

Studies on the catalytic oxidation of epoxides to α -diketones by $\text{Bi}^{(0)}/\text{O}_2$ in DMSO

Sylvain Antoniotti^a, Elisabet Duñach^{a,b,*}

^a Laboratoire Arômes, Synthèses et Interactions, Université de Nice-Sophia Antipolis, Parc Valrose, 06108 Nice Cedex 2, France

^b Laboratoire de Chimie Bio-Organique, UMR CNRS 6001, Université de Nice-Sophia Antipolis, Parc Valrose, 06108 Nice Cedex 2, France

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Abstract

Catalytic oxidation of internal epoxides by bismuth derivatives under molecular oxygen in DMSO affords the corresponding α -diketones. The influence of several parameters such as of the nature of the catalyst, $\text{Bi}^{(\text{III})}$ salts or $\text{Bi}^{(0)}$, the solvent, the presence of additives and other oxidants has been examined. The preparation of a series of linear and cyclic, aliphatic and aromatic α -diketones is reported in 31–77% yields. © 2003 Elsevier B.V. All rights reserved.

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1. Introduction

We have been interested in the selective oxidation of epoxides and we have recently reported that some $\text{Bi}^{(\text{III})}$ -carboxylates constituted novel catalysts to effect the transformation of terminal aryl epoxides into the corresponding carboxylic acids according to Scheme 1 [1,2]. The catalytic oxidation of styrene oxide derivatives has been described using molecular oxygen and DMSO with bismuth(III)-mandelate as the catalyst. The C–C oxirane bond cleavage occurred and led to the corresponding carboxylic acids and CO_2 . The yields of carboxylic acids were in the range of 42–64%.

This novel catalytic oxidation process was interesting because epoxides, easily prepared from olefins or carbonyl compounds [3], are known to be versatile intermediates in organic synthesis. Epoxides can be easily converted into a large number of functional groups, by various ring-opening additions [4] and isomerisation reactions [5]. In spite of the high number of papers dealing with epoxide transformations, oxidation reactions have only received a limited interest.

Most of the methods described for epoxide oxidation involve the oxidative cleavage of the carbon–carbon bond leading to carbonyl compounds or carboxylic acids [6].

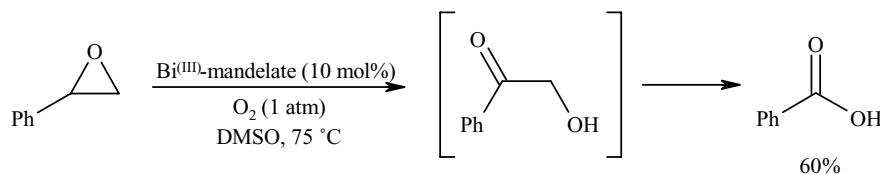
However, oxidative cleavage has mainly been reported for terminal aromatic epoxides.

Oxidation of epoxides without C–C bond cleavage affording α -functionalised ketones has also been reported. Among these reactions, the acid-catalysed oxidation of epoxides by DMSO leads to α -hydroxyketones, though with a limited synthetic scope, due to the low product yields and selectivity [7].

In recent years, the Lewis acid character of several bismuth(III) compounds has been described. Bismuth(III) salts have been used as catalysts for the deprotection of acetals [8] and *S,S*-acetals [9], the isomerisation of epoxides [10], the sulfonylation reaction [11], the acetylation and benzoylation of alcohols [12], the Diels–Alder reaction [13,14], the Biginelli reaction [15], the Mukaiyama aldol reaction [16], as well as other organic transformations [17]. However, the use of $\text{Bi}^{(\text{III})}$ derivatives as catalysts in oxidation reactions has been limited. Stoichiometric $\text{Bi}^{(\text{V})}$ processes with NaBiO_3 are known for the oxidation of alcohols and diols [18], and the stoichiometric use of Bi_2O_3 in refluxing acetic acid has also been reported for the oxidation of α -ketols to α -diketones [19].

Besides the oxidation of epoxides, the catalytic use of $\text{Bi}^{(\text{III})}$ derivatives in oxidation reactions has been extended to the oxidative cleavage of α -ketols and α -hydroxyacids to the corresponding carboxylic acids [20]. These reactions have been shown to proceed through a $\text{Bi}^{(\text{III})}/\text{Bi}^{(0)}$ or $\text{Bi}^{(\text{III})}/\text{Bi}^{(\text{I})}$ redox couple under molecular oxygen.

* Corresponding author. Tel.: +33-492076142; fax: +33-492076151.
E-mail address: dunach@unice.fr (E. Duñach).

Scheme 1. Bi^(III)-mandelate-catalysed oxidation of styrene oxide in a DMSO/O₂ system.

Recently, we have been working on the use of bismuth-based catalytic systems for the oxidation of internal epoxides. The reaction conditions used in Scheme 1 did not allow to selectively convert internal epoxides to α -diketones. Herein we describe the modifications effected on the Bi-catalysed reaction system to be adapted to the oxidation of 1,2-substituted epoxides for the selective synthesis of α -diketones. A first communication of this work has been reported [21].

2. Experimental

2.1. Materials

2.1.1. Preparation of epoxides

Most of the epoxides used in this work are commercially available. Epoxides **e**, **h**, **i** were prepared according to classical epoxidation procedure by *m*CpBA [22].

2.1.2. Reagents

Bi⁽⁰⁾ powder, triflic acid, copper(II) triflate, bismuth(III) chloride, bismuth(III) bromide, bismuth(III) acetate are commercially available. Bismuth(III) mandelate [23] and bismuth(III) triflates [24] were prepared according to literature procedures.

2.2. General procedure for epoxide oxidation catalysed by Bi⁽⁰⁾/O₂ in the presence of an additive

A mixture of the appropriate amount of bismuth(0) (0.25–0.50 mmol) and the additive (**CAUTION!**: triflic acid is highly corrosive) in freshly distilled DMSO (15 ml) is heated at 100 °C under O₂ (1 atm from a cylinder). The epoxide (5 mmol) in DMSO (5 ml) is then introduced through a serum cap and the mixture is stirred at this temperature until complete consumption of the epoxide, and complete consumption of the α -ketol intermediate (monitored by GC). The reaction mixture is then hydrolysed with brine (50 ml) and extracted with diethyl ether (3 \times 50 ml). The combined organic layers are dried over MgSO₄ and evaporated in vacuo. The crude product is purified by column chromatography over silica gel with a gradient pentane/dichloromethane as the eluent.

Five- and six-membered cyclic α -diketones were only observed in their enol form under analytical conditions [25]. Thus, non-symmetrical cyclic diketones may be observed as

a couple of different enolised forms, described separately in this section. All compounds were characterised by comparison with authentic samples (**1a**, **1f**, **1h** purchased from Aldrich company) or literature data (**1b** [26], **1c** [27], **1d** [26], and **1e** [28]).

2.2.1. New compounds

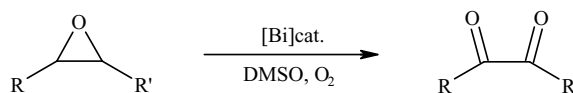
2-Hydroxy-4-vinyl-cyclohex-2-en-1-one **1g**: ¹H NMR (200 MHz, CDCl₃, 20 °C): δ = 5.6 (d, *J* = 3.9 Hz, 1H), 5.4 (m, 1H), 4.8–4.6 (m, 2H), 2.8 (m, H), 2.3–1.9 (m, 4H). ¹³C NMR (200 MHz, CDCl₃, 20 °C): δ = 194.7 C(O), 147.0 C(O)–C(OH)=C, 139.8 –CH=CH₂, 120.1 C(OH)=CH, 115.6 –CH=CH₂, 41.6 C(O)–CH₂, 38.3 C₄, 34.3 C₅. MS (EI): *m/z*(%) = 138(64) [M⁺], 110(32), 109(100), 95(73), 84(10), 81(51), 67(52), 56(17), 55(49), 53(50), 39(50).

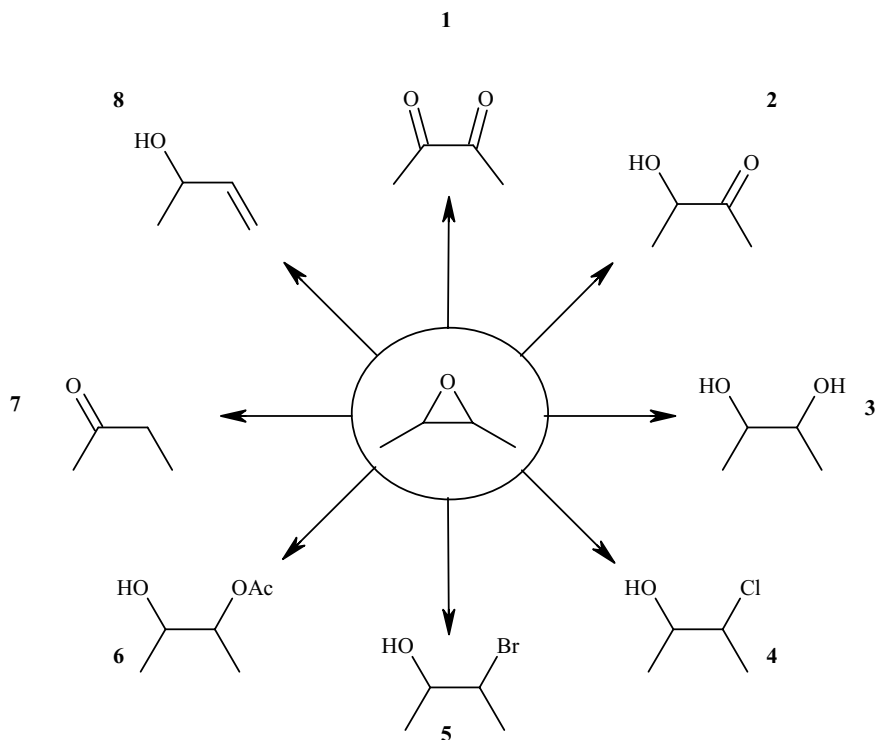
2-Hydroxy-5-vinyl-cyclohex-2-en-1-one **1g'**: ¹H NMR (200 MHz, CDCl₃, 20 °C): δ = 5.7 (dd, *J* = 3.4 Hz, *J* = 5.9 Hz, 1H), 5.4 (m, 1H), 4.8–4.6 (m, 2H), 2.4 (m, 1H), 2.1 (m, 2H), 1.8 (m, 2H). ¹³C NMR (200 MHz, CDCl₃, 20 °C): δ = 194.7 C(O), 147.0 C(O)–C(OH)=C, 139.1 –CH=CH₂, 116.9 C(OH)=CH, 114.8 –CH=CH₂, 41.6 C(O)–CH₂, 39.2 C₅, 29.7 C₄. MS (EI): *m/z*(%) = 138(22) [M⁺], 110(78), 109(16), 95(34), 84(56), 81(18), 67H(29), 56(100), 55(95), 53(29), 39(45).

Elemental analysis for **1g** and **1g'**: formula C₈H₁₀O₂·0.1DMSO·0.3H₂O. Calculated: C% 64.8; H% 7.5; O% 25.6. Found: C% 64.0; H% 7.7; O% 25.5.

3. Results and discussion

We have been working on a bismuth-based catalytic system for the oxidation of internal epoxides, searching for a selective transformation of an internal epoxide to an α -diketone (Scheme 2). α -Diketones are generally prepared by oxidation of other functional groups such as α -hydroxyketones [19,29], α -diols [30], alkynes [31], or by oxidation of methylene groups vicinal to a carbonyl group [32]. However, their direct preparation from epoxides has, to our knowledge and apart our own work [21], not yet been reported.

Scheme 2. Bi-catalysed oxidation of internal epoxides under O₂ (1 atm).



Scheme 3. Products from epoxide transformations.

Due to the versatility of the oxirane ring, different products have been obtained during this work. The chart depicted in Scheme 3 reports the product numbers used throughout the text.

Epoxide oxidation compounds such as **1** and **2** have been observed, as well as epoxide hydrolysis or ring-opening compounds **3–6** and isomerisation products **7** and **8**.

3.1. Oxidation of terminal versus internal epoxides by $\text{Bi}^{(\text{III})}$

The previously reported oxidation of terminal aryl epoxides was carried out in the presence of 10 mol% of $\text{Bi}^{(\text{III})}$ -mandelate [1] in DMSO under molecular oxygen at 75 °C to afford the corresponding carboxylic acid (Scheme 1). Other $\text{Bi}^{(\text{III})}$ -carboxylates such as $\text{Bi}^{(\text{III})}$ -2-pyridine carboxylate or $\text{Bi}^{(\text{III})}$ -phthalate could also be used [2].

The same reaction conditions applied to 1,2-disubstituted epoxides such as cyclohexene oxide or cyclooctene oxide did not form any α -diketones. Several other $\text{Bi}^{(\text{III})}$ -carboxylates were also used as catalysts in reactions at 80, 100 or 120 °C, and the only products formed in low yields resulted from isomerisation and hydrolysis of the starting epoxides (Scheme 4).

These results indicated that the oxidative ring-opening of the cyclic epoxides did not take place under the experimental conditions used.

In the proposed mechanism for the oxidation of terminal aryl epoxides [20], the $\text{Bi}^{(\text{III})}$ species, acting as a

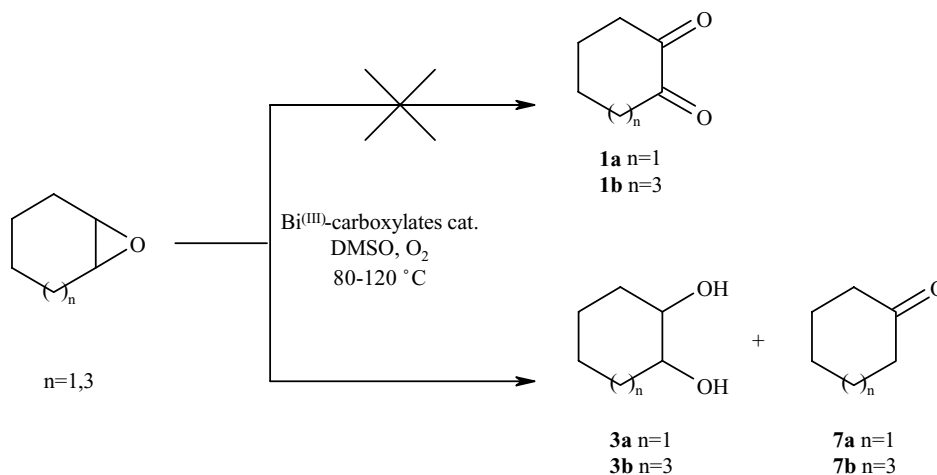
Lewis acid, may activate the epoxide function and allow its ring-opening combined with the DMSO-based addition and further oxidation of the oxirane to an α -ketol intermediate. In a second step, the oxidation of the α -ketol to an α -diketone compound should be catalysed by the $\text{Bi}^{(\text{III})}/\text{O}_2$ system (Scheme 5).

In such a mechanism, terminal epoxides are sterically favoured as compared to internal ones for the nucleophilic attack of DMSO. In order to activate internal epoxides for an oxidative ring opening, the Lewis acidity of the $\text{Bi}^{(\text{III})}$ derivative should be increased as well as the nucleophilic ability of the oxidant acting as oxygen transfer agent to the epoxide. Several $\text{Bi}^{(\text{III})}$ derivatives were therefore tested as the catalysts.

3.2. Influence of the nature of the $\text{Bi}^{(\text{III})}$ catalysts

Cyclohexene oxide was taken as a model compound in this study. Different kind of bismuth(III) compounds were used for the oxidation of cyclohexene oxide: $\text{Bi}^{(\text{III})}$ carboxylates, chloride, bromide and triflate. The results are summarised in Table 1. The reactions were carried out with 5–10 mol% of $\text{Bi}^{(\text{III})}$ under molecular oxygen (1 atm) in DMSO at 100 °C and were stopped after complete conversion.

When $\text{Bi}^{(\text{III})}$ -mandelate (10 mol%) was used as the catalyst, no α -diketone **1a** was formed from cyclohexene oxide even after 46 h, and the partial hydrolysis to *trans*-1,2-cyclohexanediol **3a** was observed in 15% yield (entry 1). This diol **3a** may result from the attack of DMSO

Scheme 4. Oxidation test of cyclic epoxides by $\text{Bi}^{\text{(III)}}$ -carboxylates under DMSO/O_2 .

on the epoxide to form an α -hydroxysulfonium intermediate, which would be slowly converted to the glycol derivative, as reported by Swern and co-workers [7] or from the acidic hydrolysis of the reaction mixture.

Under the same reaction conditions, but in the absence of $\text{Bi}^{\text{(III)}}$ catalyst, no oxidation product was observed. After 5 h, 60% of the starting material had disappeared, probably after a partial polymerisation during heating at $100\text{ }^\circ\text{C}$.

The reaction of cyclohexene oxide in the presence of bismuth(III) chloride led mainly to the formation of 2-chlorocyclohexanol **4a** in 24% yield, resulting from the ring opening of the oxirane by chloride ions, and the expected diketone **1a** in 22% yield (entry 2). Increasing the catalyst ratio mainly resulted in increased amounts of 2-chlorocyclohexanol **4a** in up to 41% yield. The isomerised cyclohexanone **7a** was also obtained in 20% yield together

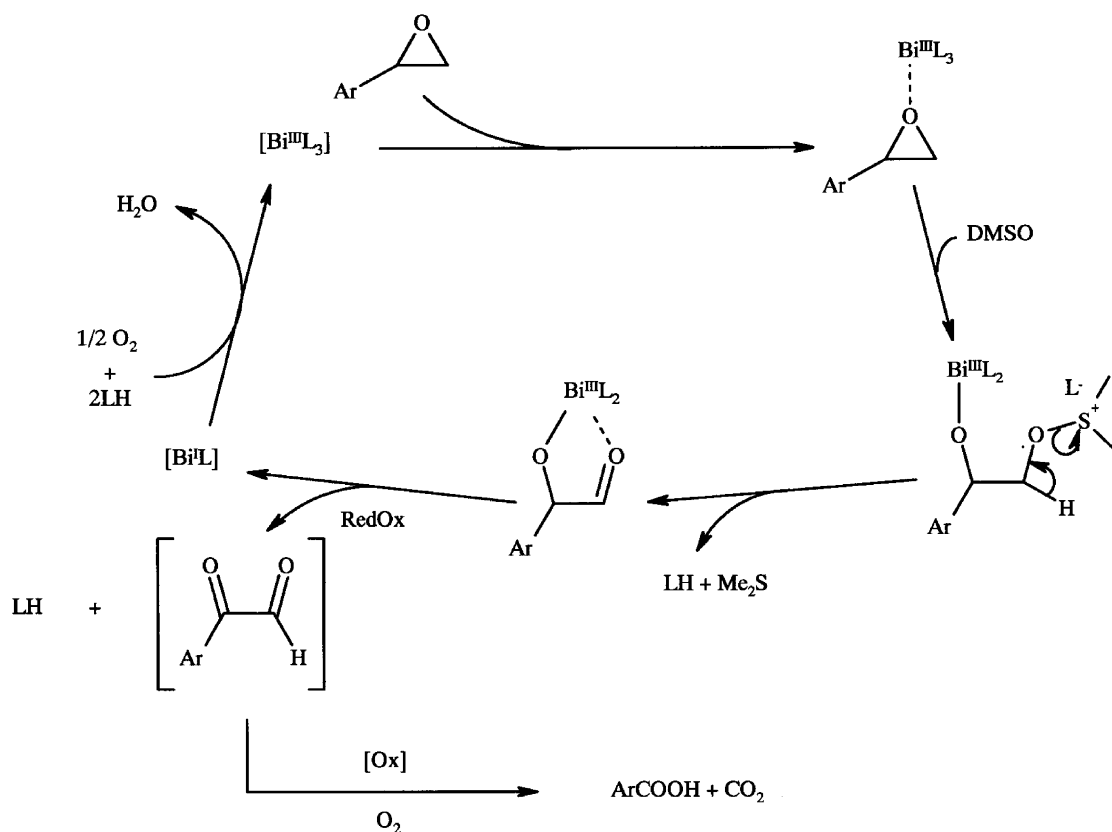
Scheme 5. Proposed mechanism of the $\text{Bi}^{\text{(III)}}$ -catalysed oxidation of terminal aryl epoxides in DMSO/O_2 .

Table 1
Oxidation of cyclohexene oxide catalysed by Bi^(III) derivatives in DMSO at 100 °C under molecular oxygen (1 atm)

Entry	Bi ^(III) derivative (equivalents)	Time (h)	Products	Yield (%)
1	Bi-mand (0.10)	46	3a	15
2	BiCl ₃ (0.09)	2.6	1a 4a 7a	22 24 <1
3	BiCl ₃ (0.50)	5	1a 4a 7a	9 41 20
4	BiBr ₃ (0.10)	5	1a 3a 5a	16 12 16
5	Bi(OAc) ₃ (0.09)	7	1a 6a	15 15
6	Bi(OTf) ₃ (0.05)	1.3	1a 3a	51 13

with the α -diketone **1a** (9% yield), the only oxidation product (entry 3).

Bismuth bromide and acetate reacted similarly to BiCl₃. The ring opening products were preferentially formed compared to the oxidation products. Thus, BiBr₃ used in 10 mol% afforded 1,2-cyclohexanedione **1a** in 16% yield, 2-bromocyclohexanol **5a** in 16% yield, and the α -diol **3a** in 12% yield (entry 4). With Bi(OAc)₃ the yield of 1,2-diketone **1a** was of 15% (entry 5).

Interestingly, the use of Bi(OTf)₃ was more selective towards the oxidation of the epoxide and the reaction with 5 mol% of catalyst led to 1,2-cyclohexanedione **1a** in 51% isolated yield after 1.3 h reaction (entry 6). The presence of the non-nucleophilic triflate anions prevented the formation of ring opening products (Scheme 6).

On the other hand, bismuth(III) triflate [24] presents a high Lewis acid activity and is also a very hygroscopic material, which can explain the presence of 1,2-cyclohexanediol **3a**.

3.3. Use of Bi⁽⁰⁾ as the catalyst

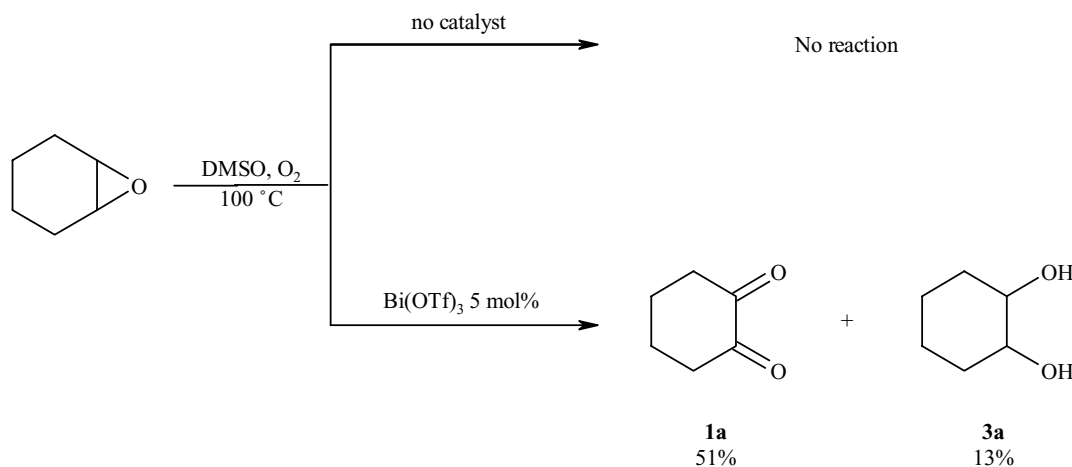
We have reported that the oxidation of α -ketols and of α -hydroxy acids to the corresponding carboxylic acids, involving an oxidative C–C bond cleavage, could be effected by the catalytic system Bi^(III)/O₂ in several solvents. Moreover, the same reactions could be carried out with Bi⁽⁰⁾ as the catalyst, after the addition of a carboxylic acid and the dissolution of Bi⁽⁰⁾ powder [20].

In the present reaction of internal epoxides oxidation, a redox step involving Bi^(III)/Bi⁽⁰⁾ or Bi^(III)/Bi^(I) can be proposed to explain the oxidation of the α -ketol intermediate to the α -diketone (Scheme 5). The reduced Bi⁽⁰⁾ or Bi^(I) species should be further reoxidised to Bi^(III) in the presence of molecular oxygen.

Based on the results obtained for the cyclohexene oxide oxidation by Bi(OTf)₃, we examined the catalytic system based on Bi⁽⁰⁾ in the presence of TfOH, and the results are shown in Table 2. The in situ generation of the active bismuth species should avoid the problem of preparation and handling of a hygroscopic material such as Bi(OTf)₃.

When the reaction of cyclohexene oxide was carried out in the presence of 8–10 mol% of Bi⁽⁰⁾ powder in DMSO/O₂ at 100 °C, no reaction occurred and the black Bi⁽⁰⁾ powder remained undissolved. However, with the addition of triflic acid (22 mol%) the oxidation to the α -diketone **1a** took place in 49% yield (entry 1). The reaction carried out at room temperature with a high catalyst ratio did not allow the formation of **1a**; however, ketol **2a** was formed in 21% yield (entry 2).

The reactivity was also examined in the presence of metallic bismuth and with copper(II) triflate as the additive. Thus, as shown in entry 3, with 8 mol% of Bi⁽⁰⁾ and 2.5 mol% of Cu(OTf)₂, the oxidation reaction of cyclohexene oxide led to 1,2-cyclohexanedione **1a** in 74% isolated yield. These reaction conditions seem to be the best compromise between the oxidation to the diketone and the epoxide polymerisation. A similar reaction at 80 °C resulted in an isolated yield of 52% (entry 4).



Scheme 6. Role of bismuth(III) in the oxidation of cyclohexene oxide.

Table 2

Oxidation of cyclohexene oxide catalysed by Bi⁽⁰⁾ in the presence of an additive, in DMSO under molecular oxygen (1 atm)

Entry	Bi ⁽⁰⁾ (equivalents) additive (equivalents)	Temperature (°C)	Time (h)	Products	Yield (%)
1	Bi ⁽⁰⁾ (0.08) TfOH (0.22)	100	2.0	1a	49
2	Bi ⁽⁰⁾ (0.50) TfOH (1.50)	20	46.0	2a	21
3	Bi ⁽⁰⁾ (0.08) Cu(OTf) ₂ (0.025)	100	2.0	1a	74
4	Bi ⁽⁰⁾ (0.1) Cu(OTf) ₂ (0.05)	80	2.8	1a	52

Kinetic experiments of the reactions catalysed by the systems Bi⁽⁰⁾/TfOH and Bi⁽⁰⁾/Cu(OTf)₂ were carried out under the conditions of entries 1 and 3 (Table 2). The conversion of the epoxide was followed in situ by ¹H NMR using DMSO-*d*₆ as the solvent at 100 °C. Fig. 1 illustrates the results obtained, indicating that the Bi⁽⁰⁾/TfOH system was kinetically more efficient, although the yield of the resulting 1,2-cyclohexanedione **1a** was lower, most possibly due to the increased epoxide polymerisation in the presence of the strong acid.

The association of Bi⁽⁰⁾/triflic acid acted as a stronger activating agent than Bi⁽⁰⁾/copper(II) triflate for the ring opening of cyclohexene oxide. However, the rate of diketone formation was found to be higher under the Bi⁽⁰⁾/Cu(OTf)₂ system. This fact can be explained by a faster oxidation of the reduced bismuth species in the presence of copper(II), already known to occur with palladium in the Wacker process [33]; a redox reaction between Bi⁽⁰⁾ and Cu(II) should not be excluded. On the other hand, it was checked that Cu(OTf)₂ alone was a catalyst for the epoxide oxidation and for the

oxidation of the α-ketol intermediate to the α-diketone. Indeed, the oxidation of cyclohexene oxide in DMSO in the presence of 10 mol% of Cu(OTf)₂ under an oxygen atmosphere afforded 28% yield of 1,2-cyclohexanedione **1a** and 50% yield of α-hydroxycyclohexanone **2a** after 2.2 h at 100 °C. The comparison between these different Bi⁽⁰⁾, Bi^(III), Cu(II) and mixed catalytic systems is shown in Scheme 7, and clearly illustrates the superiority of the use of metallic bismuth combined with copper(II) triflate in terms of α-diketone yield, relatively to the use of metallic bismuth combined with triflic acid, or bismuth(III) triflate itself.

3.4. Influence of the solvent and of the presence of molecular oxygen

The oxidative ring opening of cyclohexene oxide by both Bi⁽⁰⁾/Cu(OTf)₂ or Bi⁽⁰⁾/TfOH systems under molecular oxygen was examined in solvents such as DMF and acetonitrile. In DMF at 100 °C, or in acetonitrile at reflux, no oxidation reaction occurred.

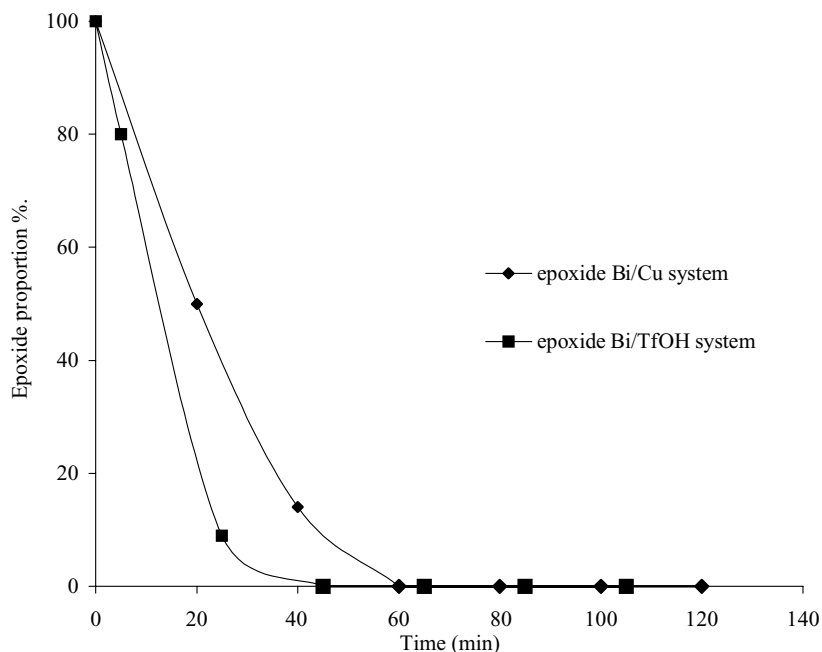
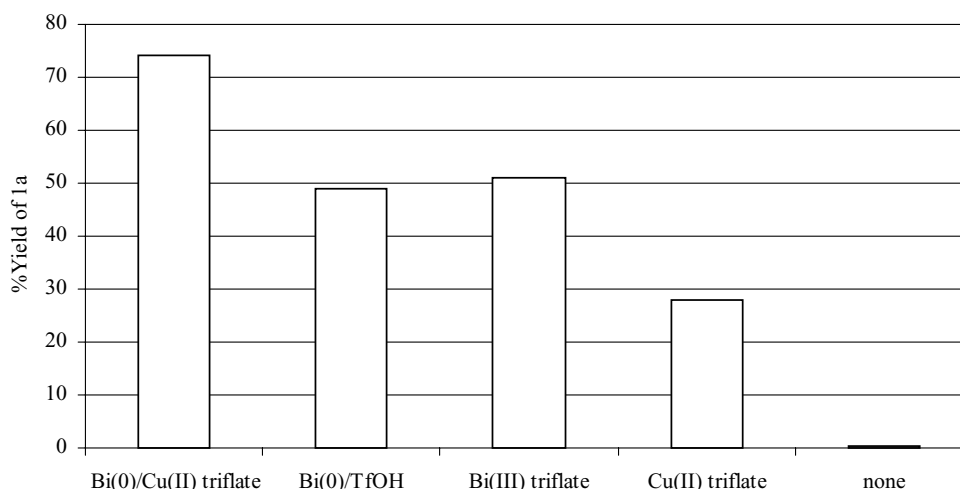


Fig. 1. Kinetics of the consumption of cyclohexene oxide in the Bi⁽⁰⁾/Cu(OTf)₂ and Bi⁽⁰⁾/TfOH-catalysed oxidations. The reaction was monitored by ¹H NMR analysis.

Scheme 7. Yield of 1,2-cyclohexanedione **1a** for different catalytic systems (after total conversion of cyclohexene oxide).

In a mixture of DMSO/toluene (1:1) the reaction mixture was heterogeneous and the oxidation of the epoxide did not occur.

We could conclude that the oxidative epoxide ring opening needs the presence of DMSO, which acts as an oxidant as well as a solvent. DMSO is the oxidant in the first step of oxidative ring opening, converting the epoxide into the corresponding α -ketol intermediate, in the presence of a Lewis acid.

When the oxidation of cyclohexene oxide was carried out in DMSO at 100 °C in the presence of Bi⁽⁰⁾ and Cu(OTf)₂, respectively in 9 and 14 mol%, but under a nitrogen atmosphere, only 22% of the expected α -diketone **1a** was formed after 2 h reaction, together with 19% of the α -ketol intermediate **2a** and 24% of the diol **3a**. A black Bi⁽⁰⁾ powder was present after the reaction.

Molecular oxygen is therefore needed as oxidant in the process. The oxygen consumption has been measured to be of 1.5 equivalents in the case of the oxidation of an α -ketol to the corresponding carboxylic acid via the oxidative cleavage by Bi^(III) compounds [34]. Molecular oxygen is involved,

together with Bi^(III), in a redox process with the α -ketol and leading to the α -dicarbonyl compound.

It was already shown, that under DMSO/O₂ but in the absence of bismuth species, no epoxide oxidation to the α -diketone was taking place.

3.5. Alternative oxygen sources

The Bi-catalysed oxidative system for internal epoxides to α -diketones is based on two different oxidants, DMSO, and molecular oxygen.

In the context of an increasing demand of environmentally friendly reactions, particularly in the area of oxidation reactions, we were interested in a substitute for DMSO as an oxygen transfer agent. *N*-oxides, as well as *t*-butyl hydroperoxide or hydrogen peroxide were tested as possible oxygen transfer agents for the oxidation of cyclohexene oxide.

The use of aqueous H₂O₂ led to the exclusive formation of the glycol derivative from epoxide hydrolysis (Table 3, entries 1 and 2). Anhydrous *t*-BuOOH in nonane in the presence of 2 mol% of Cu(OTf)₂ in dichloromethane was used,

Table 3
Oxidation of cyclohexene oxide with various oxygen transfer agents

Entry	Oxygen source (equivalents)	Catalyst temperature (°C)	Solvent time (h)	Conversion	Products, yield
1	H ₂ O ₂ (40)	Bi(OTf) ₃ 12 mol% (17)	H ₂ O (0.5)	100%	3a , 91%
2	Aq. H ₂ O ₂ (2.0)	Cu(OTf) ₂ 1 mol% (80)	CH ₃ CN (7.0)	100%	3a , <1%
3	2Na ₂ CO ₃ ·3H ₂ O ₂ (1.1)	– (70)	CH ₃ CN (17.0)	0%	–
4	2Na ₂ CO ₃ ·3H ₂ O ₂ (1.3)	Cu(OTf) ₂ 1 mol% (40)	CH ₂ Cl ₂ (20.0)	0%	–
5	Pyridine <i>N</i> -oxide (1.4)	Cu(OTf) ₂ 6 mol% (80)	CH ₃ CN (22.0)	8 ^a	2a , <1%
6	Trimethylamine <i>N</i> -oxide·2H ₂ O (1.5)	Cu(OTf) ₂ 8 mol% (80)	CH ₃ CN (7.5)	100%	Complex mixture of 3a and 7a as major products
7	Pyridine <i>N</i> -oxide (1.4)	Bi ⁽⁰⁾ 8 mol% TfOH 28 mol%	CH ₃ CN (8.0)	100%	–

^a Determined by GC.

leading to a non-selective mixture of products. The use of sodium percarbonate has been already mentioned in organic transformations, this reagent acting as an oxygen donor [35]. However, in refluxing acetonitrile or dichloromethane, no conversion of the epoxide was observed (entries 3 and 4).

N-Oxide derivatives such as pyridine *N*-oxide or trimethylamine *N*-oxide acted as weak nucleophiles. Cyclohexene oxide was only poorly converted into the corresponding α -ketol (entry 5).

In order to correlate these experimental results with the intrinsic nucleophilicity of *N*-oxides, some ab initio calculations with Gaussian 98 [36] were carried out. The optimised geometries of *N*-oxides were calculated and compared to that of DMSO, in particular regarding charges on oxygen and vicinal atoms. Becke's three-parameters exchange functionals [37] and the gradient-corrected functionals of Lee et al. [38] (B3LYP) level of theory was chosen, with the basis set 3-21+G*. Results are summarised in Table 4. Charges were estimated on the optimised geometry by means of a natural population analysis (NPA).

The calculated charges on oxygen atoms were close to -0.5 for pyridine *N*-oxide, to almost -0.7 for trimethylamine *N*-oxide and to -0.9 for DMSO. Even though it is known that a basis set of a reduced size, particularly with limited polarisation functions, stabilizes the sulfenate form relatively to the sulfoxide one [39], this values are consistent with our experiments, showing that, although DMSO is described as a poor nucleophile, it was able to act as an

oxygen transfer agent to the epoxide, more efficiently than the *N*-oxide derivatives. Calculations were done for 2,5- and 2,6-lutidine to illustrate the delocalisation phenomena and showed that lowest charges were theoretically located on carbon atoms.

Among the oxidants tested, DMSO remained the best oxygen transfer agent, playing also the role of solvent, polar enough to solve the Bi-chelated intermediates, and allowing reactions to be run at 100 °C without decomposition.

3.6. Influence of the substrate

In order to determine the scope of the oxidation of epoxides to α -diketones, several cyclic, linear and functionalised epoxides were submitted to the catalytic oxidation by the Bi⁽⁰⁾/O₂/DMSO system.

We observed that cyclic epoxides such as cyclopentene oxide, cyclohexene oxide, and cyclododecene oxide were readily converted into their corresponding α -diketones in good yields using the catalytic system Bi⁽⁰⁾ with added Cu(OTf)₂ or TfOH.

The results from the oxidation of cyclic epoxides by Bi⁽⁰⁾ in the presence of Cu(OTf)₂ or TfOH as the additives are summarised in Table 5. For five- and six-membered ring epoxides (entries 1 and 2) the use of Cu(OTf)₂ as the additive gave better yields of α -diketone (**1c**: 52% and **1a**: 74%) than the use of TfOH (compare entries 2 and 3).

Cyclooctene oxide was treated by both Bi⁽⁰⁾/Cu(OTf)₂ and Bi⁽⁰⁾/TfOH. When Cu(OTf)₂ has been used as the additive, the reaction presented a low conversion of 24% after 6 h, with only traces of α -diketone **1b** (entry 4). Isomerisation, ring-opening and polymerisation products were the main products. In the presence of TfOH (entry 5), a mixture of 2-hydroxycyclooctanone **2b**, cyclooctanone **7b** and 3-hydroxycyclooctene **8b** was obtained, in 20, 21 and 14% yield, respectively.

For less strained macrocyclic epoxides such as cyclododecene oxide (entries 6, 7), a better activation was obtained with the combination Bi⁽⁰⁾/TfOH (entry 7). 1,2-Cyclododecanedione **1d** was obtained in 51% yield, together with 10% of isomerised cyclododecanone **7d** and 27% of dodecanedioic acid, from the oxidative cleavage of the C–C bond of 1,2-cyclododecanedione **1d**.

The results of the oxidation behaviour of aromatic and aliphatic linear epoxides are presented in Table 6.

The oxidation of 4-nonene oxide, afforded 4,5-nonanedione **1e** in 57% yield with the system Bi⁽⁰⁾/TfOH. Butanoic and pentanoic acids, resulting from the oxidative C–C bond cleavage of the diketone **1e**, were found each in 24% yield.

Aromatic epoxides (entries 2–5) reacted unselectively with both TfOH or Cu(OTf)₂ as the activating agents. While 1,2-disubstituted epoxides such as stilbene oxide led to a mixture of benzil **1f**, small amounts of benzaldehyde and benzoic acid and isomerisation products (benzophenone 32%, 1,2-diphenylethanone **7f** 15%), terminal aryl epoxides such as styrene oxide led preferentially to oxidative

Table 4
Atomic charges calculated by DFT method (B3LYP/3-21+G*) for *N*-oxides and DMSO


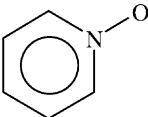
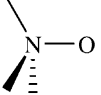
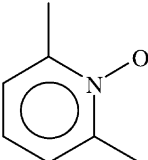
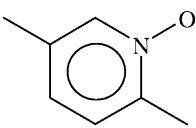
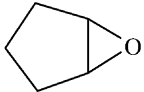
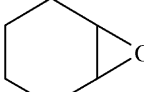
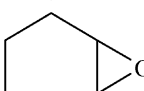
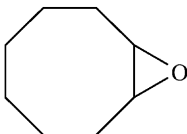
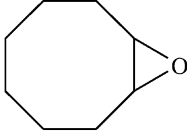
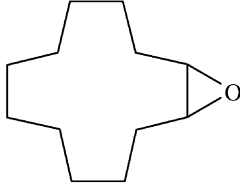
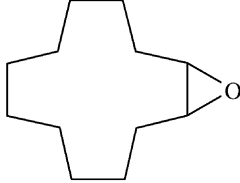
Entry	Nucleophile	Atomic charges (natural population analysis)
1		O atom: -0.93 , S atom: 1.18
2		O atom: -0.53 , N atom: -0.02
3		O atom: -0.67 , N atom: -0.13
4		O atom: -0.56 , N atom: -0.02 , methyl C atom: -0.74
5		O atom: -0.54 , N atom: -0.01 , 2-methyl C atom: -0.74 , 5-methyl C atom: -0.71

Table 5
Oxidation of cyclic epoxides catalysed by Bi⁽⁰⁾ in the presence of additives in DMSO at 100 °C under molecular oxygen (1 atm)

Entry	Starting epoxide	Catalyst (equivalents) additive (equivalents)	Time (h)	α -Diketone	Yield (%)
1		Bi ⁽⁰⁾ (0.06) Cu(OTf) ₂ (0.07)	1.8	1c	52
2		Bi ⁽⁰⁾ (0.08) Cu(OTf) ₂ (0.025)	2.0	1a	74
3		Bi ⁽⁰⁾ (0.08) TfOH (0.22)	2.0	1a	49
4		Bi ⁽⁰⁾ (0.17) Cu(OTf) ₂ (0.07)	6.2	1b	<2 ^a
5		Bi ⁽⁰⁾ (0.09) TfOH (0.12)	27.7	None	–
6		Bi ⁽⁰⁾ (0.05) Cu(OTf) ₂ (0.10)	22.5	1d	– ^b
7		Bi ⁽⁰⁾ (0.02) TfOH (0.06)	9.0	1d	51

^a Reaction stopped after that maximum conversion was reached (monitored by GC).

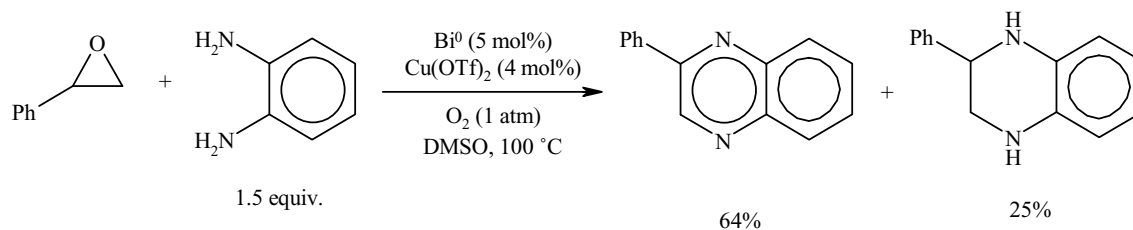
^b Conversion 13%; cyclododecanone **7d** 3%.

cleavage products, and the expected phenylglyoxal was not observed (entry 4).

Nevertheless, when the same reaction was carried out in the presence of 1.5 equivalents of phenylene diamine, 2-phenylquinoxaline was obtained in 64% yield, and 1,2,3,4-tetrahydro-2-phenylquinoxaline in 25% yield

(Scheme 8, and Table 6, entry 5). Both products were formed simultaneously during the reaction, and the proportion of tetrahydroquinoxaline and quinoxaline was kept constant.

We can assume that the quinoxaline ring results from the trapping of the 1,2-dicarbonyl compound, resulting from the oxidation of epoxide function by Bi⁽⁰⁾/O₂/DMSO, in



Scheme 8. Oxidation of styrene oxide in the presence of phenylene diamine, with trapping of the glyoxal intermediate.

Table 6

Oxidation of linear epoxides catalysed by Bi⁽⁰⁾ in the presence of additives in DMSO at 100 °C under molecular oxygen (1 atm)

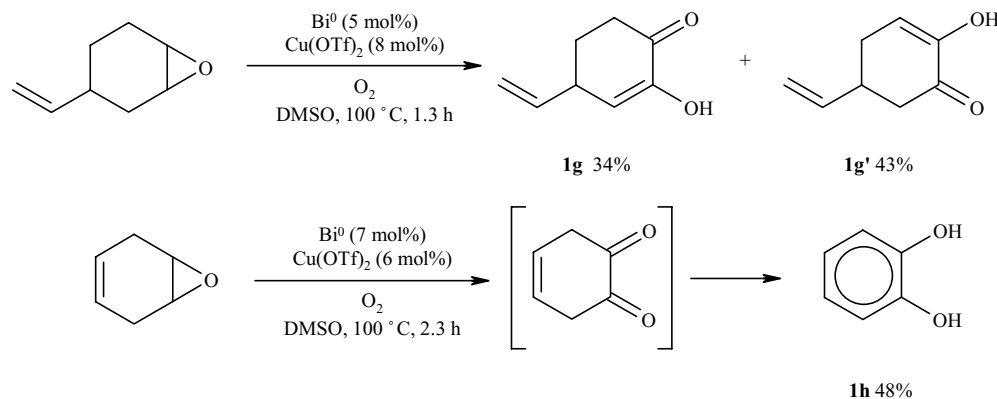
Entry	Epoxide	Catalyst (equivalents) additives (equivalents)	Time (h)	Oxidation products	Yield (%)
1		Bi ⁽⁰⁾ (0.10) TfOH (0.20)	2.3	1e	57
2		Bi ⁽⁰⁾ (0.13) TfOH (0.36)	20.0	1f	31
3		Bi ⁽⁰⁾ (0.05) Cu(OTf) ₂ (0.03)	3.0	1f	31
4		Bi ⁽⁰⁾ (0.04) Cu(OTf) ₂ (0.06)	3.3	PhCHO PhCOOH	41 16
5		Bi ⁽⁰⁾ (0.05) Cu(OTf) ₂ (0.04) Phenylene diamine (1.5)	3.7		64
6		Bi ⁽⁰⁾ (0.09) Cu(OTf) ₂ (0.07)	3.0	C ₆ H ₁₃ CHO, C ₆ H ₁₃ COOH, and C ₆ H ₁₃ COCO ₂ H	Complex mixture, non-isolated products
7		Bi ⁽⁰⁾ (0.05) TfOH (0.16)	16.0	C ₆ H ₁₃ COOH	13

the presence of Cu(OTf)₂. This strategy has been applied for a new catalytic synthesis of various quinoxaline derivatives [40]. In the absence of the aromatic diamine to trap the α -ketoaldehyde intermediate, it undergoes an oxidative cleavage to benzaldehyde and benzoic acid, as already described [20]. The tetrahydroquinoxaline resulted from the nucleophilic attack of phenylene diamine to the epoxide.

An aliphatic terminal epoxide such as 1-octene oxide (entry 6), led, in the presence of Bi⁽⁰⁾/Cu(OTf)₂, to a complex mixture containing heptanal, heptanoic acid, 2-oxooctanoic acid and 1,2-octanediol. The yield of heptanoic acid was in-

creased to 13% by the use of TfOH instead of Cu(OTf)₂ (entry 7). Attempts to trap the 2-oxooctanal intermediate by phenylene diamine were unsuccessful.

In order to examine the tolerance of the oxidative system towards functional groups, some experiments were carried out using functionalised epoxides. Thus, 4-vinylcyclohexene oxide and 1,2-epoxycyclohex-4-ene were converted into their corresponding α -diketones **1g** (and isomeric **1g'**) and **1h** in 77 and 48% yield, respectively (Scheme 9), indicating that both the intra- and the exocyclic double bonds remained unchanged during the transformation. However,



Scheme 9. Bi-catalysed oxidation of olefin containing epoxides.

the oxidation of 4-decenol oxide bearing a hydroxyl function showed that alcohol function on the epoxide was not compatible with the Bi⁽⁰⁾ oxidative system.

4. Conclusion

In conclusion, we showed that a Bi⁽⁰⁾/O₂/DMSO system could be efficient for the catalytic one-pot oxidation of internal epoxides to α -diketones, in the presence of an acid additive, preferentially providing triflate anions. The choice of the additive, copper(II) triflate or triflic acid, is closely related to steric hindrance, strain, and polymerisation of the epoxide. The use of DMSO as an oxygen transfer agent to epoxides is efficient in the absence of any strong nucleophile. It was shown to be the best among several common oxidants tested. The reaction is catalysed by a Bi^(III) active species generated in situ from bismuth powder. These results constitute a further development of the activation of molecular oxygen by bismuth, the heaviest metal of the periodic table, and one of the least toxic. This work, including the preliminary communication, constitutes the first example of the direct conversion of epoxides to α -diketones. This new transformation provides a two-steps pathway from olefins to α -diketones, using commercially available reagents in catalytic amounts.

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