The regio- and stereo-chemistry of 1,3-dipolar cycloaddition of a chiral methylenenitrone to 1,2-disubstituted alkenes

Shaikh A. Ali* and Muhammad Z.N. Iman

Chemistry Department, King Fahd University of Petroleum and Minerals, Dhahran 31261, Saudi Arabia

A study of regio- and stereo-selectivity in the cycloaddition reactions of a series of symmetrical and unsymmetrical 1,2-disubstituted alkenes to the chiral, internally H-bonded *N*-(2-hydroxy-1-phenyl)methylenenitrone, has been carried out. The regioselectivity observed in the addition reactions is explained in terms of frontier orbital interactions. The alkenes having a hydroxymethyl substituent at the allylic position are found to undergo regio- as well as highly stereo-selective cycloaddition reactions in the presence of anhydrous magnesium bromide.

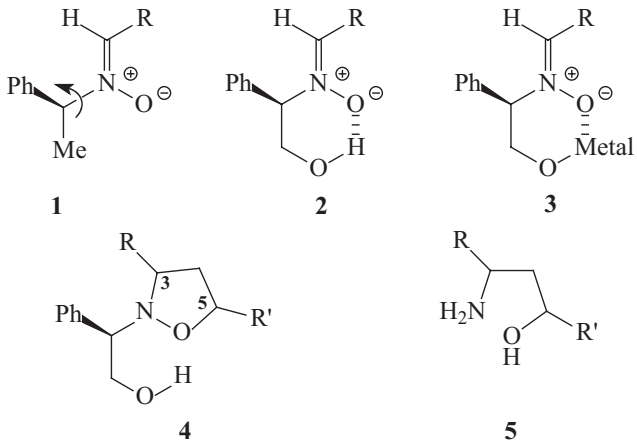
Keywords: dipolar cycloddition, asymmetric induction, Lewis acid catalyst, diastereoselection, chiral methylenenitrone

The nitrone-alkene cycloaddition reaction is the best method for constructing isoxazolidines in high yields.[1,2] Remarkable regio-, stereo-, face- and chemo-selectivity along with efficient incorporation of multiple stereocentres in a single step have made nitrone cycloaddition a powerful tool in organic synthesis. In recent years, asymmetric nitrone cycloaddition reactions[3-7] leading to optically active isoxazolidines have received considerable attention and have been reviewed by various authors.[8-13] A cyclic nitrone having a chirogenic centre embedded in the ring skeleton allows an alkene to approach the energetically favourable face of the nitrone. Even though a chiral acyclic nitrone (*e.g.* **1**) could allow an approaching alkene to choose between the faces, poor stereoselectivity is observed[14] in its cycloadditions and this has been attributed to its conformational flexibility by virtue of easy N–C bond rotation (Scheme 1). However, the conformational mobility is somewhat or completely arrested in the intramolecularly H-bonded *(R)*-chiral nitrone **2** or its tightly metal-chelated form **3**. As a result, the nitrone **2** is receiving increasing attention owing to its efficacy in transferring chirality to the newly created stereocentres of the resulting isoxazolidines in intramolecular[15,16] (having R containing an alkene moiety), as well as intermolecular[15,17] (R = H, alkyl) cycloaddition reactions. Another important advantage that is bound to make the nitrone **2** a very popular reactant, is the facile reductive cleavage of the chiral auxiliary as well as N–O bond of the isoxazolidine **4** thereby providing simple and efficient access to a variety of synthetically important chiral 1,3-aminoalcohols **5.**

Although the nitrone cycloaddition reactions of *C,N*-disubstituted nitrones with various kind of alkenes have been studied in great detail,[1,2] the chemistry of *N*-substituted nitrones (*i.e.* methylenenitrones) with mono- and 1,1-disubstituited alkenes has only been investigated to a limited extent.[15,17,18-21] The reactions involving methylenenitrones and 1,2-disubstituted alkenes are scarcely even mentioned in the literature.[19] Most recently, we have reported[17] a systematic study detailing the regio- and stereo-chemical features associated with the cycloaddition of the chiral methylenenitrone **2** (R = H) to a series of mono- and 1,1-disubstituted alkenes. In our continuing study involving methylenenitrones we report herein the cycloaddition of chiral methylenenitrone **2** (R = H) to *trans* and *cis*-1,2-disubstituted alkenes [(7) and (12) respectively] so as to provide a composite picture that reflects the scope and limitations associated with the addition reactions of the methylenenitrone.

Results and discussion

The stereochemical details of the addition of nitrone **2** to several *trans*-alkenes (**7**) (Scheme 2) along with the reaction



Scheme 1

temperatures, isolated yield, and composition of the isomeric cycloadducts are given in Table 1.

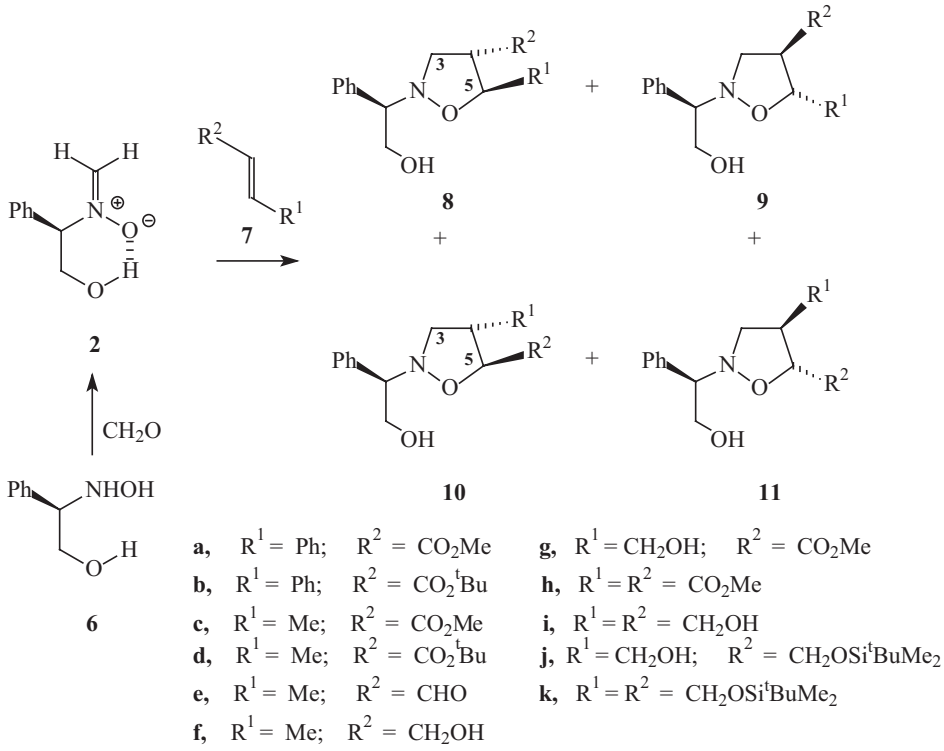
While the reaction of nitrone **2** with methyl cinnamate (**7a**) gave a mixture of isomers **8a**–**11a** in a ratio of 73 : 8 : 13:6, the

Table 1 Regio- and stereo-chemistry of the cycloaddition[a,b] of the nitrone **2** to *trans*-disubstituted alkenes **7**

Alkene **7**	Temp /°C	Time /h	Lewis Acid	Isolated yields/%	Isomeric ratio **(8:9:10:11)**
a	90	8	None	87	73:8:13:6
b	90	8	None	85	76:7:12:5
c	90	8	None	84	57:9:18:16
	80	12	$BF_3.OEt_2$	60	59:13:15:13
	80	12	$ZnCl_2$	65	58:14:17:11
d	90	8	None	82	53:9:22:16
e	85	6	None	90	32:26:19:23
f	90	8	None	89	38:7:45:10
	65	48	$MgBr_2$	96	0: 0: 9:91
g	90	8	None	79	50:13:30:7
	65	48	$MgBr_2$	76	19:81:0:0
h	65	12	None	91	**(8h = 10h)/ (9h = 11h)** 70:30
i	105	12	None	92	**(8i = 10i)/ (9i = 11i)** 80:20
	65	36	$MgBr_2$	74	6:94
j	105	12	None	89	56:24:13:7
	65	36	$MgBr_2$	88	4:96:0:0
k	105	12	None	73	**(8a = 10k)/ (9k = 11k)** 75:25

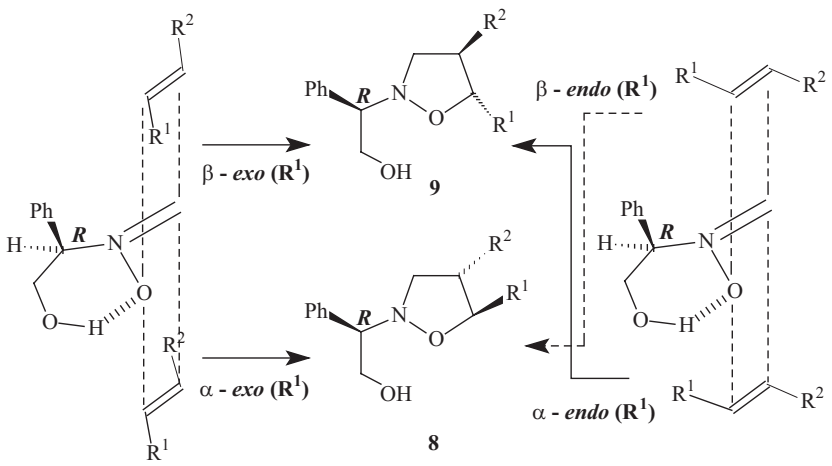
[a]In toluene in the absence of Lewis acid catalyst. [b]In the presence of one equivalent of Lewis acid in CH_2Cl_2 except for the addition reaction of alkene **7c** in toluene.

* Correspondent. E-mail: shaikh@kfupm.edu.sa



Scheme 2

addition of *t*-butyl cinnamate (**7b**) afforded adducts **8b–11b** in a ratio of 76 : 7 : 12 : 5, respectively. The stereochemistry of the *t*-butyl cinnamate adducts **8b–11b** was correlated with the methyl cinnamate adducts **8a–11a** by ester exchange with methanol/HCl. The structures of the regioisomers were assigned on the basis of characteristic chemical shifts of C(5)Hs (Experimental). The nitrone **2** is expected to be internally H-bonded as shown in Scheme 3. This would place the phenyl group on the β-face of the nitrone, while the H on the stereocentre remains on the α-face. While both the 'α-*exo* (R^1 = Ph) approach' (*i.e.* the approach of the alkene with *exo*-oriented R^1 group toward the α-face of the nitrone) and 'β-*endo* (R^1) approach' of the alkene would lead to the same diastereomer **8**, the 'α-*endo* (R^1)' and 'β-*exo* (R^1)' approaches give the other diastereomer **9**. The face selectivity in the addition reaction of methylene-nitrones, such as **2**, cannot be determined since, for instance, the formation of the diastereomer **8** is the combined outcome of the approach of the alkene to both faces of the nitrone. Likewise, the stereoselectivity in each face (*exo*/*endo* ratio) cannot be determined, since each diastereomer can be obtained by both the *exo* and *endo* mode of attack. This problem does not arise in the case of *N,C*-disubstituted chiral nitrones, since their regioselective addition reactions with disubstituted alkenes would create four chiral centres, and as such, each of the approaches would generate a different diastereomer, thus allowing the determination of face selectivity as well as stereoselectivity of each face. For the current nitrone **2**, it can be presumed that the α-face of the nitrone will be preferentially attacked, and the steric interactions would then dictate the *exo* (R^1 = Ph) mode of approach while the secondary orbital interactions would augment the stereoselection by allowing CO_2R (*i.e.* R^2) *endo*-oriented in the transition state. In line with this reasoning, the *trans*-cinnamate cycloadditions resulted in the formation of major adduct **8a** and **8b** predominantly *via* 'α-*exo* (R^1)



Scheme 3

approach', while its minor stereoisomer **9a** and **9b** is the product of 'α-*endo* (R^1) approach'. For the formation of the corresponding regiosomers **10** and **11**, the Scheme 3 has to be modified with the positions of R^1 and R^2 reversed. In the cinnamate additions, the major regioisomer was assigned the stereochemistry as depicted in **11** obtained via 'α-*exo* (R^2 =CO_2R) approach' as a result of unfavourable steric hindrance in the transition state (*vide infra*).

trans-Crotonates **7c** and **7d** underwent additions to give **8c–11c** and **8d–11d** in ratios of 57 : 9 : 18 : 16 and 53 : 9 : 22 : 16, respectively. The cycloaddition of **7c** in the presence of Lewis acid catalysts $BF_3.Et_2O$ or $ZnCl_2$ did not change the isomeric compositions (Table 1). The stereochemistry of the *t*-butyl crotonate adducts **8d–11d** was correlated to the methyl crotonate adducts **8c–11c** by ester exchange with methanol/HCl. Based on the earlier discussion, the major adduct **8c** was obtained *via* 'α-*exo* (R^1) approach' (Scheme 3). The stereochemistry of the isomers **8c–11c** was confirmed by lithium aluminum hydride (LAH) reduction to *trans*-crotyl alcohol (**7f**) adducts **8f–11f** (*vide infra*). The addition reaction of *trans*-crotonal **(7e)** was also found to be non regioselective; the cycloadducts **8e–11e** were obtained in a ratio of 32 : 26 : 19 : 23, respectively. The configuration of adducts **8e–11e** was correlated by $NaBH_4$ reduction to *trans*-crotyl alcohol (**7f**) adducts **8f–11f**.

While the methylenenitrone–crotonate addition reaction is scarcely mentioned in the literature, in one such cycloaddition the achiral *N*-benzylmethylenenitrone gave a mixture of regiomers having ester functionality attached to the C(4) and C(5) in a ratio of 67 : 33, respectively.[22] Recently, the reaction of *N*-tetrahydropyran-2-ylmethylenenitrone with methyl cinnamate **(7a)** has been reported[23] to undergo regioselective addition to give a single adduct having an ester functionality attached to the C(4) of the isoxazolidine. The report contradicts our findings: the methylenenitrone-cinnamate or -crotonate cycloadditions in this work are found to be non-regioselective; the preferred regioisomers (**8** and **9)** were the ones having the electron-withdrawing carbonyl groups attached to the C(4) of the isoxazolidines. The results discussed above are in general agreement with the frontier orbital treatment of the nitrone 1,3-dipolar cycloadditions.[24-30] In the case of cinnamates and more so in the case of crotonates, both the HOMO–LUMO combinations do not offer any clear-cut regiochemical preference since the nitrone as well as the alkene HOMO orbitals have a similar magnitude of orbital coefficients at both the oxygen and carbon terminals of the methylenenitone[31,32] and carbon terminals of the alkenes (Fig. 1).[33] As such a mixture of regioisomers is expected to be formed in the addition reactions of methylene nitrones with 1,2-disubstituted alkenes. Based on the small differences in the orbital coefficients, one may conclude that the nitrone (HOMO)-crotonate (LUMO) or nitrone (LUMO)-cinnamate (HOMO) prefer the formation of $C(4)CO_2R$ regioisomers by uniting the larger terminal coefficients in the transition state (Fig. 1).[31,32]

The stereochemistry of the minor regioisomers **10b/11b** and **10d/11d** was correlated by using the similarity in the chemical shift values of their ^{t}Bu protons in toluene-d_6; while the ^{t}Bu protons of **10b** and **11b** appeared at δ 1.36 and 1.32, the corresponding signals for **10d** and **11d** were displayed at δ 1.37 and 1.35, respectively. The major adduct was assigned the stereochemistry as in **8a** or **8b** with *endo*-oriented R^2 (*i.e.* CO_2R) as a result of favourable secondary orbital interactions. The stereoisomeric preference for the *endo*-oriented CO_2R in isomers **8** over *exo*-oriented CO_2R in **9** was found to be much higher than that in their regioisomeric counterparts **10** and **11** (Table 1). As is evident from Table 1, while the ratio of **8a (***endo*-CO_2Me**)** and **9a** is 73 : 8, that of **10a** and **11a** (*endo*-CO_2Me) is found to be 13 : 6. A look at the corresponding transition states **A** and **B** might reveal the reasons for the differences in the *exo/endo* ratios (Figure 2). The oxygen terminal of the nitrone apparently becomes a part of the six-membered ring as a result of the H-bonding. The increased steric encumbrance of the oxygen-terminal in the presence of H-bonding thereby encourages the substituent (CO_2Me) to have **a** greater *endo* preference *via* transition state **A** rather than via **B**. In the transition state **A** involving the H-bonded nitrone, the OMe group does not experience steric crowding as much as in transition state **B** where the OMe group will be subjected to non-bonded repulsions with the substituent at the nitrogen. The results thus revealed that an *endo*-oriented group is better tolerated at the carbon terminal of the nitrone than at the oxygen terminal. This is clearly demonstrated in the addition reaction of crotyl alcohol (**7f**) which gave **8f–11f** in a ratio of 38 : 7 : 45 : 10. The regiochemical preference is lost in this addition reaction owing to the presence of 'normal' substituents (*i.e.* CH_3 *vs.* CH_2OH) at both ends of the alkene; a regioisomeric mixture of **8f/9f** and **10f/11f** was obtained in ratio of 45 : 55. The formation of major regiomers **8f** (*endo*-CH_2OH) and **10f** (*endo*-Me), both having a substituent at C(4)

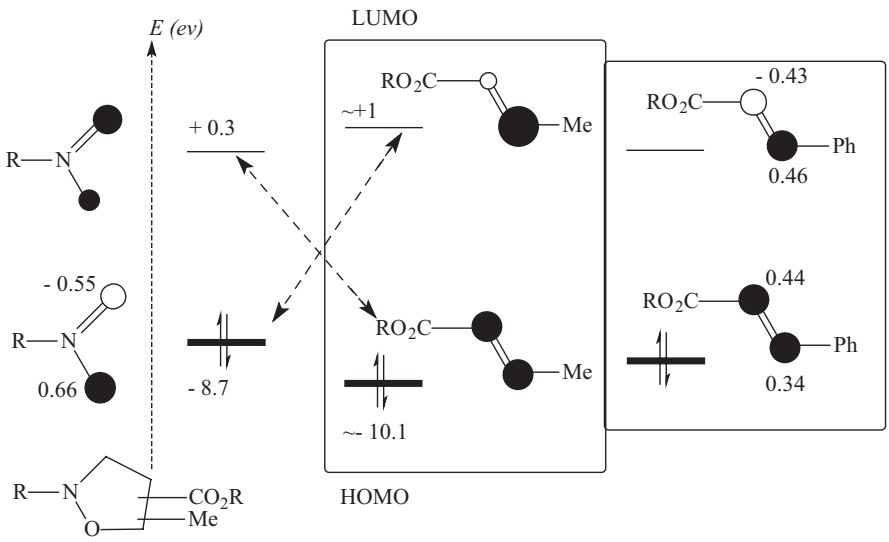
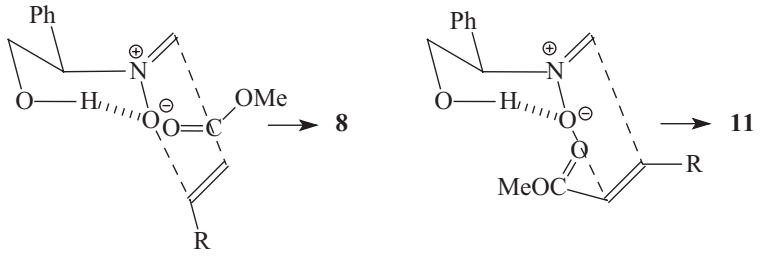


Fig. 1 A qualitative representation of the frontier orbital energies and coefficients of methylenenitrone and a 1,2-disubstituted alkene.



A: α–*endo*(CO_2Me) **B:** β–*endo*(CO_2Me)

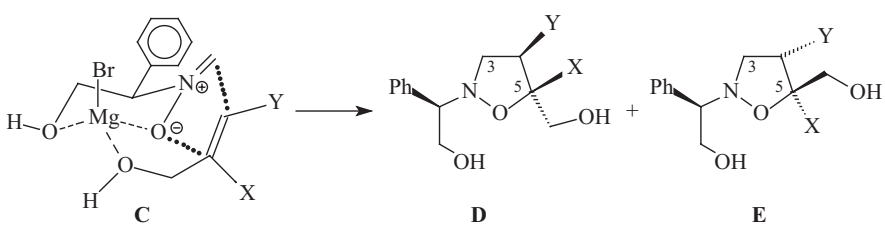
Fig. 2 Steric effects and secondary orbital interactions in the transition states.

endo-oriented, is a result of the preferred *endo* orientation of the alkene substituent at the carbon terminal of the nitrone in the transition states.

Effective utilisation of the cycloaddition reactions under study, however, demands a better regio- as well as stereo-selectivity than has been observed so far. In search of a better selectivity and proof for the stereochemistry assigned so far, we next studied the cycloaddition of several *trans*-alkenes containing hydroxy groups at the allylic position in the presence of $MgBr_2$. As documented in the recent literature,[15-17] the magnesium-chelated *endo* approach of the CH_2OH group of the allyl alcohol from the less hindered face of the nitrone as depicted in **C** afforded **D** and **E** (X = Y = H) in a ratio of 96 : 4 (Fig. 3).[15] Likewise, methallyl alcohol gave the cycloadducts **D** and **E** (X = Me, Y = H) in a 97 : 3 ratio.[17] It is gratifying to see that the metal-chelated transition state is equally effective in controlling regio- as well as stereo-selection in the addition reaction of a *trans*-alkeneol like crotyl alcohol **7f**. The ratio of 38 : 7 : 45 : 10 for adducts **8f–11f** in the absence of $MgBr_2$ was changed to 0 : 0 : 9 : 91 in the presence of $MgBr_2$; a complete reversal of the regiochemistry has thus been achieved. The configuration of the overwhelmingly predominant adduct **11f** is consistent with a magnesium-chelated *endo* approach of the CH_2OH group of the crotyl alcohol from the less hindered face of the nitrone as depicted in **C** (X = H, Y = Me) (Fig. 3). This reaction was particularly helpful in establishing the stereochemistry of the addition products of alkenes **7c–7f** since the stereochemistry of adducts was correlated with each other by chemical conversions (*vide supra*). The ^1H NMR spectroscopic analysis was helpful in determining the regioisomeric distributions. The C(5)Me protons of cycloadducts **8** and **9**, obtained from the addition reactions of alkenes **7c, 7d** and **7f**, invariably appeared downfield by virtue of being closer to the ring oxygen, while the C(4)Me of the regioisomeric **10** and **11** appeared upfield.

While the addition reaction of nitrone **2** with *trans*-methyl γ–hydroxycrotonate **(7g)** was found to be non-regioselecetive as expected, giving adducts **8g–11g** in a ratio of 50 : 13 : 30 : 7, the reaction became regioselective in the presence of $MgBr_2$ to afford **8g–11g** in a ratio 0 : 0 : 19 : 81, respectively. If the assignment of the regio- and stereochemistry is correct, then a mixture of adducts **8g–11g** in a ratio of 50 : 13 : 30 : 7 is expected to give, after LAH reduction, the triols **8i** and **9i** in a ratio of (50 + 30) : (13 + 7), respectively, as a result of the following conversions: **(8g, 10g)→ 8i**; and **(9g, 11g)→ 9i.** The formation of triols **8i** and **9i** in a ratio of ~80 : 20 provides evidence of the correctness of the assignment of the stereochemistry of adducts **8g–11g**. Likewise, the mixture of adducts **10g** and **11g** (obtained via $MgBr_2$-catalysed reaction) in a 19 : 81 ratio was converted into **8i** and **9i** in a ratio of ~19 : 81 as expected.

Next, we pursued the cycloaddition reaction of symmetrical *trans*-alkenes so as to eliminate the regiochemeical complication. Thus the addition reaction of nitrone **2** with dimethyl fumarate **(7h)** and *trans*-but-2-en-1,4-diol **(7i)** gave a mixture cycloadducts **8h, 9h** and **8i, 9i,** respectively, in a ratio of 70 : 30 and 80 : 20. The major adducts (*i.e.* **8h** and **8**i) were obtained *via* 'α-*exo* (R^1) approach' (Scheme 3). The stereochemistry of the fumarate adducts **8h** and **9h** was correlated by LAH reduction to adducts **8i** and **9i**. The stereoselectivity of the addition of *trans*-diol **7i** was dramatically reversed in the presence of $MgBr_2$; adducts **8i** and **9i** were obtained in a ratio of 6 : 94, respectively. While the addition of unsymmetrical silyloxy alkeneol **7j** gave the cycloadducts **8j–11j** in a ratio of 56 : 24 : 13 : 7, the symmetrical disilyloxy alkene **7k** afforded **8k** and **9k** in a ratio of 75 : 25, respectively. The ratio of 80 : 20 for the regioisomers (**8j + 9j**) vs. (**10j + 11j**) validates the earlier discussion that the alkene carbon bearing the bulkier $CH_2OSi^tBuMe_2$ substituent prefers to be away from the oxygen terminal and attaches itself to the carbon terminal of the nitrone. The stereochemistry of the mono- and di-silyloxy adducts was confirmed by their conversion into adducts **8i** and **9i** by treatment with MeOH/HCl. The formation of **8i** and **9i** in a ratio of ~69 : 31 from the above mixture of **8j–11j** (in a ratio of 56 : 24 : 13 : 7) as a result of the following conversions: **(8j, 10j)→ 8i**; and (**9j, 11j**)→ **9i**, provided further evidence of the correctness of the assignment of the stereochemistry**.** The regio- as well as stereo-



X=Y=H; (**D**/**E**) = 96:4

X= Me; Y=H; (**D**/**E**) = 97:3

X= H; Y = Me; (**11f**/**10f**) i.e. (**D**/**E**) = 91:9

Fig. 3 Metal-chelated transition state for the cycloaddition reactions.

selectivity of the addition of silyloxy alkeneol **7j** was changed in the presence of $MgBr_2$; adducts **8j–11j** were obtained in a ratio of 4 : 96 : 0 : 0, respectively. The configuration of the overwhelmingly predominant adduct **9j** is consistent with the magnesium-chelated *endo* approach of the CH_2OH toward the less hindered face of the nitrone (Fig. 3). As before, the mixture of adducts **8j** and **9j** (obtained via $MgBr_2$-catalysed reaction) in a 4 : 96 ratio was converted into **8i** and **9i** in a ratio of ~4 : 96 as expected.

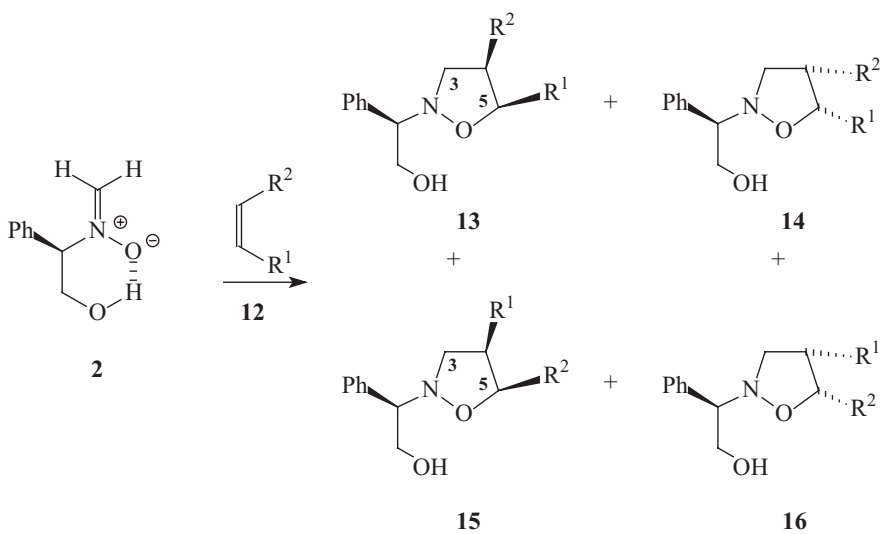
Finally, we studied the cycloaddition of nitrone **2** with several *cis*-alkenes **12**. The stereochemical details along with the reaction temperatures, isolated yield, and composition of isomeric cycloadducts are given in Table 2 (Scheme 4). The addition of dimethyl maleate **12a** afforded adducts **13a** and **14a** in a ratio of 40 : 60, which was changed to 53 : 47 in the presence of $MgBr_2$. The emergence of **14a** as the major product certifies the dominance of secondary orbital interaction over steric effects in dictating the stereochemical outcome of the reaction. The addition of *cis*-diol **12b** in the absence and presence of $MgBr_2$ afforded **13b** and **14b** in a ratio of 48 : 52 and 20 : 80, respectively. The metal-chelated transition state thus confirmed the stereochemistry of **14b** as having *endo*-oriented hydroxymethyl substituents. The stereochemistry of dimethyl adducts **13a** and **14a** was correlated to adducts **13b** and **14b** by LAH reduction. While the addition of the unsymmetrical monosilyloxy alkene **12c** in the absence of $MgBr_2$ afforded adducts **13c–16c** in a ratio of 55 : 23 : 15 : 7, the addition reaction in the presence of $MgBr_2$ became regioselective to give the adducts in a ratio of 20 : 80 : 0 : 0. The addition of symmetrical disilyloxyalkene **12d** gave the adducts **13d** and **14d** in a ratio of 72 : 28, while the ratio became 90 : 10 in the presence of $MgBr_2$ in a low yielding reaction. The stereochemistry of adducts from the addition reaction of alkenes **12c** and **12d** as correlated to that of alkene **12b** by treatment with MeOH/HCl. The formation of triols **13b** and **14b** in a ratio of ~70 : 30 from the above mixture of **13c–16c** (in a ratio of 55 : 23 : 15 : 7), provides further evidence of the correctness of the assignment of the stereochemistry of adducts **13c–16c** as a result of the following conversions: **(13c, 15c)→ 13b**; and **(14c, 16c)→ 14b.**

While the use of ^1H NMR coupling constant using the Karplus equation is highly successful in assigning configuration of six-membered rings, such applications often do not work well with isoxazolidines or any five-membered ring systems. The configuration of the isoxazolidines in the current work is indeed very complex to elucidate with any certainty. The complexity arises from the fact that the relatively slow nitrogen inversion makes the proton signals broader at ambient temperature. The five-membered ring does not have the well-defined conformation of six-membered systems. The constantly changing conformation (half chair/envelope/near planar), flap of the envelope, as well as configuration (owing to nitrogen inversion), make it a rather difficult task to deduce the configuration of the isoxazolidines.

Table 2 Regio- and stereo-chemistry of the cycloaddition[a,b] of the nitrone **2** to *cis*-disubstituted alkenes **12**

Alkene **12**	Temp/°C	Time/h	Lewis Acid	Isolated yields/%	Isomeric ratio **(13:14:15:16)**
					(13a = 15a)/14a = 16a)
a	85	12	None	90	40:60
	65	36	$MgBr_2$	45	53:47
					(13b = 15b)/14b = 16b)
a	95	6	None	93	48:52
	65	36	$MgBr_2$	72	20:80
c	105	12	None	92	55:23:15:7
	65	48	$MgBr_2$	84	20:80:0:0
					(13d = 15d)/14d = 16d)
d	105	12	None	89	72:28
	65	48	$MgBr_2$	8	90:10

[a]In toluene in the absence of Lewis acid catalyst. [b]In the presence of one equivalent of Lewis acid in CH_2Cl_2.



a, $R^1 = R^2 = CO_2Me$ **c,** $R^1 = CH_2OH$; $R^2 = CH_2OSi^tBuMe_2$

b, $R^1 = R^2 = CH_2OH$ **d,** $R^1 = R^2 = CH_2OSi^tBuMe_2$

Scheme 4

The measurement of NOE is of not much help in this situation. All the isoxazolidines in this work are liquids and as such X-ray diffraction analysis cannot be carried out. Added to these difficulties was the fact that most of the adducts were non-separable; a few were separated with great difficulty.

It is important to know that the disubstitituted alkenes in this study, like the monosubstituted ones,[17] gave the major products via *exo*-oriented transition state at the *N*-terminal of the nitrone **2**. The *endo*-oriented C(5)H of the isoxazolidines derived from the additions of monosubstituted alkenes, are known[17] to appear downfield in compare to that of the *exo*-oriented C(5)H. Further evidence of the correctness of the assignment of configuration in this work is based on the observation that the *endo*-oriented C(5)H in **8, 10, 13** or **15** invariably appeared downfield in comparison to that of the *exo*-oriented C(5)H in **9, 11, 14** or **16**, respectively (Table 3). We have no rationale to offer for such a difference in the chemical shifts; however, it is a diagnostic trend that would enable the assignment of the stereochemistry of this important class of cycloaddition reactions.

A systematic study of asymmetric reactions of the chiral methylenenitrone **2** with several 1,2-di-substituted alkenes has been carried out for the first time. The distereoselection observed in our study reflects the scope and limitations inherent in these important cycloaddition reactions. The remarkable regio- and stereo-selectivity observed in the magnesium-chelated cycloadditions paves the way for the synthesise of isoxazolidines having a variety of functionalities.

Experimental

General

Elemental analysis was carried out on a EuroVector Elemental Analyser Model EA3000. All melting points are uncorrected. IR spectra were recorded on a Perkin Elmer 16F PC FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ at 20°C using TMS as internal standard on a JEOL LA 500 MHz spectrometer. Silica gel chromatographic separations were performed with Silica Gel 100 from Fluka Chemie AG (Buchs, Switzerland). Paraformaldehyde, *cis*-but-2-ene-1,4-diol, dimethyl maleate, dimethyl fumarate, *trans*-methyl crotonate, *trans*-methyl cinnamate, *trans*-crotonaldehyde, *m*-chloroperbenzoic acid (70% purity), D(-)-α–phenylglycinol (*i.e.* (*R*)-phenylglycinol), hydroxylamine hydrochloride from Fluka were used as received.

trans-Crotyl alcohol **(7f)** was obtained by $NaBH_4$ reduction of *trans*-crotonaldehyde, while *trans*-but-2-ene-1,4-diol **(7i)** was prepared by reduction of dimethyl fumarate with DIBAH using the procedure as described.[34] *trans*-*t*-butyl –crotonates[35] and –cinnamates[36] were prepared as described.

Silyloxy alkenes **(7j, 7k)** and **(12c, 12d)** were prepared from but-2-ene-1,4-diols **7i** and **12b**, respectively, using ^{t}BuMe$_2$SiCl in the presence of imidazole in DMF. Thus to a solution of *trans*-but-2-ene-1,4-diol **(7i)** (2.02 g, 23.0 mmol) in anhydrous distilled DMF (20 cm^3) was added imidazole (5.18 g, 76 mmol) followed by *t*-butyldimethylsilyl chloride (5.72 g, 38 mmol). The reaction mixture was stirred under N_2 at 20°C for 6 h, and then taken up in ether (40 cm^3) and washed with water (4 × 15 cm^3). The organic layer was dried, concentrated and chromatographed using chloroform as eluant to give the disilylated *trans*-1,4-di-*t*-butyldimethylsilyloxybut-2-ene **(7k)** as a colourless liquid (2.30 g, 32%); (Found: C, 60.4; H, 11.3. $C_{16}H_{36}O_2Si_2$ requires C, 60.69; H, 11.46%.); ν_{max} (neat) 2953, 2889, 2857,1467, 1367, 1254, 1129, 1044, 998, 968, 935, 839 and 776 cm^{-1}; δ_H ($CDCl_3$) 0.068 (12H, s), 0.91 (18H, s), 4.18 (4H, d, J = 2.5 Hz), 5.76 (2H, t, J = 2.3 Hz); δ_C ($CDCl_3$) –5.2, 18.4, 26.0, 63.3, 129.3. Continued elution with 20 : 1 $CHCl_3$/methanol afforded the *trans*-4-*t*-butyldimethylsilyloxybut-2-en-1-ol **(7j)** (1.94 g, 42%); (Found: C, 59.5; H, 11.1. $C_{10}H_{22}O_2Si$ requires C, 59.35; H, 10.96%.); ν_{max} (neat) 3347, 2931, 2857,1466, 1380, 1255, 1129, 1096, 1061, 1007, 906, 839, and 778 cm^{-1}; δ_H ($CDCl_3$) 0.078 (6H, s), 0.92 (9H, s), 1.98 (1H, br, OH), 4.14 (2H, dd, J = 1.3, 5.2 Hz), 4.19 (2H, dd, J = 1.6, 3.1 Hz), 5.79 (1H, ttd, J = 1.2, 4.6, 15.3 Hz), 5.86 (1H, ttd, J = 1.5, 5.2, 15.3 Hz); δ_C ($CDCl_3$) –5.3, 18.4, 25.9, 63.0, 63.1, 129.0, 130.8.

Using a similar procedure to that described above *cis*-1,4-di-*t*-butyldimethylsilyloxybut-2-ene **(12d)** (colourless liquid) (27%) and *cis*-4-*t*-butyldimethylsilyloxybut-2-en-1-ol **(12c)** (colourless liquid) (36%) were obtained from *cis*-but-2-ene-1,4-diol **(12b)**. *cis*-1,4-di-*t*-Butyldimethylsilyloxybut-2-ene **(12d):** (Found: C, 60.5; H, 11.3. $C_{16}H_{36}O_2Si_2$ requires C, 60.69; H, 11.46%.); ν_{max} (neat) 3026, 2953, 2930, 2889, 2857,1467, 1405, 1362, 1255, 1085, 1005, 940, 840 and 777 cm^{-1}; δ_H ($CDCl_3$) 0.068 (12H, s), 0.90 (18H, s), 4.23 (4H, d, J = 2.8 Hz), 5.55 (2H, t, J = 2.8 Hz); δ_C ($CDCl_3$) –5.2, 18.3, 25.9, 59.6, 130.2. *cis*-4-*t*-Butyldimethylsilyloxybut-2-en-1-ol **(12c):** (Found: C, 59.1; H, 10.8. $C_{10}H_{22}O_2Si$ requires C, 59.35; H, 10.96%.); ν_{max} (neat) 3351, 3024, 29.53, 2930, 2886, 2857, 1469, 1407, 1361, 1255, 1088, 1035, 939, 838 and 777 cm^{-1}; δ_H ($CDCl_3$) 0.088 (6H, s), 0.91 (9H, s), 2.50 (1H, br, OH), 4.19 (2H, d, J = 5.2 Hz), 4.25 (2H, d, J = 5.2 Hz), 5.65 (1H, td, J = 5.5, 11.3 Hz), 5.69 (1H, td, J = 5.5, 11.3 Hz); δ_C ($CDCl_3$) –5.2, 18.3, 25.9, 58.7, 59.6, 130.1, 131.2.

Methyl γ-hydroxycrotonate **(7g)** was prepared as described.[37] $MgBr_2$ was freshly prepared by reaction of Mg with 1,2-dibromoethane in THF. The chiral hydroxylamine (*R*)-3-hydroxyamino-2-phenylethanol **(6)** was prepared in 80% yield according to the literature procedures,[38,39] m.p. 68–68.5°C (methanol–ether) (lit.[39] m.p. 67–68°C); $[\alpha]^{23}_D$ –62 (*c* 2.00, methanol) (lit.[39] $[\alpha]^{20}_D$ –38 (*c* 0.99, $CHCl_3$). All solvents were of reagent grade. Dichloromethane was passed through alumina before use.

General procedure for the cycloaddition reactions

In all the cycloadditions involving electron deficient conjugated alkenes, a mixture of hydroxylamine **6** (2.0 mmol), paraformaldehyde (3.0 mmol) and toluene (6 cm^3) was stirred in a closed flask at 65°C for 2 h to generate the nitrone **2**. The nitrone solution was then treated with anhydrous $MgSO_4$ (0.5 g) and the alkene. The conjugated alkene was not added prior to the formation of the nitrone to avoid any Michael addition of the hydroxylamine. For the additions involving normal alkenes, all the reactants and anhydrous $MgSO_4$ were added in the beginning, and the reaction mixture was directly heated at the specified temperatures (Tables 1 and 2). For the reaction involving *trans*- **(7i)** and *cis*-but-2-en-1,4-diol **(12b)**, the alkenes were found to be insoluble in the system; ethanol (1 cm^3) was added so as to make the system homogeneous. The alkenes used, with the amount in mmol written in parentheses, were as follows: **7a** (3), **7b** (3), **7c** (15), **7d** (4), **7e** (10), **7f** (10), **7g** (4), **7h** (2.5), **7i** (5), **7j** (4), **7k** (4), **12a** (3), **12b** (5), **12c** (4), **12d** (4). The reaction temperatures, time, solvent used, composition of adducts, and isolated yields are given in Tables 1 and 2. The reaction mixture was filtered, evaporated to remove the solvent and excess alkene (if volatile) to give crude residues containing the cycloadducts which were then purified and analysed.

Cycloaddition of nitrone **2** *with methyl cinnamate* **(7a)**: The crude mixture of cycloadducts was purified by chromatography over silica using hexane/ether as eluant to give a non-separable mixture of isomers **8a–11a** (87%) as a colourless liquid. ^{1}H NMR analysis of the crude and purified samples gave similar composition of the isomers.

Mixture of isomers **8a–11a**: (Found: C, 69.5; H, 6.5; N, 4.2. $C_{19}H_{21}NO_4$ requires C, 69.71; H, 6.47; N, 4.28%.) ν_{max} (neat) 3440, 3063, 3030, 2951, 2881, 1735, 1597, 1494, 1453, 1436, 1348, 1207, 1178, 1053, 1022, 939, 908, 760, and 700 cm^{-1}. The ^{1}H NMR signals of the major isomer **8a** were as follows: δ_H ($CDCl_3$) 2.50–3.50 (4H, m), 3.73 (3H, s), 3.88 (1H, m), 4.10 (1H, m), 4.15 (1H, m), 5.50 (1H, br), 7.32 (10H, m). The ^{1}H NMR spectrum in $CDCl_3$ revealed the presence of **8a–11a** as indicated by the presence of four methyl singlets at δ 3.73, 3.71, 3.82, 3.80 ppm, respectively.

Table 3 ^{1}H NMR chemical shifts of C(5)H signals of some isoxazolidines

Isoxazolidine	*endo*-C(5)H δ (ppm)	Isoxazolidine	*exo*-C(5)H δ (ppm)
8a	5.50	**9a**	5.29
8b	5.45	**9b**	5.20
8c	4.54	**9c**	4.28
8d	4.48	**9d**	4.20
8g	4.59	**9g**	4.37
8h	4.99	**9h**	4.89
8i	4.10	**9i**	3.98
8j	4.07	**9j**	3.95
8k	4.03	**9k**	3.90
10c	4.12	**11c**	4.09
13a	4.90	**14a**	4.75
13b	4.42	**14b**	4.22
13c	4.43	**14c**	4.24
13d	4.41	**14d**	4.17

The phenyl group at C(5) in **8a** and **9a** was indicated by the presence of signals at δ 5.50 (broad, major) and 5.29 (d, *J* = 6.4 Hz, minor) which were assigned to the C(5)Hs in similar cases.[40] The C(5)H of **10a** appeared at δ 4.60 (d, *J* = 4.6 Hz). The spectrum in toluene-d_8 revealed the presence of the corresponding methyl singlets of **8a–11a** free of any overlapping signals at δ 3.24**,** 3.20, 3.32, 3.30 ppm in a ratio of 73 : 8 : 13 : 6, respectively. The downfield methyl singlets were attributed to the C(5)CO_2Me signals of **10a** and **11a**, as a result of their proximity to the ring oxygen.

Cycloaddition of nitrone **2** *with t-butyl cinnamate* **(7b)***, and conversion of cycloadducts* **8b–11b** into methyl cinnamate adducts **8a–11a**: The crude mixture of cycloadducts was purified by chromatography over silica using hexane/ether as eluant to give a non-separable mixture of isomers **8b–11b** (85%).

Mixture of isomers **8b–11b**: ^{1}H NMR analysis of the crude and purified samples gave similar composition. (Found: C, 71.3; H, 7.2; N, 3.7. $C_{22}H_{27}NO_4$ requires C, 71.52; H, 7.37; N, 3.79%.) ν_{max} (neat) 3443, 3060, 3031, 2976, 2933, 2882, 1727, 1600, 1493, 1454, 1368, 1251, 1154, 1052, 845, 759, and 700 cm^{-1}. The ^{1}H NMR signals of the major isomer **8b** were as follows: δ_H ($CDCl_3$) 1.44 (9H, s), 2.50–3.50 (4H, m), 3.80 (1H, m), 4.10 (1H, m), 4.15 (1H, m), 5.45 (1H, br), 7.32 (10H, m). The *t*-butyl proton signals for **8b–1b** appeared in $CDCl_3$ at δ 1.44, 1.43, 1.52, 1.47 ppm, respectively in a ratio of 76 : 7 : 12 : 5. The *t*-butyl singlets were well separated and free of any competing signals. The C(5) H of **8b** and **9b** appeared at δ 5.45 ppm (broad, major) and 5.20 (d, *J* = 6.4 Hz, minor), respectively. As a result of nitrogen inversion most of the signals were very broad.

The mixture of *t*-butyl cinnamate adduct **8b–11b** in a ratio of 76 : 7 : 12 : 5 (50.0 mg, 0.153 mmol) in 5 : 1 (w/w) methanol/HCl (1 cm^3) was stirred at 20°C for 6 h. After removal of methanol, the residual liquid was taken up in CH_2Cl_2 (15 cm^3) and washed with 5% K_2CO_3 (5 cm^3). The organic layer was dried (Na_2SO_4) and concentrated to give methyl cinnamate adducts **8a–11a** as a colourless liquid (48 mg, 97%). The ^{1}H NMR spectrum as analysed above revealed isomers **8a–11a** (hence **8b–11b**) in a ratio of 78 : 7 : 10 : 5, respectively. The ^{1}H NMR spectrum revealed the absence of *t*-butyl protons thereby implying complete ester exchange with methanol.

Cycloaddition of nitrone 2 with trans-methyl crotonate **(7c)** in the absence and presence of Lewis acid catalysts, and lithium aluminium hydride reduction of cycloadducts **8c–11c** to **8f–11f**: The crude mixture of cycloadducts was purified by chromatography over silica using CH_2Cl_2 as eluant to give a non-separable mixture of **8c–10c**. Continued elution gave a mixture of all four isomers followed by a pure sample of **11c** as a colourless liquid. The combined yield of the cycloadducts was found to be 84%. Careful ^{1}H NMR analysis of the crude and the separated fraction revealed the ratio of the isomers **8c–11c** as 57 : 9 : 18 : 16, respectively. The ^{1}H NMR spectra at 20°C in toluene-d_8 were helpful in the determination of isomeric composition; the C(5)-methyl protons of **8c** and **9c**, and C(4)-methyl of **10c** and **11c** appeared at δ 1.13 (d, *J* = 6.1), 1.16 (d, *J* = 6.1), 0.83 (d, *J* = 7.0), 0.78 (d, *J* = 6.8), while the corresponding CO_2Me appeared as singlets at δ3.25, 3.22, 3.30, 3.33 ppm, respectively.

Mixture of isomers **8c–10c**: (Found: C, 63.2; H, 7.2; N, 5.2. $C_{14}H_{19}NO_4$ requires C, 63.38; H, 7.22; N, 5.28%.) ν_{max} (neat) 3453, 3030, 2954, 1739, 1603, 1494, 1453, 1380, 1204, 1062, 912, 846, 761, and 703 cm^{-1}. Careful analysis of the spectra of the mixture **8c–10c** identified the following signals belonging to the major isomer **8c:** δ_H ($CDCl_3$) 1.41 (3H, d, *J* = 6.2 Hz), 2.75–3.50 (4H, m), 3.71 (3H, s), 3.70–4.10 (3 H, m), 4.54 (1H, m) 7.30 (5H, m). The C(5)-methyl of **9c** and C(4)-methyl of **10c** appeared at δ 1.44 (d, *J* = 6.1 Hz) and 1.22 (d, *J* = 6.8 Hz), respectively, while the corresponding CO_2Me singlet appeared at δ 3.69 and 3.80 ppm, respectively. Most of the signals were broad due to nitrogen inversion. The broad signal at δ 4.54 ppm for C(5)H of **8c** became a distinct quintet at –40°C (*J* = 6.1 Hz), while the corresponding signal for the minor isomer **9c** at δ 4.28 also became a distinct quintet (quintet, *J* = 6.2 Hz). The spectrum revealed the C(5)H of the isomer **10c** as a doublet at δ 4.12 ppm (*J* = 5.3 Hz).

11c: (Found: C, 63.3; H, 7.1; N, 5.3. $C_{14}H_{19}NO_4$ requires C, 63.38; H, 7.22; N, 5.28%.) ν_{max} (neat) 3500, 3027, 2956, 2875, 1741, 1493, 1453, 1440, 1366, 1277, 1209, 1086, 1057, 1031, 787, 759, and 702 cm^{-1}; δ_H ($CDCl_3$) 1.20 (3H, d, *J* = 6.6 Hz), 2.60 (1H, br), 2.83 (1H, m), 3.06 (1H, m), 3.46 (1H, br, OH), 3.78 (1H, m), 3.82 (3H, s), 3.97 (1H, dd, *J* = 3.7, 7.5 Hz), 4.09 (1H, br), 4.18 (1H, dd, *J* = 7.5, 11.3 Hz), 7.32 (5H, m).

The above reaction was repeated in the absence of $MgSO_4$ using hydroxylamine **6** (1.0 mmol) in toluene (10 cm^3). The resultant nitrone solution was concentrated to a volume of 5 cm^3 by blowing a gentle stream of N_2 at 60°C. This was done to ensure the removal of moisture. To the nitrone solution was then added $BF_3.OEt_2$ (1.0 mmol) and the reaction mixture was heated at 80°C for 12 h. A similar experiment was carried out using $ZnCl_2$ (1.0 mmol) instead of $BF_3.OEt_2$. After removal of the solvent, the reaction mixture was taken up in water (10 cm^3), basified (K_2CO_3), and extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic layers was dried (Na_2SO_4), concentrated and purified by silica gel chromatograpy using 97 : 3 CH_2Cl_2/methanol as eluant to give a mixture of **8c–11c** as a colourless liquid in 60 and 65% yields in $BF_3.OEt_2$ and $ZnCl_2$, respectively, in a ratio of 59 : 13 : 15 : 13 and 58 : 14 : 17 : 11.

A mixture of cycloadducts **8c–11c** in a ratio of 58 : 14 : 17 : 11 was reduced with $LiAlH_4$. To a stirred solution of **8c–11c** (107 mg, 0.40 mmol) in ether (15 cm^3) was added lithium aluminium hydride (100 mg, 2.7 mmol) at room temperature. The reaction was complete in 10 min as indicated by TLC experiment (silica, ether). To the reaction mixture was added water (0.1 g), 10% NaOH solution (0.1 g) and water (0.4 g). The mixture was stirred for 1 h, decanted and the residue washed with CH_2Cl_2. The organic layer was dried (Na_2SO_4), concentrated, and purified by silica gel chromatography using a 95 : 5 CH_2Cl_2/methanol as the eluant to give a non-separable mixture of alcohols **8f–11f** as a colourless liquid (95%). The ^{1}H NMR spectrum revealed the presence of **8f–11f** in an almost similar ratio of ~58 : 14 : 17 : 11.

Cycloaddition of nitrone **2** *with t-butyl crotonate* **(7d)***, and conversion of cycloadducts* **8d–11d** *into methyl crotonate adducts* **8c–11c**: The crude mixture of cycloadducts was purified by chromatography over silica using hexane/ether as eluant to give a non-separable mixture of four isomers **8d–11d** as a colourless liquid (252 mg, 82%). (Found: C, 66.3; H, 8.1; N, 4.5. $C_{17}H_{25}NO_4$ requires C, 66.43; H, 8.20; N, 4.56%.) ν_{max} (neat) 3465, 3029, 2975, 2928, 2871, 1727, 1454, 1368, 1247, 1219, 1156, 1089, 1061, 905, 845, 760, and 701 cm^{-1}. ^{1}H NMR analysis of the crude and purified samples gave similar composition. The ^{1}H NMR signals in $CDCl_3$ were broadened due to nitrogen signals. However in toluene-d_8, the non-overlapping methyl signals of **8d–11d** appeared as doublets at δ 1.17 (*J* = 6.1 Hz), 1.20 (*J* = 6.4 Hz), 0.86 (*J* = 6.7 Hz), 0.82 (*J* = 6.7 Hz) ppm, respectively in a ratio of 53 : 9 : 22 : 16, respectively. The pair of downfield methyl doublets were attributed to the C(5) Me of **8d** and **9d** as a result of their proximity to the ring oxygen in compare to C(4)Me of **10d** and **11d**. The *t*-butyl singlets of **8d–11d** toluene-d_8 appeared at δ 1.26, 1.25, 1.37, and 1.35 ppm, respectively. The C(5)H of **8d** and **9d** in $CDCl_3$ appeared at δ 4.48 (m) and 4.20 (m), respectively.

The mixture of *t*-butyl crotonate adducts **8d–11d** (50.0 mg, 0.162 mmol) was converted into methyl crotonate adducts **8c–11c** as a colourless liquid (41 mg, 95%) using the ester exchange reaction. The NMR spectrum revealed **8c–11c** (hence **8d–11d)** in a ratio of 55 : 10 : 21 : 17, respectively.

Cycloaddition of nitrone **2** *with trans-crotonaldehyde* **(7e)** *and sodium borohydride reduction of cycloadducts* **8e–11e** *to* **8f–11f**: The crude mixture of cycloadducts **8e–11e** in methanol (5 cm^3) was treated with $NaBH_4$ (200 mg) and stirred at 20°C for 1 h. After removal of the solvent by a gentle stream of N_2, the reaction mixture was taken up in a saturated K_2CO_3 solution (10 cm^3), and extracted with CH_2Cl_2 (3 × 15 cm^3). The combined organic layers were dried (Na_2SO_4), concentrated and the residual liquid was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/methanol as eluant gave a non-separable mixture of diols **8f–11f** as a colourless liquid (90%). The ^{1}H NMR revealed the presence of **8f–11f** in a ratio of 32 : 26 : 19 : 23, respectively.

Cycloaddition of nitrone **2** *with trans-crotyl alcohol* **(7f)**: The crude mixture of cycloadducts was purified by chromatography over silica using 95 : 5 CH_2Cl_2/methanol as eluant to give a non-separable mixture of diols **8f–11f** as a colourless liquid (89%).

Mixture of isomers **8f–11f**: (Found: C, 65.6; H, 7.9; N, 5.8. $C_{13}H_{19}NO_3$ requires C, 65.80; H, 8.07; N, 5.90%.) ν_{max} (neat) 3386, 3030, 3060, 2963, 2928, 2873, 1494, 1454, 1411, 1380, 1314, 1212, 1061, 1028, 895, 760 and 702 cm^{-1}; δ_H ($CDCl_3$) 1.00–1.40 (3H, four doublets), 1.60–3.40 (5H, m), 3.60–4.10 (6H, m), 7.32 (5H, m). ^{1}H NMR spectrum revealed the presence of the C(5)Me of **8f** and **9f**, and C(4)Me of **10f** and **11f** at δ 1.35 (d, overlapping), 1.36 (d, *J* = 6.1), 1.09 (d, *J* = 6.8), 1.06 (d, *J* = 6.4) ppm, respectively, in a ratio of 38 : 7 : 45 : 10. Adduct **10f** and **11f** are further characterised below.

Cycloaddition of nitrone **2** *with trans-methyl γ–hydroxycrotonate* **(7g)***, and lithium aluminium hydride reduction of cycloadducts* **8g–11g** *to* **8i** *and* **9i**: The crude mixture of cycloadducts was purified by chromatography over silica using 95 : 5 CH_2Cl_2/methanol as eluant to give a non-separable mixture of adducts **8g–11g** as a colourless

liquid (79%) in a ratio of 50 : 13 : 30 : 7, respectively, as determined by ^{1}H NMR integration or peak height of the CO_2Me singlets which appeared at δ 3.70 (for **9g**), 3.72 (for **8g**), 3.82 (for **11g**), and 3.88 (for **10g**). The pair of downfield singlets were assigned to the C(5)CO_2Me of **10g** and **11g** as a result of their proximity to the ring oxygen.

Mixture of isomers **8g–11g**: (Found: C, 59.6; H, 6.6; N, 4.8. $C_{14}H_{19}NO_5$ requires C, 59.78; H, 6.81; N, 4.98%.) ν_{max} (neat) 3391, 3060, 3025, 2952, 2877, 1734, 1729, 1494, 1453, 1431, 1355, 1209, 1058, 761 and 703 cm^{-1}; δ_H ($CDCl_3$) 1.70–2.30 (2H, broad), 2.50–3.50 (5H, m), 3.60–4.60 (9H, m including the four CO_2Me singlets), 7.32 (5H, m).

Using the procedure as described, the above mixture of isomers **8g–11g** in a ratio of 50 : 13 : 30 : 7 was reduced with $LiAlH_4$. Because of the presence of three polar hydroxy groups, the lithium salts were extensively washed with CH_2Cl_2/MeOH (90 : 10) to ensure the extraction of the triols into the organic layer. The product was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/MeOH as eluant to give a mixture of **8i** and **9i** as a colourless liquid(70%) in a ~78 : 22 ratio.

Cycloaddition of nitrone **2** *to dimethyl fumarate* **(7h)***, and lithium aluminium hydride reduction of cycloadducts* **8h, 9h** *to* **8i, 9i**: The crude mixture of cycloadducts was separated by chromatography over silica using 98 : 2 dichloromethane/ether as eluant to give **8h** followed by **9h** as colourless liquid in a total yield of 91%. Spectroscopic analysis of the crude as well as the isolated yields revealed the presence of the **8h** and **9h** in a ratio of 70 : 30, respectively.

8h: (Found: C, 58.0; H, 6.0; N, 4.5. $C_{15}H_{19}NO_6$ requires C, 58.25; H, 6.19; N, 4.53%.) ν_{max} (neat) 3500, 3055, 3026, 3002, 2954, 2886, 2847, 1738, 1494, 1437, 1376, 1222, 1087, 1061, 1024, 937, 761, 733, and 703 cm^{-1}; δ_H ($CDCl_3$) 2.65 (1H, m), 3.20 (1H, m), 3.37 (1H, t, *J* = 9.0 Hz), 3.73 (3H, s), 3.83 (3H, s), 3.65–4.05 (4H, m), 4.99 (1H, d, *J* = 4.0 Hz), 7.30 (5H, m); δ_C ($CDCl_3$) 50.7, 52.6, 52.7, 56.6, 66.7, 71.8, 76.9, 128.1 (2C), 128.3, 128.6 (2C), 137.9, 171.5, 171.6.

9h: (Found: C, 58.3; H, 6.1; N, 4.4. $C_{15}H_{19}NO_6$ requires C, 58.25; H, 6.19; N, 4.53%.) ν_{max} (neat) 3473, 3055, 3026, 2997, 2954, 2857, 1741, 1494, 1437, 1381, 1219, 1060, 932, 856, 761, 734, and 703 cm^{-1}; δ_H ($CDCl_3$) 2.5–3.5 (3H, m), 3.71 (3H, s), 3.82 (3H, s), 3.65–4.0 (3H, m), 4.15 (1H, m), 4.89 (1H, m), 7.33 (5H, m). δ_C ($CDCl_3$) 50.6, 52.6, 52.7, 55.1, 65.8, 70.9, 76.7, 128.2, 128.5, 136.0, 171.0, 171.5.

Using the procedure as described above, **8h** (421 mg, 1.36 mmol) was reduced with $LiAlH_4$. Because of the presence of three polar hydroxy groups, the lithium salts were extensively washed with CH_2Cl_2/MeOH (90 : 10) to ensure the extraction of the triols into the organic layer. The product was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/MeOH as eluant to give **8i** as a colourless liquid (215 mg, 62%).

8i: (Found: C, 61.4; H, 7.5; N, 5.4. $C_{13}H_{19}NO_4$ requires C, 61.64; H, 7.56; N, 5.53%.) ν_{max} (neat) 3355, 3031, 3007, 2927, 2876, 1452, 1420, 1386, 1218, 1061, 923, 875, 756, and 703 cm^{-1}; δ_H($CDCl_3$) 2.10–3.45 (6H, m), 3.50–3.85 (m, 6H), 4.05 (1H, dd, *J* = 6.9, 11.5 Hz), 4.10 (1H, m), 7.31 (5H, m); δ_C ($CDCl_3$) 46.7, 58.0, 63.2, 64.6, 67.9, 73.7, 81.3, 128.1, 128.3 (2C), 128.7 (2C), 137.7.

Using the procedure as described above, **9h** (250 mg, 0.81 mmol) was reduced with $LiAlH_4$. Because of the presence of three polar hydroxy groups, the lithium salts were extensively washed with CH_2Cl_2/MeOH (90 : 10) to ensure the extraction of the triols into the organic layer. The product was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/MeOH as eluant to give **9i** as a colourless liquid (125 mg, 61%).

9i: (Found: C, 61.5; H, 7.4; N, 5.4. $C_{13}H_{19}NO_4$ requires C, 61.64; H, 7.56; N, 5.53%.) ν_{max} (neat) 3354, 3031, 3002, 2927, 2876, 1492, 1452, 1386, 1352, 1218, 1032, 889, 757 and 702 cm^{-1}; δ_H ($CDCl_3$) 2.50–3.30 (6H, m), 3.50–3.85 (m, 6H), 3.98 (1H, m), 4.07 (1H, m), 7.31 (5H, m); δ_C ($CDCl_3$) 45.8, 57.3, 63.2, 63.6, 67.8, 73.7, 83.0, 128.0, 128.2 (2C), 128.8 (2C), 137.8.

Cycloaddition of nitrone **2** *to trans-but-2-ene-1,4-diol* **(7i)**: The crude mixture of cycloadducts was purified by chromatography over silica using 95 : 5 CH_2Cl_2/MeOH as eluant to give a non-separable mixture **8i** and **9i** as a colourless liquid (92%). Careful analysis of the ^{1}H and ^{13}C spectra (Section 3.2.8) (signals at δ 83.01 for **9i** versus and 81.34 ppm for **8i, as** well as 45.81 for **9i** versus and 46.70 ppm for **8i**) revealed the presence of the **8i** and **9i** in an approximate ratio of 80 : 20.

Cycloaddition of nitrone **2** *to trans-4-t-butyldimethylsiloxy-2-butene-1-ol* **(7j)***, and conversion of cycloadducts* **8j–11j** *into* **8i, 9i**: The crude mixture of cycloadducts was purified by chromatography over silica using 98 : 2 $CHCl_3$/MeOH as eluant to give a mixture adducts **8j–11j** (89%) as a colourless liquid. Spectroscopic analysis of the crude as well as the purified adducts revealed the presence of the **8j–11j** in a ratio of 56 : 24 : 13 : 7, respectively, as determined by integration and peak heights of several proton signals (belonging to Si^{t}BuMe_2) of the crude as well as purified adducts.

Mixture of isomers **8j–11j:** (Found: C, 61.8; H, 8.8; N, 3.6. $C_{19}H_{33}NO_4Si$ requires C, 62.09; H, 9.05; N, 3.81%.) δ_H ($CDCl_3$) ~0.035 (6H, singlets), ~0.9 (9H, singlets), 2.25–3.25 (4 H, m), 3.50–4.15 (9H, m), 7.31 (5 H, m). The Me_2Si protons appeared at δ 0.032 (s) for **8j**; δ 0.017 (s) and 0.024 (s) for **9j;** δ 0.114 (s) for **10j**; δ 0.108 (s) for **11j**. The C(5)H of **8j** appeared around 4.07. The *t*-buytl Si protons appeared at δ 0.87 (s) for **8j**; δ 0.855 (s) for **9j;** δ 0.917 (s) for **10j** and **11j**. The downfield singlets of ^{t}BuSi and Me_2Si were assigned to **10j** and **11j** as a result of their proximity to the ring oxygen. Compound **9j** is further analysed below.

To a solution of the above mixture of isomers **8j–11j** in a ratio of 56 : 24 : 13 : 7 (70 mg), in methanol (2 cm^3) was added 300 mg of a 3 : 1 (w/w) MeOH/HCl mixture. The reaction mixture was stirred at 20°C for 20 min. After removal of the solvent by a gentle stream of N_2, the residual liquid was taken up in a saturated K_2CO_3 solution (1 cm^3) and extracted with CH_2Cl_2 (3 × 5 cm^3). The organic layer was dried (Na_2SO_4), concentrated to give the triols **8i** and **9i** in an almost quantitative yield in a ratio of 70 : 30, respectively, as analysed above.

Cycloaddition of nitrone **2** *to trans-1,4-di-*^{t}*butyldimethylsiloxybut-2-ene* **(7k),** *and conversion of cycloadduct* **8k** *to* **8i**: The crude mixture of cycloadducts was purified by chromatography over silica using 5 : 1 hexane/ether as eluant to give **8k** followed by a mixture of **8k/9k** and finally **9k** as colourless liquids in a total yield of 73%. Spectroscopic analysis of the crude as well as separated fractions revealed the presence of the **8k** and **9k** in a ratio of 75 : 25, as determined by integration and peak heights of several proton signals of the crude as well as separated fractions.

Major isomer **8k:** (Found: C, 62.0; H, 9.6; N, 2.8. $C_{25}H_{47}NO_4Si_2$ requires C, 62.32; H, 9.83; N, 2.91%.) ν_{max} (neat) 3543, 3063, 3031, 2953, 2887, 2857, 1469, 1389, 1361, 1254, 1098, 1006, 938, 840, 778, and 702 cm^{-1}; δ_H ($CDCl_3$) 0.022 (6H, s), 0.092 (6H, s), 0.87 (9H, s), 0.91 (9H, s), 1.67 (1H, br OH), 2.36 (2H, m), 3.03 (1H, m), 3.50–3.85 (7H, m), 4.03 (1H, m), 4.07 (1H, dd, *J* = 7.8, 11.5 Hz), 7.30 (5H, m).

Minor isomer **9k:** (Found: C, 62.4; H, 9.9; N, 2.8. $C_{25}H_{47}NO_4Si_2$ requires C, 62.32; H, 9.83; N, 2.91%.) ν_{max} (neat) 3500, 3064, 3031, 2929, 2857, 1468, 1388, 1362, 1255, 1097, 1007, 938, 838, 778, and 702 cm^{-1}; δ_H ($CDCl_3$) 0.00 (3H, s), 0.003 (3H, s), 0.084 (3H, s), 0.094 (3H, s), 0.86 (9H, s), 0.91 (9H, s), 2.49 (1 H, m), 2.60 (1 H, m), 2.76 (1 H, m), 3.61 (2 H, m), 3.71 (2 H, m), 3.79 (2 H, m), 3.90 (1 H, m), 4.06 (1H, dd, *J* = 7.3, 11.3 Hz), 7.30 (5H, m).

The cycloadduct **8k** was hydrolysed in methanolic HCl as above to obtain the alcohol **8i** in an almost quantitative yield.

Cycloaddition of nitrone **2** *with dimethyl maleate* **(12a)***, and lithium aluminium hydride reduction of cycloadducts* **13a** *and* **14a** *to* **13b** *and* **14b**: The crude mixture of cycloadducts was purified by chromatography over silica using 98 : 2 dichloromethane/ether as eluant to give **13a** followed by a mixture of **13a/14a** and finally **14a** as colourless liquids in a total yield of 90%. Spectroscopic analysis of the crude as well as the separated fractions revealed the presence of the **13a** and **14a** in a ratio of 40 : 60 as determined by integration of the C5(H) signals at δ 4.90 (minor) and 4.75 (major) ppm as well as by peak heights of the CO_2Me singlets.

Minor isomer **13a**: (Found: C, 58.1; H, 6.2; N, 4.4. $C_{15}H_{19}NO_6$ requires C, 58.25; H, 6.19; N, 4.53%.) ν_{max} (neat) 3474, 3031, 3002, 2953, 2881, 1743, 1494, 1437, 1349, 1290, 1214, 1065, 940, 822, 761, and 703 cm^{-1}; δ_H ($CDCl_3$) 2.98 (2H, m), 3.35 (1H, m), 3.68 (3H, s), 3.77 (3H, s), 3.82 (2H, m), 3.96 (2H, m), 4.90 (1H, d, *J* = 9.5 Hz), 7.34 (5H, m); δ_C ($CDCl_3$) 49.8, 52.3, 52.4, 55.4, 66.6, 71.7, 76.7, 128.1 (2C), 128.2, 128.7 (2C), 137.8, 169.6, 170.2.

Major isomer **14a**: (Found: C, 58.3; H, 6.3; N, 4.5. $C_{15}H_{19}NO_6$ requires C, 58.25; H, 6.19; N, 4.53%.) ν_{max} (neat) 3474, 3031, 3002, 2953, 2886, 1743, 1494, 1438, 1353, 1290, 1214, 1059, 942, 763 and 704 cm^{-1}; δ_H ($CDCl_3$) 2.70–3.25 (3H, m), 3.63 (1H, m), 3.67 (3H, s), 3.77 (3H, s), 3.81 (1H, m), 4.02 (1H, dd, *J* = 4.2, 7.0 Hz), 4.11 (1H, m), 4.75 (1H, d, *J* = 8.8 Hz), 7.33 (5H, m); δ_C ($CDCl_3$) 50.0, 52.3, 52.4, 55.8, 66.2, 73.1, 76.9, 128.3 (2C), 128.7 (3C), 137.1, 169.6, 170.2.

13a (166 mg, 0.536 mmol) was reduced with $LiAlH_4$. Because of the presence of three polar hydroxy groups, the lithium salts were extensively washed with CH_2Cl_2/MeOH (90 : 10) to ensure the extraction of the triols into the organic layer. The product was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/MeOH as eluant to

give **13b** as a colourless liquid (95 mg, 70%). **13b**: (Found: C, 61.4; H, 7.3; N, 5.4. $C_{13}H_{19}NO_4$ requires C, 61.64; H, 7.56; N, 5.53%.) ν_{max} (neat) 3330, 3031, 2934, 2881, 1603, 1492, 1453, 1415, 1386, 1218, 1046, 856, 758 and 703 cm^{-1}; $\delta_H(CDCl_3)$ 2.93 (3H, m), 3.10–4.00 (9H, m), 4.04 (1H, dd, *J* = 6.4, 11.6 Hz), 4.42 (1H, br), 7.32 (5H, m); $\delta_C(CDCl_3)$ 45.1, 56.0, 60.3, 61.1, 67.3, 72.0, 78.9, 128.2 (2C), 128.3, 128.8 (2C), 137.7.

14a (233 mg, 0.75 mmol) was reduced with $LiAlH_4$. The product was purified by silica gel chromatography using 95 : 5 CH_2Cl_2/MeOH as eluant to give **14b** as a colourless liquid (145 mg, 76%).

14b: (Found: C, 61.5; H, 7.4; N, 5.3. $C_{13}H_{19}NO_4$ requires C, 61.64; H, 7.56; N, 5.53%.) ν_{max} (neat) 3355, 3026, 3002, 2934, 2876, 1602, 1497, 1453, 1420, 1391, 1218, 1045, 893, 851, 756, and 702 cm^{-1}; δ_H ($CDCl_3$) 2.10–3.5 (6H, m), 3.60–3.95 (6H, m), 4.08 (1H, dd, *J* = 8.0, 12.5 Hz), 4.22 (1H, br), 7.32 (5H. m); δ_c ($CDCl_3$) 45.7, 57.3, 60.31 (2C), 67.6, 74.1, 79.3, 128.3 (2C), 128.7 (3C), 137.6.

Cycloaddition of nitrone **7** *with cis-but-2-ene-1,4-diol* **(12b)**: The crude mixture of cycloadducts was purified by chromatography over silica using 95 : 5 CH_2Cl_2/MeOH as eluant to give a non-separable mixture **13b** and **14b** as a colourless liquid (93%). Careful ^1H (several proton signals) and ^{13}C (signals at δ 78.89 for **13b** versus 79.31 ppm for **14b**) spectroscopic analysis of adducts revealed the presence of the **13b** and **14b** in an approximate ratio of 48 : 52, respectively. The C(5)H of **13b** and **14b** appeared at δ4.42 and 4.22 ppm, respectively.

Cycloaddition of nitrone **2** *with cis-4-t-butyldimethylsiloxybut-2-ene-1-ol* **(12c)**, *conversion of cycloadducts* **13c–16c** *to* **13b** *and* **14b**: The crude mixture of cycloadducts was purified by chromatography over silica using 98 : 2 $CHCl_3$/MeOH as eluant to give a non-separable mixture adducts **13c–16c** (92%) as a colourless liquid. Spectroscopic analysis of the crude as well as the separated fractions revealed the presence of **13c–16c** in a ratio of 55 : 23 : 15 : 7, respectively, as determined by integration and peak heights of several proton signals (belonging to Si^tBuMe_2) of the crude as well as separated fractions.

Mixture of isomers **13c–16c:** (Found: C, 61.8; H, 8.8; N, 3.6. $C_{19}H_{33}NO_4Si$ requires C, 62.09; H, 9.05; N, 3.81%); δ_H ($CDCl_3$) ~0.04 (6H, singlets), ~0.85 (9H, singlets), 2.60–3.30 (4 H, m), 3.50–4.50 (9H, m), 7.31 (5 H, m). The Me_2Si protons appeared at δ0.035 (s) and 0.043 (s) for **13c**; δ0.047 (s) and 0.051 (s) for **14c;** δ0.13 (s) for **15c**; δ0.14 (s) for **16c**. The ^{t}BuSi protons appeared at δ0.86 (s) for **13c**; δ0.87 (s) for **14c;** δ0.915 (s) for **15c**; δ0.923 (s) for **16c**. The downfield singlets were assigned to the ^{t}BuSi and Me_2Si of **15c** and **16c** as a result of their proximity to the ring oxygen.

The above mixture of isomers **13c–16c** in a ratio of 55 : 23 : 15 : 7 was hydrolysed as described above to give triols **13b** and **14b** in an almost quantitative yield in a ratio of ~70:30, respectively, as analysed above.

Cycloaddition of nitrone **2** *with cis-1,4-di-t-butyldimethylsiloxybut-2-ene* **(12d)**, *and conversion of cycloadduct* **13d** *to* **13b**: The crude mixture of cycloadducts was purified by chromatography over silica using 4:1 hexane/ether as eluant to give **13d** followed by a mixture of **13d/14d** and finally **14d** as colourless liquids in a total yield of 89%. Spectroscopic analysis of the crude as well as the separated fractions revealed the presence of the **13d** and **14d** in a ratio of 72:28, respectively, as determined by integration and peak heights of several proton signals of the crude as well as separated fractions.

Major isomer **13d**: (Found: C, 61.9; H, 9.6; N, 2.7. $C_{25}H_{47}NO_4Si_2$ requires C, 62.32; H, 9.83; N, 2.91%.) ν_{max} (neat) 3533, 3063, 3031, 2932, 2859, 1465, 1393, 1361, 1254, 1095, 939, 840, 777, and 701 cm^{-1}; δ_H ($CDCl_3$) 0.0079 (6H, s), 0.085 (6H, s), 0.85 (9H, s), 0.91 (9H, s), 2.78 (1H, m), 2.87 (2H, m), 3.52 (1H, m), 3.66 (1H, m), 3.73 (1H, m), 3.76 (1H, m), 3.87 (1H, m), 3.92 (1H, d, *J* = 5.5 Hz), 4.12 (1H, dd, *J* = 7.9, 11.6 Hz), 4.41 (1H, m), 7.30 (5H, m).

Minor isomer **14d**: (Found: C, 62.0; H, 9.6; N, 2.8. $C_{25}H_{47}NO_4Si_2$ requires C, 62.32; H, 9.83; N, 2.91%.) ν_{max} (neat) 3545, 3063, 3031, 2930, 2886, 2857, 1468, 1391, 1361, 1255, 1093, 1007, 938, 908, 838, 777, and 701 cm^{-1}; δ_H ($CDCl_3$) 0.00 (6H, s), 0.084 (3H, s), 0.095 (3H, s), 0.85 (9H, s), 0.91 (9H, s), 2.75(1H, m), 3.07 (1H, t, *J* = 8.2 Hz), 3.25 (1H, m), 3.60 (1H, dd, *J* = 6.9, 10.2 Hz), 3.65–3.90 (5H, m), 4.10 (1H, dd, *J* = 7.7, 11.3 Hz), 4.17 (1H, m), 7.30 (5H, m).

As described above, adduct **13d** was hydrolysed by MeOH/HCl to give the triol **13b** in almost quantitative yield. The spectroscopic analysis revealed that the alcohol **13b** obtained from **13d** matches with the stereochemistry of the alcohol **13b** obtained from $LiAlH_4$ reduction of **13a**.

Cycloaddition of nitrone **2** *in the presence of* $MgBr_2$

Cycloaddition of nitrone **2** *to trans-crotyl alcohol* **(7f)** *in the presence of* $MgBr_2$: To a solution of hydroxylamine **6** (153 mg, 1.0 mmol) in dichloromethane (20 cm^3), was added paraformaldehyde (34 mg, 1.13 mmol) and the mixture was stirred in a closed vessel under N_2 at 65°C for 2 h. Thereafter, the solution was cooled to room temperature and the volume of the solution was reduced to 5 cm^3 by gently blowing N_2 at 40°C. This process is expected to remove moisture (H_2O) by evaporation along with CH_2Cl_2. Then $MgBr_2$ (184 mg, 1.0 mmol) was added to the solution. After stirring the resulting suspension under N_2 was stirred at 20°C for 15 min, crotyl alcohol **7f** (1.1 mmol) was added. The reaction mixture was then stirred at 65°C in the closed vessel under N_2 for 48 h. During the reaction, a precipitate of magnesium salts was observed. After the elapsed time, the reaction mixture was cooled to room temperature and was taken up in 10% K_2CO_3 (10 cm^3) and extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic layers was dried (Na_2SO_4), concentrated, and purified by silica gel chromatography using CH_2Cl_2/MeOH (95 : 5) as eluent to give a non-separable mixture of alcohols **10f** and **11f** as a colourless liquid (222 mg, 96%)**.** The ^1H NMR spectrum revealed the presence of **10f** and **11f** in a ratio of 9:91, respectively, as determined by integration of the C(5)Me doublets.

Mixture of 9:91 **10f**/**11f:** (Found: C, 65.6; H, 7.8; N, 5.8. $C_{13}H_{19}NO_3$ requires C, 65.80; H, 8.07; N, 5.90%.) ν_{max} (neat) 3387, 3030, 3060, 2963, 2928, 2873, 1494, 1453, 1381, 1222, 1060, 1028, 898, 844, 761, and 702 cm^{-1}; $\delta_H(CDCl_3)$ 1.06 (3H, d, *J* 6.4), 2.30–3.30 (5H, m), 3.55–3.98 (5H, m), 4.10 (1H, m), 7.32 (5H, m). The minor C(5)Me doublets of the minor isomer **10f** appeared at δ 1.09.

Cycloaddition of nitrone ***2*** *to trans-methyl γ–hydroxycrotonate* ***(7g)*** *in the presence of* $MgBr_2$, *and lithium aluminium hydride reduction of cycloadducts* **8g** *and* **9g** *to* **8i** *and* **9i**: As described above, the addition reaction was carried out using trans-methyl γ–hydroxycrotonate (**7g**) instead of **7f** at 65°C for 48 h. After usual work up, the residual liquid was purified by chromatography over silica using 95 : 5 CH_2Cl_2/MeOH as eluant to give a non-separable mixture of alcohols **8g** and **9g** as a colourless liquid (76%)**.** The ^1H NMR spectrum revealed the presence of **8g** and **9g** in a ratio of 19 : 81, respectively, as determined by integration of the $C(5)CO_2Me$ singlets. The NMR spectra of the crude as well as purified mixture failed to detect the presence of regioisomers **10g** and **11g**. The C(5)H of the isomers **8g** and **9g** appeared at δ4.59 and 4.37, respectively, as broad signals due to nitrogen inversion.

Mixture of 19:81 **8g**/**9g**: (Found: C, 59.9; H, 6.9; N, 4.8. $C_{14}H_{19}NO_5$ requires C, 59.78; H, 6.81; N, 4.98%.) ν_{max} (neat) 3379, 3081, 3060, 3025, 2952, 2877, 1736, 1731, 1494, 1453, 1431, 1355, 1207, 1176, 1055, 962, 890, 849, 788, 761 and 702 cm^{-1}. Signals attributed to the major isomer **9g**: δ_H ($CDCl_3$) 2.50–3.50 (5H, m), 3.60–4.10 (5H, m), 3.70 (3H, s), 4.37 (1H, m), 7.32 (5H, m).

The mixture of isomers **8g** and **9g** in a ratio of 19:81 upon LAH reduction gave triols **8i** and **9i** as a colourless liquid(73%) in a ~20 : 80 ratio.

Cycloaddition of nitrone **2** *to trans-2-butene-1,4-diol* **(7i)** *in the presence of* $MgBr_2$: The addition reaction was carried out using *trans*-but-2-ene-1,4-diol (**7i**) instead of **7f** at 65°C for 36 h. After usual work up (using saturated K_2CO_3) the residual liquid was purified by chromatography to give adducts **8i** and **9i** (74%). Careful analysis of the ^1H and ^{13}C spectra revealed the presence of the **8i** and **9i** in a ratio of 6:94, respectively.

Cycloaddition of nitrone **2** *with trans-4-t-butyldimethylsiloxybut-2-ene-1-ol* **(7j)** *in the presence of* $MgBr_2$, *and conversion of* **9j** *to* **9i**: The addition reaction was carried out using *trans*-4-t-butyldimethylsiloxybut-2-ene-1-ol (**7j**) instead of **7f** at 65°C for 36 h. After usual work up the residual liquid was purified by chromatography to give adducts **8j** and **9j** (88%) as a colourless liquid. Spectroscopic analysis of adducts revealed the presence of the **8j** and **9j** in an approximate ratio of 4:96, respectively.

9j: (Found: C, 61.7; H, 8.8; N, 3.7. $C_{19}H_{33}NO_4Si$ requires C, 62.09; H, 9.05; N, 3.81%.) ν_{max} (neat) 3376, 3063, 3031, 2954, 2857, 1493, 1469, 1389, 1361, 1255, 1092, 938, 838, 777, and 702 cm^{-1}; δ_H ($CDCl_3$) 0.018 (3H, s), 0.026 (3H, s), 0.86 (9H, s), 2.5–3.1 (5H, m), 3.5–3.85 (6H, m), 3.95 (1H, m), 4.04 (1H, dd, *J* = 7.6, 10.7 Hz), 7.30 (5H, m). The singlet at δ0.87 indicated the presence of the minor adduct **8j**.

The cycloadduct **9j** (containing about 4% of the minor isomer **8j)** was hydrolysed in methanolic HCl to obtain alcohol **9i** (containing minor amount of **8i**) in an almost quantitative yield.

Cycloaddition of nitrone **2** *to dimethyl maleate* **(12a)** *in the presence of* $MgBr_2$: The addition reaction was carried out using dimethyl maleate (**12a**) instead of **7f** at 65°C for 36 h. After usual work up the residual liquid was purified by chromatography to give adducts **13a** and **14a** as a colourless liquid (150 mg, 45%)**.** Spectroscopic analysis of the crude as well as the purified adducts revealed the presence of the **13a** and **14a** in a ratio of 53:47.

Cycloaddition of nitrone **2** *with cis-but-2-ene-1,4-diol* **(12b)** *in the presence of* $MgBr_2$: The addition reaction was carried out using *cis*-but-2-ene-1,4-diol (**12b**) instead of **7f** at 65°C for 36 h. After usual work up (using K_2CO_3) the residual liquid was purified by chromatography to give adducts **13b** and **14b** (182 mg, 72%). Careful analysis of ^1H (several proton signals) and ^{13}C spectra revealed the presence of **13b** and **14b** in an approximate ratio of 20 : 80.

Cycloaddition of nitrone **2** *to cis-4-t-butyldimethylsiloxybut-2-ene-1-ol* **(12c)** *in the presence of* $MgBr_2$ *and conversion of cycloadducts* **13c** *and* **14c** *to* **13b** *and* **14b**: The addition reaction was carried out using cis-4-^{t}butyldimethylsiloxybut-2-ene-1-ol (**12c**) instead of **7f** at 65°C for 48 h. After usual work up the residual liquid was purified by chromatography to give adducts **13c** and **14c** (84%) as a colourless liquid. Spectroscopic analysis of adducts revealed the presence of the **13c** and **14c** in an approximate ratio of 20 : 80, respectively.

Mixture of 20 : 80 **13c**/**14c:** (Found: C, 61.8; H, 9.0; N, 3.6. $C_{19}H_{33}NO_4Si$ requires C, 62.09; H, 9.05; N, 3.81%.) ν_{max} (neat) 3391, 3061, 3031, 2930, 2858, 1492, 1468, 1392, 1361, 1255, 1092, 939, 839, 777, 737, and 702 cm^{-1}; $\delta_H(CDCl_3)$ 0.038 (0.20 × 3H, s, minor), 0.045(0.20 × 3H, s, minor), 0.051 (0.80 × 3H, s, major), 0.054 (0.80 × 3H, s, major), 0.86 (0.20 × 9H, s, minor), 0.88(0.80 × 9H, s, major), 1.70 (1H, m), 2.55-3.15 (3H, m), 3.50-3.80 (7H, m), 4.07 (1H, m), 4.24 (0.80 × 1H, m, major), 4.43 (0.20 × 1H, m, minor), 7.32 (5H, m).

A portion of the above mixture of cycloadducts **13c** and **14c** in a ratio of 20 : 80, respectively, was hydrolysed in methanolic HCl to obtain a mixture of alcohols **13b** and **14b** in a ratio of ~20 : 80 in an almost quantitative yield.

Cycloaddition of nitrone **2** *to cis-1,4-di-t-butyldimethylsiloxybut-2-ene* **(12d)** *in the presence of* $MgBr_2$: The addition reaction was carried out using *cis*-1,4-di-^{t}butyldimethylsiloxybut-2-ene (**12d**) instead of **7f** at 65°C for 48 h. After usual work up the residual liquid was purified to give adducts **13d** and **14d** (40 mg, 8.3%) in a ratio of 9 : 1. As determined by careful analysis of the ^1H NMR spectra.

The facilities provided by the King Fahd University of Petroleum and Minerals, Dhahran, are gratefully acknowledged. We thank Mr. M. Arab for recording NMR spectra.

Received 13 November 2007; accepted 26 Janaury 2008
Paper 07/4939 *doi: 10.3184/030823408X287087*

References

1 J.J. Tufariello in *1,3-Dipolar cycloaddition chemistry*, ed. A. Padwa, Wiley-Interscience, New York 1984**,** *2*, Chap 9, pp 83-168.
2 P.N. Confalone and E.M. Huie, *Organic reactions,* 1988, **36**, 1.
3 S. Kanemasa, *Synlett,* 2002, 1371.
4 X. Ding, K. Taniguchi, Y. Ukaji and K. Inomata, *Chem. Lett.,* 2001, 468.
5 W.S. Jen, J.J.M. Wiener and D.W.C. MacMillan, *J. Am. Chem. Soc.,* 2000, **122**, 9874.
6 K.V. Gothelf and K.A. Jorgensen, *Chem. Commun.,* 2000, 1449.
7 G. Zecchi and G. Broggini, *Synthesis,* 1999, 905.
8 H. Pellissier, *Tetrahedron*, 2007, **63**, 3235.
9 S. Karlsson and H. –E. Högberg, *Org. Prep. Proc. Int.,* 2001, **33**, 103.
10 K.V. Goethelf and K.A. Jorgensen, *Chem. Rev.,* 1998, **98**, 863.
11 M. Frederickson, *Tetrahedron,* 1997, **53**, 403.
12 J. Revuelta, S. Cicchi, A. Goti and A. Brandi, *Synthesis,* 2007, 485.
13 A.E. Koumbis and J.K. Gallos, *Curr. Org. Chem.,* 2003, **7**, 585.
14 C. Belzecki and I. Panfil, *J. Org. Chem*., 1979, **44**, 1212.
15 R. Hanselmann, J. Zhou, P. Ma and P.N. Confalone, *J. Org. Chem*., 2003**,** **68**, 8739.
16 Q. Zhao, F. Han and D.L. Romero, *J. Org. Chem.,* 2002, **67**, 3317.
17 S.A. Ali and M.Z.N. Iman, *Tetrahedron,* 2007, **63**, 9134.
18 S.A. Ali, A. Hassan and M.I.M. Wazeer, *Spectrochim. Acta Part A,* 1995, **51**, 2279.
19 M.I.M. Wazeer and S.A. Ali, *Canad. J. Appl. Spectro.,* 1995, **40**, 53.
20 A. Hassan, M.I.M. Wazeer, H.P. Perzanowski and S.A. Ali, *J. Chem. Soc., Perkin Trans***.** *2,* 1997, 411.
21 E.J. Fornefeld and A.J. Pike, *J. Org. Chem*., 1979, **44**, 835.
22 M.I.M. Wazeer and S.A. Ali, *Canad. J. Appl. Spectro.,* 1995, **40**, 53.
23 R.S. Jones, J. Sutherland and D.F. Weaver, *Synth. Commun.,* 2003, **33**, 43.
24 R. Huisgen, *J. Org. Chem*., 1976, **41**, 403.
25 K. Fukui, *Acc. Chem. Res*., 1971, **4**, 57.
26 R. Sustmann, *Pure Appl Chem.,* 1974, **40**, 569.
27 K.N. Houk, J. Sims, R.E. Duke, R.W. Strozier and J.K. George, *J. Am. Chem. Soc.,* 1973, **95**, 7301.
28 J. Sims and K.N. Houk, *J. Am. Chem. Soc.,* 1973, **95**, 5798.
29 C.M. Joucla and J. Hamelin, *J. Chem. Res*., 1978, (*S*), 276; (*M*), 3535.
30 H. Seidl, R. Huisgen and R. Knorr, *Chem. Ber*., 1969, **102**, 904.
31 K.N. Houk, *Acc. Chem. Res*., 1975, **8**, 361.
32 M.D. Gordon, P.V. Alston and A.R. Rossi, *J. Am. Chem. Soc*., 1978, **100**, 5701.
33 M. Joucla, F. Tonnard, D. Gree and J. Hamelin, *J. Chem. Res*., 1978, (*S*), 240; (*M*), 2901-2912.
34 A.E.G. Miller, J.W. Biss and L.H. Schwartzman, *J. Org. Chem*., 1959, **24**, 627.
35 A.L. McCloskey, G.S. Fonken, R.W. Kluiber and W.S. Johnson, *Org. Synth., Coll.*, 1963*,* **4***,* 261.
36 C.R. Hauser, B.E. Hudson, B. Abramovitch and J.C. Shivers, *Org. Synth. Coll.,* 1955*,* **3**, 142.
37 J.J. Tufariello and J.P. Tette, *J. Org. Chem*., 1975, **40**, 3866.
38 P.W. Wovkulich and M.R. Uskovic, *Tetrahedron,* 1985, **41**, 3455.
39 O. Tamura, K. Gotanda, J. Yoshino, Y. Morita, R. Terashima, M. Kikuchi, T. Miyawaki, N. Mita, M. Yamashita, H. Ishibashi and M. Sakamoto, *J. Org. Chem.,* 2000, **65**, 8544.
40 S.A. Ali and H.P. Perzanowski, *J. Chem. Res. (S),* 1992, 146-147; *(M),* 1992, 1074.