension was diluted with ether (20 ml). After extraction with ether (10 ml×2), organic layer was washed with sat. $NaHCO_3$ and brine successively, and dried over sodium sulfate. Concentration and purification by preparative TLC (hexane–ethyl acetate=10:1) gave cyclododecanone (0.36 g, 98%).

Oxidation of 3-(2-Hydroxyethyl)cyclopentanol: The diol (0.23 g, 1.8 mmol) and CAN (0.1 g, 0.18 mmol) were added to a suspension of sodium bromate (0.27 g, 1.8 mmol) in aq acetonitrile. The whole was heated at reflux for 30 min and the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and poured into water. After extraction with ethyl acetate, the combined organic layer was dried over sodium sulfate. Concentration followed by purification by silica-gel column chromatography (hexane–ethyl acetate=3:1) gave 3-(2-hydroxyethyl)-cyclopentanone (0.20 g, 89%).

Oxidation of 1,10-Undecanediol with Cerium(IV) Sulfate (CS)/$NaBrO_3$: The diol (0.37 g, 2.0 mmol) and CS (0.07 g, 0.2 mmol) were added to a suspension of sodium bromate (0.3 g, 2.0 mmol) in aq acetonitrile (10 ml) and the whole was refluxed for 2 h. Extractive workup and purification by silica-gel column chromatography (hexane–ethyl acetate=2:1) gave 11-hydroxy-2-undecanone (0.32 g, 86%).

General Procedure for the Oxidation of Secondary Alcohols with $RuCl_3/NaBrO_3$ in the Presence of a Phase Transfer Reagent (Reaction Conditions A): Tetrabutylammonium bromide (ca. 10 mg) and a solution of cyclododecanol (0.18 g, 1.0 mmol) in dichloromethane (2.0 ml) were added successively to a solution of sodium bromate (0.15 g, 1.0 mmol) and ruthenium trichloride (0.01 g, 0.05 mmol) in deionized water (2.0 ml). The mixture was stirred at 25 °C and the alcohol was consumed completely within 30 min. The resulting dark brown solution was diluted with ether, then poured into ice cooled sat. sodium hydrogensulfite. After extraction with ethyl acetate (20 ml×2), the combined organic layer was dried over sodium sulfate and concentrated. The residual oil was purified by silica-gel column chromatography (hexane–ethyl acetate=10:1) to yield cyclododecanone (0.18 g) quantitatively.

General Procedure for the Oxidation of Alcohols with $RuCl_3$/$NaBrO_3$ without a Phase Transfer Catalyst (Reaction Conditions B): A solution of cyclododecanol (0.18 g, 1.0 mmol) in 1,2-dichloroethane was added to a mixed solution of sodium bromate (0.15 g, 1.0 mmol) and ruthenium trichloride (0.01 g, 0.05 mmol) in deionized water (2.0 ml). The mixture was stirred at 70 °C for 3 h. Workup and purification by silica-gel column chromatography gave cyclododecanone in quantitative yield.

General Procedure for the Oxidation of Primary Alcohols with $RuCl_3 \cdot nH_2O$/$NaBrO_3$ (Reaction Conditions C): Sodium bromate (0.15 g, 1.0 mmol) and ruthenium trichloride (0.01 g, 0.05 mmol) were dissolved in the buffer solution (2.0 ml, pH=10). 1,2-Dichloroethane (1.0 ml) was added and the whole was stirred for 30 min at 25 °C. A solution of 1-dodecanol (0.19 g, 1.0 mmol) in 1,2-dichloroethane (1.0 ml) was added and the resulting mixture was stirred for 20 min at 70 °C. Workup and purification gave dodecanal in 86% yield.

General Procedure for the Oxidation of Primary Alcohols with $Ru_3(CO)_{12}$/$NaBrO_3$ (Reaction Conditions D): A solution of 1-dodecanol (0.19 g, 1.0 mmol) in 1,2-dichloroethane (2.0 ml) was added to a solution of dodecacarbonyltriruthenium(0) (0.01 g, 0.05 mmol of ruthenium element) and sodium bromate (0.3 g, 2.0 mmol) in deionized water (2.0 ml). The whole was stirred for 1 h at 70 °C and the mixture was poured into ice-cooled water and extracted with ethyl acetate. Purification by preparative TLC gave dodecanal (0.13 g) in 68% yield.

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13) 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 mmol each) with CAN (0.1 mmol) and $NaBrO_3$ (1.0 mmol) gave 4-dodecanone in 98% yield together with recovered 1-dodecanol (95%).

14) Under the same reaction conditions, cyclododecanol was converted into cyclododecanone in 95% yield.

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