Tetrahedron Vol. 44, No. 14, pp. 4645 to 4652, 1988
Printed in Great Britain.

0040-4020/88 $3.00+.00

DIASTEREOSELECTIVE NITRILE OXIDE CYCLOADDITIONS TO CHIRAL ALLYL ETHERS DERIVED FROM 1,1-DITHIO-3-BUTEN-2-OLS.

Rita Annunziata, Mauro Cinquini,* Franco Cozzi,*
and Laura Raimondi
Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università, Via C. Golgi 19, 20133 Milano, Italy.

(*Received in UK* 22 *April* 1988)

Summary. Highly diastereoselective cycloaddition of nitrile oxides to the title compounds gives masked polyfunctional products amenable to a variety of synthetic elaboration; an entry to enantiomerically pure derivatives is described.

4,5-Dihydroisoxazoles (Δ^2-isoxazolines), easily obtained by cycloaddition of nitrile oxides to alkenes,[1] are versatile synthons for the stereocontrolled preparation of various classes of highly functionalized acyclic compounds such as β-ketols, polyols and amino polyols.[2]

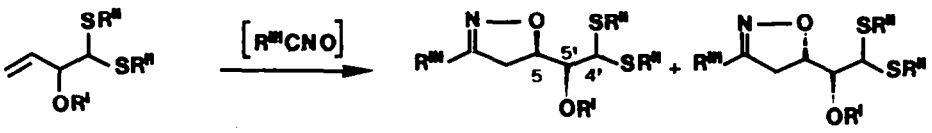
Chiral allyl ethers can be conveniently used to control simoultaneously the relative and absolute configuration of the stereocenters in the cycloadducts, both in intermolecular[3,4] and intramolecular reactions.[5] In particular it was shown that the level of stereoselection increases with increasing steric requirement of the alkyl substituent at the allyl stereocenter.[4] In this line we examined the cycloaddition of nitrile oxides to allyl derivatives (1-4) in which the bulkiness of the dithioacetals moiety should secure good stereoselectivity and afford products amenable to further synthetic elaboration.

Alkenes (1-4), easily prepared by condensation of acrolein with the corresponding formaldehyde dithioacetals,[6] and subsequent protection of the hydroxyl group, were reacted with various nitrile oxides (generated *in situ* following Huisgen procedure[1]) to give mixture of diastereoisomeric isoxazolines (5a,b-13a,b) (Scheme 1). As can be seen from the data reported in Table 1, chemical yields range from good to excellent, with the remarkable exception of entries F, H, and I.[§] More interestingly, the diastereoselection of the cycloaddition is constantly high and virtually independent of the bulkiness of the oxygen protecting group (entries A and B)** or of the sulphur substituent (entries B-D), and of the nature of the nitrile oxides (entries D-I).

[§] Nitrile oxide residues that mask oxygenated function as in (9),[2] (10),[7], (12),[2,3] and (13)[2,3] are particularly useful in sugar and aminosugar syntheses.

** It must be noted that a cycloaddition carried out on an un-protected alcohol (namely 1,1-diphenylthio-3-buten-2-ol) was poorly diastereoselective, affording a 68:32 ratio of *anti*:*syn* products as demonstrated by correlation with (6a,b).Nitrile oxide cycloadditions to chiral allyl alcohols generally feature low *syn* selectivity.[3,4]

Scheme 1.



(1-4) (5a-13a) (5b-13b)

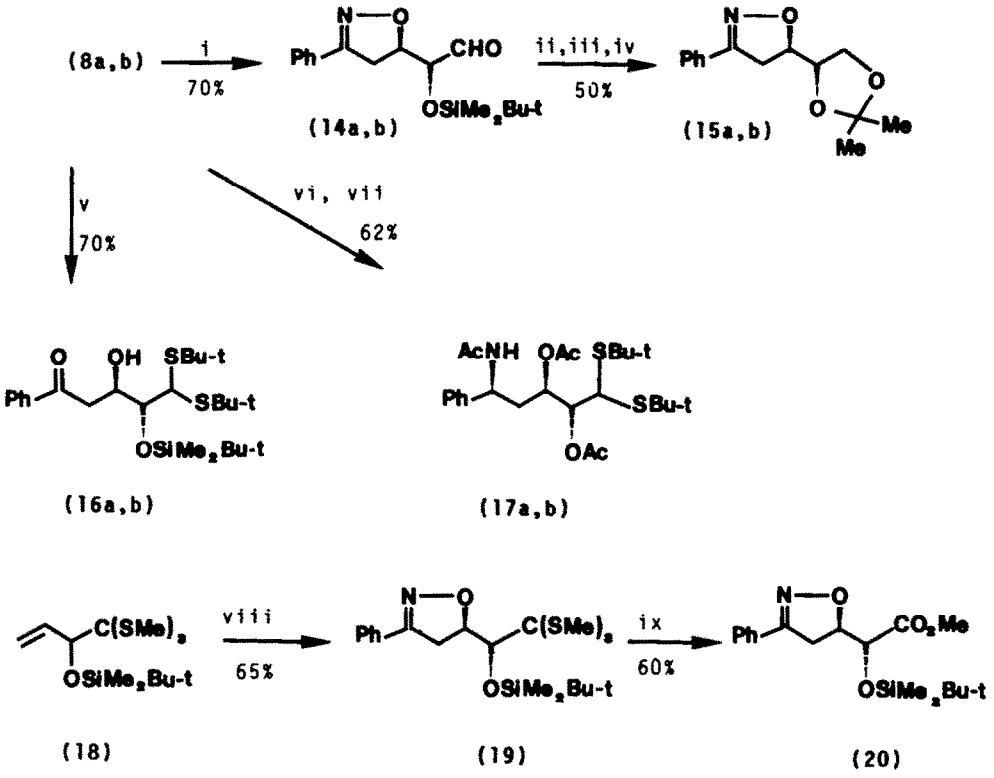
(1),	(5)	R' = CH_2Ph;	R'' = Ph;	R''' = Ph
(2),	(6)	R' = $SiMe_2But$;	R'' = Ph;	R''' = Ph
(3),	(7)	R' = $SiMe_2But$;	R'' = $-(CH_2)_3-$	R''' = Ph
(4),	(8)	R' = $SiMe_2But$;	R'' = But;	R''' = Ph
	(9)	R' = $SiMe_2But$;	R'' = But;	R''' = p-$MeOC_6H_4$
	(10)	R' = $SiMe_2But$;	R'' = But;	R''' = 2-thiazolyl
	(11)	R' = $SiMe_2But$;	R'' = But;	R''' = Me
	(12)	R' = $SiMe_2But$;	R'' = But;	R''' = COOEt
	(13)	R' = $SiMe_2But$;	R'' = But;	R''' = CH_2OCH_2Ph

Table 1. Synthesis of isoxazolines (5-13).

Entry	Compound	Yield %	Diastereoisomeric ratio a:b
A	(5a,b)	92	90:10
B	(6a,b)	87	91: 9
C	(7a,b)	78	91: 9
D	(8a,b)	98	92: 8
E	(9a,b)	60	89:11
F	(10a,b)	32	95: 5
G	(11a,b)	65	⩾98: 2
H	(12a,b)	26	94: 6
I	(13a,b)	25	⩾98: 2

Anti[8] isomers (5a-13a) always predominate on their syn[8] counterparts (5b-13b) as expected on the basis of experimental[3-5] and theoretical[4] results obtained for related reactions. The structural assignment resides on inspection of 300 MHz ^1H n.m.r. spectra and on chemical correlation. Indeed, in products (5a-13a) HC-5, HC-5', and HC-4'(Scheme 1 and Table 2) generally resonate at lower field with respect to the same protons of isomers (5b-13b), clearly showing that all the major diastereoisomers (and thus all the minor ones) feature the same relative configuration at C-5 and C-5'. Furthermore, the HC-5/HC-5' coupling constants values are constantly smaller for the predominant isomers, a trend already observed by Kozikowski for similar substrates.[3] As a further proof of the anti diastereoselectivity shared by these cycloadditions, compound (8a,b) was converted, via aldehyde (14a,b), into the known[3,4,9] derivative (15a,b) (Scheme 2).

Scheme 2.



Reagents: i, $HgCl_2$, $CaCO_3$, CH_3CN, H_2O, reflux, 4h; ii, $NaBH_4$, EtOH, RT, overnight; iii, $Bu_4N^+F^-$, THF, H_2O, RT, 2h; iv, $(MeO)_2CMe_2$, PTSA, RT, overnight; v, Ni-Ra, H_2, H_3BO_3, MeOH, H_2O, RT, overnight; vi, $LiAlH_4$, Et_2O, reflux, 36h; vii, Ac_2O, Et_3N, RT, overnight; viii, PhC(Cl)NOH, Et_3N, Et_2O, 0° ⟶ RT, overnight; ix, $HgCl_2$, HgO, CH_3OH, H_2O, reflux, 4h.
For compounds (14-17) only major diastereoisomers indicated.

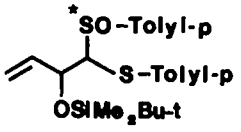
The stereochemical outcome of the cycloaddition can be nicely rationalized in terms of the proposed transition structure ruled by the "inside alkoxy effect".[4]

Some of the synthetic opportunities offered by products such as (5-13) are illustrated by the transformations of isoxazoline (8a,b), chosen as a model compound, reported in Scheme 2.

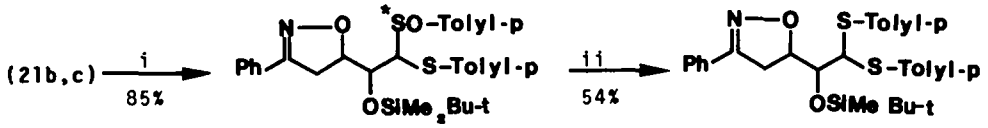
Selective un-masking of the aldehyde group (14a,b),[10] or of the β-ketol moiety (16a,b)[11] is achieved in 70% yield without epimerization at the stereocenters. The γ-aminoalcohol function embedded in the heterocyclic ring is delivered by $LiAlH_4$ reduction, a reaction known[2] to proceed in an extremely stereoselective fashion. Indeed, acetylation of the crude reduction mixture and subsequent flash chromatography allows the isolation of the diastereoisomerically pure product indicated in Scheme 2, together with trace amounts (17a:17b=97:3) of another unidentified isomer. For sake of completeness the cycloaddition of benzonitrile oxide to alkene (18) was also studied: isoxazoline (19) was isolated as the only product, from which highly functionalized ester (20) was obtained[12] in good yield.

Finally, access to enantiomerically pure derivatives was also achieved (Scheme 3). Compound (S_S)-(21a,b,c,d) was obtained as 17(a):58(b):12(c): 13(d) (elution order) mixture of isomers from enantiomerically pure (+)-(S)-*p*-tolyl-*p*-tolylthiomethyl sulphoxide.[13] Isomers (21b,c), for which n.O.e. experiments suggested the same configuration at the allylic stereocenter, when reacted with benzonitrile oxide, gave a mixture of diastereoisomeric products (22) from which, after sulphoxide deoxygenation,[14] isoxazoline (23a,b) was obtained in 91:9 anti:syn ratio. The major product was shown to be enantiomerically pure by 300 MHz ^1H n.m.r. analysis carried out in the presence of $Eu(hfc)_3$ in condition pre-established on racemic (23).

Scheme 3.



(S_S)-(21a,b,c,d)



(22) (23a,b)

Reagents: i, PhC(Cl)NOH, Et_3N, Et_2O, 0° ⟶ RT, overnight; ii, NaI, Me_3SiCl, CH_3CN, RT, 1h.

Experimental

Infrared spectra were recorded on a Perkin-Elmer 247 instrument. ^{1}H and ^{13}C NMR spectra were obtained on Varian EM 390 and Varian XL-300 spectrometer in $CDCl_3$ as solvent. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Elemental analyses were performed with a Perkin-Elmer 240 instrument. Silica gel was used for analytical and flash chromatography. Organic extracts were dried over Na_2SO_4 and filtered before removal of the solvent under reduced pressure. All reactions employing dry solvents were run under Argon.

General procedure for the synthesis of ethers (1-4) and (8). To a stirred solution of dithioacetal (1 mmol) in THF (10 ml) cooled at -30°C, n-BuLi (1.3 M solution in hexanes, 1.13 mmol) was added dropwise: after 1 h stirring, the mixture was cooled down to -78°C and acrolein (3 mmol) was added as such in one portion. After 2 min the reaction was quenched with a saturated aqueous solution of NH_4Cl and worked-up in the usual way. The crude alcohols were purified by flash chromatography with diethylether-hexanes mixtures. Conversions to the t-butyldimethylsilylethers[15] and to the benzylether[16] were performed as described, the products were purified by flash chromatography with a 95:5 hexanes: diethylether mixture as eluant.

Compound (1). Found: C% 72.78; H% 5.90. $C_{23}H_{22}OS_2$ requires: C% 72.97; H% 5.86. ^{1}H NMR: δ 7.10-7.50 (m, 15H); 5.90-6.40 (m, 1H); 5.25-5.50 (m, 2H); 4.50-4.85 (m, 3H); 4.10-4.25 (m, 1H). Overall yield 50%. n_D^{22} = 1.5810.

Compound (2). Found: C% 65.42; H% 7.50. $C_{22}H_{30}OS_2Si$ requires: C% 65.62; H% 7.51. ^{1}H NMR: δ 7.10-7.50 (m, 10H); 5.90-6.35 (m, 1H); 5.15-5.40 (m, 2H); 4.45-4.60 (m, 2H); 0.95 (s, 9H); 0.00 and -0.05 (2s, 6H). Overall yield 71%. n_D^{22} = 1.5560.

Compound (3). Found: C% 53.96; H% 8.94. $C_{13}H_{26}OS_2Si$ requires: C% 53.74; H% 9.02. ^{1}H NMR: δ 5.45-5.90 (m, 1H); 4.85-5.10 (m, 2H); 3.85-4.05 (m, 1H); 3.75 (d, J = 6 Hz, 1H); 2.55-2.70 (m, 4H); 1.60-2.00 (m, 2H); 0.80 (s, 9H); -0.05 and -0.10 (2s, 6H). Overall yield 60%. n_D^{26} = 1.5128.

Compound (4). Found: C% 59.41; H% 10.64. $C_{18}H_{38}OS_2Si$ requires: C% 59.60; H% 10.56. ^{1}H NMR: δ 5.65-6.10 (m, 1H); 4.85-5.15 (m, 2H); 4.15-4.35 (m, 1H); 3.70 (d, J = 4.5 Hz, 1H); 1.25 (s, 18H); 0.75 (s, 9H); -0.05 and -0.10 (2s, 6H). Overall yield 60%. n_D^{27} = 1.4790.

Compound (18) was similarly prepared from acrolein and tris(methylthio)methane at -70°C and subsequent reaction with t-butyldimethylsilylchloride. Found: C% 48.41; H% 8.72. $C_{13}H_{28}OS_3Si$ requires: C% 48.10; H% 8.69. ^{1}H NMR: δ 6.05-6.40 (m, 1H); 5.10-5.35 (m, 2H); 4.20 (d, J = 7 Hz, 1H); 2.15 (s, 9H); 0.90 (s, 9H); 0.00 and -0.05 (2s, 6H). Overall yield 59%. n_D^{18} = 1.5096.

General procedure for the synthesis of isoxazolines (5)-(13),(19). To a stirred solution of allyl ether (1 mmol) and hydroxymoyl chloride (3 mmol) in diethylether for (5)-(9),(19) or chloroform for (10)-(13) (20 ml) cooled at 0°C, triethylamine (3 mmol) in the same solvent (5 ml) was added dropwise over a 10 min period. After 1h external cooling was removed and the mixture stirred overnight at room temperature. Water was then added, the aqueous phase separated, extracted twice with the organic solvent, and the combined organic extracts dried. The products were purified by flash chromatography with the indicated hexanes:diethylether eluting mixtures. For compounds (5)-(13) yields and diastereoisomeric ratios are collected in Table 1; relevant NMR data in Table 2.

Isoxazoline (5). Eluting mixture 80:20. Found: C% 72.21; H% 5.50; N% 2.83. $C_{30}H_{27}NO_2S_2$ requires: C% 72.40; H% 5.47; N% 2.81. n_D^{27} = 1.6249.

Isoxazoline (6). Eluting mixture 85:15. Found: C% 66.66; H% 6.71; N% 2.69. $C_{29}H_{35}NO_2S_2Si$ requires: C% 66.75; H% 6.76; N% 2.68. n_D^{25} = 1.5881.

Isoxazoline (7). Eluting mixture 90:10. Found: C% 58.78; H% 7.59; N% 3.40. $C_{20}H_{31}NO_2S_2Si$ requires: C% 58.63; H% 7.63: N% 3.42. n_D^{26} = 1.5617.

Isoxazoline (8). Eluting mixture 95:5. Found: C% 62.21; H% 8.88; N% 2.93. $C_{25}H_{43}NO_2S_2Si$ requires: C% 62.31; H% 9.00; N% 2.91. n_D^{26} = 1.5295.

Isoxazoline (9). Eluting mixture 80:20. Found: C% 60.81; H% 8.90; N% 2.77. $C_{26}H_{45}NO_3S_2Si$ requires: C% 61.01; H% 8.86; N% 2.74. n_D^{20} = 1.5700.

Isoxazoline (10). Eluting mixture 80:20. Found: C% 53.91; H% 8.32; N% 5.70. $C_{22}H_{40}N_2O_2S_3Si$ requires: C% 54.05; H% 8.25; N% 5.73. M.p. of (10a): 100-102°C.

Isoxazoline (11). Eluting mixture 80:20. Found: C% 57.04; H% 9.91; N% 3.36. $C_{20}H_{41}NO_2S_2Si$ requires: C% 57.22; H% 9.85; N% 3.38. n_D^{26} = 1.5855.

Isoxazoline (12). Eluting mixture 90:10. Found:C% 55.01; H% 9.15; N% 2.96.

$C_{22}H_{43}NO_4S_2Si$ requires: C% 55.30; H% 9.07; N% 2.93. M.p. of (12a) 64-66°C.
Isoxazoline (13). Eluting mixture 80:20. Found: C% 61.14; H% 9.10; N% 2.64. $C_{27}H_{47}NO_3S_2Si$ requires: C% 61.66; H% 9.01; N% 2.66. n_D^{24} = 1.5220.
Isoxazoline (19). Eluting mixture 90:10. Found: C% 54.36; H% 7.58; N% 3.15. $C_{20}H_{33}NO_2S_2Si$ requires: C% 54.13; H% 7.50; N% 3.16. M.p. 79-80°C. Yield 65%. ^{1}H NMR: δ 7.33-7.66 (m, 5H); 5.49 (t, J = 11.4 Hz, 1H); 4.43 (s, 1H); 3.42-3.63 (m, 2H); 2.20 (s, 9H); 0.87 (s, 9H); 0.23 and 0.00 (2s, 6H).
Synthesis of aldehyde (14). This product was obtained in 70% yield from (8a,b) (1 mmol) following the described procedure;[10] it was purified by flash chromatography with a 1:1 hexanes:diethylether mixture as eluant. Found: C% 64.01; H% 7.80; N% 4.34. $C_{17}H_{25}NO_3Si$ requires: C% 63.90; H% 7.89; N% 4.38. n_D^{28} = 1.5232. ^{1}H NMR of (14a): δ 9.73 (s, 1H); 7.33-7.66 (m, 5H); 4.99-5.06 (m, 1H); 4.41 (d, J = 2.9 Hz, 1H); 3.33 (ddd, J = 6.6, 7.2, 10.7, 2H); 0.92 (s, 9H); 0.06 and 0.12 (2s, 6H).
Synthesis of isoxazoline (15). This product was obtained in three steps from (14). The aldehyde (0.05 mmol, 0.160 g) was reduced with $NaBH_4$ (1 mmol, 0.038g) in absolute EtOH (5 ml) at room temperature overnight. Usual work-up afforded the crude alcohol that was treated with $Bu_4N^+F^-.3H_2O$ (3 mmol, 0.945g) in THF (10 ml) for 2h at room temperature. The reaction mixture was filtered through a short column of silica gel (diethylether as eluant) and the organic solvents evaporated under vacuum. The oily residue was dissolved in 2,2-dimethoxy propane and a catalytic amount of PTSA was added. After overnight stirring at room temperature and usual work-up, isoxazoline (15a,b) (0.25 mmol, 0.100g) was obtained by flash chromatography as described.[9] Overall yield 50%. (15a): m.p. 69-70°C; (15b): m.p. 74-75°C.

Table 2. Relevant NMR data for isoxazolines (5)-(13).

	HC-5	HC-5'	HC-4'	J 5-5'	J 5'-4'
(5a)	5.21	4.06	4.88	5.9	2.4
(5b)	5.19	3.97	4.71	7.0	3.0
(6a)	5.19	4.33	4.65	3.9	2.6
(6b)	5.00	4.22	4.48	6.8	1.5
(7a)	4.99	4.23	4.23	1.6	-[a]
(7b)	4.88	3.92	4.31	6.4	2.8
(8a)	5.07	4.21	4.24	4.9	2.0
(8b)	4.85	4.27	4.18	7.5	1.0
(9a)	5.02	4.17	4.27	5.3	2.0
(9b)	4.85	4.25	4.18	7.3	1.5
(10a)	5.17	4.28	4.14	4.0	2.3
(10b)	5.03	4.21	4.11	8.0	1.2
(11a)	4.84	4.10	4.15	4.9	2.0
(12a)	5.16	4.24	4.08	4.0	2.5
(12b)	4.97	4.17	4.04	6.5	1.6
(13a)	4.91	4.12	4.19	5.3	2.0

[a] Undetermined because of peak overlap.

Synthesis of β-ketol (16). A mixture of isoxazoline (8) (0.7 mmol, 0.330g), boric acid (1.4 mmol, 0.087g), W-4 Raney nickel (1.5g wet material) in 21 ml of a 6:1 MeOH/H_2O solution was shaken under H_2 atmosphere for 18h at room temperature.[11,12] The reaction mixture was filtered through a celite pad, concentrated in vacuum, and purified by flash chromatography with a 9:1 hexanes :diethylether mixture as eluant to give (16), m.p. 73-74°C, in 70% yield. Found: C% 61.71; H% 9.05. $C_{25}H_{44}O_3S_2Si$ requires: C% 61.93; H% 9.15. ^{1}H NMR of (16a): δ 7.43-7.93 (m, 5H); 4.55 (d, J = 1 Hz, 1H); 4.36-4.45 (m, 1H); 4.06 (dd, J = 1, 7.5 Hz, 1H); 3.69 (bs, 1H); 3.30 (ABX system, J = 2.3, 9, 18 Hz, 2H); 1.43 (s, 18H); 0.97 (s, 9H); 0.33 and 0.18 (2s, 6H).

Synthesis of triacetylderivative (17). To a refluxing stirred solution of (8) (1.5 mmol, 0.720g) in diethylether (50 ml), $LiAlH_4$ (12 mmol, 0.460 g) was added portionwise, and the reaction stirred for 36h. Usual work-up gave the crude aminoalcohol that was treated with excess acetic anhydride and triethylamine in dichloromethane at room temperature overnight. The reaction mixture was poured into water, extracted twice with dichloromethane, the organic phase washed with dilute hydrochloric acid and water. Evaporation of the solvent gave the crude product that was purified by flash chromatography with a 2:1 diethylether:ethylacetate mixture as eluant to give compound (17a) (0.93 mmol, 0.463 g), m.p. 139-140°C, in 62% yield, along with trace amounts of an unidentified isomer (17b). Found: C% 60.00; H% 7.98; N% 2.84. $C_{25}H_{39}NO_5S_2$ requires: C% 60.33; H% 7.90; N% 2.81. ^{1}H NMR: δ 7.27-7.33 (m, 5H); 6.53 (bd, 1H); 5.47 (dd, J = 2.4, 7.3 Hz, 1H); 5.09 (dt, J = 5.5, 7.1 Hz, 1H); 4.98 (dd, J = 7.0, 8.2 Hz, 1H); 4.16 (d, J = 2.5 Hz, 1H); 2.27-2.38 (m, 2H); 2.20, 2.01, 2.00 (3s, 9H); 1.36, 1.32 (2s, 18H).

Synthesis of isoxazoline (20). A suspension of (19) (0.23 mmol, 0.100 g), HgO (0.4 mmol, 0.087 g), $HgCl_2$ (1.12 mmol, 0.280 g) in MeOH:water 12:1 (13 ml) was refluxed for 4h. The described work-up followed by flash chromatography with a 7:3 hexanes:diethylether mixture as eluant, gave the product, n_D^{28} = 1.5111, (0.048 g) in 60% yield. Found: C% 61.48; H% 7.71; N% 3.97. $C_{18}H_{27}NO_4Si$ requires: C% 61.86; H% 7.79; N% 4.01. ^{1}H NMR: δ 7.37-7.66 (m, 5H); 5.04 (ddd, J = 2.6, 7.0, 9.6 Hz, 1H); 4.56 (d, J = 2.7 Hz, 1H); 3.77 (s, 3H); 3.20-3.50 (m, 2H); 0.83 (s, 9H); 0.10, 0.07 (2s, 6H).

Synthesis of allylether (21). This product was prepared in 60% yield by condensation of (+)-(S)-p-tolyl-p-tolylthiomethyl sulphoxide with acrolein, according to the literature procedure,[13] and reaction with t-butyldimethylsilyl-chloride of the diastereoisomeric mixture. Purification by flash chromatography with a 80:20 hexanes:diethylether mixture as eluant allowed the isolation of (21a), $[\alpha]_D^{22}$ = -103.2 (c 1.2, $CHCl_3$), (21b,c), $[\alpha]_D^{22}$ = +109.3 (c 1, $CHCl_3$), and (21d), $[\alpha]_D^{22}$ = +88.4 (c 0.9, $CHCl_3$). The elemental analysis was performed on (21b,c). Found: C% 64.83; H% 7.59. $C_{24}H_{34}O_2S_2Si$ requires: C% 64.52; H% 7.67. (21b,c) was shown by ^{1}H NMR to be a 4.8:1 mixture of diastereoisomers. ^{1}H NMR: δ 6.80-7.55 (m, 8H); 6.00-6.32 (m, 1H); 5.27-5.55 (m, 2H); 4.98-5.02, major, and 4.54-4.61, minor (m, 1H); 4.0 major, and 3.82, minor (d, J = 3.7 and 4.6, respectively, 1H); 2.38, minor and 2.33, major (2s, 3H); 2.25, minor and 2.23, major (2s, 3H); 0.90 (s, 9H); 0.11 (s, 6H). ^{1}H NMR data for olefins (21a,b,c,d) gave hints for tentative configurational assignment; indeed, with (21a) and (21c) irradiation of HC-3 caused n.O.e.'s (6%) with HC-1 for both compounds, and with HC-2 (7%) only for (21a); this suggested that HC-3 and HC-1 are on the same side of the molecule and that the configuration at C-2 changes from (21a) to (21c). On irradiation of HC-3 in (21b) and (21d) no n.O.e. effect was observed on HC-1, while irradiation of HC-2 revealed n.O.e. with (21b) HC-3 (8%) and with (21d) HC-1 (5%); thus in (21b) and (21d) HC-1 and HC-3 should be on opposite sides and the configuration at C-2 changes on passing from (21b) to (21d). The possibility that (21b,c) have the same configuration at C-2 was confirmed by the e.e. determination on (23a) (see below).

Synthesis of isoxazoline (23). This product was prepared in two steps by reaction of (21b,c) with benzhydroxymoyl chloride as described above to give (22) (purified by flash chromatography with a 70:30 hexanes:diethylether mixture as eluant, 85% yield), followed by deoxygenation.[14] The crude product was purified by flash chromatography (90:10 hexanes:diethylether) to give (23a,b) as a 91:9 mixture of isomers in 54% yield. Found: C% 67.46; H% 7.10; N% 2.51. $C_{31}H_{39}NO_2S_2Si$ requires: C% 67.71; H% 7.15; N% 2.55. For (23a,b): $[\alpha]_D^{22}$ = -40.3 (c 1.4, $CHCl_3$). ^{1}H NMR: δ 7.00-7.73 (m, 13H), 5.16, major (ddd, J = 3.6, 7.0, 9.7 Hz) and 4.96, minor (m), (overall 1H); 4.45, major (d, J = 2.7 Hz) and 4.44, minor (d), (overall 1H); 4.28-4.30 (m, 1H); 3.16-3.68 (m, 2H); 2.33, major and 2.29, minor (2s) (overall 3H); 2.32, major and 2.28, minor (2s) (overall 3H). (23a) was shown to be enantiomerically pure by ^{1}H NMR analysis in the presence of $Eu(hfc)_3$ in condition pre-established on racemic (23); this confirms that (21b,c) feature the same configuration at C-2.

Acknowledgements. Partial financial support by Ministero Pubblica Istruzione - Roma is gratefully acknowledged.

References.

1) P. Caramella and P. Grünanger, in "1,3-Dipolar Cycloaddition Chemistry"; A. Padva Ed.; Wiley-Interscience: New York, 1984; Vol. 1, pp. 291-392.

2) V. Jäger, I. Muller, R. Schohe, M. Frey, E. Ehrler, B. Häfele, and D. Schröter, Lect. Heterocycl. Chem., 1985, 8, 79; A.P. Kozikowski, Acc. Chem. Res., 1984, 17, 410.

3) A.P. Kozikowski and A.K. Ghosh, J. Org. Chem., 1984, 49, 2762; V. Jäger and R. Schohe, Tetrahedron, 1984, 40, 2199.

4) K.N. Houk, S.R. Moses, Y.D. Wu, N.G. Rondan, V. Jäger, R. Schohe, and F.R. Fronczek, J. Am. Chem. Soc., 1984, 106, 3880; K.N. Houk, H.Y. Duh, Y.D. Wu, and S.R. Moses, J. Am. Chem. Soc., 1986, 108, 2754.

5) R. Annunziata, M. Cinquini, F. Cozzi, and L. Raimondi, J. Chem. Soc., Chem. Commun., 1987, 529; R. Annunziata, M. Cinquini, F. Cozzi, C. Gennari, and L. Raimondi, J. Org. Chem., 1987, 52, 4674; R. Annunziata, M. Cinquini, F. Cozzi, G. Dondio, and L. Raimondi, Tetrahedron, 1987, 43, 2369.

6) E.J. Corey and D. Seebach, Angew. Chem., Ind. Ed. Engl., 1965, 4, 1075.

7) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, Synthesis, 1987, 998.

8) S. Masamune, S.A. Ali, D.L. Snitman, and D.S. Garvey, Angew. Chem. Int. Ed. Engl., 1980, 19, 557.

9) R. Annunziata, M. Cinquini, F. Cozzi, L. Raimondi, and A. Restelli, Helv. Chim. Acta, 1985, 68, 1217.

10) E.J. Corey and B.W. Erickson, J. Org. Chem., 1971, 36, 3553.

11) D.P. Curran, J. Am. Chem. Soc., 1983, 105, 5826.

12) R.A. Ellison, W.D. Woessner, and C.C. Williams, J. Org. Chem., 1972, 37, 2757.

13) L. Colombo, C. Gennari, C. Scolastico, G. Guanti, and E. Narisano, J. Chem. Soc., Perkin Trans. I, 1981, 1278.

14) G.A. Olah, S.C. Narang, B.G.B. Gupta, and R. Malhotra, Synthesis, 1979, 61.

15) E.J. Corey and A. Venkateswarlu, J. Am. Chem. Soc., 1972, 94, 6190.

16) S.Czernecki, C. Georgoulis, and C. Provelenghiou, Tetrahedron Lett., 1976, 3535.