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Oxygen atom transfer from a chiral oxaziridinium salt. Asymmetric epoxidation of unfunctionalized olefins.

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Abstract: The synthesis of an optically pure oxaziridinium salt from (1S,2R)-(+)-norephedrine and the study of the asymmetric oxygen transfer reactions from this reagent to unfunctionalized olefins are described.

INTRODUCTION

The first example of an oxaziridinium salt was obtained on a steroidal skeleton and shown to behave as an electrophilic oxygen atom transfer agent towards nucleophiles.[1] A second oxaziridinium salt, derived from tetrahydroisoquinoline, was synthesized some time later.[2] The oxygenation of carbon-carbon double bonds,[3] sulfides,[4] amines and imines[5] by this salt has been described. Concerning olefins, a catalytic oxaziridinium-mediated epoxidation method was also developed using Oxone® as oxygen source.[6]

The possibility of performing not only stoichiometric but also catalytic epoxidation by an oxaziridinium salt incited to tackle the question of asymmetric epoxidation[7] and particularly the asymmetric epoxidation of unfunctionalized olefins.[8,9] A chiral oxaziridinium, derived from a 3,4-disubstituted chiral tetrahydroisoquinoline substrate, was then described and the usefulness of chiral oxaziridinium salts in the asymmetric (stoichiometric and catalytic) epoxidation of unfunctionalized olefins was established.[10]

Following these results, some others reports concerning the catalytic (asymmetric or not) oxaziridinium-mediated epoxidation of unfunctionalized olefins by oxone® have appeared. In the asymmetric field, a C_2-symmetry binapthyl-derived iminium salt[11] and a series of chiral 3,4-dihydroisoquinolinium salts unsubstituted at the isoquinoline C-atoms but chiral at the exocyclic nitrogen substituent[12] has been used to catalyze the epoxidation of unfunctionalized alkenes leading to ee's up to 71%[11] and 73%[12] respectively. In the racemic field, it has been shown that acyclic iminium salts can catalyze the epoxidation of olefins by oxone.[13] In addition, it has also been reported that the treatment of unsaturated oxaziridines with methyl triflate resulted in intramolecular epoxidation, presumably via oxaziridinium salts.[14]

We describe here the full details of the synthesis of the new oxaziridinium salt **10** from 1S,2R-(+)-norephedrine **2** and the study of the asymmetric oxygen transfer reactions from this reagent to unfunctionalized olefins.

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(1S,2R)-norephedrine **2** was N-benzylated in two steps, i.e. condensation with benzaldehyde leading to the (equilibrium) mixture of the imino-alcohol **3** and the cyclic forms **4**[15] (two diastereoisomeric oxazolidines) followed by sodium borohydride reduction. The resulting amino-alcohol **5** was cyclized to the tetrahydroisoquinoline **6** which was oxidized to the dihydroisoquinoline **7** through the intermediate chloramine. The key step in the synthesis of **7** is the stereospecific cyclization leading to **6** (in 80 % yield from **5**) which was performed under the conditions described by S.G. Davies for similar substrates[16]. In the crude product of the two step oxidation of **6** (N-chlorination followed by alkaline dehydrohalogenation leading to the dihydroisoquinoline **7**) the corresponding aromatic derivative (**12**, scheme 3) was present as by product (5 % as shown by ^{1}H NMR). Both products were isolated by column chromatography and fully characterized. The dihydroisoquinoline **7** was thus obtained in 50 % yield from norephedrine **2**.

Two pathways led from imine **7** to the oxaziridinium **10** which could be prepared either through the iminium salt **8** or through the oxaziridine **9**.

In the first, the dihydroisoquinoline **7** was methylated with the Meerwein's salt $MeO^+F_4B^-$. The resulting dihydroisoquinolinium fluoroborate **8** was stereospecifically oxidized by metachloroperbenzoic acid (mCPBA) at room temperature. The oxaziridinium salt **10** was isolated by crystallization from the crude product in 46 % global yield from **8** and could be completely characterized. The structure of the oxaziridinium **10** was established by X-ray diffraction[10,17]. The three membered oxaziridinium ring is syn to the C_3-methyl group (Me_3) and is axially oriented, being thus essentially perpendicular to the plane of the aromatic ring of the tetrahydroisoquinoline skeleton. The substituents C_3-methyl and C_4-phenyl are both equatorial. The trans-diaxial arrangement of H_3 and H_4 in solution, suggested by the coupling constant between H_3 and H_4 in ^{1}H NMR ($J_{3,4}$ = 10Hz), was so confirmed in the solid state (scheme 2, left side).

In the second pathway to **10**, the dihydroisoquinoline **7** was first oxidized in order to obtain the oxaziridine **9**. This latter, having the same conformation and absolute configuration than the target oxaziridinium as also indicated by NMR and established by X-ray diffraction[10,17] (scheme 2, right side) led quantitatively to **10** when methylated with the same Meerwein's reagent as above.

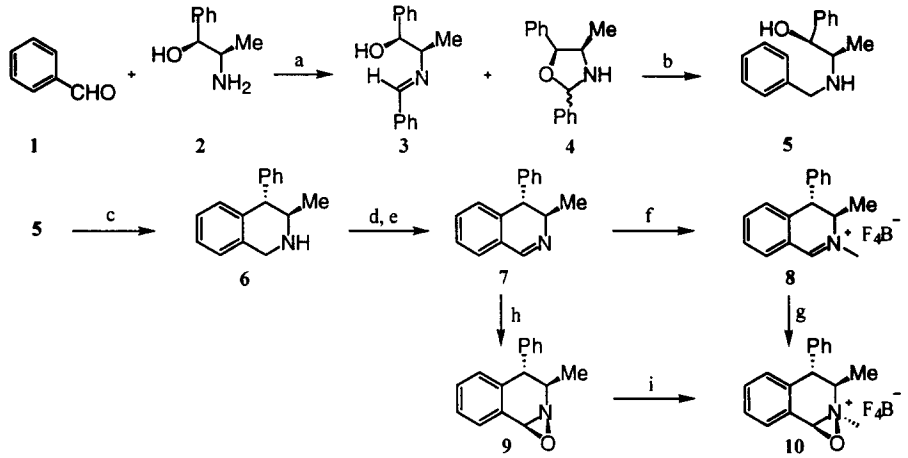
The principal difference between the two pathways lay into the oxidation steps. While the peracidic oxidation of the iminium **8** was stereospecific at room temperature, that of the parent imine **7** had to be performed at (strictly controlled) low temperature to allow a proper and practically stereospecific reaction (entry 2, scheme 3) from which the oxaziridine **9** could be obtained in high yield directly by crystallization from the crude product. At room temperature the peracidic oxidation of the tetrahydroisoquinoline **7** was not stereospecific and even not chimioselective[18] (entry 1, scheme 3). In one hand, the two possible diastereoisomeric oxaziridines **9** and **11** were formed, and on the other hand, the nitrone **13** (resulting from the electrophilic oxygen atom transfer from the peracid to the iminic nitrogen) was also produced†. Moreover, the desired oxaziridine **9** was partly decomposed under that reaction conditions, which was not the case of the minor diastereoisomer **11**. The first step of this base-catalyzed dehydration leading to the isoquinoline **12** is the isomerisation of the oxaziridine **9** into the carbinol-imine **14** (scheme 3). It has been shown that an antiperiplanar arrangement between the oxaziridine three membered ring and the C_β-H bond is required for the isomerisation of cyclic oxaziridines into imino-carbinols.[19]

† The nitrone **13** and the isoquinoline **12**, which are also new compounds, have been isolated and fully characterized (see exp.).

RESULTS and DISCUSSION

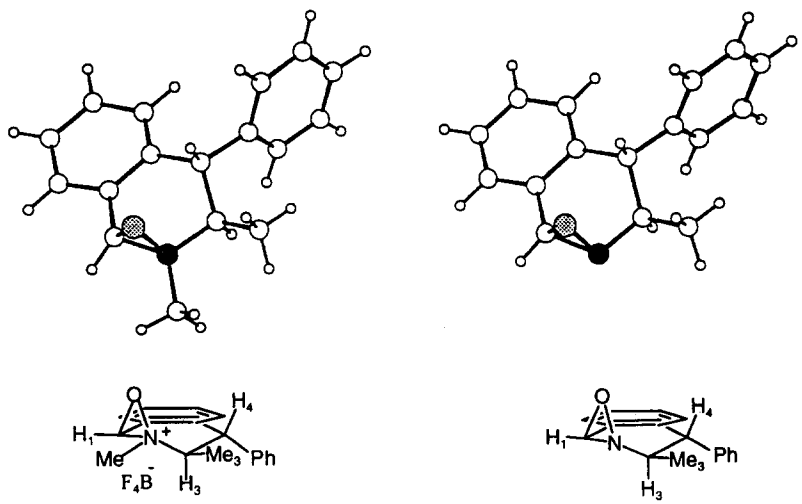
Synthesis of the chiral oxaziridinium salt 10

The enantiomerically pure oxaziridinium salt **10** was synthesized from imine **7** which was prepared from norephedrine **2** as shown in scheme 1.



a) $MgSO_4$ / CH_2Cl_2; b) $NaBH_4$ / EtOH; c) CF_3CO_2H / H_2SO_4 (1:1); d) $NaOCl_{aq}$ / CH_2Cl_2; e) NaOH / MeOH / CH_2Cl_2; f) $Me_3O^+F_4B^-$ / CH_2Cl_2; g) mCPBA / CH_2Cl_2 / 20°C; h) mCPBA / CH_2Cl_2 / -45°C; i) $Me_3O^+F_4B^-$ / CH_2Cl_2.

scheme 1

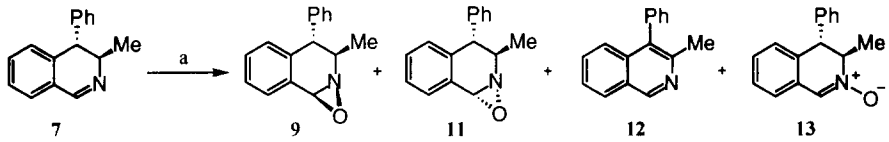


10: ^{1}H NMR, Cl_3CD
H_1: 6.50 ppm s
Me_3: 1.53 ppm d J = 6 Hz
H_3: 4.63 ppm dq J = 10Hz J = 6Hz
H_4: 3.98 ppm d J = 10Hz

9: ^{1}H NMR, Cl_3CD
H_1: 5.13 ppm s
Me_3: 1.33 ppm d J = 6.5 Hz
H_3: 3.24 ppm dq J = 9.8Hz J = 6.5Hz
H_4: 3.62 ppm d J = 9.8Hz

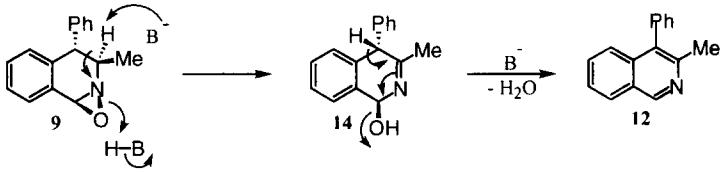
scheme 2

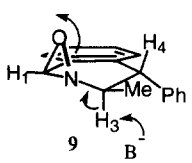
Therefore the isomerisation of the minor oxaziridine **11**, which showed in ^{1}H NMR a coupling constant of 1Hz between H_3 and H_4 thus indicating a trans diequatorial arrangement of those hydrogens and consequently a pseudoaxial oxaziridine ring, trans to the C_3-methyl group, is not a favored process.



	9	11	12	13
20 °C [b,d]	50	5	35	10
-45 °C [c,d]	99	1	-	-

a) mCPBA / CH_2Cl_2 ($NaHCO_3$); b) mCPBA added portionwise in the solid state to a 0.1M solution of **7** in CH_2Cl_2; c) 0.01M solution of mCPBA in CH_2Cl_2 slowly added to a 0.05M solution of **7** in CH_2Cl_2; d) ratio in the crude product determined by ^{1}H NMR.





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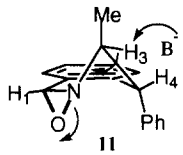

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^{1}H NMR, Cl_3CD
H_1: 4.92 ppm s
Me: 1.20 ppm d J = 6.7Hz
H_3: 4.34 ppm dq J = 1Hz J = 6.7Hz
H_4: 4.05 ppm d J = 1Hz

scheme 3

*Oxygen transfer from **10** to unfunctionalized olefins*

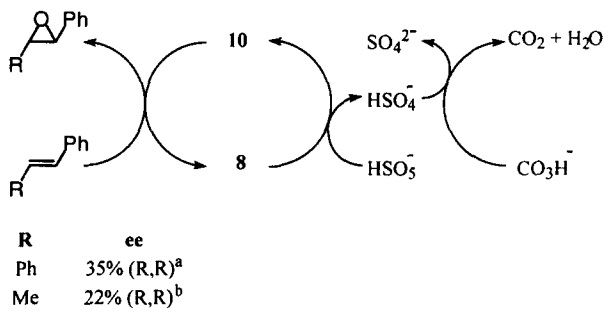
The epoxidation of some rather unhindered (mono-, di- and tri-substituted) unfunctionalized olefins was performed in dichloromethane, stoichiometrically at first, with the oxaziridinium **10**. While the conversions of the alkenes into the corresponding epoxides were high, the enantioselectivities, observed after work up and chromatographic isolation of the products were moderate to low (table 1).

The epoxidations of the olefins leading to the higher enantioselectivities were, in a second time, performed catalytically using a substoichiometric amount (5 mol%) of the iminium salt **8** and potassium monopersulfate (from oxone®) to *in situ* generate the oxaziridinium salt **10**. Under the conditions shown in scheme 4, the conversions olefin/epoxide were high (typically 70-80% for R = Me and 80-90% for R = Ph) and the enantioselectivities of the same order than those observed in the stoichiometric epoxidations.

Table 1. Stoichiometric epoxidations.[a, b]

Entry	Substrate	% Yield[c]	% e.e.[d]	Abs. conf.[e]
1	*trans*-stilbene	63 (100)	42	(R,R)
2	β-methyl-styrene	50 (87)	23	(R,R)
3	styrene	10 (55)	12	-[f]
4	1-phenyl-cyclohexene	65 (90)	5[g]	(R,R)

a) recrystallized oxaziridinium salt **10** (100% of active oxygen by iodometry) was used.
b) all reactions in CH_2Cl_2 at r.t.. Molar ratio oxaziridinium **10**:olefin = 1.1:1, olefin concentration 0.2M.
c) yield of epoxides isolated by preparative TLC on silicagel and in parentheses the conversion olefin/epoxide determined by ^1H NMR analysis of the crude product.
d) determined by HPLC using a DAICEL CHIRALPAK OT(+) column.
e) determined by polarimetry
f) not determined
g) determined by ^1H NMR using $Eu(hfc)_3$ as chiral shift reagent.



R	ee
Ph	35% (R,R)[a]
Me	22% (R,R)[b]

Conditions: molar ratio olefin : iminium **8** : $KHSO_5$: $NaHCO_3$ = 1 : 0.05 : 2 : 4, solvent: CH_3CN-H_2O (3%), mixture stirred overnight at room temperature, epoxides isolated by TLC on silicagel.
a)- determined by HPLC using a DAICEL CHIRALPAK OT(+) column. b) determined by ^1H NMR

scheme 4

As shown in table 1, the enantioselectivities were better for the disubstituted olefins than for the mono- or trisubstituted ones. Moreover, the presence of two aromatic rings on the opposite ends of the disubstituted double bond seem to favor the "transfer of chirality" from the oxaziridinium salt to the epoxide resulting from the oxygen transfer.

Otherwise, the more substituted olefin led to the lowest enantiomeric purity of the corresponding epoxide (table 1, entry 4). Curiously the same olefin, 1-phenylcyclohexene, led to the highest enantioselectivity when compared with *trans*-stilbene, β-methylstyrene and styrene in the oxaziridinium mediated epoxidation catalyzed by a C_2-symmetry iminium salt, recently reported by others[11] and performed according to the catalytic method developed in our laboratory.[6,10]

The temperature and the solvent effects upon the epoxidation by the oxaziridinium salt **10** were also examined using *trans*-stilbene as substrate. The results are summarized in table 2.

To evaluate the temperature effect, the epoxidations were performed in dichloromethane (entries 1-4). As expected, the lowering of the reaction temperature led to enhanced enantioselectivities while longer reactions times were necessary to attain high olefin to epoxide conversions. Thus, on going from room temperature (entry 1) to -32 °C (entry 3) a 45% improvement in the stereoselectivity was observed but, in spite of a reaction period more than fifteen times longer (at -32 °C than at room temperature), the conversion (of *trans*-stilbene) to *trans*-stilbene oxide only reached 89% (*vs* 100% at r.t.) and some unreacted oxaziridinium salt (7%) was still present as shown by a positive potassium iodide test and confirmed by quenching with dimethylsulfide followed by ^{1}H NMR analysis of the crude product. On further lowering of the temperature the epoxidation was considerably slowed down and the active oxygen of the oxaziridinium salt was partially lost without concomitant epoxidation. Thus, at -60 °C the olefin to epoxide conversion was too low (about 5%) after a reaction period of 48 hours with a concomitant sevenfold conversion (35%) of the oxaziridinium **10** into the iminium **8**, and no epoxidation was observed after 72 h at -78 °C (entry 4) while one half of the initial oxaziridinium salt **10** evolved into the iminium **8**.

Table 2. Effects of Solvent and Temperature.[a,b]

Entry	Solvent	Temp. (°C)	Time (hours)	% yield[c]	% ee[d]
1	Cl_2CH_2	20	3	63 (100)	42
2	Cl_2CH_2	0	24	66 (98)	50
3	Cl_2CH_2	-32	48	57 (89)	61
4	Cl_2CH_2	-78	72	-[e]	-
5	benzene	20	24	53 (75)	1
6	toluene	20	7	45 (67)	5
7	pentane	20	43	61 (70)	35
8	nitrobenzene	20	10 min.	60 (77)	39
9	nitromethane	20	20 min.	70 (87)	45

a)- recrystallized oxaziridinium salt **10** (100% of active oxygen by iodometry) was used.
b)- molar ratio olefin:**10** = 1.1:1.
c)- yield of epoxides isolated by TLC on silicagel and in parentheses the conversion olefin/epoxide determined by ^{1}H NMR analysis of the crude products.
d)- Always in favor of the (R,R)-epoxides. Determined by HPLC using a DAICEL CHIRALPAK OT(+) column.
e)- 50% of **10** disappeared but no epoxidation was observed.

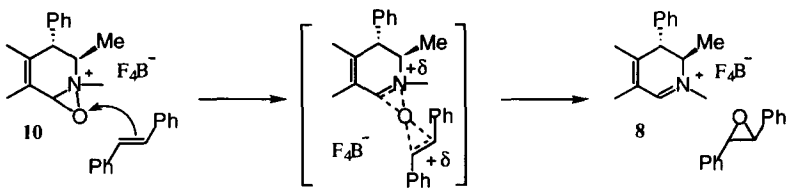
To evaluate the solvent effect, the epoxidations were performed at room temperature (entries 1 and 5-9). As first outstanding observation, the enantioselectivity was practically lost in aromatic solvents such as toluene and particularly in benzene (entries 5 and 6 *vs* entry 1). The oxaziridinium **10** is only slightly soluble in those solvents, and especially in benzene, which may account for the low epoxidation rates (relative to that observed in dichloromethane) but not for the drastic fall in the enantioselectivity of the epoxidation as suggested by the results obtained in pentane (entry 7). In this solvent, the reaction is still slower than those in

benzene and toluene, but an enantioselectivity level close to that in dichloromethane (ee 35% *vs* ee 42%) was observed in spite of the fact that the oxaziridinium salt **10** is almost insoluble in pentane. Accordingly, the lack of polarity of the solvent (and the subsequent poor solubility of the reagent) seems to play an important role relative to the epoxidation rate but on the contrary, either this factor is not relevant concerning the enantioselectivity of the oxygen transfer or, at the most, plays a minor role.

As another important fact, no loss in the enantioselectivity of the epoxidation resulted in an electron-poor aromatic solvent as nitrobenzene. Practically the same enantiomeric excess as in dichloromethane was observed while the reaction was sensibly faster (entry 8 *vs* entry 1). Moreover, a similar result was observed when the epoxidation was carried out in nitromethane (entry 9) suggesting once more a decisive link between polarity of the solvent and epoxidation rate, and on the other hand, the limited influence of this factor upon the stereochemistry of the reaction within this series of polar aprotic solvents.

The acceleration of the epoxidation by an oxaziridinium salt in the more polar aprotic solvents (entries 8 and 9 *vs* entry 1) is likely to be related to the ionic character of the oxygen transfer reaction. To the difference from the classical peracidic epoxidation[20] and those by dioxirane[21] and sulfonyloxaziridines,[22] in the epoxidation by an oxaziridinium (as for example **10**) the reagent and the transition state are cationic in nature, scheme 5, each one bearing a counterion (as here F_4B^-).

In one hand the epoxidation is faster in nitromethane and in nitrobenzene (entries 8 and 9), which have higher dissociating powers[23] than dichloromethane (entry 1). On the other hand, nitrobenzene has a dissociating power very close to that of nitromethane but a higher donating power[23] than nitromethane. It should thus be able to better stabilize the initial state. Nevertheless the epoxidation is faster in nitrobenzene than in nitromethane (entry 8 *vs* entry 9). It is evident from scheme 5 that the positive charge is dispersed in the transition state. The observed acceleration should be in connection with the dispersion of the charge on going from the initial to the transition state. The solvation by nitrobenzene (a solvent which positive and negative poles are delocalized) should be larger on the transition state (a softer cation owing to the dispersion of the charge) than on the initial state.



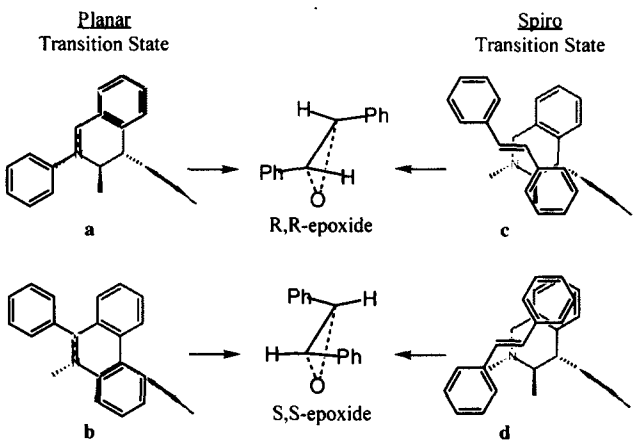
scheme 5

The solvent effect on the stereochemistry of the oxygen transfer reflected by the enantiomeric excesses in table 2 (entries 1 and 5-9) and especially by the severe restriction of the asymmetric induction in toluene (entry 6) and, more drastically, its suppression in benzene (entry 5) appears less straightforward to rationalize at first glance. Nevertheless, a reasonable hypothesis accounting for these facts may be proposed following an examination of the transition state involved in the epoxidation of *trans*-stilbene by the oxaziridinium **10**.

The epoxidations of non particularly activated olefins by electrophilic oxygen atom transfer reagents are assumed to be S_N2-type displacements[24] and are usually rationalized in terms of two energetically preferred

transition states. Either a *planar* transition state in which the electrophilic oxygen containing functional group of the reagent and the developing epoxide lay within a plane (as in the now classic "butterfly" arrangement early proposed by Bartlett for the transition state of the epoxidation by peracides[25]) or a *spiro* transition state in which the electrophilic oxygen containing functional group of the reagent and the developing epoxide are mutually perpendicular. Theoretical studies (M.O. calculations) on the epoxidation of model simple unhindered olefins by model unhindered electrophilic oxygen atom transfer reagents have revealed that a spiro transition state seems preferred over a planar transition state in the epoxidations by performic acid,[26,27] dioxirane,[21] dimethyldioxirane[21,28] and trifluoromethyldioxirane.[28] For the hypothetical[‡] epoxidation of alkenes by oxaziridine it was first proposed that there were no stereoelectronic factors that favor a planar or a spiro transition state orientation[24,29] and it has been suggested that in the case of epoxidations by sulfonyloxaziridines, the transition state is rather steric in origin.[29] A planar transition state was thus thought to better explain the stereochemistry than a spiro transition state. More accurate computational methods[30] have then allowed to show a preference for an asynchronous spiro transition state in the epoxidations by oxaziridine and for a synchronous transition state in the epoxidations by performic acid and dioxirane. The terms synchronous and asynchronous describing equal or unequal C-O bond formation respectively in the transition state.[30]

The planar (**a** and **b**) and the spiro (**c** and **d**) transition state structures for the epoxidation of *trans*-stilbene by the oxaziridinium **10** are depicted in scheme 6.



scheme 6

We have already pointed out that the epoxidation by an oxaziridinium is different in nature from the epoxidation by neutral species as peracids, dioxirane and oxaziridines. The electronic preferences for spiro transition states above mentioned are thus not directly extrapolable to the epoxidation by an oxaziridinium salt. Nevertheless, considering first the hypothesis of a spiro transition state also applying to the epoxidation by **10** and on the basis of a qualitative evaluation of the steric interactions in the spiro arrangements **c** and **d** it seems

[‡] M.O. calculations performed in order to model the epoxidation of olefins by Davis sulfonyloxaziridines but which concerns a hypothetical reaction as oxaziridine is actually an electrophilic aminating agent towards nucleophiles.[31,32,33] (i.e. a nitrogen transfer agent) and not an oxygen atom transfer reagent.

that, if any, the selectivity to be expected from such transition states should be at the opposite of the experimentally observed one which always favors the (R,R)-epoxide (table 2, entries 1 and 5-9). The spiro pro-(R,R) geometry **c** seems less favored as it sets one of the phenyls of *trans*-stilbene over the 3β-Me and the 4β-H of **10**. Considering now the hypothesis of a planar transition state (**a** and **b** in scheme 6) and also on the basis of a qualitative evaluation of the steric interactions in each geometry, it is also not obvious to clearly determine which arrangement is actually favored even if, as for the spiro geometries but in the opposite direction, a small preference for the pro-(R,R) transition state may be assumed from the fact that the pro-(S,S) transition state **b** sets one of the phenyls of *trans*-stilbene over the 3β-Me and the 4β-H of **10** while the pro-(R,R) planar transition state **a** fits one of the phenyl groups of the substrate over the tetrahydroisoquinoline aromatic ring of the reagent. However, we have observed a significant solvent effect, the loss of the enantioselectivity in benzene, from which it seems possible to find a reasonable solution for this problem. As the tetrahydroisoquinoline aromatic ring of **10** is electron-demanding while *trans*-stilbene is relatively electron-rich, it may be thought that a sort of attractive donor-acceptor interaction[§] should greatly contribute to favor the pro-(R,R) planar geometry (**a**) over the pro-(S,S) planar one (**b**). Thus, considering a planar transition state for the epoxidation of *trans*-stilbene by the oxaziridinium **10**, the preference for the pro-(R,R) arrangement (**a**) should be seriously diminished or even lost if the above stacking factor disappears. This assumption allows the rationalization of the experimental results concerning the solvent effect on the stereochemistry of the epoxidation as, in agreement with the proposed hypothesis, the observed ee's are extremely low when solvents able to disturb the attractive substrate-reagent interaction in the transition state are used. Indeed, to the difference from the also aromatic but electron-poor solvent nitrobenzene in which a "normal enantioselectivity" was observed (entry 8), toluene and benzene may serve as substitute for the phenyl ring of the substrate as they are able to exert a similar π-electron donor effect towards the electron-poor oxaziridinium skeleton thus preventing the decisive fitting factor in the transition state to play, and consequently bringing closer in energy the pro-(R,R) and the pro-(S,S) arrangements which results in the almost complete canceling of the asymmetric induction in those solvents.

In conclusion, an optically pure oxaziridinium salt has been prepared. The asymmetric epoxidation of unfunctionalized olefins has been performed with this salt. This chiral oxaziridinium has been obtained stereospecifically from the corresponding iminium salt which allows to carry out the oxygen transfer onto olefins in a catalytic system. It is thus not necessary to isolate it to perform asymmetric epoxidations as the asymmetric inductions in the catalytic process are essentially the same as in the corresponding stoichiometric epoxidations. On the other hand, significant solvent effects on the rate and on the enantioselectivity of these oxygen transfer reactions have been observed. They may be helpful for the pursuit of the studies of the reactivity of the oxaziridinium function.

Acknowledgment: We thank Dr. A. Loupy for helpful discussions on solvent effects.

[§] A similar π-π interaction seems also possible in the pro-(S,S) spiro transition state **d**. If this effect operates, it should enhance the pro-(S,S) preference already evoked when a spiro transition state was considered. Such a preference is contrary to the experimental results.

EXPERIMENTAL

General. ^1H and ^{13}C NMR were recorded in $CDCl_3$ using a Bruker A-250 (250 MHz for ^1H and 62.5 MHz for ^{13}C), AC-300 (300 MHz for ^1H and 75 MHz for ^{13}C) and AC-400 (400 MHz for ^1H). Chemical shifts (δ) are given in ppm relative to TMS (tetramethylsilane) and coupling constants (J) are given in Hertz (Hz). The molar ratios in the crude products were determined by ^1H NMR from integration curves relative to a reference [triphenylmethane, δ 5.55 ppm (s, 1H)]. Mass spectrum were carried out with AEI MS-50 (70 eV, EI), MS-59 (IC) and MS-80 (FAB) instruments. Melting points were measured using a Leitz-Wetzler apparatus and are not corrected. Elemental analysis were performed at the microanalytical laboratory of CNRS. Dichloromethane was dried over P_2O_5. TLC were performed with silicagel coated foils Schleicher & Schuell ($F1500/LS_{254}$), staining with Dragendorff reagent. Column chromatographies were performed using silicagel Merck 60 (230-400 mesh) and preparative thin layer chromatographies (TLC) were performed on glass plates precoated silicagel Merck $60F_{254}$. Metachloroperbenzoic acid, mCPBA, and the oxaziridinium salt **10** were titrated by iodometry and by ^1H NMR using an excess of *para*-tolylmethylsulfide in presence of an internal reference [*trans*-stilbene oxide, δ 3.92 ppm (s, 2H)]. The presence of oxidizing species in reaction mixtures was monitored by potassium iodide test. Recrystallized oxaziridinium **10** (100% active oxygen) was used for the stoichiometric epoxidations. The olefins are commercially available and the epoxides are known products (*trans*-stilbene oxide and styrene oxide,[34] β-methylstyrene oxide,[35] 1-phenylstyrene oxide[36]). The conversions were determined with an aliquot of the crude product analyzed by ^1H NMR in $CDCl_3$ in presence of a reference (triphenylmethane). The enantiomeric excesses were determined by HPLC using a DAICEL CHIRALPAK OT(+) chiral column and by ^1H NMR using $Eu(hfc)_3$ as chiral shift reagent. These methods were validated with each racemic epoxide, prepared by peracidic oxidation (mCPBA) of the corresponding olefin. The rotatory powers were determined using a Perkin-Elmer 241 MC instrument.

Synthesis of the oxaziridinium salt 10.

(3R,4S)-3-methyl-4-phenyl-3,4-dihydroisoquinoline (7): A solution of (1S,2R)-(+)-norephedrine **2** (free-base from the alkaline treatment of 10.33 g (55.44 mmol) of (+)-norephedrine hydrochloride) and 8 ml (78.93 mmol) of benzaldehyde **1** in 100 ml of CH_2Cl_2 was stirred over anhydrous $MgSO_4$ overnight. Filtration and concentration *in vacuo* afforded a mixture of **3** and **4** as a yellow oil (15.3 g, molar ratio **3**:**4** = 7:3), ^1H NMR (determined in the mixture), **3**: 1.12 (d, J=6, 3H); 3.67 (m, 1H); 4.87 (d, J=7.5, 1H); 7.17-7.50 (m, 10H); 8.33 (s, 1H). **4** (two diastereoisomeric oxazolidines, molar ratio: 2:1): 0.78 (d, J=6, 3H); 3.83 (m, 1H); 5.17 (d, J=3, 1H); 5.76 (s, 1H major isomer); 6.12 (s, 1H minor isomer); de 7.50-7.95 (m, 10H). The reduction of this crude product with an excess of $NaBH_4$ (2.2 g, 58 mmol) in EtOH (100 ml) gave, after the usual work up, 12.9 g of crude **5**,[37] ^1H NMR: 0.85 (d, J=6.5, 3H); 2.98 (qd, J=6.5 J=3.7, 1H); 3.87 (s, 2H); 4.76 (d, J=3.7, 1H); 7.30 (m, 10H). Trifluoroacetic acid (20 ml) and then sulfuric acid (20 ml) were added to crude **5** at 0 °C and the mixture was stirred 2 hours at 80 °C, then poured onto ice and basified with aqueous NaOH. The organic layer was decanted and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give 9.9 g of **6** as yellow oil, ^1H NMR: 1.10 (d, J=6, 3H); 3.10 (qd, J=6 J=9.5, H_3); 3.65 (d, J=9.5, H_4); 4.10 (d, J=15, H_1); 4.30 (d, J=15, H_1); 6.77 (m, 1H); 7.11 (m, 5H); 7.31 (m 3H).

MS(IC$^+$): 259; 225, hydrochloride mp 198 °C, Anal.: Calcd for $C_{16}H_{18}NCl$: C 73.77%; H 6.98%; N 5.39%; Cl 13.65%. Found: C 73.77%; H 7.02%; N 5.32%; Cl 13.75%. A solution of crude **6** in CH_2Cl_2 (100 ml) was vigorously stirred at r.t. with excess aqueous NaOCl (150 ml). The reaction, monitored by TLC (Et_2O/ NH_4OH), was complete in 2 hours. The organic layer was decanted and then it was added dropwise at r.t. to a methanolic solution of sodium hydroxide (2-3 equivalents of NaOH). At the end of the addition the reaction was complete (TLC, Et_2O/NH_4OH). The solvents were evaporated. The residue, diluted in Et_2O, was washed with aqueous NaOH (10%). The ether layer was dried (Na_2SO_4) and concentrated *in vacuo* to give 9.0 g of a mixture of **7** and **12** (molar ratio **7**:**12** = 95:5) as an oil. Chromatography on silicagel (ether/petroleum ether 1:1) afforded pure **7** (6.1 g, 50 % from **2**), $[\alpha]_D$ +33 (c=2.37; $CHCl_3$), ^{1}H NMR: 1.29 (d, J=6.5, 3H); 3.76 (d, J=11, H_4); 3.94 (dqd, J=11 J=6.5 J=2.5, H_3); 6.82 (m, 1H); 7.10-7.46 (m, 8H); 8.39 (d, J=2.5, H_1), ^{13}C NMR: 21.44 (Me); 49.09 (C_4); 59.01 (C_3); 127.01; 127.20; 127.34; 127.99; 128.84; 129.11 et 131.54 (CH); 127.92; 139.33 et 142.33 (C), MS(EI): 221 ($M^{+\cdot}$); 178 (M-43)$^{+\cdot}$, Anal.: Calcd for $C_{16}H_{15}N$: C 86.84%; H 6.83%; N 6.33%. Found: C 86.62%; H 7.01%; N 6.46%, and also pure **12**: mp: 40-44 °C. $bp_{(0.2)}$: 150 °C. ^{1}H NMR: 2.50 (s, 3H); 7.27 (m, 2H); 7.47 (m, 6H); 7.95 (m, 1H); 9.20 (s, H_1). ^{13}C NMR: 23.14 (Me); 125.01; 126.08; 127.52; 127.63; 128.70; 130.13 et 130.29 (CH); 126.90; 130.85; 135.89; 137.80 et 149.09 (C); 151.34 (C_1). MS(IC$^+$): 220 $(M+H)^+$. Anal.: Calcd for $C_{16}H_{13}N$: C 87.64%; H 5.98%; N 6.39%. Found: C 87.65%; H 6.16%; N 6.19%.

(3R,4S)-N-methyl-3-methyl-4-phenyl-3,4-dihydroisoquinolinium tetrafluoroborate (8): To 1.56 g (10.6 mmol) of trimethyloxonium tetrafluoroborate (Me_3OF_4B) in dry CH_2Cl_2 were added, under nitrogen, 1.78 g (8.05 mmol) of **7** in 60 ml CH_2Cl_2. The suspension was stirred at room temperature until **7** disappeared (TLC). The reaction mixture was then concentrated to dryness and the residue filtered through a silicagel pad. The vacuum evaporation of the elution solvent (CH_2Cl_2/Et_2O 2:1) gave crude **8** (2.5 g) as a white solid, mp 50-58 °C. $[\alpha]_D$ +148 (c=1.25; $CHCl_3$). ^{1}H NMR: 1.54 (d, J=6.5, 3H); 3.72 (s, 3H); 4.25 (dq, J=6.5 J=2.5, H_3); 4.33 (d, J=2.5, H_4); 6.92 (m, 1H); 7.29 (m, 4H); 7.58 (m, 1H); 7.76 (m, 1H); 8.09 (m, 1H); 9.27 (s, H_1). ^{13}C NMR: 17.82 (Me); 47.32 (C_4); 48.69 (C_3); 65.67 (N-Me); 107.05; 110.24; 111.22; 112.35; 112.43; 112.76; 117.73; 119.54; 121.61 et 122.05 (C and CH); 167.67 (C_1). MS(FAB): 236 (M^+-tetrafluoroborate). Anal.: Calcd for $C_{17}H_{18}NBF_4$ (1/4 H_2O): C 62.32%; H 5.69%; N 4.27%. Found: C 62.18%; H 5.60%; N 4.26%.

(1S,2R,3R,4S)-1,2-oxydo-3-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline (9): *Oxidation of 7 at -45 °C.* To a solution of 1 g (4.53 mmol) of **7** in 90 ml CH_2Cl_2 (0.01M) cooled to -45 °C were added under stirring 4 g (10 equivalents) of $NaHCO_3$ and dropwise (in 5 hours) 1 g of mCPBA titrating at 90% of active oxygen in 580 ml CH_2Cl_2. The mixture was allowed to warm to room temperature and washed with aqueous $NaHCO_3$ and then with water. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to give 1 g of crude product, a mixture of **9** and **11** (molar ratio **9**:**11**= 99:1). This crude product residue was recrystallized from pentane affording pure **9** as white needles (65 % in two crops), mp 89°C (pentane). $[\alpha]_D$ -13.8 (c=4.9; $CHCl_3$). ^{1}H NMR: 1.33 (d, J=6.5, 3H); 3.24 (dq, J=6.5 J=9.8, H_3); 3.62 (d, J=9.8, H_4); 5.13 (s, H_1); 6.62 (m, 1H); 7.15 (m, 2H); 7.33 (m, 6H); 7.60 (m, 1H). ^{13}C NMR: 19.42 (Me); 46.21 (C_4); 60.44 (C_3); 75.90 (C_1); 126.57; 127.21; 127.66; 128.87; 129.69; 129.75 et 129.85 (CH); 128.74; 139.16 et 140.21 (C). MS(IE): 237 ($M^{+\cdot}$); 221 ($M^{+\cdot}$-

16, m*=206.08); 195 ($M^{+\cdot}$-42, m*=160.44). Anal.: Calcd for $C_{16}H_{15}NO$: C 80.98%; H 6.37%; N 5.90%; O 6.70%. Found: C 81.07%; H 6.29%; N 5.58%; O 6.65%. *Oxidation of 7 at Room Temperature.* To a solution of 924 mg (4.18 mmol) of **7** in 40 ml CH_2Cl_2 were added 4 g (47.6 mmol) of $NaHCO_3$ and, portionwise, in the solid state, 971 mg of mCPBA titrated at 80% of active oxygen. After the disappearance of **7** (TLC, Et_2O/NH_4OH) the reaction mixture was diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$ and then with water, dried (Na_2SO_4) and concentrated *in vacuo* to give 920 mg of crude product (a mixture of **9**, **11**, **12** and **13** in the molar ratio 50:5:35:10). These products were separated by chromatography. A first one, elution Et_2O/MeOH (gradient), afforded pure **13** (18% from **7**) and pure **12** (already characterized, 15% from **7**) and a mixture of **9** and **11** (molar ratio **9**:**11** = 9:1). The nitrone **13** was recrystallized from ether, mp: 114-116 °C (ether). $[\alpha]_D$: +157.5 (c=0.55; $CHCl_3$). ^1H NMR: 1.54 (d, J=7, 3H); 4.12 (d, J=3, H_4); 4.31 (qd, J=7 J=3, H_3); 7.10 (m, 2H); 7.30 (m, 7H); 7.74 (s, H_1). ^{13}C NMR: 17.95 (Me); 49.48 (C_4); 70.14 (C_3); 124.79; 126.84; 127.49; 128.39; 128.57 et 129.12 (CH); 127.18; 131.04 et 140.57 (C); 131.61 (C_1). MS(IE): 237 ($M^{+\cdot}$). Anal.: Calcd for $C_{16}H_{15}NO$: C 80.98%; H 6.37%; N 5.90%; O 6.70%. Found: C 80.81%; H 6.58%; N 6.05%; O 6.51%. Two further chromatographies (elution ethyl acetate/petroleum ether 1:4) of the above mixture of the oxaziridines afforded pure **9** (already characterized, 30% from **7**) and a fraction enriched in the minor oxaziridine (molar ratio **9**: **11** = 1:9) from which **11** was characterized by ^1H NMR: 1.20 (d, J=6.7, 3H); 4.05 (d, J=1, H_4); 4.34 (qd, J=6.7 J=1, H_3); 4.92 (s, H_1); 6.94 (m, 1H); 7.25 (m, 4H); 7.47 (m, 2H); 7.68 (m, 1H).

(1S,2R,3R,4S)-N-methyl-1,2-oxydo-3-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline tetrafluoroborate (10). *Oxidation of 8:* To a solution of 3.9 g (12.1 mmol) of **8** in 25 ml CH_2Cl_2 were added under stirring 3 g (36.7 mmol) of $NaHCO_3$ and a solution of mCPBA (titrated at 75%, 5.6 g, 2 equivalents of active oxygen) in CH_2Cl_2 (65 ml). Two cycles of concentration-filtration and a final evaporation of the solvent gave 5.1 g of crude product (white solid). A recrystallization (acetone/pentane) afforded 1.9 g (46 %) of **10** as white needles, mp: 124 °C (acetone/pentane). $[\alpha]_D$ -130 (c=0.31; acetone). ^1H NMR: 1.53 (d, J = 6, 3H); 3.90 (s, 3H); 3.98 (d, J = 10, H_4); 4.63 (dq, J = 10 J = 6, H_3); 6.50 (s, H_1); 6.67 (m, 1H); 7.30 (m, 3H); 7.45 (m, 4H); 7.93 (m,1H). ^{13}C NMR: 14.14 (Me); 48.14 (C_4); 48.81 (C_3); 64.47 (N-Me); 87.81 (C_1); 121.47; 128.77; 128.95; 129.40; 130.37; 130.57; 133.17; 134.05; 137.07 et 137.65 (C and CH). MS(FAB): 252 ($M^{+\cdot}$-tetrafluoroborate). Anal.: Calcd for $C_{17}H_{18}NOBF_4$: C 60.21%; H 5.35%; N 4.13%. Found: C 59.97%; H 5.25%; N 4.03%. *Methylation of* ***9***: To a suspension of 151 mg (1.03 mmol) of trimethyloxonium tetrafluoroborate (Me_3OF_4B) in dry CH_2Cl_2 (5 ml) was added dropwise, under nitrogen, a solution of **9** (236 mg, 0.99 mmol) in CH_2Cl_2 (2 ml). The reaction mixture was stirred 15 minutes at room temperature and concentrated *in vacuo* to give **10**, quantitatively, as a white solid.

Oxygen transfer to unfunctionalized olefins

Stoichiometric epoxidations *(table 1). (entries 1,2,4):* To a solution of the olefin (12 mg, 0.6 mmol) in dichloromethane (3 ml) was added the oxaziridinium salt **10** (20 mg, 0.66 mmol). The reaction mixture was stirred at room temperature until the olefin disappeared (monitored by TLC), and then the solvent was evaporated *in vacuo*. In the epoxidation of styrene, sodium bicarbonate (3 mmol) was also added and the

heterogeneous reaction mixture was stirred at room temperature until the oxaziridinium disappeared (negative potassium iodide test). The sodium bicarbonate was separated by filtration. In all cases the solvent was evaporated *in vacuo* and the conversions olefin/epoxide were determined by ^{1}H NMR (Cl_3CD, with triphenylmethane as reference) of an aliquot of the crude product. The epoxides were isolated by preparative TLC. *trans-stilbene oxide* (entry 1): yield 63% (TLC eluting with petroleum ether-dichloromethane 2:1); ee 42% (HPLC); $[\alpha]_D$ +156,4 (c=0.75, benzene), (R,R)-epoxide [lit[30] data for (+)-(R,R)-stilbene oxide of 95% optical purity, $[\alpha]_D$ +357 (c 0.56, benzene)]. *β-methylstyrene oxide* (entry 2): yield 50% (TLC eluting with pentane-ether 9:1); ee 23% (HPLC); $[\alpha]_D$ +15,4 (c 1.5, ethanol), (R,R)-epoxide [lit[31] data for (1R,2R)-trans-β-methylstyrene oxide of 95% optical purity, $[\alpha]_D$ +70.8 (c 4.44, ethanol)]. *Styrene oxide*: yield 10% (TLC eluting with pentane-ether 9:1); ee 12% (HPLC). *1-phenylcyclohexene oxide* (entry 4): yield 65% (TLC eluting with petroleum ether-dichloromethane 4:1); ee 5% (^{1}H NMR); $[\alpha]_D$ +4,7 (c 1.7, benzene, (R,R)-epoxide [lit[32] data for pure (1R,2R)-(+)-1,2-epoxy-1-phenylcyclohexane, $[\alpha]_D$ +121.4 (c 0.78, benzene)].

Catalytic epoxidations *(scheme 4).* A mixture of the olefin [5 mmol, (R = Ph, 0.9 g), (R = Me, 0.59 g)], Oxone® (4 g, 6.5 mmol, 2 eq of active oxygen), the iminium salt **8** (80 mg, 0.25 mmol, 0.05 eq) and $NaHCO_3$ (1.7 g, 20 mmol) in 30 ml CH_3CN and 1 ml H_2O was stirred overnight at room temperature. The heterogeneous reaction mixture was filtered and the solvent was evaporated *in vacuo*. The conversions olefin/ epoxide were determined by ^{1}H NMR of an aliquot of the crude product (Cl_3CD, with triphenylmethane as reference). The epoxides were isolated by preparative TLC as above. *trans-stilbene oxide*: conversion 92%; yield 79%; ee 35% (HPLC). *β-methylstyrene oxide*: conversion 75%; yield 67%; ee 22% (^{1}H NMR).

Effects of solvent and temperature *(table 2). Low temperature reactions* (entries 2-4): A solution of the oxaziridinium **10** (20 mg, 0.06 mmol) in dichloromethane (0.6 ml) and a solution of trans-stilbene (12 mg, 0.06 mmol) were cooled to the appropriate temperature and then mixed. The reaction mixture was stirred at this temperature and quenched at the time indicated with excess dimethylsulfide and then allowed to warm to room temperature. The solvent was evaporated *in vacuo*. The conversions olefin/epoxide were determined as above. Trans-stilbene oxide was not produced in the reaction at -78°C (entry 4) but only 0.5 equivalents of dimethylsulfoxide were formed on quenching with dimethylsulfide as shown by the ^{1}H NMR analysis of the crude product. Trans-stilbene oxide from the other runs was isolated by preparative TLC as above. The ee's were determined by HPLC. *entry 2* (0°C): yield 66%, ee 50%, (R,R)-epoxide; *entry 3* (-32°C): yield 57%, ee 61%, (R,R)-epoxide. *Solvent effect* (entries 5-9): The oxaziridinium **10** (20 mg, 0.06 mmol) was added to a solution of trans-stilbene (12 mg, 0.06 mmol) in the appropriate solvent (1 ml). The reaction mixture was stirred at r.t. until the oxaziridinium disappeared (negative potassium iodide test, entries 7-9) or quenched with excess dimethylsulfide at the times indicated in table 2 (entries 5 and 6) and then concentrated *in vacuo*. The conversions olefin/epoxide were determined as above (^{1}H NMR). Trans-stilbene oxide was isolated in each case as above (TLC eluting with petroleum ether-dichloromethane 2:1). The ee's, determined by HPLC, always favored the (R,R)-epoxide. *entry 5* (benzene): yield 53%, ee 1%; *entry 6* (toluene): yield 45%, ee 5%; *entry 7* (pentane): yield 61%, ee 35%; *entry 8* (nitrobenzene): yield 60%, ee 39%; *entry 9* (nitromethane): yield 70%, ee 45%.

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