Pergamon

Tetrahedron, Vol. 53, No. 5, pp. 1759-1776, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(96)01087-3

Diastereoselective Addition of Metal-Coordinated and "Naked" Nucleophilic Reagents to Norephedrine Derived 2-Acyl-N-tosyl-Oxazolidines

Giovanni Poli,* [a] Elisa Maccagni,[a] Leonardo Manzoni,[b] Tullio Pilati,[c] and Carlo Scolastico [b]

a) Dipartimento di Chimica Organica dell'Università di Firenze, Centro CNR per lo Studio dei Composti Eterociclici, Via Gino Capponi 9, I-50121, Firenze, Italy;

b) Dipartimento di Chimica Organica e Industriale, Universita' di Milano, Centro CNR per lo Studio delle Sostanze Organiche Naturali, via Venezian 21, I-20133, Milano, Italy

c) Centro per lo Studio delle Relazioni tra Struttura e Reattivita' Chimica, Via Golgi 19, I-20124, Milano, Italy

Abstract: The addition of tri-*s*-butyl borohydrides to the 2-acetyl-1,3-oxazolidine **1** could be directed with high selectivity to either the *Si* or the *Re* π-carbonyl face under chelating or non-coordinating conditions respectively. Addition of hydrides to the corresponding phenyl ketone **2** was highly *Si* selective only in the former conditions. Grignard reagents and organolithiums add to the methyl ketone **1** with remarkable *Si* and *Re* π-face selectivity respectively. With phenyl ketone **2** only organomagnesium reagents follow the above trend. This data are in accord with a *Felkin-type* or a stereochemically opposite *chelated* mode of addition of these nucleophiles in the absence or in the presence of chelating metal counterions respectively.

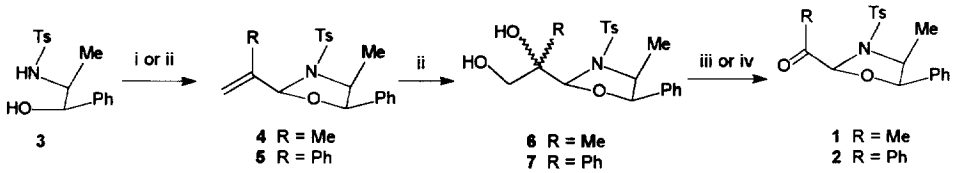
Introduction

The diastereoface differentiating addition of nucleophilic reagents to chiral carbonyl compounds is an important topic in organic synthesis and has led to a considerable amount of experimental[1] as well as theoretical[2] work. Our contribution to this field has been devoted to the asymmetric transformation of 2-substituted oxazolidines of nor-ephedrine derivation.[3] In this full account we report our results in the stereoselective addition of hydrides[4] and carbanionic reagents[5] to 2-oxy-substituted oxazolidines, which may be viewed as chirally modified glyoxal derivatives.[6]

We chose as substrates for our study the methyl ketone **1** and the phenyl ketone **2**. These compounds could be obtained via a common three-step procedure as follows. Acid-promoted condensation between methacrolein or atropic aldehyde diethylacetal and N-tosyl-norephedrine **3** gave the corresponding 2-alkenyl oxazolidines **4** and **5** as the only ($S_{C\text{-}2}$) epimers.[7] Catalytic osmylation of these alkenes gave diols **6** and **7** as

epimeric mixtures, which, upon oxidative cleavage of the crude products, afforded the respective ketones **1** and **2** (Scheme 1).

Scheme 1

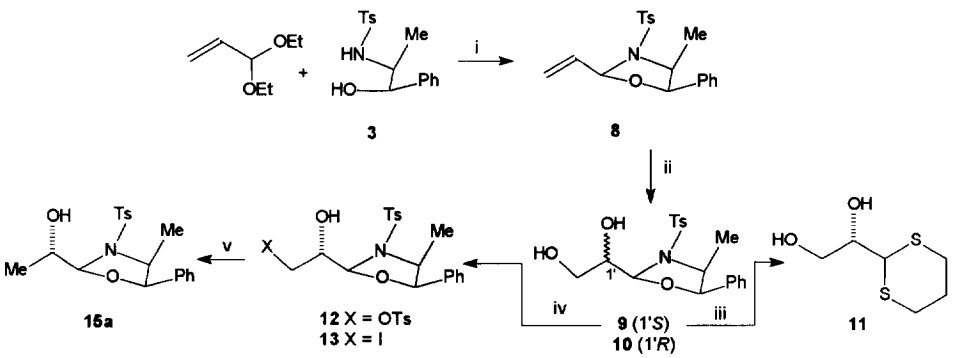


[a] Key: i: H_2C=CMeCHO, $HC(OMe)_3$, Py·Ts, PhH ↑↓; ii H_2C=CPhCH$(OEt)_2$, Py·Ts, PhH ↑↓; iii: $OsCl_3$ cat., $Me_3NO{\cdot}2H_2O$, CH_2Cl_2; iv $NaIO_4$, MeOH.

In order to be able to directly determine the stereochemical outcome of the reduction of ketone **1**, an authentic sample of one epimeric carbinol (of the two possible) was first synthesized and correlated to a derivative of known absolute configuration (Scheme 2).

Pyridinium tosylate-promoted condensation between acrolein diethylacetal and N-tosyl-norephedrine **3** gave the 2-vinyl oxazolidine **8**, again as the only $S_{C\text{-}2}$ epimer.[7] Catalytic osmylation[8] of this compound gave the diols **9** and **10** as a chromatographically separable 75:25 epimeric mixture. The absolute configuration of the former diol was easily assessed by its conversion into the known *S* dithiane **11**.[9] Reductive removal of the primary hydroxyl group in **9**, according to a monotosylation / iodination / reduction sequence, gave the carbinol **15a** of known 1'*S* absolute configuration (Scheme 2).

Scheme 2

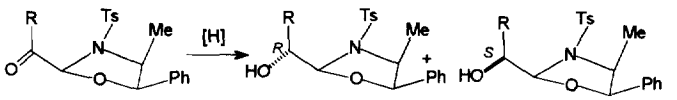


[a] Key: i: Py·Ts, PhH ↑↓; ii, $OsCl_3$ (0.05 equiv.), $Me_3NO{\cdot}2H_2O$, aq. acetone; iii, $HS(CH_2)_3SH$, $BF_3{\cdot}Et_2O$, CH_2Cl_2; iv: TsCl, pyridine, then NaI, acetone, ↑↓; v, Bu_3SnH, α,α'-azoisobutyronitrile (0.01 equiv.), toluene, ↑↓.

Addition of hydrides

In a first set of reductions on ketone **1** (Scheme 3, Table 1, entries 1-6) the tested hydrides gave the carbinols **14a** and **15a** (Scheme 3) with poor stereocontrol ranging from 65:35 to 37:63.

Scheme 3



R = Me: **1** **14a** **15a**
R = Ph: **2** **14b** **15b**

More gratifying results were instead obtained with the bulky metal tri-s-butyl borohydrides,[10] (Table 1, entries 7-9) which gave an increasing **14a**:**15a** ratio in the order: Li < K < Na. Such dramatic stereochemical changes suggest that the different geometric requirements in the interactions between the metal cations and the available oxygen atoms (i.e. carbonyl-, sulphone-, oxazolidine-, and THF-oxygens) are crucial.

In order to gain more information on the role of the cation, the above reduction was then studied in the presence of cation complexing agents such as crown ethers and criptands.[11] These polyethers are expected to generate "naked" trialkyl borohydrides whose reducing behavior can be different, in terms of reactivity and selectivity, from the parent hydrides. Pioneering work in this field was done by Pierre and Handel[12] who observed total inhibition of the reducing power of $LiAlH_4$ in the presence of criptands. The reduction of a chiral 2-acyl-1,3-oxathiane with tri-s-butyl borohydride in the presence and absence of crown ethers was reported by Eliel.[13] In that case, no noticeable stereochemical change was noted.

In our hands, the "naked" borohydrides behaved quite differently from the parent ones. The first apparent trend was the dramatic reversal of π-face discrimination upon cation complexation. In keeping with the less effective complexing power of crown ethers with respect to criptands, such a trend was moderate in the former case and maximum in the latter.

The reduction of the phenyl ketone **2** was totally *Si* selective with either $LiAlH_4$ or KBu^s_3BH (entries 16 and 17). However, the latter reduction, when performed in the presence of 18-crown-6, gave **14b** and **15b** in a 68:32 ratio (entry 18). This result indicates that the nature of the acyl substituent in the oxazolidine substrate strongly affects the stereochemical outcome of the reduction. In fact, in the case of the phenyl ketone, *Si* selectivity is attained easier than for the methyl ketone **1**, but "naked" conditions are not capable of effecting a clean reversal of selectivity.

Addition of carbanionic reagents

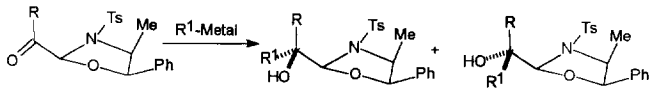
The addition of organolithium and Grignard reagents to the methyl ketone **1** to has been studied next.[5] Different proportions of the corresponding adducts have been obtained depending on the nature of the organometallic reagent and the reaction conditions used (Scheme 4, Table 2). Organolithium reagents in THF constantly favored the *1'R* epimers **16a-c** giving diastereomeric ratios in the range of 90:10 (entries 1, 14, and 16). In line with the selectride experiments mentioned above, addition of 18-Crown- totally inhibited the condensations, whereas 15-Crown-5 or Kriptofix 222 caused only a marked rate decrease (entries 3-5).

Interestingly, addition of the organolithium compatible[14] Lewis acids $BF_3 \cdot Et_2O$ or $^tBuMe_2SiOTf$, which are expected to enhance and/or modify the carbonyl reactivity, slightly improved the chemical yield and the diastereomeric ratio (entries 7 and 8). The Grignard reagents have been generated and reacted in Et_2O, or better, obtained via $MgBr_2 \cdot Et_2O$ mediated transmetallation of the corresponding organolithium reagents in CH_2Cl_2. In contrast to the lithium reagents,[15,16] these organomagnesium derivatives showed preference for the *1'S* epimers **17a-c** (entries 11, 12, 15 and 17). Such a selectivity was exceptionally high in three cases out of the four examined. Worthy of note, even a catalytic amount of $MgBr_2 \cdot Et_2O$ was capable of switching the carbonyl π-face selectivity from *Re* to *Si* (entry 13). *n*-Butylmagnesium chloride and iodide gave unsatisfactory results in terms of chemical yield although the latter reagent maintained the high selectivity of the corresponding bromide (entries 9, 10, and 11).

Table 1. Addition of hydrides to oxazolidines **1** and **2**

Entry	Ketone	Hydride	Additive	Solvent	T °C	Product	**14**:**15**	Yield %
1	1	$NaBH_4$	-	MeOH		**14a**:**15a**	50:50	81
2	1	$ZnBH_4$	-	Et_2O		**14a**:**15a**	50:50	78
3	1	$LiAlH_4$	-	Et_2O		**14a**:**15a**	60:40	71
4	1	$(Bu^tO)_3AlHLi$	-	THF		**14a**:**15a**	42:58	75
5	1	Bu^i_2AlH	-	CH_2Cl_2		**14a**:**15a**	37:63	88
6	1	$[MeO(CH_2)_2O]_2AlH$	-	Tol		**14a**:**15a**	65:35	97
7	1	s-Bu_3BHLi	-	THF	-78	**14a**:**15a**	55:45	96
8	1	s-Bu_3BHK	-	THF	-78	**14a**:**15a**	83:17	88
9	1	s-Bu_3BHNa	-	THF	-78	**14a**:**15a**	93:7	98
10	1	s-Bu_3BHLi	18-Crown-6	THF	-78	**14a**:**15a**	52:48	79
11	1	s-Bu_3BHLi	Kriptofix-211	THF		**14a**:**15a**	<1:>99	98
12	1	s-Bu_3BHK	18-Crown-6	THF	-78	**14a**:**15a**	21:79	70
13	1	s-Bu_3BHK	Kriptofix 222D	THF	-78	**14a**:**15a**	<1:>99	83
14	1	s-Bu_3BHNa	12-Crown-4	THF	-78	**14a**:**15a**	55:45	80
15	1	s-Bu_3BHLi	$MgBr_2Et_2O$	CH_2Cl_2-THF	-78	**14a**:**15a**	96:4	90
16	2	$LiAlH_4$	-	Et_2O	0	**14b**:**15b**	≥99: ≤1	43
17	2	s-Bu_3BHK	-	THF	-78	**14b**:**15b**	≥99: ≤1	88
18	2	s-Bu_3BHK	18-Crown-6	THF	-78	**14b**:**15b**	68:32	60

Scheme 4



R = Me: **1**
R = Ph: **2**

R = Me, R' = *n*-Bu	**16a**	**17a**
R = Me, R' = *n*-Pent	**16b**	**17b**
R = Me, R' = *n*-Vinyl	**16c**	**17c**
R = Ph, R' = *n*-Bu	**16d**	**17d**
R = Ph, R' = Me	**16e**	**17e**

The absolute configuration of adducts **16b** and **17b** has been unequivocally assigned as follows (Scheme 5). The diastereomeric mixture of diols **6**, previously obtained from **4**, was chromatographically separated into

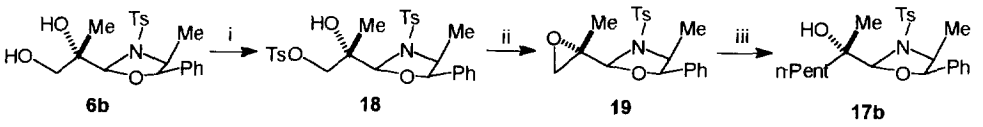
epimers **6a** and **6b**. The latter epimer was monotosylated to give **18** and then treated with DBU to give the epoxide **19**. Subsequent addition of the higher order cyanocuprate n-Bu_2CuLi_2CN gave the carbinol **17b**, which was identical to the major diastereomer obtained from n-pentylmagnesium bromide addition to **1** (Table 2, entry 15). The x-ray structure of the crystalline epimer **6a** (Figure 1) unravelled the C-1' absolute configuration of the products.

Table 2. Addition of organometallic reagents to oxazolidines **1** and **2**

Entry	Ketone	RM	equiv.	Additive	Solvent	T °C	Product	16:17	Yield %
1	1	n-BuLi	1.5	-	THF	-78	**16a**:**17a**	90:10	74
2	1	n-BuLi	3.0	-	DME	-78	**16a**:**17a**	79:21	73
3	1	n-BuLi	2.0	15-Crown-5	THF	-78	**16a**:**17a**	84:16	72
4	1	n-BuLi	2.0	18-Crown-6	THF	-78	**16a**:**17a**	-	-
5	1	n-BuLi	2.0	K-222D	THF	-78	**16a**:**17a**	90:10	70
6	1	n-BuLi	1.5	$CeCl_3$	THF	-78	**16a**:**17a**	-	-
7	1	n-BuLi	2.0	$BF_3{\cdot}Et_2O$	THF	-78	**16a**:**17a**	90:10	80
8	1	n-BuLi	1.5	$^tBuMe_2SiOTf$	THF	-78	**16a**:**17a**	92:8	88
9	1	n-BuMgCl	2.0	-	Et_2O	0	**16a**:**17a**	33:67	≤10
10	1	n-BuMgI	2.0	-	Et_2O	0	**16a**:**17a**	1:99	≤10
11	1	n-BuMgBr	2.0	-	Et_2O	0	**16a**:**17a**	1:99	60
12	1	n-BuLi	1.5	$MgBr_2{\cdot}Et_2O$	CH_2Cl_2	-78	**16a**:**17a**	≤1:≥99	90
13	1	n-BuLi	1.5	$MgBr_2{\cdot}Et_2O$[a]	CH_2Cl_2	-78	**16a**:**17a**	25:75	76
14	1	n-PentLi	1.5	-	THF	-78	**16b**:**17b**	89:11	76
15	1	PentMgBr	1.5	-	Et_2O	0	**16b**:**17b**	≤1:≥99	36
16	1	VinylLi	1.5	-	THF	-78	**16c**:**17c**	90:10	80
17	1	VinylMgBr	1.5	-	Et_2O	-78	**16c**:**17c**	34:66	82
18	2	n-BuLi	1.5	-	THF	-78	**16d**:**17d**	40:60	35
19	2	n-BuLi	1.5	$MgBr_2{\cdot}Et_2O$	CH_2Cl_2	-78	**16d**:**17d**	3:97	46
20	2	MeLi (Et_2O)	1.5	-	THF	-78	**16e**:**17e**	60:40	23
21	2	MeMgBr	1.5	-	Et_2O	0	**16e**:**17e**	3:97	60

a) 0.1 equiv. of $MgBr_2{\cdot}Et_2O$

Scheme 5



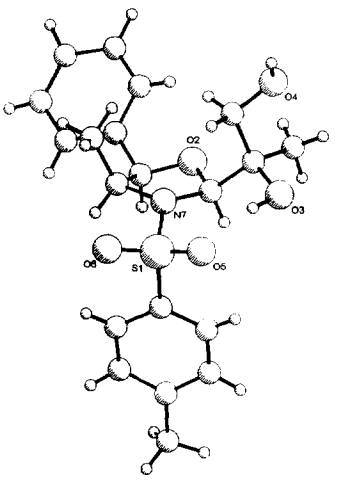
6b **18** **19** **17b**

[a] Key: i) TsCl, NEt_3, p-$Me_2NC_5H_4N$, 0°C RT; iii) DBU, THF, RT; iv) $Bu_2CuCNLi$, THF, -78°C.

The regular diastereoselective trend observed in Table 2, coupled with some relevant features distinguishing the ^{1}H-NMR spectra of the "Li-products" from those of the "Mg-products" allowed the safe configurational assignment of the remaining diastereomeric pairs **16a**/**17a**, and **16c**/**17c**.

The behavior of the phenyl ketone **2a** paralleled only partially that observed for ketone **1**. In fact, in this case, the Mg reagents maintained the exceptionally high levels of chelation controlled *Si* π-face selectivity (entries 19 and 21), whereas the lithium reagents behaved unselectively. (entries 18 and 20).

Figure 1



X-ray crystal structure of diol **6a**

Discussion

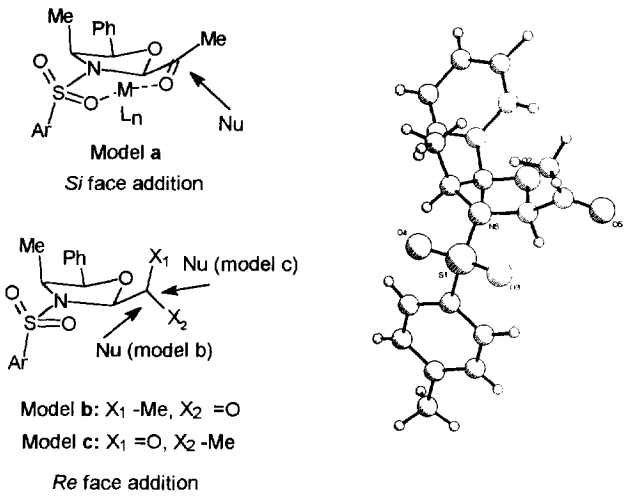
The above results appear to be consistent with a preferred *Si* face addition on a chelated SO_2/OC intermediate when metal - coordination is possible (Fig. 2, model a). In the case of the addition of selectrides to ketone **1** such a chelated form is expected to be more favored and/or reactive[17] than a "non-chelated" or an "O_{ring} chelated" one in the following decreasing order: Na > K > Li. Thus, appropriate counterions are expected to bring about S=O---M---O=C chelation thereby "forcing" the natural disposition (see later) of the carbonyl and the sulfonyl fragments. As a consequence, *Si* face addition is favored. In agreement with the above hypothesis, the presence of a bicoordinating Lewis acid such as $MgBr_2 \cdot Et_2O$ dramatically improved the selectivity of s-Bu_3BHLi from 55:45 to 96:4 (Table 1, entries 7 and 15).[18] On the other hand, with "naked" reagents tight coordination or chelation phenomena should be absent. A reactive conformation[19] akin to that found in the crystal structure of **1** is thus likely to be involved in this case. A 6.4% NOE effect between HC_2 and the aromatic hydrogen *ortho* to the sulfonamide group, in combination with the absence of that between $MeC_{1'}$ and HC_2, confirms a similar conformation in solution. Given the above assumption, hydride addition antiperiplanar to the electronegative oxazolidine oxygen atom on a $syn_{C=O/C-H}$ conformated substrate well rationalizes the observed *Re* face selectivity (Fig. 2, model b). Alternatively, Hoppe suggested for a related system[6d] an $anti_{Nu/C-N}$ addition of the nucleophile on an $anti_{C=O/C-H}$ conformation (Fig. 2, model c).

However, the results obtained with the phenyl ketone **2** indicate that the face selectivity of these N-sulfonylated oxazolidines in the absence of magnesium ions is rather substrate dependent. In this case, in fact, the *Re* preference is lost.

In order to obtain a deeper insight into this problem we undertook a theoretical study[20] on the model substrate 2-acetyl-3-mesyl oxazolidine. A first conformational search using PM3 method[21] located three minimum energy conformations. Further geometrical optimization on the 3-21G* potential energy hypersurface gave only two conformers A and B with energies of -979.8641136 a.u. and -979.857919 a.u. respectively (Figure 3). According to the Boltzman equation the A:B ratio at 195°K, is thus 99.9956 : 0.0044. Interestingly, neither of the two conformers located were akin to that found in the solid state of **1**. Furthermore, B is found to

adopt the an $anti_{C=O/C-H}$ disposition, as in model c of Scheme 5. The atomic charges[22] associated to the ring oxygen and the mesyl moiety[23] were found to be -0.55 and -0.39 for A and -0.58 and -0.45 for B respectively.

Figure 2



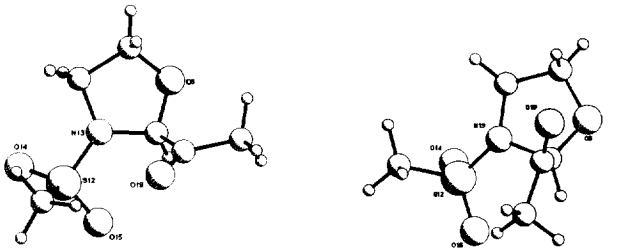
Left: stereochemical models for the addition of nucleophilic reagents to ketones **1** and **2**; a: chelated model; b and c: open models. Right: X-ray crystal structure of ketone **1**.

It thus appears that, although bulkier, the sulfonamide moiety has a less electronwithdrawing power than oxygen. MO analysis proved also of interest. In fact, the LUMO's of both A and B were found to be asymmetrically extended at the carbonyl π faces, the *Re* face resulting more diffuse than the *Si* one in both cases.[24] This data suggests an intrinsic bias of both A and B to react through the *Re* face, a finding in agreement with the experimentally observed *Re* selectivity shown by methyl ketone **1** in the absence of coordinating metal ions. However, it should be pointed out that an A-type conformation would severely hinder the carbonyl *Re* face in the specific case of the methyl ketone **1**. A type-B conformation thus appears as the one presumably adopted by the transition state; a result in accordance with model c of Figure 2.[25]

In order to further support the above proposed Mg chelation the ^{1}H-NMR of the methyl ketone **1** has been recorded in the presence of additional amounts of $MgBr_2 \cdot Et_2O$. Plotting the observed chemical shift variations ($\Delta\delta$) versus the equivalents of $MgBr_2 \cdot Et_2O$ added, gave a curve for each nucleus examined. Such a Lewis acid induced shift analysis thus allowed to individuate and qualitatively rank the protons lying in the vicinity of the coordination sites according to the following decreasing order: H_A, CH_3CO, H_B, and H_C (Figure 4). As expected, these data are in full accord with the S=O---Mg---O=C chelation. Interestingly, all the plots

reach a *plateau* at two equivalents of added Lewis acid. This suggests that the oxazolidine **1** should ultimately engage two molecules of the Lewis acid.[26]

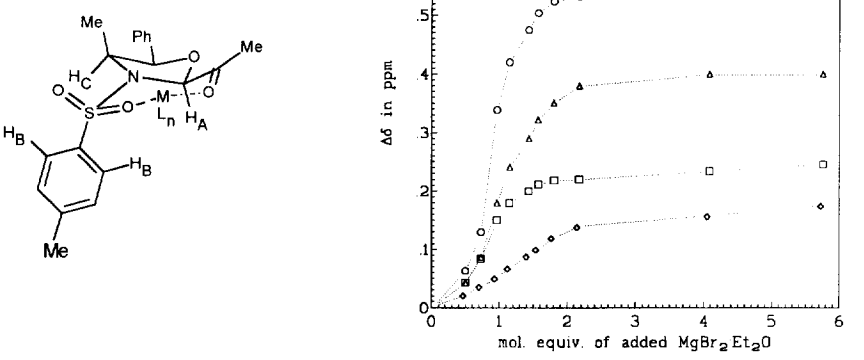
Figure 3



A -979.86411 a.u. (0.0 kcal/mol) **B** -979.857919 a.u. (+3.89 kcal/mol)

HF/3-21G* optimized structures for 2-acetyl-3-mesyl oxazolidine. Absolute and relative energies (vibrationless) are indicated.

Figure 4

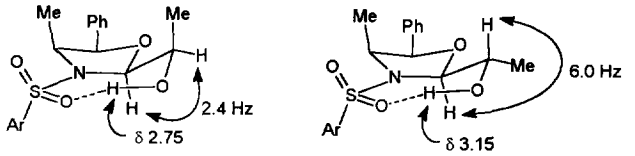


^{1}H-NMR chemical shift variations in ketone **1** as a function of $MgBr_2 \cdot Et_2O$ added (H_A: o; CH_3CO: Δ; H_B: □; H_C: ◊).

The intrinsic coordinating ability of the sulfonamide group was also apparent in the carbinols **14a** and **15a**, as deduced from their ^{1}H-NMR spectra in $CDCl_3$. In fact, the dilution-independent chemical shifts of the hydroxyl protons and the relative values of their $J_{C\text{-}2\text{-}Cl'}$ are only consistent with an intramolecular SO···HO interaction (Figure 5).[27] A similar hydrogen bonded conformation has been also observed in the crystal

structure of **6a**. Estimation[28] of $J_{C2\text{-}C1'}$ on models of **14a** and **15a**, obtained by incorporating the carbinols into the crystal structure of **6a**, afforded the following values: **14a**, $J_{C2\text{-}C1'}$= 2.8 Hz; **15a**, $J_{C2\text{-}C1'}$= 7.7 Hz. Such a feature has been useful in the configuration assignment of the other carbinol pair **14b** and **15b**.

Figure 5



14a (1'*R*) **15a** (1'*S*)

Postulated conformations of carbinols **14a** and **15a** and their relevant spectroscopic features.

Thus, it appears that addition of tri-*s*-butyl borohydrides and carbanionic reagents to the acetyl-oxazolidine **1** may be conveniently directed to either of the carbonyl π-faces with exceptionally high selectivity and high yield. Locking of the acetyl moiety through metal chelation allows a virtually exclusive *Si* face selectivity, whereas removal of the electrophilic activation by making the borohydrides "naked", affords the alternative *Re* topicity. On the other hand, the behavior of the phenyl ketone **2** suggests that the nature of the acyl substituent in the oxazolidine substrate can strongly affect the stereochemical outcome of the nucleophilic addition.

Conclusions

In summary, the present paper has shown the potential of oxazolidines for the asymmetric formation of secondary and tertiary alcohols in chiral glyoxal derivatives. These findings are in agreement with and complement those recently presented by Hoppe[6d-e] with (*R*)-phenylglycinol- and norpseudoephedrine-derived N-tosyl oxazolidines and by Agami[6f-i] with norephedrine-derived N-Boc oxazolidines. The commercial availability of norephedrine in both enantiomeric forms at low cost, coupled with the unique stereodivergent behavior of **1** as a function of the reaction conditions make the present method particularly attractive from the synthetic point of view. We believe that the present study confirms norephedrine-derived oxazolidines as effective chiral templates for asymmetric synthesis, and stimulates interest in new ways of selectivity control.

EXPERIMENTAL SECTION

General. ^{1}H and ^{13}C-NMR spectra were recorded in $CDCl_3$ as indicated, at 200 and 50.3 MHz, respectively (the usual abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The positive chemical shift values are given in ppm and the coupling constants in Hz. Elemental analyses were performed with a Perkin-Elmer 240 instrument. Mass spectra were obtained with a VG 7070 EQ spectrometer. Optical rotations were measured in 1-dm cells of 1-mL capacity by using a Perkin-Elmer 241 polarimeter. Thin-layer chromatography (TLC) was carried out using Merck precoated silica gel F-254 plates. Flash chromatography was carried out with Merck Silica Gel 60, 200-400 mesh. Solvents were dried with standard procedures and reactions requiring anhydrous conditions were performed under a positive nitrogen atmosphere. Final product solutions were dried over Na_2SO_4, filtered and evaporated under reduced pressure on a rotary evaporator.

***(2S,4S,5R)*-2-isopropenyl-4-methyl-5-phenyl-3-(toluene-4'-sulfonyl)-oxazolidine (4).** To a solution of N-toluene-4-sulfonyl-norephedrine **3**[29] (2.0 g, 6.56 mmol) in dry benzene (41 ml) were added methyl orthoformate (1.39 g, 13.1 mmol), methacrolein (0.918 g, 13.1 mmol), and pyridinium tosylate (0.411 g, 1.6 mmol). The resulting mixture was refluxed with a bypassed dropping funnel filled with 4Å molecolar sieves placed between the flask and the reflux condenser. After 4 h refluxing the mixture was cooled and treated with saturated aqueous $NaHCO_3$. The organic layer was extracted with Et_2O, dried (Na_2SO_4), filtered and the solvent was removed under reduced pressure. The crude oil was purified by flash-chromatography (hexane-AcOEt 80:20) affording pure **4** (2.346 g, 50.2 %) as a colorless oil. IR ($CHCl_3$): ν 1730, 1590, 1490, 1340, 1160, 910 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, J = 7.0 Hz), 1.9 (s, 3H), 2.5 (s, 3H), 4.15 (m, 1H), 4.5 (d, 1H, J = 5.0 Hz), 5.18 (s, 1H), 5.35 (s, 2H), 7-8 (m, 9H). Anal. Calcd. for $C_{20}H_{23}NO_3S$: C, 67.20; H,6.49; N, 3.92. Found: C, 67.24; H, 6.52; N, 3.89.

***(2S,4S,5R)*-4-methyl-5-phenyl-2-(1-phenyl-vinyl)-3-(toluene-4'-sulfonyl)-oxazolidine (5).** To a solution of N-toluene-4-sulfonyl-norephedrine **3**[29] (1.181 g, 3.87 mmol) in dry benzene (24 ml) were added atropic aldehyde diethylacetal[30] (0.799 g, 3.87 mmol), and pyridinium tosylate (0.242 g, 1 mmol). The resulting mixture was refluxed with a bypassed dropping funnel filled with 4Å molecolar sieves placed between the flask and tyhe reflux condenser. After 4 h refluxing the mixture was cooled and treated with saturated aqueous $NaHCO_3$. The organic layer was extracted with Et_2O, dried (Na_2SO_4), filtered and the solvent was removed under reduced pressure. The crude oil was purified by flash-chromatography (hexane-AcOEt 8:2) affording pure **5** (1.3 g, 80 %) as a white solid. ^{1}H-NMR ($CDCl_3$): δ 0.62 (d, 3H, J = 5.5 Hz), 2.5 (s, 3H), 4.15 (m, 1H), 4.5 (d, 1H, J = 5.5 Hz), 5.51 (d, 1H, J = 1 Hz), 5.8 (d, 2H, J = 3.5 Hz), 7-8 (m, 14H). Anal. Calcd. for $C_{25}H_{25}NO_3S$: C, 71.57; H, 6.01; N, 3.34. Found: C, 71.53; H, 6.04; N, 3.39.

***(2RS,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-propane-1,2-diol (6).** To a solution of **4** (2.3 g, 6.4 mmol) in acetone/water 8 : 1 (50 ml) was added at room temperature $OsCl_3$ (0.191 g, 0.644 mmol) and $Me_3NO{\cdot}2H_2O$ (1.43 g, 12.8 mmol). After 1 h stirring was added Na_2SO_3, and the organic layers were extracted with AcOEt, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash-chromatography gave the two diastereoisomeric products in 1:1 ratio (2.001 g, 80 %). ***(1S)*-6b**: ^{1}H-NMR ($CDCl_3$ + D_2O): δ 0.88 (d, 3H, J = 5.6 Hz), 1.25 (s, 3H), 2.5 (s, 3H), 3.6 (d, 1H, J = 12.0 Hz), 4.0 (d, 1H, J = 12.0 Hz), 4.1 (m, 1H), 4.21 (d, 1H, J = 6.0 Hz), 5.05 (s, 1H), 7-8 (9H); ***(1R)*-6a**: ^{1}H-NMR ($CDCl_3$ + D_2O): δ 0.88 (d, 3H, J = 6.5 Hz), 1.25 (s, 3H), 2.5 (s, 3H), 3.6 (d, 1H, J = 11.5 Hz), 4.0 (d, 1H, J = 11.5 Hz), 4.1 (m, 1H), 4.21 (d, 1H, J = 6.0 Hz), 5.05 (s, 1H), 7-8 (9H). Anal. Calcd. for $C_{20}H_{25}NO_5S$: C,

61.36; H, 6.44; N, 3.58. Found: C, 61.43; H, 6.40; N, 3.61. Crystal data for **6a.** $C_{20}H_{25}NO_5S$, Fw. = 391.48, orthorhombic, space group $P2_12_12_1$, a = 9.833(2), b = 12.154(4), c = 16.872(5) Å, V = 2016(1) Å^3, Z = 4, D_x = 1.290 Mg.m^{-3}, μ (Mo-$K\alpha$) = 0.18 mm^{-1}; crystal dimensions 0.24x0.24x0.30 mm^3, λ = 0.71073 Å (Mo-$K\alpha$ radiation, graphite monochromator, Enraf-Nonius CAD4 diffractometer). Data callection at room-temperature, ω-2θ scan mode, 2θ < 50°, *hkl* limits 0←12, 0←15, 0←21; 2613 unique reflections [1772 with $I_o > 1.\sigma(I_o)$ were considered observed]; no significant decay, no absorption correction. The structure was solved by MULTAN[31] routine and refined by full-matrix least-squares with anisotropic thermal parameters for non-hydrogen atoms; H atoms were refined isotropically with the exclusion of those of methyl of tosyl group that were rotationally disordered and were included in calculation but not refined. Atomic scattering factors were those given by Enraf-Nonius SDP[32] system of computing programs. The final refinement gave R = 0.034 and R_w = 0.036 for 1772 observed reflections with weights $w = 4\ I_oLp^2/[\sigma^2(I_o)+0.0009I_o^2]$, were Lp is the Lorentz-polarization factor. The maximum residue on the final difference Fourier map was 0.14 e. Å^{-3}. The absolute configuration was chosen according to that known of the precursors. Final coordinates have been deposited at CCDF. Bond distances and bond angles do not present any noticeable feature; the conformation of the molecule in the crystal is essentially determined by two hydrogen bonds, the first and stronger intramolecular O2...H(4)-O4 [with distance O2...O4 of 2.721(2) Å], the second intermolecular be O5-H...$O4_{1/2+x,-1/2-y,-z}$ [with O5...$O4_{1/2+x,-1/2-y,-z}$ 2.842(3) Å]

***(2S,4S,5R)*-1-[4-methyl-5-phenyl-3-(toluene-4'-sulfonyl)-oxazolidin-2-yl]-ethanone (1).** To a solution of **6** (2.565 g, 6.56 mmol) in dioxane/water 4 : 1 (20 ml) was added $NaIO_4$ (3.51 g, 16.4 mmol). After 1 h stirring CH_2Cl_2 was added, and the organic layer was extracted with AcOEt, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash-chromatography (hexane:AcOEt 6:4) gave 1.9 g of **1** (81 %) as a white solid. IR (CH_2Cl_2): ν 2860, 1729, 1350, 1170 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.70 (d, 3H, J = 5.6 Hz), 2.3 (s, 3H), 2.35 (s, 3H), 3.98 (m, 1H), 4.5 (d, 1H, J = 6.0 Hz), 5.2 (s, 1H), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 16.9, 21.7, 58.6, 82.8, 90.0, 125.9, 127.9, 128.3; Anal. Calcd. for $C_{19}H_{21}NO_4S$: C, 63.49 ; H, 5.89; N, 3.90. Found: C, 63.43; H, 5.92; N, 3.86. Crystal data for **1**: $C_{19}H_{21}NO_4S$, orthorombic, space group $P2_12_12_1$, a = 9.738(1), b = 11.059(1), c = 17.630(1), V = 1898.6(3) Å^3, Z = 4, D_c = 1.258 g cm^{-3}, Mo Ka radiation (l =0.71073 Å), μ(Mo Ka) = 1.83 cm^{-1}: a crystal of 0.30 x 0.28 x 0.24 mm^3 was sealed in a glass capillary to avoid intensity decay. Nonius CAD4 diffractometer; 2473 reflection collected up to 24 = 55 , 1373 observed [I . s(I)]. The structure is MULTAN-resistent; it was solved by using the program RISCON[33] . A molecular model for **1**, requested by this routine, was derived from ***(1R)*-6a**; refinement by full-matrix least-squares with weights w = $1/s^2(F_\wedge)$; R = 0.042, R_w = 0.040; hydrogen atoms of two methyls are disordered; they were introduced in calculated positions but not refined. S, O, N, C, atoms anisotropic, H isotropic; no particular residue on the last 6 Fourier map. Atomic coordinates, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Center.

***(1RS,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-1-phenyl-ethane-1,2-diol (7) and *(2S,4S,5R)*-[4-methyl-5-phenyl-3-(toluene-4-sulfonyl)-oxazolidin-2-yl]-phenyl-methanone (2).** To a solution of **5** (0.532 g, 1.3 mmol) in acetone/water 8 : 1 (12 ml), $OsCl_3$ (0.0377 g, 0.127 mmol) and $Me_3NO{\cdot}2H_2O$ (0.283 g, 2.54 mmol) were added at r.t. After 1 h stirring Na_2SO_3 was added and the organic layers were extracted with AcOEt, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash-chromatography gave the diol **7** as a 1:1 mixture of two diastereoisomeric products (0.46 g, 80 %). To a solution of **7** (0.575 g, 1.27 mmol) in dioxane/water 4 : 1 (10 ml) was added $NaIO_4$ (0.678 g, 3.17 mmol). After 1 h stirring at r.t. was added CH_2Cl_2, and the organic layer was extracted with AcOEt, dried over

Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash-chromatography (hexane:AcOEt 8:2) gave 0.214 g of **2** (40 %). ^{1}H-NMR ($CDCl_3$): δ 0.71 (d, 3H, J = 5.7 Hz), 2.5 (s, 3H), 4.2 (m, 1H), 4.95 (d, 1H, J = 5.5 Hz), 6.45 (s, 1H), 7-8.3 (14H). Anal. Calcd. for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32. Found: C, 68.48 H, 5.48; N, 3.29.

General procedures for the reduction of ketones 1 and 2

I) reductions with selectrides®

Method A (without additive, Table 1, entries 7-9, and 17). To a 0.1 M solution of **1** or **2** in THF was added dropwise at -78°C the appropriate selectride (1.5 mol. equiv, 1.0 M soln in THF). After 30 min stirring the reaction was quenched with phosphate buffer solution, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

Method B (in the presence of additive, Table 1, entries 10-14, and 18). To a 0.1 M solution of the appropriate additive (see Table 1) in THF was added in one portion at -78°C the appropriate selectride (1.5 mol. equiv, 1.0 M soln in THF). After 10 min stirring a 0.1 M solution of **1** or **2** in THF was added dropwise. After 2 h the reaction was quenched with phosphate buffer solution, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

Method C (in the presence of $MgBr_2{\cdot}Et_2O$, Table 1, entry 15). To a 0.1 M solution of **1** (0.0158 g, 0.044 mmol) in THF, $MgBr_2{\cdot}Et_2O$ (0.0171 g, 0.066 mmol) was added at -78°C. After 10 min L-selectride (0.066 mmol., 0.066 ml) was added dropwise. After 2 h stirring the reaction was quenched with phosphate buffer solution, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

II) reductions with the other hydrides

Method A (Table 1, entries 4-6). To a 0.05 M solution of **1**, in the solvent and at the temperature indicated in table 1, the appropriate hydride solution (1.5 mol. equiv.) was added dropwise. After 2 h stirring the reaction was quenched with phosphate buffer, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

Method B (Table 1, entry 3 and 16). To a solution of $LiAlH_4$ (0.0205 g, 0.54 mmol) in Et_2O (1.35 ml) was added at 0°C a solution of **1** (0.0242 g, 0.067 mmol) in Et_2O (0.5 ml). After 2 h stirring the reaction was quenched with phosphate buffer, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. An identical procedure was followed for the reduction of ketone **2**.

The diastereomeric ratios were determined in each case on the crude products by ^{1}H-NMR analysis. Flash chromatography of the crude materials (hexane:AcOEt 8 : 2 for both **14a/15a** and **14b/15b**) allowed separation of the two diastereoisomers that were isolated as oils. For product ratios and yields see Table 1.

***(1R,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-ethanol (14a).** IR ($CHCl_3$): ν 3500, 3000, 2350, 1250, 1360, 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, J = 6.5 Hz), 1.35 (d, 3H, J = 6.1 Hz), 2.45 (s, 3H), 2.7 (d, 1H, J = 5.7 Hz, exchangeable), 4.05 (m, 1H), 4.1 (m, 1H), 4.25 (d, 1H, J = 6.0 Hz), 4.95 (d, 1H, J = 2.4 Hz), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 17.3, 17.6, 21.6, 58.9, 68.3, 80.9, 93.4, 125.9, 127.9, 128.0, 128.3, 130.1. Anal. Calcd. for $C_{19}H_{23}NO_4S$: C, 63.14; H, 6.41; N, 3.88. Found: C, 63.09

H, 6.48; N, 3.85. ***(1S,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4-sulfonyl)-oxazolidin-2'-yl]-ethanol (15a).** IR ($CHCl_3$): ν 3700, 3000, 1600, 1350, 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, J = 6.5 Hz), 1.42 (d, 3H, J = 6.1 Hz), 2.5 (s, 3H), 3.15 (d, 1H, J = 5.7 Hz, exchangeable), 3.98 (m, 1H), 4.12 (m, 1H), 4.22 (d, 1H, J = 6.0 Hz), 4.84 (d, 1H, J = 6.0 Hz), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 17.3, 17.8, 21.6, 59.2, 70.9, 80.8, 93.5, 125.7, 127.9, 128.0, 128.3, 130.2. Anal. Calcd. for $C_{19}H_{23}NO_4S$: C, 63.14; H, 6.41; N, 3.88. Found: C, 63.11, 6.45; N, 3.84.

***(1R,2'S,4'S,5'R)*-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-phenyl-methanol (14b).** ^{1}H-NMR ($CDCl_3$): δ 0.40 (d, 3H, J = 5.5 Hz), 2.5 (s, 3H), 3.78 (d, 1H, J = 10 Hz, exchangeable), 3.97 (m, 1H), 4.21 (d, 1H, J = 6.0 Hz), 5.16 (d, 1H, J = 5.5 Hz), 5.25 (d, 1H, J = 1.2 Hz), 7-8.0 (m, 14H). Anal. Calcd. for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 68.10 H, 5.89; N, 3.26.

***(1S,2'S,4'S,5'R)*-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-phenyl-methanol (15b).** ^{1}H-NMR ($CDCl_3$): δ 0.52 (d, 3H, J = 5.5 Hz) 2.05 (s, 3H), 3.5 (d, 1H, J = 5 Hz, exchangeable), 4.15 (m, 1H), 4.12 (d, 1H, J = 7 Hz), 4.95 (d, 1H, J = 5.5 Hz), 5.11 (s, 1H), 6.9-8.0 (m, 14H, aromatics). Anal. Calcd. for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 68.11 H, 5.87; N, 3.40.

***(1S,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-ethane-1,2-diol (9) and *(1R,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-ethane-1,2-diol (10).** To a solution of **8** (0.6447 g, 1.88 mmol), in acetone : water 8 : 1 (20 ml) $OsCl_3$ (0.0557 g, 0.188 mmol) and $Me_3NO{\cdot}2H_2O$ (0.418 g, 3.76 mmol) were added in that order at room temperature. After 3 h stirring the reaction was treated with Na_2SO_3, the organic layer was extracted with AcOEt, dried over Na_2SO_4, filtered and the solvent was evaporated at reduced pressure. Flash chromatography (acetone : CH_2Cl_2 1 :9) allowed isolation of ***(1'S)*-9** (0.454 g, 75%), oil, and ***(1'R)*-10** (0.153 g, 25%) oil. ***(1'S)*-9**: IR ($CHCl_3$): ν 3500, 3000, 1600, 1350, 1200 cm^{-1}; ^{1}H-NMR ($CDCl_3$ + D_2O): δ 0.85 (d, 3H, J = 6 Hz), 2.5 (s, 3H), 3.82 (m, 2H), 3.92 (m, 1H), 4.1 (m, 1H), 4.2 (d, 1H, J = 5 Hz), 5.1 (d, 1H, J = 6.5 Hz), 7-8 (9H). ***(1'R)*-10**: IR ($CHCl_3$): ν 3500, 3000, 1600, 1360, 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$ + D_2O): δ 0.83 (d, 3H, J = 7.0 Hz), 2.5 (s, 3H), 3.7-4.15 (4H), 4.22 (d, 1H, J = 6 Hz), 5.12 (d, 1H, J = 6.5 Hz), 7-8 (9H).

***(1'S,2''S,4''S,5''R)*-toluene-4-sulfonic acid 2'-hydroxy-2'-[4''-methyl-5''-phenyl-3''-toluene-4'''-sulfonyl)-oxazolidin-2''-yl]-ethyl ester (12).** To a solution of ***(1'S)*-9** (0.0427 g, 0.113 mmol) in pyridine (1.5 ml) TsCl (0.0214 g, 0.113 mmol) was added at room temperature. After 1 h stirring the reaction mixture was diluted with H_2O (1.5 ml), the organic layer was extracted with Et_2O, dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude was purified by flash-chromatography affording 0.024 g of **12** (41 %) oil. IR: ($CHCl_3$): 3500, 3000, 1600, 1350, 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.81 (d, 3H, J = 7.0 Hz), 2.4 (s, 3H), 2.5 (s, 3H), 3.5 (d, 1H, exchangeable), 3.8-4.15 (2H), 4.2 (d, 1H, J = 5.5 Hz), 4.22-4.51 (2H), 5 (d, 1H, J = 5.2 Hz), 7-8 (13H); Anal. Calcd. for $C_{26}H_{29}NO_7S_2$: C, 58.74; H, 5.50; N, 2.63. Found: C, 58.68 H, 5.53; N, 2.58.

***(1S,2'S,4'S,5'R)*-2-iodo-1-[4'-methyl-5'-phenyl-3'-toluene-4''-sulfonyl)-oxazolidin-2'-yl]-ethanol (13).** To a solution of **12** (0.0245 g, 0.046 mmol) in acetone (1 ml) was added NaI (0.0413 g, 0.276 mmol) and that solution was heated to reflux for 5 h. H_2O was added (3 ml) and the organic layer was extracted with Et_2O, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by flash-chromatography (hexane:AcOEt 7:3) to give 0.012 g of the title compound (53 %). IR ($CHCl_3$): 3480, 2990, 1600, 1350, 1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, J = 7.0 Hz), 2.51 (s, 3H), 3.4-3.8 (3H + 1H

exchangeable), 4.1 (dq, 1H, J = 7.0 and 6.5 Hz), 4.25 (d, 1H, J = 6.5 Hz), 5.0 (d, 1H, J= 6.0 Hz), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 8.7, 17.2, 21.5, 59.2, 73.0, 81.1, 92.0, 125.6, 127.9, 128.1, 128.3, 130.2.

Reduction of 13 to 15a. To a solution of **13** (0.0147 g, 0.03 mmol) were added Bu_3SnH (0.0174 g, 0.06 mmol) and AIBN (0.099 mg, 0.0006 mmol). The resulting solution was heated to reflux for 3 h and then treated with an aqueous KF solution. The organic layer was separated and the aqueous phase was extracted with Et_2O, dried over Na_2SO_4 and evaporated under reduced pressure. Flash-chromatography (hexane:AcOEt 8:2) of the crude product afforded 3.2 mg of pure compound (30 %). This material showed identical physico-chemical data of compound **15a** obtained from reduction of **1** (see above).

***(S)*-1-[1,3]-dithian-2-yl-ethane-1,2-diol (11).** To a solution of ***(1S)*-9** (42.9 mg, 0.113 mmol) in CH_2Cl_2 were added at room temperature 1,3-propanedithiol (122.4 mg, 1.132 mmol) and $BF_3{\cdot}Et_2O$ (48.1 mg, 0.339 mmol). After 20 min stirring the reaction was treated with a phosphate buffer solution, the organic layers were separated and the aqueous phase was extracted with Et_2O, dried over Na_2SO_4 and eavaporated under reduced pressure. The crude product was purified by flash-chromatography affording 8.3 mg of the title compound (41 %). $[\alpha]_D^{20}$ = -6.6 (c 0.83, MeOH), [lit.[9] $[\alpha]_D^{20}$ = -6.0 (c 1.08, MeOH)]; IR ($CHCl_3$): 3600, 3480, 2910, 1180, 1090; ^{1}H-NMR ($CDCl_3$-D_2O): δ 1.95-2.18 (m, 2H), 2.15-2.29 (m, 2H), 2.91-3.05 (m, 2H), 3.79-4.07 (4H); -^{13}C-NMR ($CDCl_3$): δ 25.3, 26.7, 27.3, 47.1, 63.6, 71.1.

General procedures for the additon of organolithium and organomagnesium compounds to 1 and 2.
Method A (without additives, Table 2, entries 1, 2, 9-11, 14-18, 20, 21). A solution of the organometallic reagent (1.5 mol. equiv.) was added dropwise at -78°C to a 0.1 M solution of oxazolidine **1** or **2** (1.0 mol. equiv.) in the appropriate solvent. After stirring for 30 min the mixture was quenched with sat. aq. NH_4Cl and then submitted to extractive work-up with Et_2O. Flash chromatography of the crude (n-hexane : ethyl acetate) yielded the pure products.

Method B (in the presence of additives, Table 2, entries 3-5). To a 0.1 M solution of the additive in THF at -78°C, a 1.6 M hexane solution of *n*-BuLi was added. After 10 min stirring a 0.1 M THF solution of **1** was added dropwise. After further 2 h stirring the reaction was treated with sat. aq. NH_4Cl, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure.

Method C (Table 2, entries 7-8). To a 0.1 M solution of **1** in THF the Lewis acid (2.0 mol. equiv.) and *n*-BuLi (2.0 mol. equiv.) were added dropwise at -78°C in that order. After 30 min stirring the reaction was treated with satd. aqueous NH_4Cl, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. In the case of entry 8 only 1.5 mol. equiv. of the Lewis acid and of n-BuLi were used.

Method D (Table 2, entries 12, 19) $MgBr_2{\cdot}Et_2O$ (1.0 mol. equiv.) was added in one portion to a 0.1 M solution of **1** or **2** in CH_2Cl_2 at -78 °C. After 10 min stirring a 1.6 M hexane solution of *n*-BuLi (1.5 mol. equiv.) was added dropwise. After 10 min stirring a solution of organolithium compound was added. After further 30 min stirring the reaction was quenched with a saturated aqueous solution of NH_4Cl, the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure.

The diastereomeric ratios were determined in each case on the crude products by ^{1}H-NMR analysis. The crude products were purified by flash chromatography (hexane : AcOEt). For product ratios and yields see Table 2.

***(2R,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-hexane-2-ol (16a).** ^{1}H-NMR ($CDCl_3$): δ 0.7-1.1 (6H, m), 1.15-1.8 (9H), 2.5 (s, 3H), 3.45 (s, 1H, exchangeable), 4.12 (m, 1H), 4.25 (d, 1H, J = 5.5 Hz), 4.81 (s, 1H), 7-8 (9H). Anal. Calcd. for $C_{23}H_{31}NO_4S$: C, 66.16; H, 7.48; N, 3.35. Found: C, 66.07 H, 7.52; N, 3.30.

***(2S,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-hexane-2-ol (17a).** IR ($CHCl_3$): 3500, 3000, 1350, 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.7-1.1 (6H, m), 1.15-1.8 (9H), 2.5 (s, 3H), 4.0 (s, 1H, exchangeable), 4.15 (m, 1H), 4.28 (d, 1H, J = 6.0 Hz), 4.8 (s, 1H), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 14.2, 17.3, 22.8, 23.2, 23.4, 25.2, 36.1, 59.9, 80.3, 97.0, 125.7, 128.0, 128.3, 130.1. Anal. Calcd. for $C_{23}H_{31}NO_4S$: C, 66.16; H, 7.48; N, 3.35. Found: C, 66.10 H, 7.39; N, 3.32.

***(2R,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-heptane-2-ol (16b)** ^{1}H-NMR ($CDCl_3$): δ 0.7-1.0 (6H, m), 1.1-1.8 (11H), 2.5 (s, 3H), 3.48 (s, 1H, exchangeable), 4.13 (m, 1H), 4.32 (d, 1H, J = 6 Hz), 4.8 (s, 1H), 7-8 (m, 9H, aromatics). Anal. Calcd. for $C_{24}H_{33}NO_4S$: C, 66.79; H, 7.71; N, 3.25. Found: C, 66.84 H, 7.75 N, 3.36.

***(2S,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-heptane-2-ol (17b).** ^{1}H-NMR ($CDCl_3$): δ 0.7-1.0 (6H, m), 1.1-1.8 (11H), 2.5 (s, 3H), 3.93 (s, 1H, exchangeable), 4.11 (m, 1H), 4.25 (d, 1H, J = 6.0 Hz), 4.8 (s, 1H), 7-8 (9H); ^{13}C-NMR ($CDCl_3$): δ 14.0, 17.3, 21.5, 22.2, 22.5, 29.5, 31.8, 32.4, 39.0, 59.8, 80.3, 95.9, 125.7, 127.9, 127.9, 128.2, 130.1. Anal. Calcd. for $C_{24}H_{33}NO_4S$: C, 66.79; H, 7.71; N, 3.25. Found: C, 66.85 H, 7.75 N, 3.30.

***(2R,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-but-3-en-2-ol (16c).** ^{1}H-NMR ($CDCl_3$): δ 0.82 (d, 3H, J = 6.0 Hz), 1.47 (s, 3H), 2.5 (s, 3H), 4.1 (m, 1H), 4.2 (s, 1H, exchangeable), 4.27 (d, 1H, J = 5.0 Hz), 4.88 (s, 1H), 5.3 (dd, 1H, J = 12.0 and 1.0 Hz), 5.5 (dd, 1H, J = 16.0 and 1.0 Hz), 6.15 (dd, 1H, J = 16.0 and 1.0 Hz), 7-8 (9H). Anal. Calcd. for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61. Found: C, 65.15 H, 6.43 N, 3.53.

***(2S,2'S,4'S,5'R)*-2-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-but-3-en-2-ol (17c).** ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, J = 6.0 Hz), 1.47 (s, 3H), 2.5 (s, 3H), 4-4.3 (3H, 1H is exchangeable), 4.81 (s, 1H), 5.24 (dd, 1H, J = 12.0 and 1.0 Hz), 5.58 (dd, 1H, J = 14.0 and 1.0 Hz), 6.11 (dd, 1H, J = 14.0 and 1.0 Hz.), 7-8 (9H); -^{13}C-NMR ($CDCl_3$): δ 17.4, 21.6, 24.6, 59.8, 80.5, 96.0, 114.8, 125.8, 128.0, 128.0, 128.1, 129.7, 140.2. Anal. Calcd. for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.61. Found: C, 65.13; H, 6.43 N, 3.55.

***(1S,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-1-phenyl-pentan-1-ol (16d).** ^{1}H-NMR ($CDCl_3$): δ -0.24 (d, 3H), 2.5 (s, 3H), 3.8 (m, 1H), 4.1 (d, 1H, J = 5.6 Hz), 5.0 (s, 1H), 5.1 (s, 1H), 7-8 (m, 9H, aromatics). Anal. Calcd. for $C_{28}H_{33}NO_4S$: C, 70.12; H, 6.93; N, 2.92. Found: C, 70.20; H, 7.00 N, 2.89.

***(1R,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-1-phenyl-pentan-1-ol (17d).** -^{1}H-NMR ($CDCl_3$): δ 0.05 (s, 3H), 2.4 (s, 3H), 4.12 (d, 1H, J = 5.2 Hz), 4.2 (d, 1H, J = 7.8 Hz), 4.3 (s,

1H), 4.9 (s, 1H), 7-8 (m, 9H, aromatics). Anal. Calcd. for $C_{28}H_{33}NO_4S$: C, 70.12; H, 6.93; N, 2.92. Found: C, 70.15; H, 6.90 N, 2.95.

***(1S,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-1-phenyl-ethanol (16e)** -^{1}H-NMR ($CDCl_3$): δ 0.85 (d, 3H, J = 6.5 Hz), 1.80 (s, 3H), 2.49 (s, 3H), 4.12 (m, 1H), 4.6 (s, 1H, exchangeable), 4.92 (s, 1H), 5.3 (s, 1H), 7-8 (m, 14H). Anal. Calcd. for $C_{25}H_{27}NO_4S$: C, 68.63; H, 6.22; N, 3.20. Found: C, 68.55; H, 6.20 N, 3.15.

***(1R,2'S,4'S,5'R)*-1-[4'-methyl-5'-phenyl-3'-(toluene-4''-sulfonyl)-oxazolidin-2'-yl]-1-phenyl-ethanol (17e)** -^{1}H-NMR ($CDCl_3$): δ -0.11 (d, 3H, J = 6.4 Hz), 1.81 (s, 3H), 2.5 (s, 3H), 3.9 (m, 1H), 4.12 (d, 1H, J = 6.5 Hz), 5.08 (s, 1H), 5.12 (s, 1H, exchangeable), 7-8 (14H). Anal. Calcd. for $C_{25}H_{27}NO_4S$: C, 68.63; H, 6.22; N, 3.20. Found: C, 68.50; H, 6.30; N, 3.25.

***(1'S,2''S,4''S,5''R)*-toluene-4-sulfonic acid 2'-hydroxy-2'-[4''-methyl-5''-phenyl-3''-toluene-4'''-sulfonyl)-oxazolidin-2''-yl]-propyl ester (18).** To a solution of **6b** (216.6 mg, 0.55 mmol) in CH_2Cl_2 (5 ml) were added at 0°C tosylchloride (156.9 mg, 0.825 mmol) triethylamine (100.2 mg, 0.99 mmol) and 4-dimethylaminopyridine (0.67 mg, 0.0055 mmol). After 1 h stirring the reaction was treated with a phosphate buffer solution, the organic layer was extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The crude was purified by flash-chromatography (hexane:AcOEt 8:2) affording 255 mg of **18** (85 %). ^{1}H-NMR ($CDCl_3$): δ 0.82 (d, 3H, J = 6.8 Hz), 1.3 (s, 3H), 2.3 (s, 3H), 2.5 (s, 3H), 4-4.3 (4H), 4.92 (s, 1H), 7-8 (13H). Anal. Calcd. for $C_{27}H_{31}NO_7S_2$: C, 59.43; H, 5.73; N, 2.57. Found: C, 59.50; H, 5.70; N, 2.60.

***(2S,4S,5R,1'S)*-4-methyl-2-(2'-methyl-oxiran-2-yl)-5-phenyl-3-(toluene-4''-sulfonyl)-oxazolidine (19).** To a solution of **18** (20.7 mg, 0.038 mmol) in THF was added DBU (9.83 mg, 0.064 mmol). After 1 h stirring the reaction was quenched with a phosphate buffer solution and the organic layers were extracted with Et_2O, dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude was purified by flash-chromatography (hexane:AcOEt 8:2) affording 12.6 mg of **19** (77 %). ^{1}H-NMR ($CDCl_3$): δ 0.88 (d, 3H, , J = 7.5 Hz), 1.5 (s, 3H), 2.5 (s, 3H), 2.75 (d, 1H, J = 5.0 Hz), 3.12 (d, 1H, J = 5.0 Hz), 4.1 (m, 1H), 4.3 (d, 1H, J = 6.0 Hz), 5.02 (s, 1H), 7-8 (9H); -^{13}C-NMR ($CDCl_3$) selected data: δ 14.1, 16.7, 51.7, 59.0, 81.2, 92.4, 126.0, 127.9, 128.3, 130.0.

Synthesis of 17b from 19. To a suspension of CuCN (13.3 mg, 0.148 mmol) in THF (0.2 ml) was added at -78°C under Ar atmosphere a 1.6 M solution of *n*-BuLi (0.185 ml, 0.296 mmol). After the addition the reaction temperature was let to reach -20°C in 30 min and then a solution of **19** (13.8 mg, 0.037 mmol) in THF (0.2 ml) was added dropwise. After 2 h stirring the reaction mixture was quenched with a NH_4Cl solution and the organic layer was extracted with Et_2O, dried over Na_2SO_4 and evaporated under reduced pressure. The crude oil was purified by flash-chromatography (hexane:AcOEt 9:1) affording 15.4 mg of **17b** (96 %). This material showed identical physico-chemical data as compound **17b** obtained from addition of *n*-PentLi to ketone **1** (see above).

Acknowledgement. Financial support by MURST-ITALY is gratefully acknowledged.

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(*Received in UK* 21 *October* 1996; *revised* 20 *November* 1996; *accepted* 21 *November* 1996)