

Novel and catalytic oxidation of internal epoxides to α -diketones

Sylvain Antoniotti^a and Elisabet Duñach^{*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. E-mail: dunach@unice.fr

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A catalytic system based on Bi(0)–Cu(OTf)₂ is efficient for the selective one-pot oxidation of 1,2-disubstituted epoxides to α -diketones under molecular oxygen and DMSO.

The ring opening of epoxides,¹ including stereo-, regio- and enantioselective aspects, has been widely reported for the functionalization of organic compounds. However, the oxidative ring opening of oxiranes has been poorly explored, the oxirane ring being difficult to oxidize selectively. Within epoxide oxidations, the formation of α -hydroxy ketones in the presence of dimethyl sulfoxide and an activating agent has been reported to occur in moderate yields.² The oxidative cleavage of the C–C bond of oxiranes can lead to aldehydes or to carboxylic acids, by a Ce(IV)-mediated reaction³ or by a Bi(III)-catalysed process,⁴ respectively. To our knowledge, no report in the literature deals with the direct and catalytic transformation of epoxides to α -diketones.⁵

We recently reported the use of Bi(0) under oxidative conditions for the synthesis of carboxylic acids from α -hydroxy acids or terminal aryl epoxides involving the oxidative cleavage of the terminal C–C bond.⁶ However, the reaction conditions were not well adapted to disubstituted epoxides.

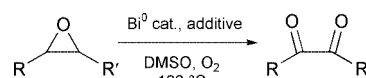
We describe here a novel and simple methodology based on the use of catalytic amounts of Bi(0) and Cu(OTf)₂ (or TfOH), able to oxidize internal epoxides to α -diketones in one step, under relatively mild conditions, using molecular oxygen–DMSO according to Scheme 1.

This reaction involves Bi(III)/Bi(0) as the catalytic system; the possibility of using commercially available Bi(0) powder is

interesting, due to its availability, its low cost and its low toxicity.⁷

The results of the oxidation of several 1,2-disubstituted epoxides are presented in Table 1. The reactions are carried out in DMSO at 100 °C and under an oxygen pressure of 1 atm in the presence of 5–10 mol% of Bi(0) powder and 2.5–20 mol% of Cu(OTf)₂ or TfOH as the additives. Interestingly, the black Bi(0) powder is dissolved in the organic medium containing the epoxide, affording a light yellow homogeneous solution, provided that the reaction is run under oxygen.

Cyclic, as well as linear 1,2-disubstituted epoxides led to the corresponding 1,2-diketones in good yields. For five and six-membered ring epoxides (entries 1–3, 6), the use of Cu(OTf)₂ (2.5–8 mol%) as the additive afforded the best results as compared to the use of other Lewis acids, such as BiCl₃, Li(NTf₂) or TfOH. Thus, epoxide **1a** afforded 74% isolated yield of cyclohexane-1,2-dione **1b**, whereas the same epoxide led to partial polymerisation in the presence of TfOH or Li(NTf₂) as the additives. On the other hand, for larger cycles ($n = 12$, **5a**) or linear epoxides such as **4a**, with less ring strain, the use of TfOH instead of Cu(OTf)₂ resulted in the best yields (entries 4, 5). The main by-products in the oxidation of **4a** and **5a** were the corresponding ketones (5–10% to 29% re-



Scheme 1

Table 1 Bi-catalysed oxidation of epoxides under O₂ (1 atm) in DMSO at 100 °C

Entry	Epoxide	Bi(0) (equiv.)	Additive (equiv.)	Time (h)	Product	Yield
1		0.08	Cu(OTf) ₂ (0.025)	2		74%
2		0.05	Cu(OTf) ₂ (0.08)	1.3		77%
3		0.08	Cu(OTf) ₂ (0.06)	2.3		48%
4		0.10	TfOH (0.2)	2.3		83%
5		0.06	TfOH (0.09)	7.0		70%
6		0.06	Cu(OTf) ₂ (0.07)	2		52%

spectively), issued from the epoxide isomerisation in acidic medium.⁸ No other by-products were detected.

The oxidation of unsaturated epoxides **2a** and **3a** indicated that olefin functions were not modified by the catalytic system.

The α -diketones in five or six-membered rings were mainly found in their enol form according to ¹H-NMR analysis (in CDCl₃ at 20 °C). Particularly in the case of entry 3, only the 1,2-dihydroxybenzene form was observed. However, diketones **4b** and **5b** were present with low enolisation (respectively 36 and 30%) under the same analytical conditions.

When a terminal epoxide such as 1-octene oxide was treated under the Bi(0)–Cu(OTf)₂ oxidation conditions (as for entry 1), the expected α -keto aldehyde underwent further C–C cleavage leading to a mixture of heptanal and heptanoic acid in 80% overall yield. This result was consistent with our previous observations on the reactivity of terminal epoxides.⁶

The presence of Bi(0) was essential for the preparation of the α -diketone. In the absence of bismuth, **1a** did not lead to **1b** but afforded 2-hydroxycyclohexanone in 55% yield. On the other hand, no diketone was obtained in the absence of O₂ (reactions under N₂) or in the absence of DMSO (reactions in DMF). This result indicates that DMSO would act as the oxygen transfer agent to the epoxide. Accordingly, dimethyl sulfide is evolved in the oxidation process. It was also shown that without any additive, the epoxide was unreactive.

In order to check if Bi(III) species were involved in the catalytic cycle, the reaction of **1a** was carried out in the presence of Bi(III)-mandelate,⁹ replacing Bi(0) (conditions of entry 1). The reaction also afforded **1b**, but in low yield (10%). This result was taken to indicate that the reaction could proceed through a Bi(0)/Bi(III) redox couple, in agreement with recent results.⁶ We observed that the Bi(0) oxidative dissolution (presumably to Bi(III)) needed molecular oxygen as well as the presence of the epoxide and the additive. Under nitrogen, the black Bi(0) precipitate persisted, and the epoxide oxidation to the α -diketone did not take place.

For the reaction mechanism, still under investigation, we propose the initial oxidative oxirane ring opening to an α -hydroxy ketone intermediate catalysed by the system Cu(OTf)₂ [or TfOH]–DMSO. The presence of a strong acid (Lewis or protic one) to activate the oxirane ring seems an important feature of this process. The presence of weakly coordinating triflate species could also have an important role in the reaction. DMSO, in association to the acid, effects the oxidative ring opening.

In a second step, in the presence of Bi(III), presumably issued from Bi(0) oxidative dissolution, a redox reaction affords the α -diketone by oxidation of the ketol. The reduced bismuth species are reoxidized to Bi(III) under molecular oxygen. The use of

oxygen at the pressure of 1 atm as the oxidant in this step is an interesting aspect of the process. Recently, another Bi(III)–O₂ system has proven its efficiency in the deprotection of *S,S*-acetals.¹⁰

In conclusion, a new synthetic transformation is described, involving the oxidative ring opening of epoxides to α -diketones, in a combined Bi(0)–Cu(OTf)₂ catalytic system under O₂–DMSO. The process uses commercially available reagents in a one-pot reaction under relatively mild conditions.

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Notes and references

General procedure for epoxide oxidation. A mixture of bismuth(0) (0.5 mmol) and the additive (0.5 mmol) in DMSO (15 ml) is heated at 100 °C under O₂ (1 atm). 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 (monitored by GC). The reaction mixture is hydrolysed with brine (50 ml) and extracted with diethyl ether (3 × 50 ml). The combined organic layers are dried over MgSO₄ and evaporated. The product is purified by column chromatography over silica gel with dichloromethane as the eluent. The products are identified by ¹H and ¹³C NMR and mass spectroscopy, and compared with authentic commercial samples or literature data.

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