



Preliminary communication / Communication

Asymmetric epoxidation of olefins via new α -fluorinated dioxiranes

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Abstract

Epoxidation of *trans*-stilbene and *trans*-methyl *p*-methoxycinnamate through dioxiranes generated in situ from chiral cyclohexanones was examined. It was shown, by comparing flexible ketones with a rigid *trans*-decalinic type ketone, that, although the Curtin–Hammett principle holds, the less populated conformer (with a fluorine equatorial) has but a negligible contribution. It was also shown that reaction conditions are important and must be fixed in each case. **To cite this article:** A. Solladié-Cavallo et al., *C. R. Chimie* 6 (2003).

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Résumé

L'époxydation du *trans*-stilbène et du *p*-méthoxycinnamate de méthyle par des dioxiranes chiraux générés in situ au départ de cyclohexanones chirales a été étudié. La comparaison entre des cétones flexibles et une cétone décalinique rigide a montré que, bien que les conditions du principe de Curtin–Hammett soient remplies, le conformère le moins peuplé, ayant son atome de fluor en position équatoriale, ne contribue que très faiblement. Il a été montré aussi que les conditions opératoires devaient être fixées dans chaque cas. **Pour citer cet article :** A. Solladié-Cavallo et al., *C. R. Chimie* 6 (2003).

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Mots clés : epoxydation asymétrique ; dioxirane fluorés

1. Introduction

Dioxiranes generated in situ from oxone and chiral ketones have appeared to be efficient reagents for

asymmetric epoxidations of *trans*-olefins [1–5]. During investigation of type-I substituted cyclohexanones as precursors of chiral dioxiranes for asymmetric epoxidation of *trans*-stilbene **1** and *trans*-methyl *p*-methoxycinnamate **2** (Fig. 1), we recently reported a 26 to 30% increase of the ee (40 to 66% ee and/or 60 to 90% ee) with ketones **3** and **4** compared with **5** (due to

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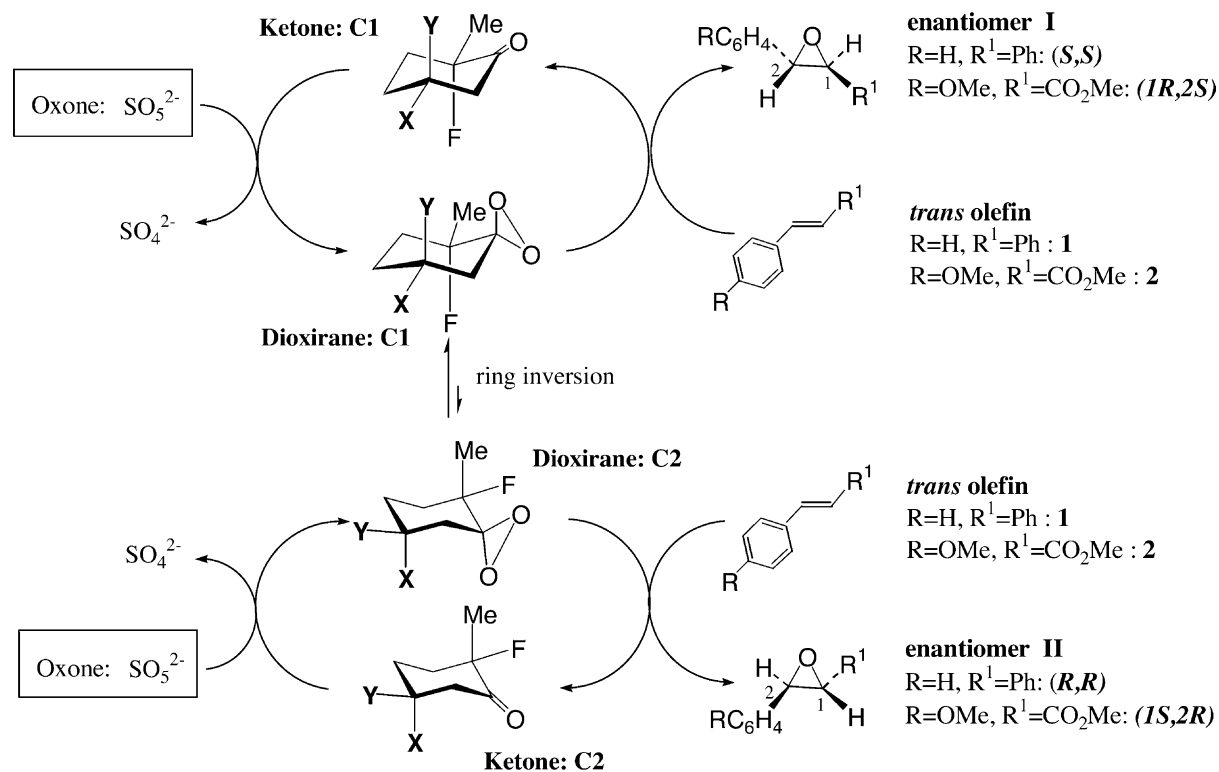


Fig. 1

de-symmetrization of the axial face of the cyclohexanone). A contribution of the axial approaches of the olefin onto the dioxirane (in addition to the main equatorial approaches) was thus envisaged [6].

However, because approaches (equatorial and axial) on the inverted ring (conformation **C2**) of the dioxirane (Fig. 1) provide the other enantiomer [7] and could be responsible for lowering the enantioselectivity, a new rigid ketone **6** similarly substituted at C2 and C5 (compared to ketone **4**) and having only conformation **C1** has been designed and synthesized.

We present here a comparison between the efficiencies of flexible ketones **3**, **4** and **7** already used by Shi [8] (in which ring inversion is possible) and that of **6** (which is rigid) for epoxidation of *trans*-stilbene **1** and *trans*-methyl *p*-methoxycinnamate **2** (Fig. 2). Moreover, different epoxidation conditions have been used.

2. Results

Ketone **6** was obtained (from commercially available (*R*)-(-)-hexahydro-4a-methyl-2-naphthalenone

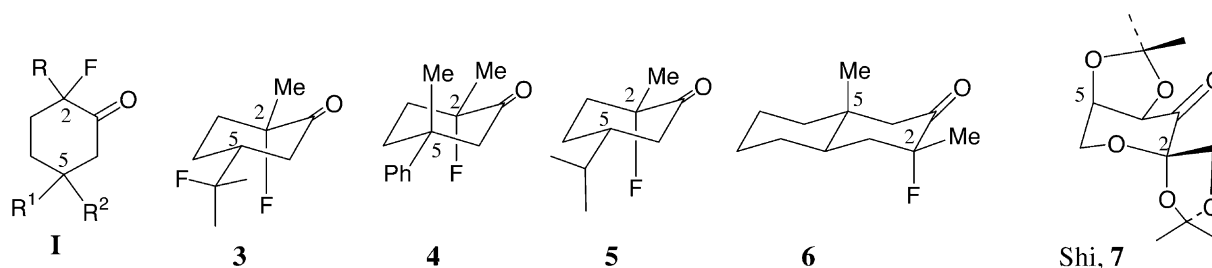


Fig. 2

Table 1
Epoxidation of olefins **1** and **2** using ketones **3**, **4**, **6** and **7**.

Ketone		3		4		6*		7	
Olef.	cond.	conv.%	ee%	conv.%	ee%	conv.%	ee%	conv.%	ee%
1	A	90	90, (-)-(SS)	95	90, (-)-(SS)	100	91*, (+)-(RR)	62	82, (+)-(RR)
1	B	100	90, (-)-(SS)					47	98, (+)-(RR)**
2	A	74	60, (-)-(RS)	90	66, (-)-(RS)	75	50*, (+)-(SR)	30	34, (+)-(SR)
2	B	100	76, (-)-(RS)					43	86, (+)-(SR)

* This ketone being 90% ee, the ee% of the epoxides have been corrected.

** 75% conv. and 97% ee (+)-(R,R) were found by Shi under the same conditions [11].

90% ee) as one diastereomer and it has been shown by NMR (in C_6D_6) that the fluorine atom was *axial* [9], as in the most populated conformer (**C1**) of ketones **3**, **4** and **6**. Shi's ketone **7** was prepared according to the described process [10]. The percentages of conversion have been determined by combining weights and 1H NMR (200 and 300 MHz) of solvent-free crude products; then the obtained and known epoxides were isolated by flash chromatography on silica gel. The ee% were determined by HPLC (Chiralcel OD), 1H NMR (400 MHz, $Eu(hfc)_3$) and the absolute configuration through the signs of optical rotations.

The results are gathered in Table 1.

In all cases, 0.3 equiv of ketone were used and the reaction conditions were either **A** (dioxane/ H_2O ; K_2CO_3 0.1 M/AcOH, 0.5%; oxone (3 equiv)/ H_2O and K_2CO_3 (6 equiv) dropwise; addition ~6 h at room temperature) or **B** (acetonitrile; $Na_2B_4O_7 \cdot 10 H_2O$, 0.05 M/ Na_2EDTA , $4 \times 10^{-4}M$; HSO_4NBu_4

(0.05 equiv); oxone (1.4 equiv)/ Na_2EDTA , $4 \times 10^{-4}M$ and K_2CO_3 (5.8 equiv) dropwise); addition ~2 h at 0 °C).

It was found that conditions **B** have a tendency to give slightly higher yields and higher ee% (compare lines 1/2 and 3/4 in columns 1 and 4).

It appeared that, under conditions **A** and for epoxidation of stilbene **1**, ketones **3**, **4** and **6** are more efficient (90–100% yield and 90–91% ee) than Shi's ketone **7** (62% yield and 82% ee); however, under conditions **B**, ketone **7** provides higher enantioselectivity (98%), but lower yield (47%).

It is worth noting that the absolute configuration of the major epoxide enantiomer obtained (Table 1) fits with the postulated model [6] of equatorial (and partly axial) approaches of the olefin on the most populated conformer **C1** of the non-rigid ketones **3**, **4** and **7** and on rigid ketone **6** (Fig. 3).

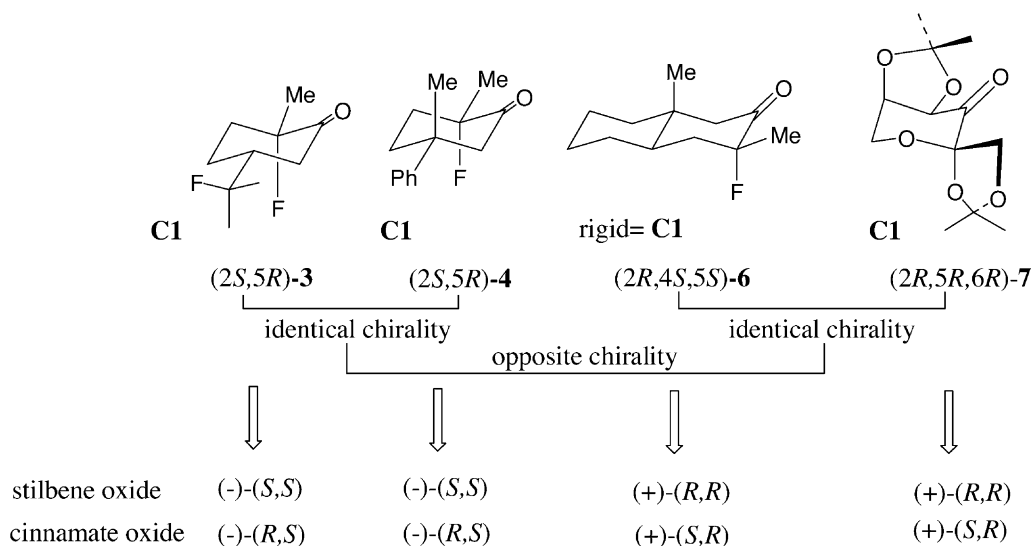


Fig. 3

We could thus conclude that, although the Curtin–Hammett principle holds to non-rigid ketones, the contribution of the olefin's approaches on the inverted ring **C2** is not significant. Moreover, direct epoxidation of the olefin by the oxone has been checked and appeared to be negligible under conditions **B** (3% epoxide formed in absence of the ketone for stilbene and 1% for methyl cinnamate), but started to become slightly significant under condition **A** (14% for stilbene and 9% for methyl cinnamate).

It thus seems that the maximum efficiency of the chiral ketones is reached and that more efficient substituents must be found. However, adjustment of the epoxidation conditions is very important and depends on both the olefin and the ketone. It is worth noting that while ketone **7** is not recovered under both conditions (**A** and **B**) for an undetermined reason (no Baeyer–Villiger product has been isolated or identified), ketones **3**, **4** and **6** are recovered (almost quantitatively

during chromatography). Only **3** undergoes 3–5% of Baeyer–Villiger product under conditions **B**.

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