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## COMMUNICATION

## Synthesis of *tert*-butyl peresters from aldehydes by Bu<sub>4</sub>NI-catalyzed metal-free oxidation and its combination with the Kharasch–Sosnovsky reaction<sup>†</sup>

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A new *tert*-butyl peresters synthesis directly from aldehydes and TBHP was developed *via*  $Bu_4NI$ -catalyzed aldehyde C-H oxidation. Mechanistic studies suggest that the protocol proceeds *via* a radical process. Combining the method with the Kharasch–Sosnovsky reaction offers a practical approach for the synthesis of allylic esters from simple aldehydes and alkenes *via* a two-step one-pot procedure.

In the past decade, aldehydes C–H activation has attracted much attention in synthetic organic chemistry.<sup>1,2</sup> These transformations relied heavily on transition-metal-catalysts. Notably, Scheidt *et al.*<sup>2d</sup> and Glorious *et al.*<sup>21,m,p</sup> described the *N*-heterocyclic carbene-catalyzed metal-free aldehydes C–H activation, respectively. In their pioneering work, Caddick *et al.*<sup>2q,r</sup> developed aerobic hydroacylation of  $\alpha,\beta$ -unsaturated esters and azodicarboxylates. We herein report a Bu<sub>4</sub>NI-catalyzed aldehyde C–H oxidation<sup>3</sup> reaction to prepare *tert*-butyl peresters.<sup>4</sup> No transition metal was required for this cross-dehydrogenative coupling (CDC) reaction<sup>5</sup> between aldehyde and *tert*-butyl hydroperoxide.

*tert*-Butyl peresters are of interest because of their rich applications across many fields of chemistry.<sup>6–11</sup> Traditionally, the synthesis of *tert*-butyl peresters relied primarily on the reaction of carboxylic acid and its derivative with *tert*-butyl hydroperoxide.<sup>12</sup> Compared to the traditional method, our methodology is distinguished by high atom economy and free of base.

Our initial work focused on the reaction of 2-naphthaldehyde (1a) with *tert*-butyl hydroperoxide. After extensive screening, we determined that 20 mol%  $Bu_4NI$  in  $H_2O$  at 40 °C for 24 h was the most effective set of conditions, giving the desired *tert*-butyl perester 3a in 92% yield (Table 1, entry 4). No reaction proceeded in the absence of  $Bu_4NI$  (Table 1, entry 1). Other ammonium iodides resulted in lower yields (Table 1, entry 5–6). In particular,  $Bu_4NCI$  or  $Bu_4NBr$  halted the formation of the desired perester 3a, which indicated that the use of iodide was critical for efficient conversion (Table 1, entries 2–3).

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 Table 1 Optimization of reaction conditions<sup>a</sup>

$\bigcirc$	$\begin{array}{c} 0 \\ H \\ H \end{array} + H0^{-0} \\ H_2O, 40 \ ^{\circ}C, 24 \ h \end{array}$	3a
Entry	Catalyst	Yield <sup>b</sup>
1		$ND^{c}$
2	Bu <sub>4</sub> NCl	<5%
3	Bu <sub>4</sub> NBr	<5%
4	Bu <sub>4</sub> NI	92%
5	<i>n</i> -Hep <sub>5</sub> NI	83%
6	Me <sub>3</sub> BnNI	79%
7	KI	<5%
8	KI	$63\%^{d}$
9	PdCl <sub>2</sub>	<5%
10	CuCl	ND
11	CuI	<5%
12	RuCl <sub>3</sub> ·nH <sub>2</sub> O	ND
13	FeCl <sub>2</sub>	<5%
a		

<sup>*a*</sup> 0.5 mmol 2-naphthaldehyde (**1a**), 1.5 mmol TBHP, 20 mol% catalyst in 2.0 mL H<sub>2</sub>O. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> Not detected. <sup>*d*</sup> 20 mol%18-crown-6 was added.

Interestingly, only trace amount of perester **3a** was generated in the presence of catalytic KI (Table 1, entry 7). Upon adding 18-crown-6 to the reaction mixture as a phase transfer catalyst, the perester **3a** was generated in a moderate yield (Table 1, entry 8). When metal catalysts were used,<sup>13</sup> poor results were observed (Table 1, entries 9–13).

To define the scope of the Bu<sub>4</sub>NI-catalyzed C–H oxidation reactions, we applied this process to a series of aldehydes as shown in Table 2. A variety of functional groups, including benzylic C–H, ether, sulfide, halide, ester, BocO, TsO, doublebond and triple-bond moieties, were tolerated under the optimized conditions. The steric effects of the aromatic aldehydes had no significant effect on reactivity, resulting in the corresponding peresters in good yields (products **3I–3n**). Heteroarenes, such as 2-thiophenecarboxaldehyde, also underwent C–H oxidation to give the corresponding perester **3s** in good yield. Notably, preliminary result demonstrated that alkyl aldehyde worked for this reaction. When cyclohexanecarbaldehyde was used as a substrate, the perester **3u** was obtained in 43%yield with cyclohexanecarboxylic acid as the byproduct.

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 $^{a}$  0.5 mmol aldehydes, 1.5 mmol TBHP, 20 mol% Bu<sub>4</sub>NI in 2.0 mL H<sub>2</sub>O.  $^{b}$  48 h.  $^{c}$  Cumene hydroperoxide was used.

Finally, cumene hydroperoxide was not a suitable reaction partner for this transformation (product 3x).

For practical purposes, the reaction was scaled up to 100 mmol scale, affording the perester 3a smoothly in 91% yield. Further investigation focused on the synthetic application of the methodology. Allylic esters serve as important building blocks in organic synthesis. The Kharasch-Sosnovsky reaction,11 Cu-catalyzed allylic C-H oxidation of alkenes using tert-butyl peresters as the oxidants, is a useful transformation for allylic ester synthesis.<sup>14</sup> Recent studies have aimed at an asymmetric version of this reaction that is catalyzed by chiral copper salts.<sup>11b-h</sup> Compared with tert-butyl perester, aldehydes are commercially available or easily prepared. We envisioned that the combination of the aldehydes C-H oxidation and the Kharasch-Sosnovsky reaction in one-pot would open a novel entry to allylic ester directly from simple olefins and aldehydes. The C-H oxidation of aldehydes was conducted for 24 h under slightly modified conditions,<sup>15</sup> followed by CuBr-catalyzed allylic oxidation of cyclohexene for 36 h, leading to the desired allylic esters in moderate to good yields. A variety of functional groups were tolerated in the two-step one-pot process as shown in Table 3. Notably, other alkenes, such as indane, 1,5-cyclooctadiene and tetrahydronaphthalene, are suitable substrates in the transformation (products 4n-4p).

A plausible catalytic cycle was proposed as shown in Scheme 1a. Initially, the *tert*-butoxyl and *tert*-butylperoxy radicals were generated in the catalytic system.<sup>16</sup> The resulting *tert*-butoxyl radical **A** traps H to form the acyl radical C.<sup>17</sup> The coupling of the acyl radical **C** and the *tert*-butylperoxy radical **B** affords the desired perester. A control experiment was





<sup>a</sup> Step 1: in 5.0 mL CH<sub>2</sub>Cl<sub>2</sub> at 40 °C for 24 h; step 2: 40 °C for 36 h.
<sup>b</sup> Step 1: In 2.0 mL benzene at 40 °C for 24 h; step 2: 80 °C for 24 h.
<sup>c</sup> Indane was used. <sup>d</sup> 1,5-Cyclooctadiene was used. <sup>e</sup> Tetrahydronaphthalene was used.



Scheme 1 Plausible reaction mechanism.

carried out to elucidate the mechanism. When TEMPO, a radical-trapping reagent, was added to the reaction, the product **5**, adduct of acyl radical and TEMPO, was obtained in nearly quantitative yield (Scheme 2a). This result indicated that an acyl radical was involved in the catalytic cycle of the transformation.

One could argue that the dehydrogenation of the hemiacetal by *in situ* generated hypoiodite cannot necessarily be ruled out in the present transformation (Scheme 1b). Recently, Ishihara *et al.* 



Scheme 2 Investigation on the reaction mechanism.

reported pioneering studies involving a C–H oxidative reaction based on *in situ* generated ammonium hypoiodite species using either H<sub>2</sub>O<sub>2</sub> or TBHP as the oxidant.<sup>18</sup> The C–H oxidation reaction worked well in the presence of stoichiometric amounts of Bu<sub>4</sub>NOH and iodine (*in situ* generation of  $[Bu_4N]^+[IO]^-$ ).<sup>19</sup> In sharp contrast, the existence of ammonium hypoiodite halted the present aldehyde C–H oxidation (Scheme 2b). Although not conclusive, we currently believe that hypoiodite is not the actual catalytic species in the aldehydes C–H oxidation reaction.

In summary, a Bu<sub>4</sub>NI-catalyzed C–H oxidation of aldehydes has been developed. This process represents the first synthesis of *tert*-butyl peresters directly from aldehydes and TBHP. Most importantly, the practicality of the method, as well as its combination with the Kharasch–Sosnovsky reaction, renders it suitable for applications in synthetic chemistry. Based on the control experiments, a radical process was proposed in the catalytic cycle. Investigations that provide a more detailed mechanism and further applications are ongoing in our laboratory.

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