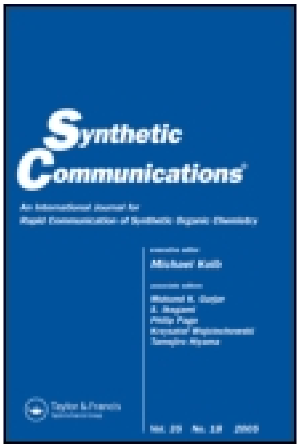

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Cerium(III) Bromate as a New Reagent in Oxidation of Organic Compounds

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ABSTRACT

Cerium(III) bromate, prepared by the reaction of barium bromate with cerium(III) sulfate, can be used for the oxidation of alkylarenes, alcohols, and sulfides. Products are obtained in high yields under mild conditions. $Ce(BrO_3)_3$ is an unique, dual property reagent in which the anion is the oxidant and the cation a catalyst. Stoichiometric studies indicate that bromate is reduced to bromide under these conditions, making the process highly efficient.

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INTRODUCTION

Cerium(IV) ammonium nitrate (CAN) has been used extensively as an oxidant in organic chemistry. It has been employed both as a stoichiometric oxidant and as a catalyst in combination with other co-oxidants for the oxidation of toluene and substituted toluenes to the corresponding benzaldehydes,[1] ethylbenzene and diphenylmethane to acetophenone and benzophenone, respectively,[1,2] benzylic alcohols to aldehydes,[3] phenols to quinones[4] and sulfides to sulfoxides.[5] When coupled with a co-oxidant such as sodium bromate, cerium(IV) has also been as a catalyst for the oxidation of alcohols,[6–8] sulfides,[9] and aromatic side chains.[10] The oxidation reactions of cerium(IV) have been reviewed by several authors.[11–13]

Although very useful for many purposes, CAN suffers from a pair of disadvantages: (i) because it is a high molecular weight, one-electron transfer agent, large quantities are required for certain applications. In particular, the oxidation of alkylarene, to the corresponding *alpha*-ketones, which is a four electron process, requires over 2 kg of oxidant for each mole of reductant; and (ii) since acidic conditions are required, acid sensitive compounds cannot be oxidized without causing undesirable degradations. Some of these disadvantages can be overcome by using catalytic amounts of CAN coupled with a less expensive multi-electron transfer agent such as sodium bromate; however, rather acidic conditions are still required. For example, both CAN and $Ce(SO_4)_2 \cdot 2H_2SO_4$,[7] which produce acidic aqueous solutions are active catalysts, while corresponding neutral compounds such as cerium(III) chloride,[7] cerium(IV) oxide,[7] and cerium(IV) fluoride[14] are much less active.

In continuation of our studies on the oxidation of organic compounds with bromate ion,[15–19] we wish to report that the above mentioned problems can be overcome by the use of cerium(III) bromate, which gives excellent yields in the oxidation of alkylarenes, alcohols, and sulfides under neutral conditions. $Ce(BrO_3)_3$ is a unique oxidant that contains both the catalyst, Ce^{3+}, and the co-oxidant, BrO_3^-, in a single compound. Although the preparation of $Ce(BrO_3)_3$ was first described about a century ago,[20] a search of literature failed to uncover any previous reports of its use as an oxidant for organic compounds. However, as described in the following report, we have found that it is a very convenient reagent for the oxidation of alkylarenes, alcohols, and sulfides in aqueous acetonitrile.

EXPERIMENTAL SECTION

Oxidant

$Ce(BrO_3)_3$ is easily prepared in situ by the reaction of cerium(III) sulfate with barium bromate, as in Eq. 1. Barium sulfate precipitates, leaving a solution of the oxidant that can be used without further modification.

$$3Ba(BrO_3)_2 + Ce_2(SO_4)_3 \longrightarrow 2Ce(BrO_3)_3 + 3BaSO_4 \downarrow \tag{1}$$

Reductants

The reductants used in this study were obtained commercially (Aldrich) and used without additional purification.

Products

All products are known compounds, which were identified by comparison of their physical and spectral data with literature values. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Infrared spectra were recorded as neat films or as KBr pellets on a Perkin Elmer FT-IR 1600 spectrophotometer. NMR spectra were recorded on a Bruker AC-200 spectrometer at 200 MHz with $CDCl_3$ as solvent and $(CH_3)_4Si$ as internal standard. Yields refer to isolated products or 2,4-dinitrophenylhydrazone (2,4-DNP) derivatives.[21]

A Typical Procedure for the Oxidation of Alkylarenes

Cerium(III) sulfate hydrate (0.133 g, 0.23 mmol) and barium bromate (0.295 g, 0.75 mmol) were added to indan (0.177 g, 1.50 mmol) in aqueous acetonitrile ($CH_3CN{:}H_2O = 7{:}3$; 10 mL). The reaction mixture was refluxed and the progress of the reaction monitored by TLC (eluent; hexane:ethyl acetate = 2:1). When the reaction was completed (after 2 h), the product mixture was filtered through a sinter glass funnel and the residue washed with methylene chloride (10 mL). The filtrate was treated with saturated aqueous sodium thiosulfate (5 mL) in order to reduce any residual oxidant. The resulting mixture was extracted with methylene chloride (2 × 10 mL) and the combined organic layers were dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 1-indanone (0.176 g, 1.33 mmol, 89%). This product was identified by comparison with authentic 1-indanone using TLC, melting point (41–42°C; Lit.[22] 42°C) and ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.63 (t, $J = 6.10$ Hz, 2H), 3.09 (t, $J = 6.10$ Hz, 2H), 7.08–7.80 (m, 4H).

The stoichiometry of the reaction was determined by monitoring the extent to which indan was converted to indanone by limited amounts of oxidant. Indan (0.177 g, 1.5 mmol) was dissolved in aqueous acetonitrile (CH_3CN:$H_2O = 7{:}3$; 10 mL), cerium(III) sulfate hydrate (0.133 g, 0.230 mmol) and barium bromate (0.197 g, 0.500 mmol) were added and the reaction was allowed to proceed at reflux temperature until all of the oxidant had been consumed (20 h). The extent of reaction was then established by comparing peak integrals in the ^{1}H NMR spectrum for indan (δ 2.03 and 2.88 ppm) and 1-indanone (δ 2.63 and 3.09 ppm). The experiment was repeated two more times using less barium bromate (0.375 and 0.25 mmol). From a plot ($r^2 = 0.98$) of unreacted indan vs. the amount of bromate reduced it was found that 1.50 mmol of indan reacted with 1.06 mmol BrO_3^- (or 0.35 mmol $Ce(BrO_3)_3$).

A Typical Procedure for the Oxidation of Sulfides

Cerium(III) sulfate hydrate (0.100 g, 0.17 mmol) and barium bromate (0.200 g, 0.51 mmol) were added to methyl *p*-tolyl sulfide (0.138 g, 1.00 mmol) in aqueous acetonitrile (CH_3CH:$H_2O = 7{:}3$; 10 mL). The reaction mixture was stirred at room temperature and the progress of the reaction monitored by TLC (eluant; chloroform:ethyl acetate = 1:1). When the reaction was complete (after 50 min), the product mixture was filtered through a sinter glass funnel and the residue washed with methylene chloride (10 mL). The filtrate was treated with saturated aqueous sodium thiosulfate (2.5 mL) in order to reduce any residual oxidant. The resulting mixture was extracted with methylene chloride (2 × 10 mL) and the combined organic layers were dried over anhydrous magnesium sulfate. Evaporation of the solvent gave methyl *p*-tolyl sulfoxide (0.150 g, 0.99 mmol, 97%). This product was identified by comparison with authentic methyl *p*-tolyl sulfoxide using TLC, melting point (45–46°C; Lit.[23] 44–46°C) and ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.43 (s, 3H), 3.70 (s, 3H), 7.43 (d, $J = 8.51$ Hz, 2H), 7.55 (d, $J = 8.50$ Hz, 2H).

The stoichiometry of this reaction was established as described above for the oxidation of indan to indanone. The results showed each mmol of sulfide reacted with 0.35 mmol BrO_3 (or 0.12 mmol $Ce(BrO_3)_3$).

A Typical Procedure for the Oxidation of Alcohols

Cerium(III) sulfate hydrate (0.110 g, 0.186 mmol) and barium bromate (0.393 g, 1.0 mmol) were added to 1-indanol (0.268 g, 2.0 mmol) in aqueous acetonitrile ($CH_3CN:H_2O = 7:3$; 10 mL). The reaction mixture was refluxed and the progress of the reaction monitored by TLC (eluant; hexane:ethyl acetate = 2:1). When the reaction was complete (after 2 h), the product mixture was filtered through a sinter glass funnel and the residue washed with methylene chloride (10 mL). The filtrate was treated with saturated aqueous sodium thiosulfate (5 mL) in order to reduce any residual oxidant. The resulting mixture was extracted with methylene chloride (2 × 10 mL) and the combined organic layers were dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 1-indanone (0.264 g, 2.0 mmol, 100%). This product was identified by comparison with authentic 1-indanone using TLC, melting point (41–42°C; Lit.[22] 42°C) and ^1H NMR (200 MHz, $CDCl_3$): δ 2.63 (t, $J = 6.10$ Hz, 2H), 3.09 (t, $J = 6.10$ Hz, 2H), 7.08–7.80 (m, 4H).

The stoichiometry of this reaction was then determined as described above for the oxidation of indan to indanone. The results showed 2 mmol of alcohol reacted with 0.69 mmol BrO_3^- (or 0.23 mmol $Ce(BrO_3)_3$).

RESULTS AND DISCUSSION

The Oxidation of Alkylarenes

From a quantitative study of the reaction of indan with limited amounts of oxidant it was determined that 1.5 mmol of alkylarene reacts with 0.35 mmol $Ce(BrO_3)_3$, giving the stoichiometry expressed in Eq. 2.

$$9ArCH_2R + 2Ce(BrO_3)_3 \longrightarrow 9ArCOR + 2CeBr_3 + 9H_2O \qquad (2)$$

The observed stoichiometry clearly indicates that the process is highly efficient; very little oxidant is lost to side reactions.

The results summarized in Table 1 indicate that the reaction can be used effectively to synthesize *alpha*-ketones from a wide variety of alkylarenes. Both cyclic and acyclic side chains are efficiently oxidized. Interestingly, the reaction appears to fail when there is a methoxy substituent on the aromatic ring as in Entries 6 and 8. This rather unusual observation suggests that the reaction does not likely involve a rate limiting hydride or hydrogen atom transfer because the resulting intermediate carbocations or free radicals would be

Table 1. Oxidation of alkylarenes by cerium(III) bromate.[a]

Entry	Reactant	Product	Reaction time (h)	Yield (%)
1	Ethylbenzene	Acetophenone	2	94[b]
2	4-Ethyltoluene	4-Methylacetophenone	1.3	92[b]
3	4-Ethylfluorobenzene	4-Fluoroacetophenone	2.2	94[b]
4	4-Ethylnitrobenzene	4-Nitroacetophenone	24	95[b]
5	Pentylbenzene	Butyl phenyl ketone	6	97
6	4-Ethylanisole	No reaction	10	—
7	Indan	1-Indanone	2	89
8	5-Methoxyindan	No reaction	15	—
9	Phthalan	Phthalide	2	90
10	2,3-Dihydrobenzofuran	No reaction	20	—
11	Tetralin	1-Tetralone	3.5	95
12	Isochroman	2-Chromanone	2	90
13	Diphenylmethane	Benzophenone	3	80
14	Fluorene	9-Fluorenone	24	50[b]
15	1,2-Diphenylethane	Benzyl phenyl ketone	6	85
16	Anthrone	Anthraquinone	20	97
17	Xanthene	Xanthone	24	90
18[c]	Indan	No reaction	24	—
19[d]	Indan	1-Indanone	8	10
20[e]	Indan	1-Indanone	8	15

[a] Cerium(III) sulfate (0.23 mmol) and barium bromate (0.75 mmol) were reacted with alkylarene (1.5 mmol) in aqueous acetonitrile (10 mL) under reflux.
[b] A small amount (3–6%) of the corresponding alcohol was also obtained.
[c] No cerium sulfate was used.
[d] The amount of cerium sulfate was reduced to 0.023 mmol.
[e] Cerium(III) chloride (2 mmol) and sodium bromate (1.5 mmol) were reacted with indan (1.5 mmol) in aqueous acetonitrile (10 mL).

stabilized by methoxy substituents. The unreactivity of 2,3-dihydrobenzofuran (Entry 10) is also consistent with these observations. However, one apparent exception to this pattern is xanthene (Entry 17) where the *ortho* oxygen does not seem to greatly inhibit the reaction. Although these observations are currently not well understood from a mechanistic point of view, the selectivity exhibited by the reaction may be of empirical value when this reaction is used for organic synthesis.

The low yield obtained when cerium(III) chloride and sodium bromate were used under the same conditions (Entry 20) indicates that $Ce(BrO_3)_3$ is superior to the use of other cerium(III) compounds as catalysts in the presence of sodium bromate.

Table 2. Oxidation sulfides by cerium(III) bromate.[a]

Entry	Reactant	Product	Reaction time (min)	Yield (%)
1	Thioanisole	Methyl phenyl sulfoxide	60	97
2	Methyl *p*-tolyl sulfide	Methyl *p*-tolyl sulfoxide	50	99
3	4-Fluorothioanisole	4-Fluorophenyl methyl sulfoxide	50	98
4	4-Chlorothioanisole	4-Chlorophenyl methyl sulfoxide	45	97
5	4-Bromothioanisole	4-Bromophenyl methyl sulfoxide	45	98
6	4-Nitrothioanisole	4-Nitrophenyl methyl sulfoxide	60	98
7	4-Methoxy-(methylthio) benzene	4-Methoxyphenyl methyl sulfoxide	120	97
8	Phenyl sulfide	Phenyl sulfoxide	180	99
9	Benzyl phenyl sulfide	Benzyl phenyl sulfoxide	120	98
10	Benzyl sulfide	Benzyl sulfoxide	80	95
11	Ethyl sulfide	Ethyl sulfoxide	45	98
12	Butyl sulfide	Butyl sulfoxide	45	96
13	Hexyl sulfide	Hexyl sulfoxide	60	97
14	Octyl sulfide	Octyl sulfoxide	60	98
15	Pentamethylene sulfide	Pentamethylene sulfoxide	60	99
16[b]	Thioanisole	No reaction	1400	—
17[b]	Butyl sulfide	No reaction	1400	—
18	Thioanisole	Methyl phenyl sulfoxide	1400	98[c]
19	Butyl sulfide	Butyl sulfoxide	1400	92[d]
20	Methyl phenyl sulfoxide	Methyl phenyl sulfone	1400	4
21	Butyl sulfoxide	Butyl sulfone	1400	9

[a] Cerium(III) sulfate (0.17 mmol) and barium bromate (0.50 mmol) were added to the sulfide (1.0 mmol) in aqueous acetonitrile (10 mL) and the reaction was allowed to proceed at room temperature.

[b] No cerium sulfate was used.

[c] Plus 2% methyl phenyl sulfone.

[d] Plus 8% butyl sulfone.

The Oxidation of Sulfides

Alkyl and aryl sulfides are converted into sulfoxides in quantitative yields when treated with cerium(III) bromate in aqueous acetonitrile. As the data in Table 2 (Entries 20 and 21) indicates, the rate of oxidation of sulfoxides under these conditions is so slow that the products obtained after a reasonable reaction time are not contaminated by sulfones.

Table 3. Oxidation of alcohols by cerium(III) bromate.[a]

Entry	Reactant	Product	Reaction time (h)	Yield (%)
1	Benzyl alcohol	Benzaldehyde	3	85
2	4-Fluorobenzyl alcohol	4-Fluorobenzaldehyde	3.3	70
3	4-Methylbenzyl alcohol	4-Methybenzaldehyde	3	90
4	4-Nitrobenzyl alcohol	4-Nitrobenzaldehyde	5	36[b]
5	1-Phenylethanol	Acetophenone	2	90
6	Benzhydrol	Benzophenone	6	95
7	Benzoin	Benzil	24	100
8	1-Indanol	1-Indanone	2	100
9	9-Hydroxyfluorene	9-Fluorenone	7	80
10	3-Pentanol	3-Pentanone	3.3	100
11	4-Heptanol	4-Heptanone	3.3	100
12	4-Octanol	4-Octanone	3.3	100
13	Cyclopentanol	Cyclopentanone	5	90
14	Cyclohexanol	Cyclohexanone	3	100
15	4-Methylcyclohexanol	4-Methylcyclohexanone	7	90
16	2-*tert*-Butylcyclohexanol	2-*tert*-Butylcyclohexanone	7	90
17	*Exo*-Norborneol	Norcamphor	7	90
18	2-Ethyl-1,3-hexanediol	3-Hydroxymethyl-4-heptanone	3.3	90
19	1-Phenyl-1,2-ethannediol	Hydroxymethyl phenyl ketone	3.3	90
20[c]	1-Phenylethanol	No reaction	24	—
21[c]	4-Heptanol	No reaction	24	—

[a] Cerium(III) sulfate (0.19 mmol) and barium bromate (1.0 mmol) were added to the alcohol (2.0 mmol) in aqueous acetonitrile (10 mL) and allowed to react under reflux.

[b] 4-Nitrobenzoic acid (15%) was also isolated.

[c] No cerium sulfate was used.

The reagent, therefore, shows excellent selectivity for the formation of sulfoxides.

As indicated from the data reported in the experimental section, 1.0 mmol of sulfide is completely oxidized by 0.12 mmol $Ce(BrO_3)_3$, giving the stoichiometry expressed in Eq. 3.

$$9RSR' + Ce(BrO_3)_3 \longrightarrow 9RSOR' + CeBr_3 \qquad (3)$$

The Oxidation of Alcohols

Primary alcohols are oxidized to aldehydes and secondary alcohols to ketones by cerium(III) bromate as indicated by the data in Table 3.

The yields are, in general, better for secondary alcohols and, in competitive reactions, secondary alcohols are oxidized preferentially. For example, the oxidation of 1-phenyl-1,2-ethanediol gives hydroxymethyl phenyl ketone in 90% yield (Entry 19). Similarly, 2-ethyl-1,3-hexanediol gives 2-hydroxymethyl-4-heptanone as the sole product (Entry 18). The reagent, therefore, shows excellent selectivity for the oxidation of secondary alcohols.

The results reported in the experimental section show that 2.0 mmol of secondary alcohol are completely oxidized by 0.23 mmol $Ce(BrO_3)_3$, giving the stoichiometry expressed in Eq. 4.

$$9RCHOHR' + Ce(BrO_3)_3 \longrightarrow 9RCOR' + CeBr_3 + 9H_2O \qquad (4)$$

SUMMARY

1. Cerium(III) bromate, which may be prepared in situ from the reaction of barium bromate and cerium(III) sulfate in an aqueous acetonitrile, is a unique oxidant that contains both the catalyst (Ce^{+3}) and the cooxidant (BrO_3^-) in a single compound.
2. Alkylarenes are converted into the corresponding *alpha*-ketones in good yields. The reagent does not, however, react with most alkoxy substituted alkylarenes.
3. Sulfides are oxidized to the corresponding sulfoxides in quantitative yields. The products are not contaminated by the presence of the corresponding sulfones.
4. Primary benzylic and secondary alcohols are oxidized to the corresponding aldehydes and ketones respectively. In competitive reactions with diols which contain both primary and secondary functionalities, the secondary hydroxyls are oxidized preferentially.
5. Stoichiometric studies have shown that bromate is reduced to bromide in these reactions.

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