

# Selective cerium-catalyzed oxidation of alkyl benzenes to benzyl esters by bromate salts

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## Abstract

Benzyl esters are formed catalytically at moderate temperatures from alkyl benzenes by  $\text{KBrO}_3$  in the presence of cerium ammonium nitrate (CAN). Toluene gives in acetic acid benzyl acetate. Ethylbenzene, cumene, 4-*tert*-butyltoluene, and 4-bromotoluene give similar oxidation products. *p*-xylene undergoes a selective mono-acetoxylation reaction in acetic acid. The bromate salt is acting as an oxidant for the alkylbenzene and a cooxidant for the Ce salt. The Ce salts (Ce(III), Ce(IV)) serve both as oxidation catalysts and as Lewis acids that catalyze the conversion of benzyl bromide in the reaction mixture to benzyl ester.

*Keywords:* Oxidation; Alkylbenzenes; Benzyl esters; Cerium; Bromate salts

## 1. Experimental

### 1.1. General

$^1\text{H}$  NMR spectra were recorded on a Varian XL-200 spectrometer. GCMS measurements of the products and reaction mixtures were taken on a Packard VG 5050 micromass spectrometer. The progress of the reactions was monitored on a Perkin-Elmer 8310B gas chromatograph equipped with either a 5% SE-52 or a DEGS/Chromosorb W column. All solvents were distilled prior to use. CAN was obtained from Aldrich Chemical Co. Products were identified by comparison of their physical data (NMR, IR, MS) with those of authentic samples.

### 1.2. General procedure of the oxidation reaction in acetic acid

Potassium bromate (7.5–10 mmol), CAN (0.5 mmol) and alkylbenzene (10 mmol) were added to acetic acid (15 ml) in a three necked flask under nitrogen. The mixture was stirred and heated (see Table 1 for details). The reaction was followed by GC and  $^1\text{H}$  NMR. After the desired conversion, the reaction mixture was poured into a cold mixture of water (20 ml) and dichloromethane (20 ml). Separation, washing the organic layer with water (20 ml  $\times$  3), drying with magnesium sulfate and evaporation of the solvent, leads to an oil mixture. The crude was separated on a silica-gel column chromatograph (hexane/ether).

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## 2. Introduction

Benzylic esters are usually prepared by esterification of benzylic alcohols. The formation of the alcohols requires, however the application of the fairly expensive hydride reduction of carbonyl compounds. Consequently, direct benzylic functionalization of the easily available alkylbenzenes has been intensively investigated [1–3]. The direct transformation of alkylarene involves peroxides and a variety of metal salts [4,5]. Some serious drawbacks are associated with these reactions (e.g., toxicity of some metals, stoichiometric reaction conditions, or non-generality) that may be responsible for their infrequent use for the preparation of benzylic alcohols and esters.

A limited number of metallic oxidants have been used to oxidize methylbenzenes to benzyl esters in carboxylic acids as a medium. The best known reagent is lead tetraacetate, which gives moderate yields [4].

Several research groups have however reported the use of ceric salts under stoichiometric conditions [6,7]. Oxidation of organic compounds with cerium (IV) is interesting since Ce(IV) is an unusually strong, one electron oxidant. Moreover, unique reactions of Ce(IV) with organic compounds are expected, because of specific coordination properties of the ion with various organic and inorganic ligands. Application of Ce(IV) to organic synthesis has been limited because of the large quantities of reagents required. Moreover this process lacked generality. To overcome these shortcomings we investigated systems in which catalytic amounts of Ce(IV) salts are added, and during oxidation of alkylbenzenes the Ce(IV) species is continuously replenished by the action of a less expensive oxidant. Thus Ce(IV) is reduced by the alkylbenzene, but the resulting Ce(III) ion is reoxidized by the bromate ion.

We have shown in our recent studies on the oxidation of alkylbenzenes to aldehydes, ke-

Table 1  
Oxidation of alkylbenzenes catalyzed by CAN and  $\text{KBrO}_3$  <sup>a</sup>

Substrate	$\text{KBrO}_3$ (mmol)	Temp. (°C)	Time (h)	Conversion (%)	Products (yield %)		
					ester	aldehyde	others
<b>1</b> <sup>b</sup>	7.5	90	2	100	<b>2a</b> (75)	–	<b>3</b> (5); <b>4</b> (20)
<b>1</b>	7.5	90	2	100	<b>2a</b> (92)	–	<b>3</b> (6); <b>4</b> (4)
<b>2</b> <sup>b</sup>	7.5	110	18	88	<b>6a</b> (56)	<b>7</b> (5)	<b>8</b> (23)
<b>2</b> <sup>c</sup>	7.5	110	21	98	<b>6a</b> (56)	<b>7</b> (15)	<b>8</b> (14); <b>9</b> (15)
<b>2</b>	7.5	110	18	86	<b>6a</b> (72)	<b>7</b> (7)	<b>8</b> (7)
	7.5	90	21	89	<b>6a</b> (60)	<b>7</b> (8)	<b>8</b> (10); <b>9</b> (11)
	8.75	90	24	95	<b>6a</b> (65)	<b>7</b> (12)	<b>8</b> (10); <b>9</b> (8)
<b>11</b>	10	90	23	95	<b>6a</b> (56)	<b>7</b> (22)	<b>8</b> (6); <b>9</b> (11)
	10	110	3	96	<b>12</b> (75)	<b>13</b> (12)	<b>14</b> (3); <b>15</b> (6)
<b>16</b>	7.5	110	19	86	<b>17</b> (75)	<b>18</b> (11)	
<b>19</b>	7.5	90	3	100	<b>20</b> (50)	–	<b>21</b> (50)
<b>22</b>	10	110	3.75	91	<b>23</b> (71)	<b>25</b> (5)	<b>24</b> (12); <b>26</b> (3)
	15	110	23	94	<b>23</b> (17)	<b>25</b> (29)	<b>24</b> (36); <b>26</b> (3)
<b>27</b>	7.5	90	22	86	<b>28</b> (57); <b>29</b> (11)	<b>31</b> (7)	<b>30</b> (3); <b>32</b> (11)
<b>1</b> <sup>d</sup>	10	110	3	98	<b>2b</b> (80)	–	<b>3</b> (15); <b>4</b> (3)
<b>2</b> <sup>d</sup>	10	110	22	96	<b>6b</b> (57)	<b>7</b> (14)	<b>8</b> (10)
<b>2</b> <sup>e</sup>	7.5	110	3	60	–	–	<b>8</b> (60)
<b>1</b> <sup>f</sup>	7.5	110	24	70	<b>6a</b> (33)	<b>7</b> (1)	<b>9</b> (25); <b>8</b> (11)

<sup>a</sup> Reaction conditions: 10 mmol substrate, 0.5 mmol CAN, 15 ml acetic acid.

<sup>b</sup> Without CAN.

<sup>c</sup> With 10 mmol of sodium acetate.

<sup>d</sup> Propanoic acid as a solvent.

<sup>e</sup> Formic acid as a solvent.

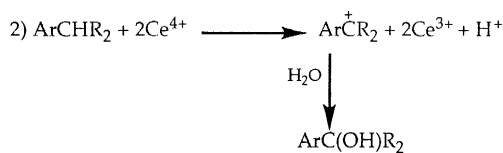
<sup>f</sup> 15 ml acetonitrile, 20 mmol acetic acid, 10 mmol substrate.

tones or alcohols by Ce(IV)/BrO<sub>3</sub><sup>-</sup> system (Scheme 1) [8] that one of the intermediates in such a catalytic system is a benzylic carbo-cation that reacts with the solvent (e.g., water) leading to the alcohols (Scheme 2). Consequently we found it conceivable that alkylbenzenes in a carboxylic acid medium could be converted to benzylic esters by oxidation with Ce(IV)/BrO<sub>3</sub><sup>-</sup> (Scheme 3).

### 3. Results and discussion

In the simplest method an alkylbenzene is dissolved in a carboxylic acid and stirred under N<sub>2</sub> with the appropriate amount of the Ce(IV) and bromate salts. After several hours the corresponding benzyl mono-ester is obtained. E.g., reaction of 10 mmol of ethylbenzene, and 7.5 mmol of KBrO<sub>3</sub>, 0.5 mmol of CAN in 15 ml acetic acid gave after 2 h at 90°C and column separation, 92% of 1-phenylethyl acetate (isolated yield). The reaction can be performed without CAN but the yield of the ester and the selectivity of the reaction is lower (Table 1). In the absence of the bromate only small amounts of oxidation products were formed. (See Scheme 4.)

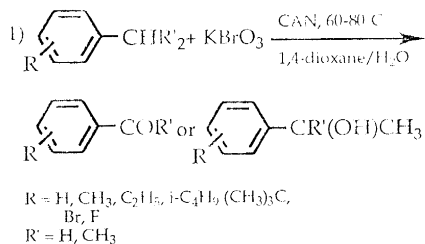
Table 1 summarizes the results with several alkylaromatics. Toluene, 4-*t*-butyltoluene and 4-bromotoluene are less selective than ethylbenzene as they gave only up to 75% yield of the ester. Oxidation of toluene at temperatures lower than 90°C (e.g., 60 for 22 h) led mainly to bromination products (*o*- and *p*-bromotoluene). Addition of sodium acetate to the reaction mix-



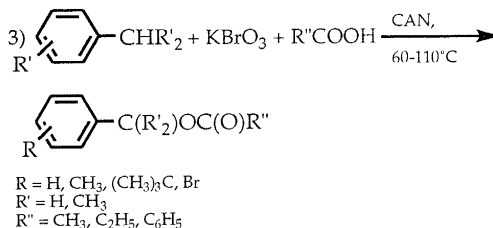
Scheme 2.

ture decreases the formation of benzyl acetate (Table 1) and increases the formation of the by-products (benzaldehyde, benzoic acid and bromination products). *p*-xylene give selectively the mono-acetate in 75% yield and the diacetate in 11% yield. This selectivity is associated with the ring deactivation by the first acetate group. While ethylbenzene gave good selectivity to the acetate ester and *p*-xylene to the mono-acetate derivative, *p*-ethyl-toluene gave less selective oxidation products (57% oxidation product at the secondary benzylic position and 11% of oxidation product at the primary benzylic position). Cumene, which has a tertiary benzylic hydrogen gave only 50% of the acetate ester, accompanied by extensive bromination products. It should be pointed out that, in the presence of 1,4-dioxane/water as solvent, it is possible to convert cumene, under mild conditions, to 2-phenyl-2-propanol in high yield (90%) [8].

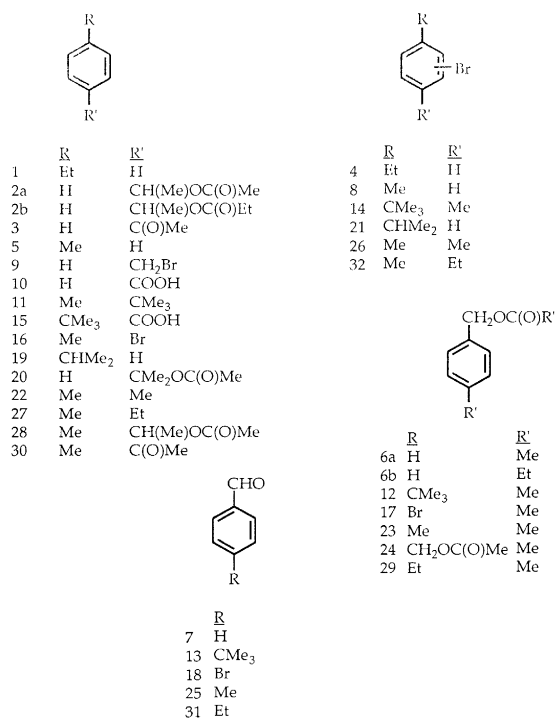
Changing the medium from acetic acid to propanoic acid leads in the case of ethylbenzene to the formation of benzyl propanoate in up to 80% yield. The oxidation system is not effective in formic acid, trichloroacetic acid and trifluoroacetic acid and only the bromination products are formed 2- and 4-bromotoluene, in the case of toluene. It should be noted that the oxidation can be carried out also in acetonitrile. In this



Scheme 1.



Scheme 3.



Scheme 4.

case the carboxylic acid can be added in stoichiometric amounts. Thus, oxidation of ethylbenzene in acetonitrile in the presence of benzoic acid and polyethyleneglycol dimethyl ether 500 as a phase-transfer agent gives 1-phenylethyl benzoate in 40% yield after 24 h. Oxidation of toluene in the presence of acetic acid and acetonitrile as solvent leads after 24 h to 33% of benzyl acetate and 25% of benzyl bromide (Table 1).

The oxidation of toluene in acetic acid was studied in detail using GC and NMR as analytical tools. The results are given in Fig. 1. Toluene reacted fast (in 2 h, ~90% conversion) giving benzyl bromide, benzyl acetate and benzaldehyde in 39%, 33% and 10% respectively. After 2 h the percentage of benzyl acetate continued to increase at a moderate rate. The accumulation of benzaldehyde increased also but at very slow rate. The amount of benzyl bromide decreased rapidly. In order to clarify how the conversion of benzyl bromide to benzyl acetate occurs, we performed the following blank ex-

periments: The reaction of 10 mmol of benzyl bromide and 15 ml of acetic acid under nitrogen at 90°C for 22 h gave 4% of benzyl acetate. A mixture of 10 mmol benzyl bromide with 15 ml acetic acid and 0.5 mmol of CAN under nitrogen for 7 h resulted in the formation of 12% of benzyl acetate and 3% of benzaldehyde and benzoic acid (1:1). In a third experiment in which we repeated the first experiment in the presence of 7.5 mmol of KBrO<sub>3</sub> at 90°C, we found that after 3 h all the benzyl bromide had disappeared and only benzoic acid and benzaldehyde in (1:4.35 ratio) was formed. After 7 h, benzoic acid was the only product in the reaction. These results indicate that after 2 h, the conversion of benzyl bromide to benzyl acetate is catalyzed only by the cerium salt. We believe that the Ce(III) salts are responsible for such reaction and acting as a Lewis acid [9].

The fact that in the presence of CAN, the oxidation reaction is more selective for the ester product indicates that while the Ce(IV) and bromate salts act as efficient oxidants, the bromate salt acts as a reoxidant for the Ce(III) ion. It is also considered as the oxidizing agent for alkyl aromatics, probably via a radical mechanism [10]. The side-chain oxidation of alkylbenzenes by CAN in acetic acid probably involves

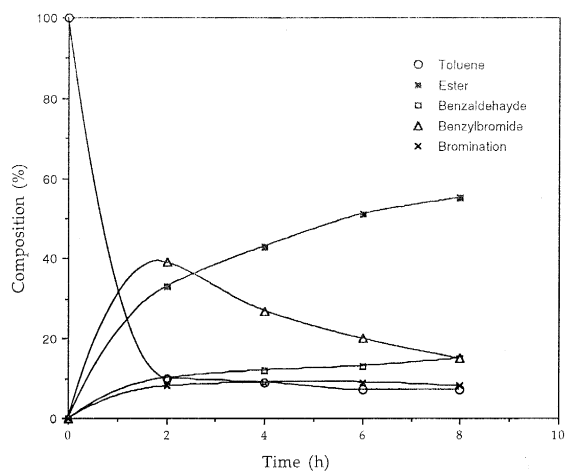
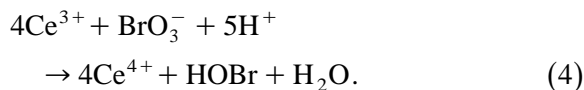
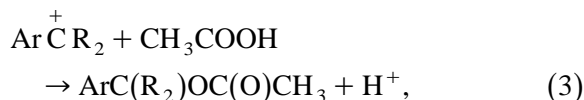
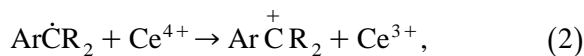


Fig. 1. Composition of toluene (○), benzyl acetate (■), benzaldehyde (□), benzyl bromide (Δ) and bromination products (×) in the oxidation of toluene by the CAN/BrO<sub>3</sub><sup>-</sup> system in acetic acid.

an electron-transfer mechanism leading to the formation of radical cations as reaction intermediates [11]. The suggested mechanism, which is similar to that generally accepted [12]<sup>1</sup> for this type of reaction is given in by



In summary, Ce(IV)/BrO<sub>3</sub><sup>-</sup> system catalyzed the selective oxidation of alkylbenzenes to the benzylic ester in good yields. This study shows that cerium (IV) salts are catalysts for oxidation of alkylbenzenes.

### Acknowledgements

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<sup>1</sup> Other proposed mechanisms in which the radical and the Ce(IV) in Eq. (2) may lead to the products might take place [13].

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