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Chemoenzymatic Synthesis of Chiral Epoxides. Preparation of 4-Phenyl-2,3-epoxybutane and 1-Phenyl-1,2-epoxypropane

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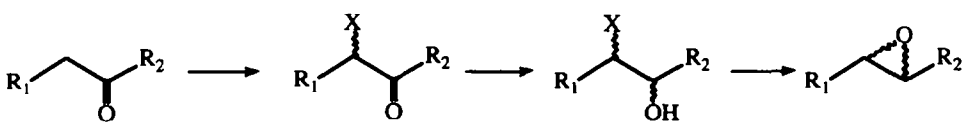
Abstract : All the stereoisomers of 4-phenyl-2,3-epoxybutane and 1-phenyl-1,2-epoxypropane (β-methylstyrene oxide) have been prepared in three steps from 4-phenyl-2-butanone and 1-phenyl-2-propanone or 1-phenyl-1-propanone respectively. The key step is the microbiological reduction of the corresponding haloketones. These results confirm those previously described[1] and demonstrate that the chemoenzymatic synthesis of homochiral 2,3-epoxides is a general method that can be used whatever the starting ketone.

The three-step preparation of chiral epoxides from a ketone has been previously described[1]. All the stereoisomers of 2,3-epoxyoctane were synthesized from 2-octanone, the key step being the microbiological reduction of 3-bromo-2-octanone. In order to verify if this chemoenzymatic method of preparing homochiral 2,3-epoxides was efficient whatever the starting ketone, the synthesis of two other epoxides from chiral halohydrins was studied. These were prepared by microbiological reduction of α-haloketones obtained from the following aromatic ketones : 4-phenyl-2-butanone **1**, 1-phenyl-2-propanone **2** and 1-phenyl-1-propanone **3**. In this paper, the chemoenzymatic syntheses of all the stereoisomers of 4-phenyl-2,3-epoxybutane **4** and of 1-phenyl-1,2-epoxypropane (β-methylstyrene oxide) **5** are described following the general scheme shown below :

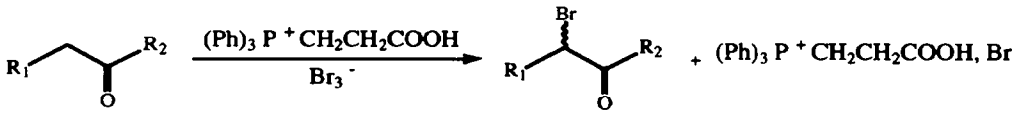


1- R_1 = Benzyl R_2 = Methyl
2- R_1 = Phenyl R_2 = Methyl
3- R_1 = Methyl R_2 = Phenyl

4- R_1 = Benzyl R_2 = Methyl
5- R_1 = Phenyl R_2 = Methyl

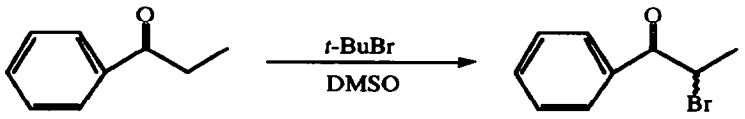
1 - Microbiological Reduction of α-Bromoketones

The first steps involved in epoxide synthesis were the preparation of α-bromoketones and the study of their microbiological reduction. 4-Phenyl-3-bromo-2-butanone **6** and 1-phenyl-1-bromo-2-propanone **7** were prepared by treating the corresponding ketones with 2-carboxyethyltriphenylphosphonium perbromide according to Armstrong *et al.*[2]. Yields were 70% and 80% respectively.



6 - R_1 = Benzyl R_2 = Methyl
7 - R_1 = Phenyl R_2 = Methyl

1-Phenyl-2-bromo-1-propanone **8** was obtained by reaction with *tert*-butyl bromide in DMSO according to the method of Armani *et al.*[3]. Yield was 80%.



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The same strains used for the microbiological reduction of 3-bromo-2-octanone[1] were retained for the microbiological reduction of the α-bromoketones **6**, **7** and **8** : bakers' yeast, *Aspergillus niger*, *Beauveria sulfurescens*, *Geotrichum candidum*, *Mortierella isabellina*, *Cunninghamella elegans*, *Lactobacillus kefir*. *Rhodotorula glutinis* and *Sporotrichum exile* were used in some cases as they have been reported to reduce α-chloro-β-ketoesters by Cabon *et al.*[4]. The yeast was used freeze-dried under non-fermenting conditions, *i.e.* suspended in water without adding sugar. Bioconversions with other microorganisms were carried out with washed resting cells except for *R. glutinis*. Growing cells were used for this microorganism.

a - Microbiological reduction of 4-phenyl-3-bromo-2-butanone **6**

Each microorganism (except *S. exile*) was assayed for a 24 h or 48 h incubation time. All the microorganisms reduced **6** after 24 h and a mixture of two diastereoisomeric bromohydrins was obtained in each case. Quantitative assays were carried out for the 24 h incubation period to determine the absolute configurations and the enantiomeric excesses of the bromohydrins formed. The results are given in Table I. All the reactions described are stereospecific: in most cases only two diastereoisomers of bromoalcohol were obtained, the reduction of the keto group being highly enantiogenic. The diastereoisomeric bromohydrins were separated by chromatography on a silica column. The chemical yields recorded in the last column of the table are overall yields of diastereoisomers after work-up. The proportions of each isomer are given in brackets.

The best results for the microorganisms giving the (2S) alcohol were with bakers' yeast, *B. sulfurescens* and *R. glutinis*. *Syn* (2S,3S) and *anti* (2S,3R) bromohydrin diastereoisomers were obtained in equivalent amounts with excellent enantiomeric excesses. With *M. isabellina*, only the *anti* (2S,3R) diastereoisomer was optically pure. Its major *syn* isomer had a low enantiomeric excess. *A. niger* and *C. elegans* gave the two other isomers of bromohydrins (the *syn* (2R,3R) and the *anti* (2R,3S) diastereoisomer respectively) with very high enantiomeric excesses. *A. niger* (as previously observed with 3-bromo-2-octanone) gave rise to a mixture of non-reactive but optically active bromoketone and (2R,3R) bromohydrin, irrespective of reaction time. The (2R) alcohol prepared with the other microorganisms (*G. candidum* and *L. kefir*) showed enantiomeric excesses too low for subsequent synthesis. In all cases, yields were very good (75-95 %). With *C. elegans*, 40 % bromoketone did not react. If the yield was calculated on the quantity of

bromoketone reduced, it would be about 70 %.

Table I : Microbiological reduction of 4-phenyl-3-bromo-2-butanone

	syn Bromohydrin			*anti* Bromohydrin			Yield
	$[\alpha]_J^{25}$	e.e.	Conf.	$[\alpha]_J^{25}$	e.e.	Conf.	
Bakers' yeast	- 28	≥ 95 %	(2S,3S)	+ 37	≥ 95%	(2S,3R)	93 % (60/40)
Mortierella isabellina	- 10	36 %	(2S,3S)	+ 35	94 %	(2S,3R)	85 % (70/30)
Beauveria sulfurescens	- 28	≥ 95 %	(2S,3S)	+ 35	94 %	(2S,3R)	75 % (50/50)
Rhodotorula glutinis	- 28	≥ 95 %	(2S,3S)	+ 29	78 %	(2S,3R)	74 % (60/40)
Aspergillus niger	+ 28	≥ 95 %	(2R,3R)	-	-	-	48% (100/0)
Cunninghamella elegans	+ 12	45 %	(2R,3R)	- 34	92 %	(2R,3S)	45 % (65/35)
Geotrichum candidum	+ 16	60 %	(2R,3R)	- 25	70 %	(2R,3S)	85 % (60/40)
Lactobacillus kefir	+ 24	85 %	(2R,3R)	- 18	50 %	(2R,3S)	83 % (60/40)

NMR was used to determine enantiomeric excesses. Diastereoisomeric esters from the reaction of each bromohydrin with the (S)-O-acetyllactic chloride were not volatile enough to be analyzed by gas phase chromatography. ^1H NMR spectra of racemic *syn* and *anti* bromohydrins in the presence of a chiral europium derivative ($Eu(tfc)_3$) showed duplication of the methyl group doublet located at 1.30 ppm. The two doublets were well separated and the proportion of each enantiomer can be determined from their integration. The only disadvantage of this method is its precision (5%). An optically pure compound is noted ee ≥ 95 %.

The absolute configuration of the bromohydrins was more difficult to determine because neither optically active 4-phenyl-3-bromo-2-butanol, nor 4-phenyl-2-butanol or 4-phenyl-3-bromobutane have been described in the literature. The absolute configuration cannot be assigned by chemical correlation. An X-Ray structural determination of a crystallized derivative obtained by the reaction of each isomer of bromohydrin (synthesized by reduction with bakers' yeast) with (1S) camphanic chloride[5] was carried out. Crystallographic and spectroscopic data will be published ulteriorly[5]. Results showed that the *syn* diastereoisomer had (2S,3S) absolute configuration and that the *anti* diastereoisomer, (2S,3R) configuration (Figure 1).

In conclusion, it has been demonstrated that all four isomers of 4-phenyl-3-bromo-2-butanol can be obtained with very high enantiomeric excesses by selection of the appropriate microorganism. Enantiomerically pure (2S,3S) and (2S,3R) diastereoisomers were obtained with bakers' yeast or *Beauveria*

sulfurescens and the (2R,3R) and (2S,3R) enantiomers with *Aspergillus niger* and *Cunninghamella elegans* respectively.

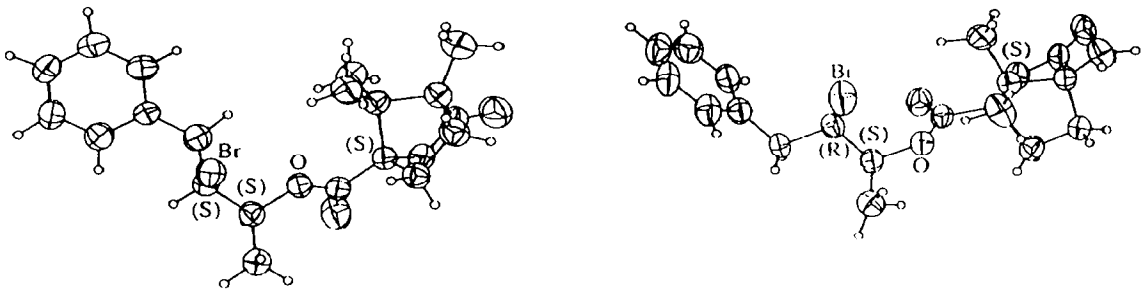


Fig. 1 : ORTEP views of (2S,3S) *(left)* and (2S,3R) *(right)* 4-phenyl-3-bromo-2-butylcamphanates

b-Microbiological reduction of 1-phenyl-1-bromo-2-propanone **7** and 1-phenyl-2-bromo-1-propanone **8**

Preliminary assays after 24 and 48 h incubation periods with several microorganisms were carried out for both ketones. The results are given in Tables II and III.

Table II : Microbiological reduction analytical assays of 1-phenyl-1-bromo-2-propanone

		1-Phenyl-2-propanone (%)	1-Phenyl-2-propanol (%)	Bromoketone (%)	*syn* Bromohydrin (%)	*anti* Bromohydrin (%)
Bakers' yeast	24 h	23	11	61	0	5
	48 h	40	12	43	1	4
Beauveria sulfurescens	24 h	35	12	50	2	1
	48 h	40	20	35	2	3
Mortierella isabellina	24 h	26	11	31	15	17
	48 h	41	22	20	10	7
Aspergillus niger	24 h	58	37	0	3	2
	48 h	53	39	0	4	4
Geotrichum candidum	24 h	30	24	35	6	6
	48 h	45	21	25	5	4

The reaction for both bromoketones did not proceed as expected. The quantities of bromohydrins formed were always very low (< 10%) with the exception of 1-phenyl-1-bromo-2-propanone with *M. isabellina*, which yielded a 32% mixture of bromohydrins. Unreacted bromoketone, large amounts of debrominated ketone (1-phenyl-2-propanone or 1-phenyl-1-propanone) and the corresponding alcohols were generally present after the incubation. Therefore the microbiological reduction of bromoketones **7** and **8** was not quantitatively assayed.

Table III: Microbiological reduction analytical assays of 1-phenyl-2-bromo-1-propanone

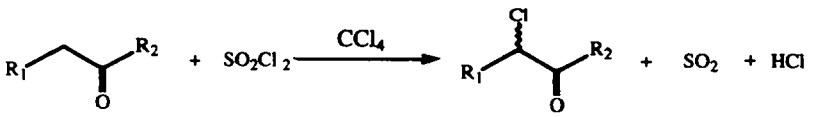
		1-Phenyl-1-propanone (%)	1-Phenyl-1-propanol (%)	Bromoketone (%)	*syn* Bromohydrin (%)	*anti* Bromohydrin (%)
Bakers' yeast	24 h	14	6	78	0	2
	48 h	34	3	59	2	2
Beauveria sulfurescens	24 h	28	3	65	0	4
	48 h	45	14	35	1	5
Mortierella isabellina	24 h	30	4	60	3	3
	48 h	40	13	40	4	3
Aspergillus niger	24 h	18	2	80	0	0
	48 h	22	3	75	0	0
Cunninghamella elegans	24 h	27	12	57	1	3
	48 h	40	15	40	2	3

Dehalogenation during the microbiological reduction of α-bromoketones has been already observed by other authors. Imuta *et al.*[6] have reported that the reduction of 1-phenyl-2-bromo-1-butanone principally results in the debrominated ketone, while reduction of the chlorinated analogue yields the chlorohydrins expected. Tanner and Stein[7] have studied the reduction of α-bromoacetophenone by horse liver alcohol dehydrogenase (HLAD) in the presence of NADH as cofactor. Acetophenone was the only product of the reaction whereas the reduction of α-chloroacetophenone gave the corresponding chlorohydrin. In contrast, α-haloacetophenone (Br or Cl) reduced by whole-cell microorganism (bakers' yeast)[8] gives the corresponding halohydrin whatever the halide. These results demonstrate that a bromine atom is more detrimental to microbiological reduction than a chlorine atom. However, dechlorination can also occur. Cabon *et al.*[4] have shown chlorine loss during microbiological reduction of α-chloro-β-ketoesters by whole-cell microorganisms.

It seemed evident that changing the nature of the halide atom and studying the microbiological reduction of chlorinated analogues of the relevant bromoketones was the next logical step to further progress.

II - Microbiological Reduction of α-Chloroketones

1-Phenyl-1-chloro-2-propanone **9** and 1-phenyl-2-chloro-1-propanone **10** were synthesized by treating 1-phenyl-2-propanone and 1-phenyl-1-propanone in a carbon tetrachloride solution with sulfuryl chloride[9].



9 - R_1 = Phenyl R_2 = Methyl

10 - R_1 = Methyl R_2 = Phenyl

After distillation or purification by chromatography on a silica column, both α-chloroketones were obtained with a 85% yield.

a - Microbiological reduction of 1-phenyl-1-chloro-2-propanone **9**

The results of the analytical study for incubation times of 24 h and 48 h are given in Table IV.

Table IV: Microbiological reduction analytical assays of 1-phenyl-1-chloro-2-propanone

		1-Phenyl-2-propanone (%)	1-Phenyl-2-propanol (%)	Chloroketone (%)	*syn* Chlorohydrin (%)	*anti* Chlorohydrin (%)
Bakers' yeast	24 h	10	9	15	41	25
	48 h	0	52	10	38	0
Beauveria sulfurescens	24 h	26	5	46	8	15
	48 h	34	11	43	6	6
Mortierella isabellina	24 h	10	43	0	28	19
	48 h	0	78	0	15	7
Aspergillus niger	24 h	12	0	79	8	1
	48 h	3	13	77	2	5
Geotrichum candidum	24 h	22	36	0	20	22
	48 h	13	51	0	33	3
Cunningha-mella elegans	24 h	5	0	94	1	0
	48 h	8	0	90	1	1
Lactobacillus kefir	24 h	42	17	12	22	7
	48 h	27	23	0	43	7
Sporotrichum exile	24 h	11	4	76	5	4
	48 h	11	5	73	3	8
Rhodotorula glutinis	24 h	4	43	0	35	18
	48 h	5	72	0	23	0

Only *C. elegans*, *A. niger* and *S. exile* did not reduce the chloroketone. The substrate totally disappeared with all the other microorganisms except for *B. sulfurescens*. A mixture of diastereoisomeric chlorohydrins with large but variable quantities of dechlorinated ketone and the corresponding alcohol was obtained. In general however, the mixture of diastereoisomeric chlorohydrins was an important part of the reaction mixture. Quantitative assays were carried out with all the microorganisms except *C. elegans*, *A. niger* and *S. exile*. The results of these assays for an incubation time of 24 h (except *L. kefir* : 48 h) are given in Table V. The yields recorded in the last column are the overall yields of diastereoisomers after work-up. The proportion of each isomer is given in brackets. These yields were quite low (< 40%) because dechlorination was consistently important.

The different constitutents of the reaction mixture were purified by column chromatography. The best results were obtained with bakers' yeast and *M. isabellina* which yielded the two (1S,2S) and (1R,2S) chlorohydrins with very high enantiomeric excesses. *B. sulfurescens* also gave these two optically pure isomers but 45% of the chloroketone did not react : the yield is too low to prepare chlorohydrins quantitatively. With *G. candidum* (strain Lab. Az.) and *R. glutinis*, only the *anti* (1R,2S) isomer showed high enantiomeric excess. *L. kefir* only gave an alcohol of (2R) configuration but the enantiomeric excesses of both chlorohydrins were low (< 20%).

Table V : Microbiological reduction of 1-phenyl-1-chloro-2-propanone

	1-Phenyl-2-propanol			*syn* Chlorohydrin			*anti* Chlorohydrin			Yield
	$[\alpha]_J^{25}$	e.e.*	Conf	$[\alpha]_J^{25}$	e.e.	Conf.	$[\alpha]_J^{25}$	e.e.	Conf.	
Bakers' yeast	+ 40	≥98%	(S)	+ 122	≥98%	(1S,2S)	- 80	≥98%	(1R,2S)	35 % (60/40)
Mortierella isabellina	+ 40	≥98%	(S)	+ 122	≥98%	(1S,2S)	- 78	97 %	(1R,2S)	18 % (55/45)
Beauveria sulfurescens	-	-	-	+ 122	≥98%	(1S,2S)	- 76	95 %	(1R,2S)	9 % (40/60)
Lactobacillus kefir (48 h)	- 39	97 %	(R)	- 15	12 %	(1R,2R)	+ 13	16 %	(1S,2R)	25 % (90/10)
G. candidum Strain CBS	- 14	35 %	(R)	+ 71	57 %	(1S,2S)	- 63	84 %	(1R,2S)	20 % (50/50)
G. candidum Strain Lab. Az	- 22	55 %	(R)	+ 10	11 %	(1S,2S)	- 80	≥98%	(1R,2S)	20 % (50/50)
Rhodotorula glutinis	- 31	78 %	(R)	+ 79	65 %	(1S,2S)	- 80	≥98%	(1R,2S)	36 % (65/35)

* From the $[\alpha]_D^{25}$ value in comparison with the literature data [10]

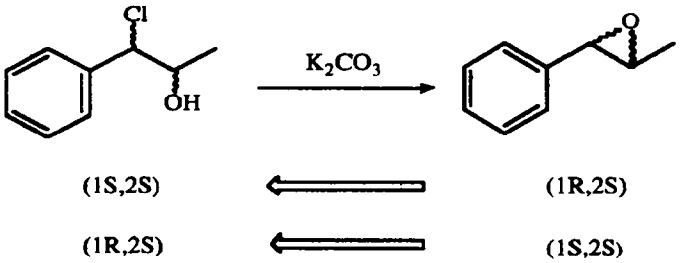
Enantiomeric excesses were determined by gas phase chromatography. Two methods were used :

- Each chlorohydrin diastereoisomer was treated by (S)-O-acetyllactic chloride and the diastereoisomeric esters were analyzed on a non chiral column.

- Each chlorohydrin was analyzed directly using a chiral phase column coated with modified γ-cyclodextrines (Lipodex E).

The enantiomeric excesses determined by these two methods were identical for each chlorohydrin diastereoisomer. The indirect method (reaction with the optically active acid chloride) was validated.

Absolute configurations of the chlorohydrins were determined by chemical correlation. Each isomer of the chlorohydrin was converted into β-methylstyrene oxide (all its isomers are described in the literature). The configuration of the chlorohydrin was deduced from the absolute configuration of epoxides formed from the chlorohydrins and from the stereochemistry of the reaction. The (1S,2S) and (1R,2S) chlorohydrins (obtained from reduction by bakers' yeast) were converted into epoxides by treatment with potassium carbonate. The *cis* or *trans* character can be assigned to the epoxides formed by comparing the ^1H NMR spectra of each epoxide with data given in the relevant literature[11]. The absolute configuration of epoxides was determined by comparing their optical rotation with those described in the literature[12]. Utaka *et al.*[13] have reported that a *syn* chlorohydrin gives a *cis* epoxide while an *anti* chlorohydrin gives a *trans* epoxide. Moreover, the epoxide formation reaction takes place with configuration inversion at the chlorine-bearing carbon atom. Therefore, the absolute configuration of chlorohydrin can be deduced from that of the epoxide from which it is derived.



1-Phenyl-2-propanol was also isolated for each microorganism. Its absolute configuration and enantiomeric excess were determined by comparing its optical rotation with that of known (2S) and (2R) enantiomers[10]. The phenomenon of dehalogenation (especially the starting compound) is gradually being elucidated by studying the characteristics of each compound obtained in the reaction. During microbiological reduction with both the strains *G. candidum* and *R. glutinis*, the carbon bearing the alcohol function had (2R) configuration for the dechlorinated alcohol and (2S) configuration for both chlorohydrins. 1-Phenyl-2-propanol can result from the reduction of 1-phenyl-2-propanone. If it was obtained from the chlorohydrins, the carbon atom bearing the hydroxyl group would have the same configuration in both compounds. This result is confirmed by comparing the enantiomeric excesses of the dechlorinated alcohol and the two chlorohydrins obtained with *L. kefir*. 1-Phenyl-2-propanol had an excellent enantiomeric excess (97 %) while those for the chlorohydrins were only 12 or 16 %. If dechlorination had taken place from the chlorohydrins, the enantiomeric excess of the dechlorinated alcohol would not have been observed to have such high optical purity. Microbiological reduction of 1-phenyl-1-chloro-2-propanone gave two optically pure diastereoisomers of chlorohydrins : (1S,2S) and (1R,2S). The (1R,2R) and (1S,2R) enantiomers had low enantiomeric excesses. In this case, an important dehalogenation reaction took place from the α-chlorinated ketone.

b - Microbiological reduction of 1-phenyl-2-chloro-1-propanone **10**

Table VI: Microbiological reduction analytical assays of 1-phenyl-2-chloro-1-propanone

		1-Phenyl-1-propanone (%)	1-Phenyl-1-propanol (%)	Chloroketone (%)	*syn* Chlorohydrin (%)	*anti* Chlorohydrin (%)
Bakers'	24 h	3	0	62	14	21
yeast	48 h	2	1	0	39	58
B. sulfurescens	24 h, 48 h	6	5	33	28	28
M. isabellina	24 h	0	0	0	60	40
Aspergillus	24 h	37	7	37	13	6
niger	48 h	5	3	12	20	60
G. candidum	24 h	10	7	0	42	41
C. elegans	24 h, 48 h	5	0	93	1	1
Lactobacillus	24 h	4	0	80	11	5
kefir	48 h	1	3	0	26	70
S. exile	24 h, 48 h	13	3	71	3	10
R. glutinis	24 h	4	3	0	45	48

The approach chosen was the same as that in previous studies. Preliminary assays were carried out for incubation periods of 24 or 48 h The results of chromatographic analyses of the reactions for each microorganism are given in Table VI.

All microorganisms reduced the 1-phenyl-2-chloro-1-propanone, with the exception of *C. elegans* and *S. exile* and a mixture of diastereoisomeric chlorohydrins always constituted the major part of reaction products. Dechlorination was low with the overall proportion of dechlorinated ketone and alcohol less than 20 %. With certain microorganisms (bakers' yeast, *A. niger*, *L. kefir*) reaction rate was slower than previously observed : 48 hours were needed for the α-chloroketone to completely disappear.

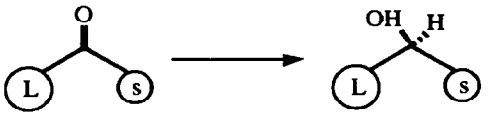
Since the analytical results were very encouraging, quantitative assays were carried out for the reduction of 1-phenyl-2-chloro-1-propanone with all the microorganisms which gave good results in the analytical assays. The results are given in Table VII. Incubation times are shown for each strain.

Table VII : Microbiological reduction of 1-phenyl-2-chloro-1-propanone

	Incubation time	*syn* Chlorohydrin			*anti* Chlorohydrin			Yield
		$[\alpha]_J^{25}$	e.e.	Conf.	$[\alpha]_J^{25}$	e.e.	Conf.	
Bakers' yeast	48 h	- 48	≥98%	(1R,2R)	- 31	≥98%	(1R,2S)	92 % (40/60)
Rhodotorula glutinis	24 h	- 48	≥98%	(1R,2R)	- 31	≥98%	(1R,2S)	95 % (50/50)
Mortierella isabellina	24 h	+ 1	2 %	(1S,2S)	+ 1.5	5 %	(1S,2R)	93 % (60/40)
Beauveria sulfurescens	24 h	+ 41	85 %	(1S,2S)	+ 2	8 %	(1S,2R)	43 % (50/50)
Aspergillus niger	48 h	+ 5	10 %	(1S,2S)	+ 19	60 %	(1S,2R)	45 % (25/75)
Geotrichum candidum	48 h	0	0	(1R,2R)	- 7	23 %	(1R,2S)	83 % (50/50)
Lactobacillus kefir	48 h	+ 44	91 %	(1S,2S)	+ 22	70 %	(1S,2R)	87 % (30/70)

Dehalogenation was low and thus the yields obtained were very good (83 to 93 %). For *A. niger* and *B. sulfurescens*, yields were comparatively lower because the reaction was incomplete. The chlorinated ketone represented 20 % and 33 % respectively of the mixture after reaction.

A surprising result was the change in chlorohydrin absolute configuration with some microorganisms in comparison to that of chlorohydrins obtained from the microbiological reduction of 1-phenyl-1-chloro-2-propanone. Bakers' yeast and *R. glutinis* yielded the (1R) alcohol and *L. kefir* the (1S) isomer, while (2S) and (2R) alcohols were obtained from 1-phenyl-1-chloro-2-propanone with the same microorganisms. This change can be explained by so-called "Prelog's rule".



(S)

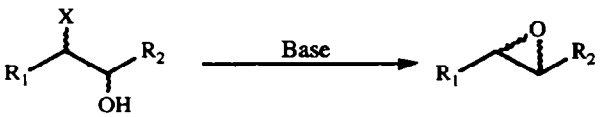
In 1-phenyl-1-chloro-2-propanone, the PhCHCl group is the bulkiest group (L) whereas the methyl group is the small substitutent (S). If the relative size of the substituents flanking the carbonyl group (shown in the above scheme) is considered then bakers' yeast and *R. glutinis* yielded the (2S) alcohol according to Prelog's rule. *L. kefir* however, which does not follow Prelog's rule, gave the (2R) alcohol. For 1-phenyl-2-chloro-1-propanone, the small group is phenyl and the large one is -CHCl-CH_3. The (L) and (S) substitutents shown in the above scheme are inverted and reaction stereochemistry is reversed. Such a change in stereochemistry has already been reported by Imuta *et al.*[6] for the reduction of 1-bromoacetophenone by bakers' yeast. The (R) alcohol was formed and not the (S) alcohol expected.

The results given in Table VII show that high yields of all 1-phenyl-2-chloro-1-propanol isomers can be obtained if the appropriate microorganism is chosen. The (1R,2R) and (1R,2S) isomers were obtained with bakers' yeast or *R. glutinis* with excellent enantiomeric excesses. The (1S,2S) and (1S,2R) isomers resulted from the action of *L. kefir*. Enantiomeric excesses were 91 % and 70 % respectively. Enantiomeric excesses were determined as before by gas phase chromatography, either after reaction with the acid chloride or by direct analysis on the chiral column. Absolute configurations were determined with the same chemical correlation method used for 1-phenyl-1-chloro-2-propanol. A *syn* and an *anti* chlorohydrin were converted into β-methylstyrene oxides. The absolute configuration of each chlorohydrin can be deduced from the configuration of the epoxide formed from the original chlorohydrin .

All these results show that microbiological reduction of α-chloroketones can be successful if the halogen atom and its position in the carbon chain are carefully chosen. Best results were obtained with the chlorine atom in position 2 and the carbonyl and the phenyl on carbon 1. In this case, the four isomers of chlorohydrin can be isolated with good yields and high enantiomeric excesses.

III - Synthesis of Chiral Epoxides

All the isomers of 4-phenyl-2,3-epoxybutane **4** and of β-methylstyrene oxide **5** were prepared by basic method for treating the different halohydrins obtained by microbiological reduction of haloketones.



4 - R_1 = Benzyl R_2 = Methyl

5 - R_1 = Phenyl R_2 = Methyl

a - Synthesis of chiral isomers of 4-phenyl-2,3-epoxybutane **4**

Each isomer of optically pure 4-phenyl-3-bromo-2-butanol was treated with sodium ethylate in ethanol according to the method of Tsuboi *et al.*[14]. The epoxides formed were purified by chromatography on a silica column and analyzed to determine their absolute configuration and optical purity. The results of these reactions are given in Table VIII.

Table VIII : Synthesis of chiral 4-phenyl-2,3-epoxybutane

Bromohydrins		Epoxides			Yield of reaction
Conf.	obtained from	$[\alpha]_J^{25}$	e.e.	Conf.	
(2S,3S)	Freeze-dried bakers' yeast	- 21	≥ 98 %	(2S,3R)	85 %
(2R,3R)	*Aspergillus niger*	+ 21	≥ 98 %	(2R,3S)	87 %
(2S,3R)	Freeze-dried bakers' yeast	- 27	≥ 98 %	(2S,3S)	90 %
(2R,3S)	*Cunninghamella elegans*	+ 25	92 %	(2R,3R)	89 %

Chemical yields were excellent. This method in three steps yielded the four isomers of 4-phenyl-2,3-epoxybutane with very high enantiomeric excesses. The *cis* or *trans* character of each epoxybutane isomer was determined first. The relevant literature[13] shows that a *syn* halohydrin gives a *cis* epoxide while an *anti* halohydrin gives a *trans* epoxide. ^{13}C NMR was used to confirm these structures. In this case the two epoxide protons had the same chemical shift and the coupling constant between these two protons could not be determined. However, data given in the literature[15] for ^{13}C NMR studies show that epoxide carbons of *trans* compounds are more deshielding than the corresponding carbons of *cis* epoxides. The *cis* or *trans* character can be assigned to each epoxide by comparing the values of the chemical shifts of C-2 and C-3.

Cis epoxide from a *syn* bromohydrin $C_2 = 52.9$ ppm $C_3 = 57.4$ ppm

Trans epoxide from an *anti* bromohydrin $C_2 = 54.6$ ppm $C_3 = 59.8$ ppm

Epoxide absolute configurations are directly deduced from these bromohydrins : the reaction takes place with configuration inversion at the bromine bearing carbon atom. A (2S,3S) bromohydrin will give a (2S,3R) epoxide. All the absolute configurations have been assigned in this way. Enantiomeric excesses were determined by direct analysis of each isomer of 4-phenyl-2,3-epoxybutane by gas phase chromatography on a chiral column (Lipodex E). All the isomers of 4-phenyl-2,3-epoxybutane were obtained by this three-step method with good yields and very high enantiomeric excesses.

b - Synthesis of chiral isomers of 1-phenyl-1,2-epoxypropane (β-methylstyrene oxide) **5**

All the chiral isomers of 1-phenyl-1,2-epoxypropane have been synthesized from the chlorohydrins obtained by microbiologically reducing 1-phenyl-1-chloro-2-propanone and 1-phenyl-2-chloro-1-propanone. The chlorohydrins in DMF solution were treated with potassium carbonate.

From 1-phenyl-1-chloro-2-propanol : As shown previously, the microbiological reduction of 1-phenyl-1-chloro-2-propanone yielded only two optically pure chlorohydrins, the *syn* (1S,2S) and the *anti* (1R,2S). These two isomers were converted into β-methylstyrene oxide, whose characteristics are given in Table IX.

Each epoxide was assigned a *cis* or *trans* character by reference to the ^1H NMR spectra. As reported in the literature[16], the coupling constant between the two epoxide protons was larger for *cis* epoxide than for *trans* epoxide. For the epoxides formed from the chlorohydrins, the following values have been determined :

Epoxide from the *syn* chlorohydrin $J_{1,2} = 4.2$ Hz

Epoxide from the *anti* chlorohydrin $J_{1,2} = 2.1$ Hz

Table IX : Synthesis of chiral 1-phenyl-1,2-epoxypropane

Chlorohydrins		Epoxides			Yield of
Conf.	obtained from	$[\alpha]_J^{25}$	e.e.	Conf.	reaction
(1S,2S)	Freeze-dried bakers' yeast	- 42	≥ 98 %	(1R,2S)	60 %
(1R,2S)	Freeze-dried bakers' yeast	- 46	≥ 98 %	(1S,2S)	55 %

The *cis* or *trans* structure of epoxide thus determined, the optical rotation sign of each epoxide was compared with those given for the two enantiomers of *cis* and *trans* β-methylstyrene oxide in the literature[11]. An absolute configuration can be assigned to both epoxides. Enantiomeric excesses were determined by direct analysis of the epoxides by GC on a chiral column (Lipodex E).

From 1-phenyl-2-chloro-1-propanol : Microbiological reduction of 1-phenyl-2-chloro-1-propanone by bakers' yeast and *L. kefir* gave three optically pure isomers of chlorohydrin : the (1R,2R), (1R,2S) and (1S,2S) isomers. The corresponding isomers of β-methylstyrene oxide have been synthesized from these three chlorohydrins. The method used is the same as previously described. The results are given in Table X.

Table X : Synthesis of chiral 1-phenyl-1,2-epoxypropane

Chlorohydrins		Epoxides			Yield of
Conf.	obtained from	$[\alpha]_J^{25}$	e.e.	Conf.	reaction
(1R,2R)	Freeze-dried bakers' yeast	- 42	≥ 98 %	(1R,2S)	70 %
(1R,2S)	Freeze-dried bakers' yeast	+ 46	≥ 98 %	(1R,2R)	65 %
(1S,2S)	*Lactobacillus kefir*	+ 38	91 %	(1S,2R)	68 %

The *cis* or *trans* structure, absolute configuration and enantiomeric excesses for each isomer of β-methylstyrene oxide were determined as described above. If the results reported in Tables IX and X are compared, it can be seen that all the optically pure isomers of β-methylstyrene oxide were obtained with good yields. Three of these isomers, (1R,2S), (1R,2R) and (1S,2R) were from the isomers of 1-phenyl-2-chloro-1-propanol while the (1S,2S) was obtained from (1R,2S)-1-phenyl-1-chloro-2-propanol.

All these results confirm those published previously[1]. The three-step chemoenzymatic synthesis of chiral 2,3-epoxides is a general method that can be used whatever the starting ketone. In some cases (R_1 = phenyl) it is necessary to manipulate the nature of the halogen and its position on the carbon chain. Yields are generally good. The choice of the microorganism is very important for success in obtaining halohydrins with excellent enantiomeric excesses during the reduction of α-haloketone. The key step to this chiral epoxide synthesis is the microbiological reduction of α-haloketone.

ACKNOWLEDGEMENTS : We gratefully acknowledge Martine Sancelme for technical assistance in microbiology.

EXPERIMENTAL SECTION

1 - GENERAL METHODS

CHROMATOGRAPHY : Gas chromatography (GC) was carried out using an instrument fitted with a flame ionisation detector and a 50 m x 0.25 mm methylsilicone capillary column (DB1) or a 50 m x 0.32 mm capillary column coated with Carbowax 20 M for analytical analysis. A 25 m x 0.25 mm capillary column coated with modified γ-cyclodextrines (Lipodex E) was also used for determining enantiomeric excesses. The carrier gas was hydrogen (65 KPa) for Carbowax and cyclodextrine columns and helium (150 KPa) for DB1 column. Oven temperatures varied according to the product and are given in each case. Reaction progress was sometimes monitored using thin layer chromatography (TLC) with Kieselgel 60 PF plates using the same eluents as for column chromatography. Plates were developed directly using UV light or a pulverised vanilin solution or a solution of ammonium molybdate derivatives. With the latter two the plates were passed in an oven at 140°C. Column chromatography was performed on a silicagel 60 Merck (70-230 mm). Eluents varied and are indicated for each product.

SPECTROSCOPY AND ANALYTICAL METHODS : After bioconversion, crude mixtures were analysed by GC or TLC and retention times (R_f) of the reduction products or epoxides were compared with those of chemically obtained racemates. Optical rotations of the compounds were determined at 25°C for the mercury J line (λ = 578 nm, c in g/mL). Enantiomeric excesses were obtained for 4-phenyl-3-bromo-2-butanols by ^1H NMR spectroscopy in the presence of a chiral derivative of europium : tris (3-(trifluoromethylhydroxymethylene)-*d*-camphorato)-europium III, $Eu(tfc)_3$. They were determined by GC analysis using the Lipodex E column for chlorohydrins and epoxides and Carbowax column for chlorohydrin esters obtained after reaction with the chloride of (-)-(S)-O-acetyllactic acid[17]. NMR analyses were carried out on purified compounds in $CDCl_3$. For ^1H (300.13 MHz) and ^{13}C (75.47 MHz) NMR spectra, the chemical shifts were relative to chloroform. High Resolution Mass Spectrometry (HRMS) and microanalyses were performed by the Service Central d'Analyses du CNRS, Vernaison (France).

MICROBIOLOGICAL METHODS : The microorganisms were all laboratory-grown with the exception of freeze-dried bakers' yeast. This was a commercial product (ANCEL S.A. Strasbourg). Preculture and culture conditions for fungi *Aspergillus niger* ATCC 9142, *Beauveria sulfurescens* ATCC 7159, *Mortierella isabellina* NRRL 1757, *Geotrichum candidum* CBS 233-76 and bacterium *Lactobacillus kefir* DSM 20587 have been described elsewhere[1,18].

Geotrichum candidum strain Azerad Laboratory (strain Lab. Az.) was cultivated on : Cornsteep (Roquette) 7g, K_2HPO_4 1g, $FeSO_4 .7H_2O$ 0.01g, $MgSO_4 .7H_2O$ 0.5g, $ZnSO_4 .7H_2O$ 0.3 g, KCl 0.5 g.and tap water making up to 1 liter.

Cunninghamella elegans var. elegans ATCC 9245 was cultivated on : Yeast extract (Difco) 5 g, soyoptim (Roquette) 5 g, sucrose 20 g, NaCl 5 g, KH_2PO_4 5g and tap water making up to 1 liter.

Rhodotorula glutinis NRRL Y 1091 was cultivated on: Sucrose 20g, Malt extract (Difco) 10g, peptone 5g and tap water making up to 1 liter.

Sporotrichum exile QM 180 was cultivated on the medium : Yeast extract (Difco) 5g, Soyoptim (Roquette) 5g, sucrose 4g, NaCl 5g, KH_2PO_4 5g and tap water making up to 1 liter.

BIOCONVERSION CONDITIONS :

• General case: Bioconversions with bakers' yeast and microorganisms in metabolic resting phase were carried out as previously described[1,19].

• *Rhodotorula glutinis* : After 60 hours of culture at 27°C, the substrate was added to the culture (50 µL/100ml of culture) under sterile conditions. After incubation at 27°C on a rotary shaker set at 200 rpm, the mixture was filtered. The liquor was worked up as described for the other microrganisms[19].

2 - MICROBIOLOGICAL REDUCTION OF α-BROMOKETONES

- Syntheses of 4-phenyl-3-bromo-2-butanone **6** and 1-phenyl-1-bromo-2-propanone **7** : A solution of 24 g of 2-carboxyethyltriphenylphosphonium perbromide in THF was added dropwise to a stirred solution of 40 mmol. of 4-phenyl-2-butanone **1** or 1-phenyl-2-propanone **2** in THF. The mixture was stirred at room temperature during 2 hours after the perbromide had been added. A white precipitate was formed and the mixture was decolourized. After filtration, the solution was concentrated under vacuum and the α-bromoketone was purified by column chromatography on silicagel, eluent : Pentane/Ether 95/5 v/v.

4-Phenyl-3-bromo-2-butanone 6 Yellow odorous lacrymatory oil. Yield 70 %. TLC : R_f (Pentane/Ether 95/5) : 0.4. GC : DB-1 column, oven temperature 130°C for 5 min, then 130°C to 280°C at 5°C/min and 5 min at 280° C. Retention time : 920 s. ^{1}H NMR, δ : 2.36 (s, 3H); AB spectrum δ_{4b} = 3.19 (dd, 1H, J_{4b-4a} = 14.4 Hz, J_{4b-3} = 7.5 Hz); δ_{4a} = 3.46 (dd, 1H, J_{4a-4b} = 14.4 Hz, J_{4a-3} = 7.5 Hz), 4.50 (t, 1H, J = 7.5 Hz); 7.15-7.40 (m, 5H). ^{13}C NMR, δ : 27.1 (C-1); 39.7 (C-4); 53.4 (C-3); 127.3 (C-8); 128.8; 129.3 (C-6, C-7); 137.2 (C-5); 201.3 (C-2). Anal. Calcd for $C_{10}H_{11}BrO$: C : 52.86; H : 4.84; Br : 35.24. Found : C : 52.92; H : 4.85; Br : 35.30.

1-Phenyl-1-bromo-2-propanone 7 Yellow odorous lacrymatory oil. Yield 80 %. TLC : R_f (Pentane/Ether 95/5) : 0.3. GC : DB-1 column, oven temperature 100°C for 5 min, then 100°C to 250°C at 5°C/min and 5 min at 250° C. Retention time : 1230 s. ^{1}H NMR, δ : 2.36 (s, 3H); 5.44 (s, 1H); 7.30-7.51 (m, 5H). ^{13}C NMR, δ : 26.3 (C-3); 56.4 (C-1); 127.6 (C-7); 128.9; 129.1 (C-5, C-6); 135.8 (C-4); 199.3 (C-2). Anal. Calcd for C_9H_9BrO : C : 50.73; H : 4.26; Br : 37.50. Found : C : 50.64; H : 4.32; Br : 36.97.

- Synthesis of 1-phenyl-2-bromo-1-propanone **8** : 1-phenyl-1-propanone was treated with *tert*-butylbromide in DMSO as previously described[1].

1-Phenyl-2-bromo-1-propanone 8 Yellow odorous and very lacrymatory oil. Yield 80 %. TLC : R_f (Pentane/Ether 95/5) : 0.3. GC : Carbowax column, oven temperature 150°C . Retention time : 880 s. ^{1}H NMR, δ : 1.90 (d, 3H, J = 7 Hz); 5.30 (q, 1H, J = 7 Hz); 7.40-7.60 (m, 3H); 8.00 (d, 2H, J = 9 Hz). ^{13}C NMR, δ : 20.2 (C-3); 62.8 (C-2); 129.1; 129.5; 133.1 (C-5, C-6, C-7); 136.2 (C-4); 198.5 (C-1). Anal. Calcd for C_9H_9BrO : C : 50.73; H : 4.26; Br : 37.50. Found : C : 50.74; H : 4.38; Br : 37.42.

- Microbiological reductions of 4-phenyl-3-bromo-2-butanone **6** : Incubation time: 24 h. The residual products were separated on a silicagel column, the eluent was pentane/ether 90/10. The yields given are overall yields for diastereoisomers after work-up. GC analysis was carried out with a DB-1 column, oven temperature 130°C for 5 min, then 130°C to 280°C at 5°C/min and 5 min at 280° C.

Bakers' yeast : The residue from fifteen flasks consisted of : 60 % (-)-(2S,3S)-4-phenyl-3-bromo-2-butanol and 40 % (+)-(2S,3R)-4-phenyl-3-bromo-2-butanol. Yield : 93 %.

(-)-(2S,3S)-4-phenyl-3-bromo-2-butanol (0.420 g). TLC : R_f (Pentane/Ether 90/10) : 0.35. GC : Retention time : 1110 s. ^{1}H NMR, δ : 1.32 (d, 3H, J = 6 Hz); 2.02 (d, 1H, exchangeable with D_2O, J = 7.6 Hz); AB

spectrum δ_{4b} = 3.23 (dd, 1H, J_{4b-4a} = 14 Hz, J_{4b-3} = 8.5 Hz); δ_{4a} = 3.39 (dd, 1H, J_{4a-4b} = 14 Hz, J_{4a-3} = 7.5 Hz); 3.66-3.79 (m, 1H); 4.23 (td, 1H, J_{3-4} = 7.5 Hz, J_{3-2} = 2.5 Hz); 7.22-7.40 (m, 5H). ^{13}C NMR, δ : 22.2 (C-1); 42.1 (C-4); 65.5 (C-3); 68.2 (C-2); 127.0 (C-8); 128.6; 129.3 (C-6; C-7); 138.4 (C-5). $[\alpha]_J^{25}$ = - 28 (c = 0.04, $CHCl_3$); ee ≥ 95 %. HRMS Calculated : 228.0150; Found : 228.0154.

(+)-(2S,3R)-4-phenyl-3-bromo-2-butanol (0.280 g). TLC : R_f (Pentane/Ether 90/10) : 0.28. GC : Retention time : 1160 s. ^1H NMR, δ : 1.38 (d, 3H, J = 7 Hz); 2.07 (d, 1H, exchangeable with D_2O, J = 7 Hz); AB spectrum δ_{4b} = 3.14 (dd, 1H, J_{4b-4a} = 14.8 Hz, J_{4b-3} = 9.5 Hz); δ_{4a} = 3.23 (dd, 1H, J_{4a-4b} = 14.8 Hz, J_{4a-3} = 5.4 Hz); 3.83-3.94 (m, 1H); 4.37-4.45 (m, 1H); 7.20-7.40 (m, 5H). ^{13}C NMR, δ : 19.2 (C-1); 40.6 (C-4); 65.1 (C-3); 69.8 (C-2); 126.9 (C-8); 128.6; 129.0 (C-6; C-7); 138.2 (C-5). $[\alpha]_J^{25}$ = + 37 (c = 0.06, $CHCl_3$); ee ≥ 95 %. HRMS Calculated : 228.0150; Found : 228.0145.

Mortierella isabellina : The residue from seven flasks consisted of : 70 % (-)-(2S,3S)-4-phenyl-3-bromo-2-butanol and 30 % (+)-(2S,3R)-4-phenyl-3-bromo-2-butanol. Yield : 85 %.

(-)-(2S,3S)-4-phenyl-3-bromo-2-butanol (0.210 g). $[\alpha]_J^{25}$ = - 10 (c = 0.02, $CHCl_3$); ee = 36 %

(+)-(2S,3R)-4-phenyl-3-bromo-2-butanol (0.090 g). $[\alpha]_J^{25}$ = + 35 (c = 0.02, $CHCl_3$); ee = 94 %

Beauveria sulfurescens : The residue from nine flasks consisted of : 20 % of 4-phenyl-3-bromo-2-butanone, 40 % (-)-(2S,3S)-4-phenyl-3-bromo-2-butanol and 40 % (+)-(2S,3R)-4-phenyl-3-bromo-2-butanol. Yield : 75%.

(-)-(2S,3S)-4-phenyl-3-bromo-2-butanol (0.135 g). $[\alpha]_J^{25}$ = - 28 (c = 0.02, $CHCl_3$); ee ≥ 95 %

(+)-(2S,3R)-4-phenyl-3-bromo-2-butanol (0.135 g). $[\alpha]_J^{25}$ = + 35 (c = 0.02, $CHCl_3$); ee = 94 %

Rhodotorula glutinis : The residue from ten flasks consisted of : 18 % 4-phenyl-3-bromo-2-butanone, 50 % (-)-(2S,3S)-4-phenyl-3-bromo-2-butanol and 32 % (+)-(2S,3R)-4-phenyl-3-bromo-2-butanol. Yield : 74 %.

(-)-(2S,3S)-4-phenyl-3-bromo-2-butanol (0.225 g). $[\alpha]_J^{25}$ = - 28 (c = 0.03, $CHCl_3$); ee ≥ 95 %

(+)-(2S,3R)-4-phenyl-3-bromo-2-butanol (0.145 g). $[\alpha]_J^{25}$ = + 29 (c = 0.02, $CHCl_3$); ee = 78 %

Aspergillus niger : The residue of fifteen flasks consisted of : 40 % of 4-phenyl-3-bromo-2-butanone and 60% of (+)-(2R,3R)-4-phenyl-3-bromo-2-butanol. Yield : 48 %.

(+)-(2R,3R)-4-phenyl-3-bromo-2-butanol (0.360 g). The NMR spectra and retention time were the same as its (2S,3S) enantiomer. $[\alpha]_J^{25}$ = + 28 (c = 0.03, $CHCl_3$); ee ≥ 95 %

Cunninghamella elegans : The residue of nine flasks consisted of : 40 % of 4-phenyl-3-bromo-2-butanone, 40 % of (+)-(2R,3R)-4-phenyl-3-bromo-2-butanol and 20 % (-)-(2R,3S)-4-phenyl-3-bromo-2-butanol. Yield : 45 %.

(+)-(2R,3R)-4-phenyl-3-bromo-2-butanol (0.130 g). $[\alpha]_J^{25}$ = + 12 (c = 0.03, $CHCl_3$); ee = 45 %

(-)-(2R,3S)-4-phenyl-3-bromo-2-butanol (0.070 g). The NMR spectra and retention time were the same as its (2S,3R) enantiomer. $[\alpha]_J^{25}$ = - 34 (c = 0.02, $CHCl_3$); ee = 92 %

***Geotrichum candidum* strain CBS** : The residue from ten flasks consisted of : 60 % (+)-(2R,3R)-4-phenyl-3-bromo-2-butanol and 40 % (-)-(2R,3S)-4-phenyl-3-bromo-2-butanol. Yield : 85 %.

(+)-(2R,3R)-4-phenyl-3-bromo-2-butanol (0.255 g). $[\alpha]_J^{25}$ = + 16 (c = 0.02, $CHCl_3$); ee = 60 %

(-)-(2R,3S)-4-phenyl-3-bromo-2-butanol (0.170 g). $[\alpha]_J^{25}$ = - 25 (c = 0.02, $CHCl_3$); ee = 70 %

Lactobacillus kefir : The residue from seven flasks consisted of : 60 % (+)-(2R,3R)-4-phenyl-3-bromo-2-butanol and 40 % (-)-(2R,3S)-4-phenyl-3-bromo-2-butanol. Yield : 83 %.

(+)-(2R,3R)-4-phenyl-3-bromo-2-butanol (0.175 g). $[\alpha]_J^{25}$ = + 24 (c = 0.02, $CHCl_3$); ee = 85 %

(-)-(2R,3S)-4-phenyl-3-bromo-2-butanol (0.115 g). $[\alpha]_J^{25}$ = -18 (c = 0.02, $CHCl_3$); ee = 50 %

3 - MICROBIOLOGICAL REDUCTION OF α-CHLOROKETONES.

- Syntheses of 1-phenyl-1-chloro-2-propanone **9** and 1-phenyl-2-chloro-1-propanone **10** : 55 g (0,41 mol.) of sulfuryl chloride was added dropwise to a stirred solution of 50 g (0.37 mol.) of 1-phenyl-2-propanone or 1-phenyl-1-propanone in 250 mL of CCl_4. The temperature of the mixture should not exceed 40° C. The solution was washed several times with water and dried on $MgSO_4$. 1-Phenyl-1-chloro-2-propanone was purified by column chromatography on silicagel, eluent : Pentane/Ether 90/10 and 1-phenyl-2-chloro-1-propanone was purified by distillation.

1-Phenyl-1-chloro-2-propanone 9 : Yellow odorous oil. Yield 90 %. TLC : R_f (Pentane/Ether 80/20) : 0.6. GC : Carbowax column, oven temperature: 150° C : Retention time : 290 s. ^1H NMR, δ : 2.20 (s, 3H); 5.38 (s, 1H); 7.25-7.50 (m, 5H). ^{13}C NMR, δ : 25.7 (C-3); 66.6 (C-1); 127.8; 129.1; 129.2 (C-5, C-6, C-7); 135.1 (C-4); 200.0 (C-2).

1-Phenyl-2-chloro-1-propanone 10 : Yellow odorous oil. E_1 = 108-110° C (Lit[9] $E_{0.3}$ = 80° C). Yield 80 %. GC : DB-1 column, oven temperature: 150° C. Retention time : 600 s. ^1H NMR, δ : 1.75 (d, 3H, J = 7 Hz); 5.27 (q, 1H, J = 7 Hz); 7.40-7.57 (m, 2H); 7.57-7.70 (m, 1H); 8.00 (d, 2H, J = 8.5 Hz). ^{13}C NMR, δ : 19.9 (C-3); 52.8 (C-2); 128.7; 128.9 (C-5, C-6); 133.6 (C-7); 134.1 (C-4) 193.5 (C-1).

- Microbiological reductions of 1-phenyl-1-chloro-2-propanone **9** : Incubation time: 24 h. The residual products were separated on a silicagel column, the eluent was pentane/ether 90/10. The yields given are overall yields for diastereoisomers after work-up. GC was carried out with a Carbowax column, oven temperature was 150°C.

Bakers' yeast : The residue from ten flasks consisted of : 10 % 1-phenyl-2-propanone, 9 % (+)-(2S)-1-phenyl-2-propanol, 15 % 1-phenyl-1-chloro-2-propanone, 41 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 25 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 35 %.

(+)-(2S)-1-phenyl-2-propanol. TLC : R_f (Pentane/Ether, 90/10): 0.04 . GC : Retention time : 390 s. ^1H NMR, δ : 1.25 (d, 3H, J = 7 Hz); 1.70 (s, 1H, exchangeable with D_2O); AB spectrum δ_{1b} = 2.70 (dd, 1H, J_{1b-2} = 7 Hz, J_{1b-1a} = 13.5 Hz); δ_{1a} = 2.79 (dd, 1H, J_{1a-2} = 5 Hz, J_{1a-1b} = 13.5 Hz); 4.04 (td, 1H, J_{2-1} = 7 Hz, J_{2-3} = 5 Hz); 7.20-7.40 (m, 5H). ^{13}C NMR, δ : 22.6 (C-3); 45.6 (C-1); 68.7 (C-2); 126.2 (C-7); 128.3; 129.3 (C-5; C-6); 138.6 (C-4). $[\alpha]_J^{25}$ = + 40 (c = 0.03, $CHCl_3$); Lit.[13] $[\alpha]_D^{25}$ = + 39.2 (c = 4.8, $CHCl_3$) and + 16.5 (ethanol); ee ≥ 98 %.

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.105 g). TLC : R_f (Pentane/Ether 90/10) : 0.15. GC : Retention time : 850 s. ^1H NMR, δ : 1.30 (d, 3H, J = 7 Hz); 2.02 (s, 1H, exchangeable with D_2O); 4.17 (q, 1H, J = 7 Hz); 4.81 (d, 1H, J = 7 Hz); 7.30-7.50 (m, 5H). ^{13}C NMR, δ : 19.5 (C-3); 71.1 (C-1); 72.0 (C-2); 127.8; 128.8 (C-5, C-6; C-7); 138.6 (C-4). $[\alpha]_J^{25}$ = + 122 (c = 0.03, $CHCl_3$); ee ≥ 98 %. Anal. Calcd for $C_9H_{11}ClO$: C: 63.35; H : 6.50; Cl : 20.77. Found : C : 63.47; H : 6.61; Cl : 20.51.

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.070 g). TLC : R_f (Pentane/Ether 90/10) : 0.10. GC : Retention time : 975 s. ^1H NMR, δ : 1.28 (d, 3H, J = 7 Hz); 1.95 (s, 1H, exchangeable with D_2O); 4.15 (qu, 1H, J = 7 Hz); 4.83 (d, 1H, J = 7 Hz); 7.25-7.45 (m, 5H). ^{13}C NMR, δ : 19.1 (C-3); 68.3 (C-1); 71.8 (C-2); 128.2; 128.7 (C-5, C-6; C-7); 138.0 (C-4). $[\alpha]_J^{25}$ = - 80 (c = 0.03, $CHCl_3$); ee ≥ 98 %. Anal. Calcd for $C_9H_{11}ClO$: C: 63.35; H : 6.50; Cl : 20.77. Found : C : 63.23; H : 6.64; Cl : 20.73.

Mortierella isabellina : The residue from twelve flasks consisted of : 10 % 1-phenyl-2-propanone, 40 % (+)-(2S)-1-phenyl-2-propanol, 28 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 22 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 18 %.

(+)-(2S)-1-phenyl-2-propanol (0.090 g). $[\alpha]_J^{25}$ = + 40 (c = 0.03, $CHCl_3$); ee ≥ 98 %

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.060 g). $[\alpha]_J^{25}$ = + 122 (c = 0.01, $CHCl_3$); ee ≥ 98 %

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.050 g). $[\alpha]_J^{25}$ = - 78 (c = 0.01, $CHCl_3$); ee = 97 %

Beauveria sulfurescens : The residue from twenty flasks consisted of : 26 % 1-phenyl-2-propanone, 4 % 1-phenyl-2-propanol, 46 % 1-phenyl-1-chloro-2-propanone, 9 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 15 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 9 %.

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.035 g). $[\alpha]_J^{25}$ = + 122 (c = 0.05, $CHCl_3$); ee ≥ 98 %

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.055 g). $[\alpha]_J^{25}$ = - 76 (c = 0.05, $CHCl_3$); ee = 95 %

Lactobacillus kefir : (Incubation time : 48 hours). The residue of twelve flasks consisted of : 27 % 1-phenyl-2-propanone, 23 % (-)-(2R)-1-phenyl-2-propanol, 43 % (-)-(1R,2R)-1-phenyl-1-chloro-2-propanol and 7 % (+)-(1S,2R)-1-phenyl-1-chloro-2-propanol. Yield : 25 %.

(-)-(2R)-1-phenyl-2-propanol (0.100 g). Same NMR spectra and retention time as observed for its (2S) enantiomer. $[\alpha]_J^{25}$ = - 39 (c = 0.03, $CHCl_3$); ee = 97 %

(-)-(1R,2R)-1-phenyl-1-chloro-2-propanol (0.135 g). The NMR spectra and retention time were the same as its (1S,2S) enantiomer. $[\alpha]_J^{25}$ = - 15 (c = 0.01, $CHCl_3$); ee = 12 %

(+)-(1S,2R)-1-phenyl-1-chloro-2-propanol (0.015 g). The NMR spectra and retention time were the same as its (1R,2S) enantiomer. $[\alpha]_J^{25}$ = + 13 (c = 0.01, $CHCl_3$); ee = 16 %

***Geotrichum candidum*, strain CBS** : The residue of twelve flasks consisted of : 20 % 1-phenyl-2-propanone, 40 % (-)-(2R)-1-phenyl-2-propanol, 20 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 20 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 20 %.

(-)-(2R)-1-phenyl-2-propanol (0.110 g). $[\alpha]_J^{25}$ = - 14 (c = 0.02, $CHCl_3$); ee = 35 %

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.060 g). $[\alpha]_J^{25}$ = + 71 (c = 0.01, $CHCl_3$); ee = 57 %

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.060 g). $[\alpha]_J^{25}$ = - 63 (c = 0.01, $CHCl_3$); ee = 84 %

***Geotrichum candidum*, strain Lab. Az.** : The residue of twelve flasks consisted of : 20 % 1-phenyl-2-propanone, 40 % (-)-(2R)-1-phenyl-2-propanol, 20 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 20 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 20 %.

(-)-(2R)-1-phenyl-2-propanol (0.110 g). $[\alpha]_J^{25}$ = - 22 (c = 0.02, $CHCl_3$; ee = 55 %

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.060 g). $[\alpha]_J^{25}$ = + 10 (c = 0.07, $CHCl_3$); ee = 11 %

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.060 g). $[\alpha]_J^{25}$ = - 80 (c = 0.03, $CHCl_3$); ee ≥ 98 %

Rhodotorula glutinis : The residue of seven flasks consisted of : 43 % (-)-(2R)-1-phenyl-2-propanol, 37 % (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol and 20 % (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol. Yield : 36 %.

(-)-(2R)-1-phenyl-2-propanol (0.100 g). $[\alpha]_J^{25}$ = - 31 (c = 0.02, $CHCl_3$); ee = 78 %

(+)-(1S,2S)-1-phenyl-1-chloro-2-propanol (0.080 g). $[\alpha]_J^{25}$ = + 79 (c = 0.03, $CHCl_3$); ee = 65 %

(-)-(1R,2S)-1-phenyl-1-chloro-2-propanol (0.045 g). $[\alpha]_J^{25}$ = - 80 (c = 0.01, $CHCl_3$); ee ≥ 98 %

- Microbiological reductions of 1-phenyl-2-chloro-1-propanone **10** : Incubation times are indicated for each microorganism. The residual products were separated on a silicagel column, the eluent was pentane/ether 98/2. The yields are given as overall yields for diastereoisomers after work-up. GC was carried out with a carbowax column, oven temperature was 150° C.

Bakers' yeast : Incubation time : 48 h. The residue from fifteen flasks consisted of : 40 % (-)-(1R,2R)-1-phenyl-2-chloro-1-propanol and 60 % (-)-(1R,2S)-1-phenyl-2-chloro-1-propanol. Yield : 92 %.

(-)-(1R,2R)-1-phenyl-2-chloro-1-propanol (0.275 g). TLC : R_f (Pentane/Ether 98/2) : 0.22. GC : Retention

time : 780 s. ^{1}H NMR, δ : 1.40 (d, 3H, J = 7.5 Hz); 2.85 (s, 1H, exchangeable with D_2O); 4.24 (qu, 1H, J = 7 Hz); 4.60 (dd, 1H, J_{1-2} = 7 Hz, J_{1-OH} = 3.5 Hz); 7.25-7.45 (m, 5H). ^{13}C NMR, δ : 21.5 (C-3); 64.1 (C-2); 79.0 (C-1); 127.1; 128.5; 128.9 (C-5, C-6; C-7); 139.7 (C-4). $[\alpha]_J^{25}$ = - 48 (c = 0.02, $CHCl_3$); ee ≥ 98 %. Anal. Calcd for $C_9H_{11}ClO$: C: 63.35; H : 6.50; Cl : 20.77. Found : C : 63.38; H : 6.60; Cl : 20.74 .

(-)-(1R,2S)-1-phenyl-2-chloro-1-propanol (0.415 g). TLC : R_f (Pentane/Ether 98/2) : 0.25. GC : Retention time : 840 s. ^{1}H NMR, δ : 1.39 (d, 3H, J = 7 Hz); 2.50 (s, 1H, exchangeable with D_2O); 4.33 (qd, 1H, J_{2-1} = 3.6 Hz, J_{2-3} = 7 Hz); 4.94 (d, 1H, J_{1-2} = 3.6 Hz); 7.30-7.45 (m, 5H). ^{13}C NMR, δ : 18.2 (C-3); 62.7 (C-2); 77.2 (C-1); 126.5; 128.1; 128.4 (C-5, C-6; C-7); 139.7 (C-4). $[\alpha]_J^{25}$ = - 31 (c = 0.02, $CHCl_3$); ee ≥ 98 %. Anal. Calcd for $C_9H_{11}ClO$: C: 63.35; H : 6.50; Cl : 20.77. Found : C : 63.18; H : 6.52; Cl : 20.50.

Rhodotorula glutinis : Incubation time : 24 hours. The residue of ten flasks consisted of : 50 % (-)-(1R,2R)-1-phenyl-2-chloro-1-propanol and 50 % (-)-(1R,2S)-1-phenyl-2-chloro-1-propanol. Yield : 95 %.

(-)-(1R,2R)-1-phenyl-2-chloro-1-propanol (0.235 g). $[\alpha]_J^{25}$ = - 48 (c = 0.01, $CHCl_3$); ee ≥ 98 %

(-)-(1R,2S)-1-phenyl-2-chloro-1-propanol (0.235 g). $[\alpha]_J^{25}$ = - 31 (c = 0.03, $CHCl_3$); ee ≥ 98 %

Mortierella isabellina : Incubation time : 24 h. The residue from nine flasks consisted of : 60 % (+)-(1S,2S)-1-phenyl-2-chloro-1-propanol and 40 % (+)-(1S,2R)-1-phenyl-2-chloro-1-propanol. Yield : 93 %.

(+)-(1S,2S)-1-phenyl-2-chloro-1-propanol (0.250 g). $[\alpha]_J^{25}$ = + 1 (c = 0.02, $CHCl_3$); ee = 2 %

(+)-(1S,2R)-1-phenyl-2-chloro-1-propanol (0.170 g). $[\alpha]_J^{25}$ = +1.5 (c = 0.03, $CHCl_3$); ee = 5 %

Beauveria sulfurescens : Incubation time : 24 h. The residue from fifteen flasks consisted of : 33 % 1-phenyl-2-chloro-1-propanone, 33 % (+)-(1S,2S)-1-phenyl-2-chloro-1-propanol and 34 % (+)-(1S,2R)-1-phenyl-2-chloro-1-propanol. Yield : 43 %.

(+)-(1S,2S)-1-phenyl-2-chloro-1-propanol (0.160 g). $[\alpha]_J^{25}$ = + 41 (c = 0.01, $CHCl_3$); ee = 85 %

(+)-(1S,2R)-1-phenyl-2-chloro-1-propanol (0.160 g). $[\alpha]_J^{25}$ = + 2 (c = 0.05, $CHCl_3$); ee = 8 %

Aspergillus niger : Incubation time : 48 h. The residue of twelve flasks consisted of : 20 % 1-phenyl-2-chloro-1-propanone, 20 % (+)-(1S,2S)-1-phenyl-2-chloro-1-propanol and 60 % (+)-(1S,2R)-1-phenyl-2-chloro-1-propanol. Yield : 45 %.

(+)-(1S,2S)-1-phenyl-2-chloro-1-propanol (0.065 g). $[\alpha]_J^{25}$ = + 5 (c = 0.01, $CHCl_3$); ee = 10 %

(+)-(1S,2R)-1-phenyl-2-chloro-1-propanol (0.200 g). $[\alpha]_J^{25}$ = + 19 (c = 0.03, $CHCl_3$); ee = 60 %

***Geotrichum candidum*, strain CBS** : Incubation time : 24 h. The residue of six flasks consisted of : 11 % 1-phenyl-1-propanone, 5% 1-phenyl-1-propanol, 42 % (-)-(1R,2R)-1-phenyl-2-chloro-1-propanol and 42 % (-)-(1R,2S)-1-phenyl-2-chloro-1-propanol. Yield : 83 %.

(-)-(1R,2R)-1-phenyl-2-chloro-1-propanol (0.125 g). $[\alpha]_J^{25}$ = 0 (c = 0.01, $CHCl_3$)

(-)-(1R,2S)-1-phenyl-2-chloro-1-propanol (0.125 g). $[\alpha]_J^{25}$ = - 7 (c = 0.01, $CHCl_3$); ee = 23 %

Lactobacillus kefir : Incubation time : 48 h. The residue from six flasks consisted of : 30 % (+)-(1S,2S)-1-phenyl-2-chloro-1-propanol and 70 % (+)-(1S,2R)-1-phenyl-2-chloro-1-propanol. Yield : 87 %.

(+)-(1S,2S)-1-phenyl-2-chloro-1-propanol (0.080 g). The NMR spectra and retention time were the same as its (1R,2R) enantiomer. $[\alpha]_J^{25}$ = + 44 (c = 0.02, $CHCl_3$); ee = 91 %

(+)-(1S,2R)-1-phenyl-2-chloro-1-propanol (0.180 g). The NMR spectra and retention time were the same as its (1R,2S) enantiomer. $[\alpha]_J^{25}$ = + 22 (c = 0.01, $CHCl_3$); ee = 70 %

4 - SYNTHESIS OF CHIRAL EPOXIDES.

- Synthesis of isomers of 4-phenyl-2,3-epoxybutane **4** : 0.5 mmol. of an isomer of 4-phenyl-3-bromo-2-butanol was added to a stirred solution of 40 mg of sodium ethylate in 4 mL of methanol at 0° C. The stirring

was continued for 0.5 hour at 0° C and overnight at room temperature. The mixture was diluted with water and extracted several times with ether. The etheral solution was dried on $MgSO_4$ and the solvent was eliminated under vacuum. The epoxide was purified on a silicagel column, eluent : pentane/ether 90/10. Analyses of epoxides in GC : Carbowax column, oven temperature : 120° C.

- 0.110g of (-)-(2S,3R)-4-phenyl-2,3-epoxybutane was prepared from 0.200g of (-)-(2S,3S)-4-phenyl-3-bromo-2-butanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield : 85 %.

(-)-(2S,3R)-4-phenyl-2,3-epoxybutane. TLC : R_f (Pentane/Ether : 90/10) : 0.40. GC : Retention time : 1000 s. ^1H NMR, δ : 1.43 (d, 3H, J = 5.5 Hz); AB spectrum δ_{4b} = 2.80 (dd, 1H, J_{4b-4a} = 14.3 Hz, J_{4b-3} = 6.3 Hz); δ_{4a} = 2.96 (dd, 1H, J_{4a-4b} = 14.3 Hz, J_{4a-3} = 5.5 Hz); 3.10-3.22 (m, 2H); 7.20-7.40 (m, 5H). ^{13}C NMR, δ : 15.4 (C-1); 34.1 (C-4); 53.0 (C-2); 57.4 (C-3); 126.6 (C-8); 128.7; 128.9 (C-6; C-7); 137.6 (C-5). $[\alpha]_J^{25}$ = - 21 (c = 0.04, $CHCl_3$); ee ≥ 98 %. HRMS : Calculated : 148.0888. Found : 148.0888

- 0.110g of (+)-(2R,3S)-4-phenyl-2,3-epoxybutane was prepared from 0.200g of (+)-(2R,3R)-4-phenyl-3-bromo-2-butanol obtained by microbiological reduction with *Aspergillus niger*. Yield : 87 %.

(+)-(2R,3S)-4-phenyl-2,3-epoxybutane. The NMR spectra and retention time were the same as its (2S,3R) enantiomer. $[\alpha]_J^{25}$ = + 21 (c = 0.01, $CHCl_3$); ee ≥ 98 %

- 0.170g of (-)-(2S,3S)-4-phenyl-2,3-epoxybutane was prepared from 0.290g of (+)-(2S,3R)-4-phenyl-3-bromo-2-butanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield : 90 %.

(-)-(2S,3S)-4-phenyl-2,3-epoxybutane. TLC : R_f (Pentane/Ether : 90/10) : 0.43. GC : Retention time : 800 s. ^1H NMR, δ : 1.34 (d, 3H, J = 6 Hz); 2.50-2.80 (m, 4H); 7.20-7.40 (m, 5H). ^{13}C NMR, δ : 17.6 (C-1); 38.6 (C-4); 54.6 (C-2); 59.7 (C-3); 126.7; 128.7; 129.0 (C-6, C-7, C-8); 137.6 (C-5). $[\alpha]_J^{25}$ = - 27 (c = 0.04, $CHCl_3$); ee ≥ 98 %. HRMS : Calculated : 148.0888. Found : 148.0889.

- 0.145g of (+)-(2R,3R)-4-phenyl-2,3-epoxybutane was prepared from 0.250g of (-)-(2R,3S)-4-phenyl-3-bromo-2-butanol obtained by microbiological reduction with *Cunninghamella elegans*. Yield : 89 %.

(+)-(2R,3R)-4-phenyl-2,3-epoxybutane. The NMR spectra and retention time were the same as its (2S,3S) enantiomer. $[\alpha]_J^{25}$ = + 25 (c = 0.01, $CHCl_3$); ee = 92 %

- Synthesis of isomers of 1-phenyl-1,2-epoxypropane **5** : 72µL of distilled water, 4 mL of DMF and 0.330 g (2.4 mmol.) of potassium carbonate was added to 0.79 mmol. of 1-phenyl-1-chloro-2-propanol or 1-phenyl-2-chloro-1-propanol. The mixture was stirred at room temperature for 24 hours and then diluted with water and extracted several times with ether. The etheral solution was washed with saturated solution of NaCl and dried on $MgSO_4$. The residue was purified by a silicagel column, eluent : Pentane. Analyses of epoxides by GC : Carbowax column, oven temperature : 120°C.

From isomers of 1-phenyl-1-chloro-2-propanol

- 0.030g of (-)-(1R,2S)-1-phenyl-1,2-epoxypropane was prepared from 0.070g of (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield: 60%.

(-)-(1R,2S)-1-phenyl-1,2-epoxypropane. TLC : R_f (Pentane) : 0.32. GC : Retention time : 340 s. ^1H NMR, δ : 1.10 (d, 3H, J = 5.5 Hz); 3.36 (qu, 1H, J = 5 Hz); 4.08 (d, 1H, J = 4.1 Hz); 7.22-7.41 (m, 5H). ^{13}C NMR, δ : 12.6 (C-3); 55.2 (C-2); 57.6 (C-1); 126.6; 127.5; 128.1 (C-5, C-6, C-7); 135.6 (C-4). $[\alpha]_J^{25}$ = - 42 (c = 0.02, $CHCl_3$); ee ≥ 98 %. Lit[11] $[\alpha]_D^{25}$ = - 47.3 (c = 1.4, $CHCl_3$).

- 0.022g of (-)-(1S,2S)-1-phenyl-1,2-epoxypropane was prepared from 0.050g of (-)-(1R,2S)-1-phenyl-1-chloro-2-propanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield : 55 %.

(-)-(1S,2S)-1-phenyl-1,2-epoxypropane. TLC : Rf (Pentane) : 0.39. GC : Retention time : 300 s. ^{1}H NMR, δ : 1.46 (d, 3H, J = 5 Hz); 3.36 (qd, 1H, J_{2-3} = 2.2 Hz, J_{2-1} = 5 Hz); 3.59 (d, 1H, J_{3-2} = 2.2 Hz); 7.25-7.40 (m, 5H). ^{13}C NMR, δ : 17.9 (C-3); 59.0 (C-2); 59.6 (C-1); 125.6; 128.1; 128.5 (C-5, C-6, C-7); 137.9 (C-4). $[\alpha]_J^{25}$ = - 46 (c = 0.02, $CHCl_3$); ee ≥ 98 %. Lit[11] $[\alpha]_D^{25}$ = - 48.5 (c = 0.9, $CHCl_3$).

From isomers of 1-phenyl-2-chloro-1-propanol

- 0.040g of (-)-(1R,2S)-1-phenyl-1,2-epoxypropane was prepared from 0.070g of (-)-(1R,2R)-1-phenyl-2-chloro-1-propanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield : 70%.

(-)-(1R,2S)-1-phenyl-1,2-epoxypropane. Identical to that obtained with (+)-(1S,2S)-1-phenyl-1-chloro-2-propanol. $[\alpha]_J^{25}$ = - 42 (c = 0.04, $CHCl_3$); ee ≥ 98 %

- 0.035g of (+)-(1R,2R)-1-phenyl-1,2-epoxypropane was prepared from 0.070g of (-)-(1R,2S)-1-phenyl-2-chloro-1-propanol obtained by microbiological reduction with freeze-dried bakers' yeast. Yield : 65%.

(+)-(1R,2R)-1-phenyl-1,2-epoxypropane. Same NMR spectra and retention time as its (1S,2S) enantiomer. $[\alpha]_J^{25}$ = + 46 (c = 0.02, $CHCl_3$); ee ≥ 98%

- 0.040g of (+)-(1S,2R)-1-phenyl-1,2-epoxypropane was prepared from 0.070g of (+)-(1S,2S)-1-phenyl-2-chloro-1-propanol obtained by microbiological reduction with *Lactobacillus kefir*. Yield : 68 %.

(+)-(1S,2R)-1-phenyl-1,2-epoxypropane. The NMR spectra and retention time were the same as its (1R,2S) enantiomer. $[\alpha]_J^{25}$ = + 38 (c = 0.04, $CHCl_3$); ee = 91 %

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