The Baeyer–Villiger rearrangement with metal triflates: new developments toward mechanism†

Piotr Latos, Agnieszka Siewniak, Magdalena Sitko and Anna Chrobok*  

Based on MS analysis, the mechanism of the Baeyer–Villiger oxidation of cyclic ketones with hydrogen peroxide using metal triflates (Ga(OTf)₃ and Er(OTf)₃) as catalysts was proposed. In the case of cyclohexanone as a substrate, dimeric, trimeric and tetrameric peroxide structures were detected. These were proved to be active catalysts in Baeyer–Villiger oxidation of 2-adamantanone, giving full conversion of ketone after short reaction time (20 minutes using 0.1 : 0.2 : 2.0 molar ratio of Sn(OTf)₂ : ketone : 30 wt% H₂O₂).  

Although the BV oxidation was discovered in 1899, attempts to establish the mechanism took the next fifty years. A generally accepted mechanism of the BV oxidation of carbonyl compounds with peracid assumes that in the first stage an attack of peracidic nucleophilic oxygen on the carbonyl carbon of the ketone occurs leading to a formation of tetraedric intermediate product, called Criegee adduct or intermediate. The second stage involves an 1,2-anionotropic rearrangement. This mechanism was confirmed by von E. Doering by a labeling experiment with benzophenone-O₂⁻. In case of using peracids as oxidants the presence of catalyst is optional. When using hydrogen peroxide as the oxidant the addition of catalyst is required. Depending on the catalyst used various BV oxidation pathways are proposed. Catalysts can activate the ketone or oxidant, or both of them, and usually one of the activation methods dominates (Fig. 1).  

Metal triflates are generally considered as Lewis acids, however some of them can partially hydrolyze to triflic acid under the influence of water. Hence, they may participate in the...

---

*Department of Chemical Organic Technology and Petrochemistry, Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice, Poland. E-mail: Anna.Chrobok@polsl.pl  
† Electronic supplementary information (ESI) available: MS spectra, experimental procedures. See DOI: 10.1039/d0ra03335a
activation of the ketone, the Criegee intermediate or hydrogen peroxide, both by Lewis or Bronsted sites.

Herein, we decided to take a deeper look at the BV oxidation mechanism with hydrogen peroxide using selected metal triflates. The studies shed light for the role of metal triflates in the non-classical approach of lactones formation concerning the high-energy compounds such as peroxides as intermediate compounds.

In the preliminary studies, two model metal triflates which significantly vary in hydrolytic stability: gallium(III) triflate and erbium(III) triflate were used to compare their stability in the presence of water. Test based on the reaction with retinyl acetate was conducted (Fig. 2). In this test, the presence of Bronsted acid in the test sample is confirmed by the formation of retinyl cation (blue color) from retinyl acetate (yellow) and detected by UV-Vis spectroscopy.\(^{12}\) Bronsted acid (triflic acid) in the studied samples of metal triflate may be formed by slow hydrolysis in the presence of traces of water. Therefore, triflic acid was used as a benchmark for these studies.

In order to limit the water content in UV-Vis tests, anhydrous nitrobenzene was used as a solvent. Results indicates (Fig. 3) that triflate with rare earth metal Er(OTf)\(_3\) was characterized by high hydrolytic stability and the presence of retinol carbocation was not observed while Ga(OTf)\(_3\) underwent partial hydrolysis as only part of the retinol acetate was converted to carbocation during tests. Due to the high reactivity of triflic acid, its amount used for the analysis was three times lower than that of metal triflates, which were used in the same molar amount.

In the case of triflic acid, all retinol acetate was transformed into retinol carbocation. The obtained results confirmed that Er(OTf)\(_3\) is hydrolytically stable Lewis acid comparing to Ga(OTf)\(_3\) which can undergo hydrolysis.

Next, the BV oxidation reactions of cyclic ketones of varied reactivity were carried out in the presence of two molar excess of 60 wt% aq. H\(_2\)O\(_2\) and Er(OTf)\(_3\) or Ga(OTf)\(_3\). The following cyclic ketones were selected: cyclobutanone, 2-adamantanone, norcamphor, 2-methylcyclohexanone and cyclohexanone. Secondary groups in cyclic ketones are more prone to migrate than primary alkyl groups in BV oxidation. Therefore, norcamphor, 2-adamantanone and 2-methylcyclohexanone are more reactive then cyclohexanone which is moreover non-strained and hardly reactive in BV oxidation. Very reactive, strained cyclobutanone is readily oxidized with H\(_2\)O\(_2\).

Results shown in Table 1 confirmed that metal triflates are highly active catalyst in BV oxidation of such cyclic ketones as 2-methylcyclohexanone, cyclobutanone and 2-adamantanone.

However, our attempts to apply the developed reaction conditions for the synthesis of \(\varepsilon\)-caprolactone showed that the selectivity towards the lactone formation dropped significantly. In the reaction products, the mixture of dimeric, trimeric or polymeric peroxides was detected. The quantitative analysis of this complex post reaction mixture was not possible, concerning the low thermal stability of peroxide species. The presence of dimeric peroxides has already reported in the literature. The formation of dimeric peroxide was postulated by Baeyer and Villiger in their early works.\(^{1-3}\) However, numerous studies have shown that this peroxide under the influence of Lewis or Bronsted acids could not be converted into the appropriate lactone with high yields and

### Table 1: Yields of lactones in the BV oxidation with hydrogen peroxide in the presence of metal triflates\(^a\)

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Metal triflate</th>
<th>Ketone conversion (%)</th>
<th>Selectivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Methylcyclohexanone</td>
<td>Ga(OTf)(_3)</td>
<td>100</td>
<td>99</td>
</tr>
<tr>
<td>2-Methylcyclohexanone</td>
<td>Er(OTf)(_3)</td>
<td>97</td>
<td>94</td>
</tr>
<tr>
<td>Cyclobutanone</td>
<td>Ga(OTf)(_3)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Cyclobutanone</td>
<td>Er(OTf)(_3)</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>2-Adamantanone</td>
<td>Ga(OTf)(_3)</td>
<td>97</td>
<td>99</td>
</tr>
<tr>
<td>2-Adamantanone</td>
<td>Er(OTf)(_3)</td>
<td>94</td>
<td>80</td>
</tr>
<tr>
<td>Norcamphor</td>
<td>Ga(OTf)(_3)</td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>Norcamphor</td>
<td>Er(OTf)(_3)</td>
<td>96</td>
<td>84</td>
</tr>
<tr>
<td>Cyclohexanone</td>
<td>Ga(OTf)(_3)</td>
<td>99</td>
<td>6</td>
</tr>
<tr>
<td>Cyclohexanone</td>
<td>Er(OTf)(_3)</td>
<td>82</td>
<td>10</td>
</tr>
</tbody>
</table>

\(^a\) Ketone, 0.67 mmol; 60 wt% aq. H\(_2\)O\(_2\), 2.01 mmol; metal triflate, 10 mol%; toluene, 5 ml; 70 °C, conversion and selectivity were determined using GC.
therefore was considered as a “dead end”.\textsuperscript{13,14,15} The unique studies conducted by Berkessel group showed that oxidation of cyclohexanone with hydrogen peroxide catalyzed by Brønsted acid, such as $p$-toluenesulfonic acid yielded $\epsilon$-caprolactone only when carried out in the presence of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as a solvent\textsuperscript{16,17} (Fig. 4). Authors postulated that perfluorinated solvent

---

**Fig. 5** Proposition of the BV oxidation mechanism of cyclohexanone with 60 wt% aq. $\text{H}_2\text{O}_2$, in the presence of Ga(OTf)$_3$. # and ## according to.\textsuperscript{17}
facilitates the conversion of dimeric peroxide to lactone by creating strong hydrogen bonds to anions.

Few examples of the formation of trimeric peroxides are known in the literature. The synthesis of trimeric peroxides from 1,1'-dihydroperoxydicycloalkyl peroxides and ketones in the presence of 70% perchloric acids was described by Sanderson and Zeiler. Vennerstrom et al. observed the formation of trimeric peroxides—hexaoxonane derivatives—during ozonolysis of tetrahydro-4H-pyran-4-one. Hong and co-workers described the synthesis of hexaoxonane derivatives in the cyclocondensation of ketones with gem-dihydroperoxide catalyzed by acid. The oxidation of acetone (linear ketone) with 30% hydrogen peroxide leading to formation of tetrameric acetone peroxide was also presented. However, to the best of our knowledge, the path of formation of trimeric peroxides and higher peroxides has not yet been presented. That encouraged us to gain an insight into the mechanism of the Baeyer–Villiger oxidation with hydrogen peroxide using metal triflates as

Fig. 6 MS spectrum of the post reaction mixture after the BV oxidation of cyclohexanone with 60 wt% aq. H$_2$O$_2$ in the presence of Ga(OTf)$_3$. The spectrum was recorded for the solution with NaI addition.

Fig. 7 Proposition of the BV oxidation mechanism of cyclohexanone with 60 wt% aq. H$_2$O$_2$, in the presence of Er(OTf)$_3$. 

This journal is © The Royal Society of Chemistry 2020
catalysts and demonstrate if the triflate groups may play the similar role as a fluorinated solvent.

For gallium(III) triflate the conversion of cyclohexanone after 3 hours reached 99% while the selectivity towards ε-caprolactone was only 6% (Table 1). In order to clarify this phenomenon, we conducted high resolution MS analysis which showed that various peroxygen substances were present in the reaction mixture. Based on the outcome, we proposed a reaction mechanism in the presence of Ga(OTf)₃ (Fig. 5). In the first stage, nucleophilic addition of hydrogen peroxide to the ketone occurs, resulting in the formation of perhydrate 2. The perhydrate reacts with the cyclohexanone molecule to give dilhydroperoxide 3. Then several paths are possible in which compound 3 undergoes further transformations. Spirobisperoxide 4 is formed in path a, which can be transformed according to the mechanism proposed by Berkessel. The transformations of 10 to 11 and of 13 to 14 proceed in exactly the same way as the transformation of 5 to 8 presented in Fig. 5, but for the sake of readability of the scheme only the final product is presented. The assumption that metal triflates can form hydrogen bonds like HFIP was used. However, gallium triflate was used in a catalytic amount, not as a solvent, so this is not the main path in which compound 3 is converted. In path b, compound 3 reacts with perhydrate to give trimeric peroxyde 9 which then rearranges to 11. All intermediates, as well as transient states, were visible and identified on the MS spectrum (Fig. 6, see also in ESI, Fig. S1†).

A completely different mechanism was observed when reactions were conducted in the presence of erbium(III) triflate which shows high hydrolytic stability. In this case, triflic acid is not formed. Thus, the hydroxyl group of cyclohexanol of intermediate 3 was not protonated and cyclized to form the six-membered cyclic peroxyde 4. Instead of them the linear peroxides were presented in the reaction mixture. The proposed mechanism was not described yet in the literature (Fig. 7 and MS spectrum see in ESI, Fig. S2†).

The experiments conducted in the same reaction conditions with 2-methylcyclohexanone, cyclobutanone and 2-adamantone showed that they can be converted to lactone in high yields (Table 1). In the presence of gallium(III) triflate the conversion of these ketones was higher than 97% and selectivity towards lactone reached 99%, while for erbium(III) triflate the conversion and selectivity were higher than 94% and 80%, respectively. MS analysis confirmed that the reaction proceeded in a similar way in the presence of both Ga(OTf)₃ and Er(OTf)₃ [see ESI, Fig. S3–S8†].

In both cases the formation of spirobisperoxide and lactone was observed according to the mechanism shown in Fig. 4 described in the literature. For the formation of a cyclic peroxyde a labile proton is required. In case of Er(OTf)₃, which is hydrolytically stable this proton could be created through the interaction between erbium(III) triflate and hydrogen peroxyde (Fig. 8). Lower selectivity may also indicate a lower strength of Brønsted acid generated in situ in the reaction mixture.

In summary, based on the MS analysis the new mechanisms were evaluated concerning the formation of dimeric and trimeric peroxydes when cyclohexanone was used as a substrate. On the other hand, when other ketones were used as the substrates the formation of spirobisperoxide was observed and the reactions proceeded with high conversion and selectivity. These studies develop the knowledge of the reactivity of cyclic ketones with hydrogen peroxyde in the presence of metal triflates.

Conflicts of interest

The authors declare no conflict of interest.

Notes and references