Optically Active Tricarbonyl(η^6-*o*-trimethylsilylbenzaldehyde)chromium(0) Complexes in Organic Synthesis: a Highly Diastereoselective 1,3-Dipolar Cycloaddition with Electron-rich Olefins[1]

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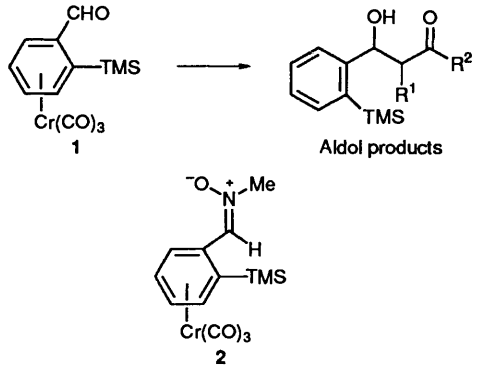
Heating of a racemic nitrone **2**, derived from tricarbonyl(η^6-*o*-trimethylsilylbenzaldehyde)chromium(0) complex **1**, with electron-rich olefins gave after decomplexation the *cis*-3,5-disubstituted isooxazolidines in a highly stereo- and regio-selective manner. Similarly, high selectivities were observed when the nitrone **9** possessing no silyl group at the *ortho* position on its benzene ring was employed instead of **2**. The corresponding non-complexed nitrones were found to provide the *cis*-isoxazolidines in a moderately selective fashion or the *trans*-ones predominantly. Treatment of chiral **2** with electron-rich olefins afforded the corresponding chiral *cis*-3,5-disubstituted isoxazolidines exclusively. The enantiomeric excess for cycloadducts thus obtained was determined to be 96–>98%. The absolute configuration of these optically active isoxazolidine derivatives was established on the basis of an X-ray crystallographic analysis.

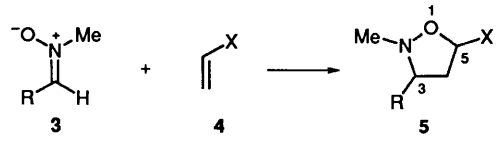
In the course of our program directed towards the development of highly stereoselective carbon–carbon bond formation mediated by tricarbonyl(η^6-arene)chromium(0) complexes, we have reported highly diastereoselective asymmetric aldol reactions[2] of optically active tricarbonyl(η^6-*o*-trimethylsilylbenzaldehyde)chromium(0) complex **1** with silyl nucleophiles. The chromium complexed aldehyde **1**, thus, has emerged as an important chiral synthon in the aldol reaction. The *ortho* trimethylsilyl (TMS) group in the complex **1** governs the geometry of the aldehyde group, whereas the chromium complexation[3] strictly controls the facial selectivity. These two intrinsically significant factors in the complex **1** can be considered to contribute mainly to the observed high stereoselectivity in the aldol reaction. Our endeavour is now focussed on taking advantage of prominent features of the complex **1** in the 1,3-dipolar cycloaddition of the nitrone **2** which should be easily derived from **1**. This paper deals with a highly diastereoselective asymmetric 1,3-dipolar cycloaddition of the chromium complexed nitrone **2** with electron-rich olefins.



Scheme 1

Results and Discussion

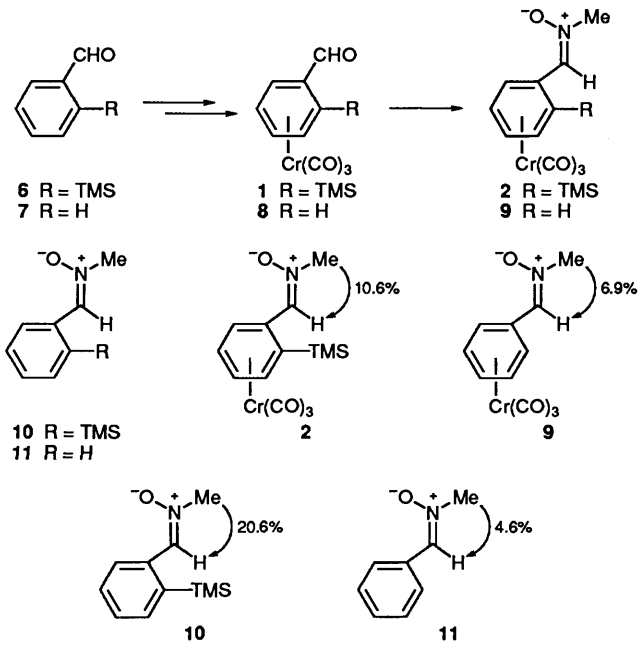
The 1,3-dipolar cycloaddition of nitrones **3**[4] has been well recognised as one of the most convenient and efficient methods for the construction of nitrogen-containing compounds.[5] The 1,3-dipolar cycloaddition of nitrones **3**[4] with various dipolarophiles **4** occurs regioselectively or nonselectively depending mainly on the electronic properties of the latter. With electron-rich dipolarophiles, the cycloaddition proceeds in a regioselective manner to afford the corresponding 3,5-disubstituted isoxazolidines **5**. However, the stereoselectivity observed was often not good enough to be considered satisfactory. We envisaged that in the reaction of the chromium complexed nitrones **2** and **9** the electron-donating functionality on the electron-rich olefins (dipolarophiles) would anchimerically release electrons to the greatly electron-deficient complexed aromatic ring[3] from the opposite face to the tricarbonylchromium moiety in the transition state. This neighbouring group participation in the transition state would control the stereochemistry of the reaction. On the basis of the above consideration we started to examine the 1,3-dipolar cycloaddition of the chromium complexed nitrones **2** and **9**.



Scheme 2

The starting chromium complexed nitrones **2** and **9** were prepared from the corresponding chromium complexed benzaldehyde derivatives **1** and **8**, respectively, by treatment[6] with *N*-methylhydroxylamine hydrochloride in methylene dichloride in the presence of sodium hydrogen carbonate. The geometry of the newly synthesised nitrones **2** and **9** was determined to be *Z* by nuclear Overhauser effect (NOE) experiments where 10.6 and 6.9% enhancement between the *N*-methyl protons and the vinylic proton were detected respectively in their ^{1}H NMR spectra. This enhancement is in good accordance with that obtained from the NOE experiment of the *N*-methylnitrone of benzaldehyde **11** (4.6% enhancement) whose regiochemistry had already been established.[4a] The *N*-methylnitrone of *o*-TMS-benzaldehyde **10** also revealed 20.6% enhancement following similar NOE studies.

The 1,3-dipolar cycloaddition was carried out by heating of the chromium complexed nitrone **9** with styrene **4a** in a sealed tube at 90 °C under a nitrogen atmosphere for 6 h to produce the cycloadduct **13a** with the chromium moiety intact. This was



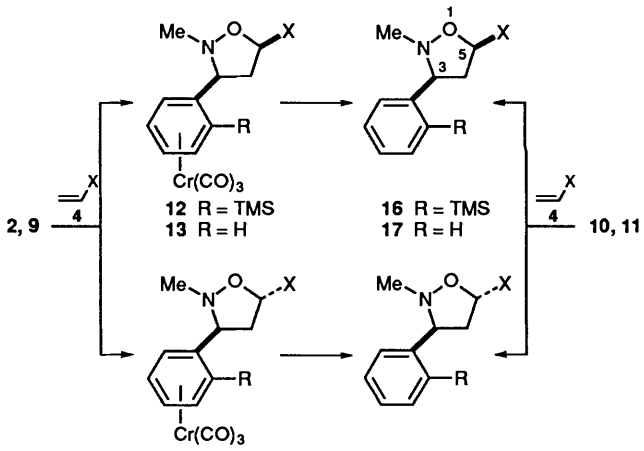
Scheme 3

Table 1 1,3-Dipolar cycloaddition of the nitrones **2**, **9**, **10**, **11** with dipolarophiles **4**

Entry	Nitrone	Dipolarophile	Product[a]		Yield (%)[b]
1	**2**	**4a**	**16a**, **18a**	>98: <2[c]	69
2	**9**	**4a**	**17a**, **19a**	>98: <2[c]	80
3	**10**	**4a**	**16a**, **18a**	18:82	96
4	**11**	**4a**	**17a**, **19a**	69:31	64
5	**11**	**4a**	**17a**, **19a**	67:33[d]	95
6	**2**	**4b**	**16b**, **18b**	>98: <2[c]	70
7	**9**	**4b**	**17b**, **19b**	>98: <2[c]	63
8	**10**	**4b**	**16b**, **18b**	28:72	91
9	**11**	**4b**	**17b**, **19b**	46:54	70
10	**11**	**4b**	**17b**, **19b**	50:50[e]	78
11	**2**	**4c**	**16c**, **18c**	74:26	51
12	**9**	**4c**	**17c**, **19c**	>98: <2[c]	85
13	**10**	**4c**	**16c**, **18c**	26:74	66
14	**11**	**4c**	**17c**, **19c**	67:33	71
15	**2**	**4d**	**16d**, **18d**	86:14[f]	15
16	**9**	**4d**	**17d**, **19d**	80:20	42
17	**10**	**4d**	**16d**, **18d**	25:75[f]	88
18	**11**	**4d**	**17d**, **19d**	40:60	54
19	**2**	**4e**	**16e**, **18e**	30:70[f]	66
20	**9**	**4e**	**17e**, **19e**	33:67[f]	64
21	**11**	**4e**	**17e**, **19e**	23:77[g]	—
22	**2**	**4f**	**16f**, **18f**	92:8	49

[a] Ratio of each isomer isolated by chromatography. [b] Isolated yields. [c] No *trans* isomer could be detected in the ^{1}H NMR spectrum. [d] The ratio taken from ref. 8. [e] The ratio taken from ref. 9. [f] Ratio of each isomer was determined by ^{1}H NMR spectrum. [g] The ratio taken from ref. 10*a*.

subsequently exposed to cerium(IV) ammonium nitrate (CAN)[7] in methanol at 0 °C to give exclusively the *cis*-3,5-disubstituted isoxazolidine **17a**[8] in 80% overall yield (Table 1, Entry 2). No regio- or stereo-isomers were detected in the reaction mixture. Similar treatment of the nitrone **2** having the TMS substituent at the *ortho* position with styrene **4a** provided again the corresponding *cis*-isomer **16a** in 69% yield (Table 1, Entry 1). The structure of **16a** was unambiguously elucidated by chemical transformation. The chromium complexed isoxazolidine **12a**, prepared from the reaction between **2** and **4a**, was desilylated with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) to yield **13a**, which was converted into **17a** by CAN treatment.[7] Conversion of **12a** into **17a** confirmed the structure of the former including, in particular, the stereochemical rearrangement. When ethyl vinyl ether **4b** was submitted to the cycloaddition with chromium complexed nitrones **2** and **9**, the corresponding *cis*-adducts **16b** and **17b**[9] were obtained exclusively in 70 and 63% yields, respectively (Entries 6 and 7). High stereoselectivity as well as regioselective control was realised in the reaction of the chromium complexed nitrones **2** and **9** with the electron-rich olefins **4a** and **4b**.



Scheme 4

Control experiments with the uncomplexed nitrones **10** and **11** strongly indicated that chromium complexation is mandatory for attaining high *cis* selectivity. Namely, upon treatment with styrene **4a** or ethyl vinyl ether **4b**, the nitrone **11** gave the adducts **17a** and **17b** either in a moderately *cis*-selective manner (Entries 4 and 5) or nonstereoselectively (Entries 9 and 10). Intriguingly, the *trans*-products **18a** and **18b** were predominantly formed when **4a** and **4b** were treated with the nitrone **10** possessing the TMS group at the *ortho* position (Entries 3 and 8).

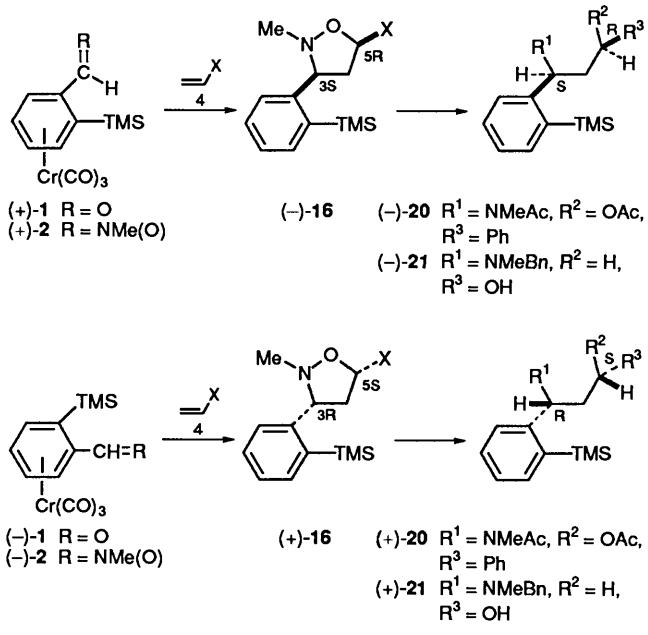
Vinyl acetate **4c** was found to afford, on exposure to the chromium complexed nitrone **9**, the *cis*-adduct **17c**[4a] exclusively in 85% yield (Entry 12). However, **4c** was unexpectedly no longer a suitable dipolarophile for highly *cis*-selective 1,3-dipolar cycloaddition with the chromium complexed nitrone **2** giving a mixture of **16c** and **18c** in a ratio of 74:26 in rather low yield (Entry 11). Changing the dipolarophile to trimethylsilylethene **4d**[6] again brought about a decrease of *cis* selectivity and poor chemical yields (Entries 15, 16). These results may reflect the differences in the electronic properties of the dipolarophiles, in other words the electron-releasing ability of substituents on the dipolarophiles. The above interpretation is supported by the fact that *cis* selectivity in the reaction of **2** with *p*-bromostyrene **4f** was slightly diminished (**16f**–**18f**, 92:8, Entry 22) compared with that for the parent styrene **4a** (**16a**–**18a**, >98: <2, Entry 1). It is worthwhile, therefore, to examine the cycloaddition of the chromium complexed nitrones **2** and **9** with the electron-deficient dipolarophile, acrylonitrile **4e** in order to gain more information about the origin of *cis* selectivity. The reactions of **2** and **9** with **4e** were performed under standard conditions. The observed ratios of **16e** to **18e** and **17e** to **19e** were 30 to 70 and 33 to 67, respectively (Entries 19 and 20). These results were in sharp contrast to those obtained from the reaction of **2** and **9** with electron-rich olefins such as **4a** and **4b**. This *trans* bias is similar to a reported result for the reaction[10] of the

uncomplexed nitrone **11** with **4e** (Entry 21). It should be mentioned that both chromium complexation and electron-rich olefins are necessary to attain high *cis* selectivity.

To sum up the results presented in Table 1 briefly: (i) the 1,3-dipolar cycloaddition of the chromium complexed nitrones with electron-rich olefins proceeds in a completely stereocontrolled way to furnish the *cis*-3,5-disubstituted isoxazolidines; (ii) the *ortho* TMS group in the chromium complexed nitrones is not essential for exclusive *cis* stereoselectivity; (iii) diastereoselectivity is markedly affected by the characteristics of the substituent on the dipolarophiles; (iv) uncomplexed nitrones show moderate stereoselectivity depending on dipolarophiles employed although it is not easy to predict. Thus, we have developed a novel way to control the stereoselectivity of this cycloaddition process by introduction of a tricarbonylchromium moiety onto the benzene ring. The most significant feature of our method is that the 1,3-dipolar cycloaddition of the chromium complexed nitrone **2** could be potentially, and easily, extended to an asymmetric situation.[2,4] The next stage of this investigation was to utilise the chiral chromium complexed nitrones, (+)- and (−)-**2** as chiral synthons in the 1,3-dipolar cycloaddition.

Asymmetric 1,3-*Dipolar Cycloaddition of Optically Active Nitrones,* (+)- *and* (−)-**2** *with Electron-rich Olefins* **4a**, **4b**.— Optically active nitrones, (+)- and (−)-**2** were prepared from the corresponding optically active aldehydes, (+)- and (−)-**1**[2d,11] according to the procedure described for the preparation of the racemic nitrone complex. The nitrone, (+)-**2** was submitted to the cycloaddition with styrene **4a**, followed by decomplexation with CAN to afford the optically active *cis*-3,5-disubstituted isoxazolidine, (−)-**16a** {$[\alpha]_D^{20}$ −210 (*c* 0.26, $CHCl_3$)} in 65% yield. Similar treatment of the enantiomeric nitrone, (−)-**2** provided (+)-**16a** {$[\alpha]_D^{16}$ +222 (*c* 0.29, $CHCl_3$)} in 68% yield. An asymmetric 1,3-dipolar cycloaddition of (+)- and (−)-**2** with ethyl vinyl ether **4b** also effected formation of an optically active isoxazolidine ring to yield, after decomplexation, (−)-**16b** {$[\alpha]_D^{21}$ −220 (*c* 0.30, $CHCl_3$)} and (+)-**16b** {$[\alpha]_D^{27}$ + 206 (*c* 0.17, $CHCl_3$)} in 62 and 60% yields, respectively. Unfortunately, optical purity of these isoxazoldine derivatives could not be directly determined by ^1H NMR spectroscopy using shift reagents such as tris[3-(heptafluoromethylhydroxymethylene)-(+)-camphorato]-europium(III) [Eu(hfc)$_3$].

In order to estimate the enantiomeric excess (e.e.) of the optically active isoxazolidines **16a** and **16b**, these compounds were converted into the corresponding amino alcohol derivatives. The nitrogen–oxygen bond of the isoxazolidine ring of (+)- and (−)-**16a** was cleaved reductively by Raney nickel[8] in ethanol in a stream of hydrogen at reflux temperature to give the corresponding amino alcohols which were subsequently acetylated with acetic anhydride and 4-(*N*,*N*-dimethylamino)-pyridine in methylene dichloride to furnish (+)- and (−)-**20** in 72 and 74% yields, respectively. ^1H NMR spectral examination of (+)- and (−)-**20** in the presence of tris[3-(trifluoromethylhydroxymethylene)-(−)-camphorato)europium(III) [Eu(tfc)$_3$] revealed that each product was made up of a single enantiomer (the corresponding peaks due to the antipode could not be detected). On the other hand, cleavage of the nitrogen–oxyen bond of (+)- and (−)-**16b** could not be realised under the conditions employed for **16a**. An alternative was conceived for fission of the nitrogen–oxygen bond of **16b**. Benzylation[12] of (+)- and (−)-**16b** with benzyl bromide in methylene dichloride in a sealed tube at 80 °C gave the ammonium salts, reduction of which with lithium aluminium hydride (LAH) in THF at refluxing temperature provided the N–O bond-cleaved products, (+)- and (−)-**21**, respectively. The e.e. measurement for these *N*-benzyl hydroxy derivatives was performed by ^1H NMR analysis in the presence of [Eu(hfc)$_3$]. The optical purity of (+)- and (−)-**21** was shown to be 96 and 97% e.e., respectively. These e.e. values for optically active **20** and **21** should reflect those of isoxazolidines, (+)- and (−)-**16a** and **16b**. Although we were not able to evaluate the e.e. of optically active isoxazolidines directly, chemical transformation of these products into the corresponding amino alcohol derivatives allowed us to estimate their e.e. to be 96–>98%.



Scheme 5

The absolute configuration of optically active isoxazolidines was determined on the basis of an X-ray crystallographic analysis. Reaction of racemic **2** with *p*-bromostyrene **4f** (*vide ante*, Scheme 4) gave racemic **12f** along with a small amount of racemic **14f**. A mixture of **12f** and **14f** was recrystallised from ethanol to furnish pure **12f** as yellow prisms suitable for an X-ray crystallographic analysis.

An X-ray crystallographic analysis of racemic **12f** showed the relative stereochemistry of the stereogenic centres on the 3 and 5 positions and benzene ring to be 3*R**,5*S**,1′*R** as described in Fig. 1. The X-ray analysis of **12f** established the absolute stereochemistry of (+)-**16** to be 3*R*,5*S*, whereas an antipode, (−)-**16** has the 3*S*,5*R* configuration because the absolute configuration[2d] of starting chromium complexed aldehydes (+)- and (−)-**1** have already been unambiguously determined. In addition, the above analysis allowed us to establish the absolute stereochemistry of the amino alcohol derivatives (+)-**20** and (+)-**21** to be 1*R*,3*S* and 1*R*, whereas (−)-**20** and (−)-**21** to be 1*S*,3*R* and 1*S*, respectively.

As mentioned earlier, there are several informative features available to understand the reaction pathway for exclusive formation of *cis*-3,5-disubstituted isoxazolidines. The first is that chromium complexation is essential and the second is that electron-releasing ability of dipolarophiles must play a significant role. Combination of these two factors results in occurrence of high *cis* selectivity. Once either of these two factors are removed or downgraded, satisfactory selectivity should not be expected. Furthermore, X-ray analysis and the determination of the absolute stereochemistry of the optically active isoxazolidines provided more information which contributed to a more precise understanding of the reaction mechanism.

Although the mechanism for this highly *cis* selective 1,3-dipolar cycloaddition of the chromium complexed nitrones **2**

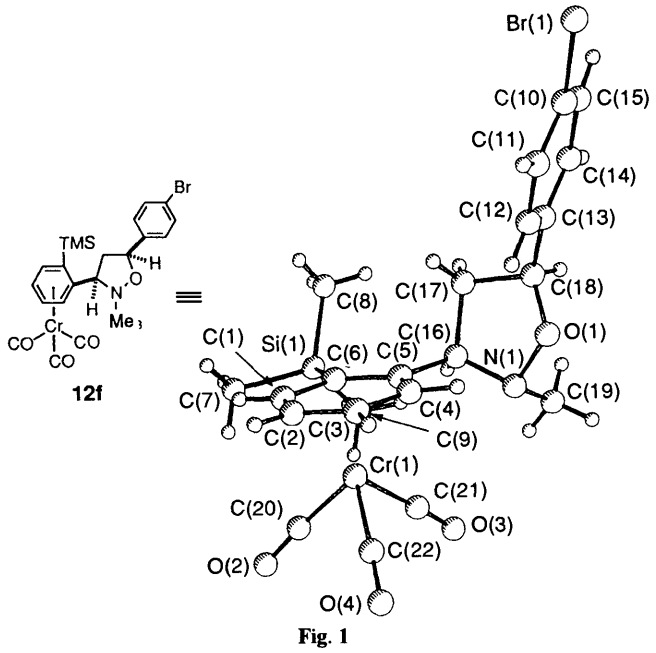


Fig. 1

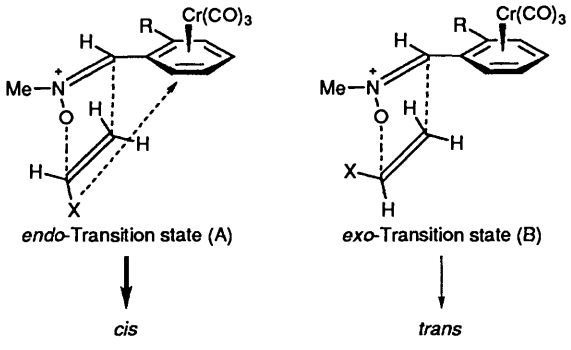


Fig. 2

and **9** with electron-rich olefins has not been, as yet, fully clarified, it can be best rationalised in terms of the possible transition states. The *endo*-transition state **A** offers the advantage of releasing electrons through space from the electron-rich substituent on the dipolarophile to the electron-deficient aromatic ring. This results in a more stable (lower energy) transition state. The corresponding *exo* transition state **B** does not have such a stabilising factor. When uncomplexed nitrones **10** and **11** are considered rather than **2** and **9**, repulsion between the *p*-orbital electrons of the benzene ring and the electron-rich substituent on the dipolarophile, in the *endo* transition state (**A**-type), would become a serious destabilising element. Preference of the *endo* transition state (**A**-type) over the *exo* transition state (**B**-type), therefore, is not expected from the stereoelectronic arguments and does not account for the formation of isoxazolidines either less selectively or nonselectively. The highly enantiomeric excess observed for (+)- and (−)-**16** can be best explained by the assumption that the trajectory of approach of dipolarophiles to the chromium complexed nitrones must be from the face opposite to that occupied by the chromium complexation. This prediction is strongly supported by consideration of the absolute configuration of products.

Thus, a highly *cis*-selective 1,3-dipolar cycloaddition between the chromium complexed nitrones and electron-rich olefins has been developed. Furthermore, it became evident that the highly enantiomeric excess for the isoxazolidine derivatives was realised when chiral nitrones were employed.

Experimental

M.p.s were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. IR spectra were measured with a JASCO A-102 spectrometer in $CHCl_3$, mass spectra with a Hitachi M-80 mass spectrometer, optical rotations with a JASCO DIP-181 digital polarimeter, ^1H NMR spectra with JEOL JNM-GX 400 and JNM-GSX 500 spectrometers in $CDCl_3$ using tetramethylsilane as an internal standard unless otherwise stated, ^{13}C NMR spectra with a JEOL EX-270 spectrometer in $CDCl_3$ with $CDCl_3$ (77.0 ppm) as an internal reference. All *J* values are in Hz and $[\alpha]_D$ values in 10^{-1} deg cm^2 g^{-1}. Methylene dichloride was freshly distilled from P_2O_5 and THF from sodium diphenylketyl prior to use. Silica gel (silica gel 60, 230–400 mesh, Nacalai Tesque) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4. Compounds **1**,[2d,11] **8**,[13] **11**[9] were prepared according to the literature procedures.

Tricarbonyl[η^6-(Z)-N-(2-*trimethylsilylbenzylidene*)*methylamine* N-*oxide*]*chromium*(0) **2**.—A solution of the chromium complexed aldehyde **1** (569 mg, 1.81 mmol) and *N*-methylhydroxylamine hydrochloride (181 mg, 2.17 mmol) in methylene dichloride (15 cm^3) was refluxed in the presence of $NaHCO_3$ (482 mg, 5.74 mmol) for 9 h. After cooling, $NaHCO_3$ was filtered off and the filtrate was concentrated to dryness. Chromatography of the residue with hexane–acetone (10:3) gave **2** (609 mg, 98%) as red needles, m.p. 108–110 °C (from hexane–benzene) (Found: C, 48.75; H, 5.0; N, 3.9. $C_{14}H_{17}CrNO_4Si$ requires C, 48.97; H, 4.99; N, 4.08%); ν_{max}/cm^{-1} 1980, 1900 (CO) and 1580 (CH=N); δ_H 7.22 (1 H, s, CH=N), 6.91 (1 H, d, *J* 6.9, aromatic-H), 5.62 (1 H, t, *J* 6.4, aromatic-H), 5.44 (1 H, d, *J* 6.9, aromatic-H), 5.25 (1 H, t-like, *J* 6.2, aromatic-H), 3.86 (3 H, s, CH_3) and 0.41 (9 H, s, TMS); δ_C 232.68, 131.99, 101.83, 98.99, 98.87, 93.89, 91.93, 90.96, 54.97 and 0.40; *m*/*z* 343 (M$^+$, 0.5), 243 (28), 192 (27), 176 (100) and 73 (9).

Tricarbonyl[η^6-(Z)-N-(*benzylidene*)*methylamine* N-*oxide*]-*chromium*(0) **9**.—According to the procedure described for the preparation of **2**, **8** (153 mg, 0.63 mmol) was treated with *N*-methylhydroxylamine hydrochloride (100 mg, 0.80 mmol) and $NaHCO_3$ (246 mg, 2.00 mmol) in methylene dichloride (5 cm^3) to give, after chromatography with hexane–acetone (10:4), **9** (163 mg, 95%) as yellow needles, m.p. 123–125 °C (from hexane–ethyl acetate) (Found: C, 48.6; H, 3.2; N, 5.2. $C_{11}H_9CrNO_4$ requires C, 48.72; H, 3.35; N, 5.16%); ν_{max}/cm^{-1} 1980, 1900 (CO) and 1590 (CH=N); δ_H 6.97 (1 H, s, CH=N), 6.36 (2 H, d, *J* 6.3, aromatic-H), 5.47 (1 H, t-like, *J* 6.0, aromatic-H), 5.31 (2 H, t-like, *J* 6.4, aromatic-H) and 3.83 (3 H, s, CH_3); δ_C 232.92, 131.54, 95.06, 93.64, 93.44, 90.42 and 54.56; *m*/*z* 271 (M$^+$, 81), 215 (63), 187 (100) and 118 (75).

(Z)-N-(2-*Trimethylsilylbenzylidene*)*methylamine* N-*Oxide* **10**.—According to the procedure described for the preparation of **2**, 2-trimethylsilylbenzaldehyde **6** (462 mg, 2.59 mmol) was treated with *N*-methylhydroxylamine hydrochloride (281 mg, 3.37 mmol) and $NaHCO_3$ (544 mg, 6.48 mmol) in methylene dichloride (15 cm^3) to give **10** (499 mg, 93%) as colourless needles, m.p. 66–68 °C (from hexane) (Found: C, 63.5; H, 8.2; N, 7.0. $C_{11}H_{17}NOSi$ requires C, 63.72; H, 8.26; N, 6.76%); δ_H 9.18 (1 H, d, *J* 7.8, aromatic-H), 7.62 (1 H, s, CH=N), 7.57–7.55 (1 H, m, aromatic-H), 7.48–7.45 (1 H, m, aromatic-H), 7.39–7.38 (1 H, m, aromatic-H), 3.90 (3 H, s, CH_3) and 0.37 (9 H, s, TMS); δ_C 139.71, 135.00, 134.95, 134.39, 129.39, 129.22, 127.94, 54.86 and 0.42; *m*/*z* 207 (M$^+$, 10), 192 (100), 134 (33) and 73 (36).

General Procedure for 1,3-*Dipolar Cycloaddition of Chromium Complexed Nitrones* **2** *and* **9** *with the Dipolarophiles* **4**.—A mixture of the nitrone and dipolarophile **4** was heated in a

sealed tube or refluxed for 6–72 h (monitored by TLC). Excess of the dipolarophile **4** was removed by evaporation or by passage through a short pad of silica gel. The crude cycloadducts were dissolved in methanol, to which CAN (3 equiv.) was added portionwise at 0 °C. The reaction mixture was stirred at 0 °C for *ca.* 30 min (decomplexation could be monitored by TLC) and methanol was evaporated off. The residue was diluted with water and extracted with methylene dichloride several times. The combined methylene dichloride layers were washed with water and brine, dried and concentrated to dryness. Chromatography of the residue gave isoxazolidines. The yields and ratio of each isomer are listed in Table 1.

(3R*,5S*)-2-*Methyl*-5-*phenyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine* **16a**.—The isoxazolidine **16a** (47 mg, 69%) was obtained from the reaction of **2** (76 mg, 0.22 mmol) with **4a** (3 cm^3) (conditions: heated in a sealed tube at 90 °C for 6 h, chromatography with hexane–ethyl acetate, 20:1). The isoxazolidine **16a** was a colourless oil (Found: M^+, 311.1712. $C_{19}H_{25}NOSi$ requires *M*, 311.1704); δ_H 7.64 (1 H, d, *J* 7.9, aromatic-H), 7.51–7.46 (3 H, m, aromatic-H), 7.39–7.33 (3 H, m, aromatic-H), 7.29–7.23 (2 H, m, aromatic-H), 5.26 (1 H, t, *J* 7.7, 5-H), 4.05 (1 H, dd, *J* 6.7 and 9.8, 3-H), 3.12 (1 H, ddd, *J* 6.7, 7.7 and 12.5, 4-H), 2.71 (3 H, s, CH_3), 2.35 (1 H, ddd, *J* 7.7, 9.8 and 12.5, 4-H) and 0.39 (9 H, s, TMS); δ_C 145.10, 143.45, 138.38, 134.25, 129.90, 128.45, 127.24, 127.04, 126.83, 125.88, 78.15, 73.05, 50.35, 43.49 and 0.99; *m/z* 311 (M^+, 74), 206 (29), 176 (58) and 28 (32). (3R*,5S*,1'R*)-*Tricarbonyl*[2-*methyl*-5-*phenyl*-3-(η^6-2-*trimethylsilylphenyl*)*isoxazolidine*]*chromium*(0) (**12a**) could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **12a** was a yellow oil (Found: M^+, 447.0939. $C_{22}H_{25}CrNO_4Si$ requires M, 447.0955; ν_{max}/cm^{-1} 1970 and 1900 (CO); δ_H 7.37–7.27 (5 H, m, aromatic-H), 5.78 (1 H, d, *J* 6.0, aromatic-H), 5.67 (1 H, t, *J* 6.0, aromatic-H), 5.40 (1 H, d, *J* 6.0, aromatic-H), 5.36 (1 H, t, *J* 8.2, 5-H), 5.12 (1 H, t, *J* 6.0, aromatic-H), 4.10 (1 H, dd, *J* 5.8 and 8.7, 3-H), 3.27 (1 H, ddd, *J* 8.2, 8.7 and 12.7, 4-H), 2.98 (3 H, s, CH_3), 2.10 (1 H, ddd, *J* 5.8, 8.2 and 12.7, 4-H) and 0.40 (9 H, s, TMS); *m/z* 447 (M^+, 6), 363 (100), 244 (46), 176 (69), 73 (5) and 28 (8).

(3R*,5S*)-2-*Methyl*-3,5-*diphenylisoxazolidine* **17a**.—The isoxazolidine **17a** (50 mg, 80%) was obtained from the reaction of **9** (70 mg, 0.26 mmol) with **4a** (3 cm^3) (conditions: heated in a sealed tube at 90 °C for 6 h, chromatography with hexane–acetone, 20:1). The isoxazolidine **17a** was a colourless oil (Found: M^+, 239.1284. $C_{16}H_{17}NO$ requires *M*, 239.1309); δ_H 7.38–7.30 (10 H, m, aromatic-H), 5.28 (1 H, t, *J* 7.6, 5-H), 3.82 (1 H, dd, *J* 6.8 and 9.8, 3-H), 3.13 (1 H, ddd, *J* 6.8, 7.6 and 12.2, 4-H), 2.66 (3 H, s, CH_3) and 2.43 (1 H, ddd, *J* 7.6, 9.8 and 12.2, 4-H); *m/z* 239 (M^+, 24), 193 (62), 134 (100) and 115 (28). (3R*,5S*,1'R*)-*Tricarbonyl*[2-*methyl*-3-(η^6-*phenyl*)-5-*phenylisoxazolidine*]*chromium*(0) **13a** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **13a** was a yellow oil (Found: M^+, 375.0526. $C_{19}H_{17}CrNO_4$ requires *M*, 375.0561); ν_{max}/cm^{-1} 1970 and 1890 (CO); δ_H 7.38–7.27 (5 H, m, aromatic-H), 5.67 (1 H, d, *J* 6.4, aromatic-H), 5.38–5.27 (4 H, m, aromatic-H and 5-H), 5.23 (1 H, d, *J* 6.4, aromatic-H), 3.78 (1 H, t *J* 7.6, 3-H), 3.24 (1 H, td, *J* 7.6 and 12.6, 4-H), 2.90 (3 H, s, CH_3) and 2.28 (1 H, td, *J* 7.6 and 12.6, 4-H); *m/z* 375 (M^+, 2), 292 (17), 187 (100) and 52 (19).

(3R*,5S*)-5-*Ethoxy*-2-*methyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine* **16b**.—The isoxazolidine **16b** (29.6 mg, 70%) was obtained from the reaction of **2** (52 mg, 0.15 mol) with **4b** (5 cm^3) (conditions: heated in a sealed tube at 90 °C for 72 h, chromatography with hexane–ethyl acetate, 20:1). The isoxazolidine **16b** was a colourless oil (Found: M^+, 279.1534. $C_{15}H_{25}NO_2Si$ requires *M*, 297.1653); δ_H 7.78 (1 H, d, *J* 7.5, aromatic-H), 7.46 (1 H, d, *J* 7.5, aromatic-H), 7.39 (1 H, t-like, *J* 7.5, aromatic-H), 7.27–7.23 (1 H, m, aromatic-H), 5.19 (1 H, dd, *J* 3.0 and 6.4, 5-H), 3.95 (1 H, qd, *J* 7.0 and 9.4, OCH_2CH_3), 3.76 (1 H, t, *J* 9.2, 3-H), 3.54 (1 H, qd, *J* 7.0 and 9.4, OCH_2CH_3), 2.91 (1 H, ddd, *J* 6.4, 9.2 and 13.4, 4-H), 2.60 (3 H, s, CH_3), 2.24 (1 H, ddd, *J* 3.0, 9.2 and 13.4, 4-H), 1.28 (3 H, t, *J* 7.0, CH_3) and 0.36 (9 H, s, TMS); δ_C 144.26, 138.62, 134.21, 129.90, 127.51, 126.97, 100.97, 72.31, 63.87, 48.43, 43.02, 15.08 and 0.96; *m/z* 279 (M^+, 6), 192 (29), 115 (100), 73 (35) and 28 (30). (3R*,5S*,1'R*)-*Tricarbonyl*[5-*ethoxy*-2-*methyl*-3-(η^6-2-*trimethylsilylphenyl*)-*isoxazolidine*]*chromium*(0) **12b** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **12b** was a yellow oil (Found: M^+, 415.0865. $C_{18}H_{25}CrNO_5Si$ requires *M*, 415.0905); ν_{max}/cm^{-1} 1970 and 1890 (CO); δ_H 5.89 (1 H, d, *J* 6.4, aromatic-H), 5.50 (1 H, dt, *J* 1.2 and 6.4, aromatic-H), 5.31 (1 H, dd, *J* 1.2 and 6.4, aromatic-H), 5.25 (1 H, dt, *J* 1.2 and 6.4, aromatic-H), 5.18 (1 H, dd, *J* 1.5 and 5.8, 5-H), 3.82 (1 H, qd, *J* 7.0 and 9.7, OCH_2CH_3), 3.71 (1 H, dd, *J* 5.5 and 9.6, 3-H), 3.44 (1 H, qd, *J* 7.0 and 9.7, OCH_2CH_3), 2.94 (1 H, ddd, *J* 5.8, 9.6 and 13.1, 4-H), 2.90 (3 H, s, CH_3), 2.10 (1 H, ddd, *J* 1.5 and 5.5 and 13.1, 4-H), 1.19 (3 H, t, *J* 7.0, CH_3) and 0.40 (9 H, s, TMS); *m/z* 415 (M^+, 1), 243 (44), 176 (100), 73 (17), 52 (16) and 28 (4).

(3R*,5S*)-5-*Ethoxy*-2-*methyl*-3-*phenylisoxazolidine* **17b**.—The isoxazolidine **17b** (26.7 mg, 63%) was obtained from the reaction of **9** (55 mg, 0.16 mmol) with **4b** (5 cm^3) (conditions: heated in a sealed tube at 90 °C for 72 h, chromatography with hexane–ethyl acetate, 10:1). The isoxazolidine **17b** was a colourless oil (Found: M^+, 207.1243. $C_{12}H_{17}NO_2$ requires *M*, 207.1257); δ_H 7.41 (2 H, d, *J* 7.9, aromatic-H), 7.35–7.27 (3 H, m, aromatic-H), 5.19 (1 H, dd, *J* 3.2 and 6.3, 5-H), 3.93 (1 H, qd, *J* 7.0 and 9.6, OCH_2CH_3), 3.52 (1 H, qd, *J* 7.0 and 9.6, OCH_2CH_3), 3.43 (1 H, t, *J* 9.6, 3-H), 2.93 (1 H, ddd, *J* 6.3, 9.6 and 13.4, 4-H), 2.58 (3 H, s, CH_3), 2.34 (1 H, ddd, *J* 3.2, 9.6 and 13.4, 4-H) and 1.27 (3 H, t, *J* 7.0, CH_3); *m/z* 207 (M^+, 8), 161 (66), 134 (29) and 118 (16). (3R*,5S*,1'R*)-*Tricarbonyl*[5-*ethoxy*-2-*methyl*-3-(η^6-*phenyl*)*isoxazolidine*]*chromium*(0) **13b** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **13b** was a yellow oil (Found: $M^+ + 1$, 344.0490. $C_{15}H_{18}CrNO_5$ requires M + 1, 344, 0490); ν_{max}/cm^{-1} 1970 and 1890 (CO); δ_H 5.55–5.52 (1 H, m, aromatic-H), 5.49 (1 H, d, *J* 6.1, aromatic-H), 5.36–5.28 (3 H, m, aromatic-H), 5.15 (1 H, dd, *J* 2.1 and 6.1, 5-H), 3.84 (1 H, qd, *J* 7.0 and 9.5, OCH_2CH_3), 3.48 (1 H, qd, *J* 7.0 and 9.5, OCH_2CH_3), 3.28 (1 H, t, *J* 8.2, 3-H), 2.99 (1 H, ddd, *J* 6.1, 8.2 and 14.1, 4-H), 2.75 (3 H, s, CH_3), 2.28 (1 H, ddd, *J* 2.1, 8.2 and 14.1, 4-H) and 1.23 (3H, t, *J* 7.0, CH_3); *m/z* 343 (M^+, 0.2), 287 (30), 171 (100) and 52 (12).

(3R*,5S*)- *and* (3R*,5R*)-5-*Acetoxy*-2-*methyl*-3-(2-*trimethylsilyphenyl*]*isoxazolidines* **16c** *and* **18c**.—The isoxazolidine **16c** (14.8 mg, 38%) and **18c** (13.3 mg, 13%) were obtained from the reaction of **2** (46 mg, 0.13 mmol) with **4c** (4 cm^3) (conditions: heated at 75 °C for 24 h, chromatography with benzene–ethyl acetate, 50:1). The isoxazolidine **16c** had m.p. 101.5–103.5 °C (from hexane–ethyl acetate) as colourless needles (Found: C, 61.4; H, 7.9; N, 4.8. $C_{15}H_{23}NO_3Si$ requires C, 61.40; H, 7.90; N, 4.77%); ν_{max}/cm^{-1} 1735 (CO); δ_H 7.76 (1 H, d, *J* 7.6, aromatic-H), 7.49 (1 H, dd, *J* 1.2 and 7.6, aromatic-H), 7.44–7.40 (1 H, m, aromatic-H), 7.30–7.26 (1 H, m, aromatic-H), 6.35 (1 H, dd, *J* 2.7 and 6.8, 5-H), 3.86 (1 H, dd, *J* 7.9 and 9.8, 3-H), 3.07 (1 H, ddd, *J* 6.8, 7.9 and 13.7, 4-H), 2.65 (3 H, s, CH_3), 2.35 (1 H, ddd, *J* 2.7, 9.8 and 13.7, 4-H), 2.16 (3 H, s, CH_3) and 0.37 (9 H, s, TMS); δ_C 170.87, 143.54, 139.01, 134.47, 122.99, 127.28, 127.01, 95.10, 71.94, 48.04, 43.09, 21.42 and 0.96; *m/z* 293 (M^+, 33), 208 (54), 176 (29), 84 (100), 73 (64) and 28 (6). The

isoxazolidine **18c** had m.p. 118–119 °C (from hexane–ethyl acetate) as colourless needles (Found: C, 61.3; H, 7.8; N, 4.7. $C_{15}H_{23}NO_3Si$ requires C, 61.40; H, 7.90; N, 4.77%); ν_{max}/cm^{-1} 1740 (CO); δ_H 7.70 (1 H, d, *J* 7.6, aromatic-H), 7.50 (1 H, dd, *J* 1.2 and 7.6, aromatic-H), 7.42–7.38 (1 H, m, aromatic-H), 7.30–7.26 (1 H, m, aromatic-H), 6.39 (1 H, d, *J* 4.0, 5-H), 4.31 (1 H, br s, 3-H), 2.81 (3 H, s, CH_3), 2.65–2.54 (2 H, m, 4-H), 2.13 (3 H, s, CH_3) and 0.39 (9 H, s, TMS); δ_C 170.03, 143.78, 138.69, 134.51, 129.91, 127.28, 126.74, 96.44, 69.11, 47.59, 46.08, 21.38 and 0.87; *m/z* 293 (M^+, 26), 208 (37), 176 (26), 84 (100), 73 (40) and 28 (19).

(3R*,5S*,1'R*)- *and* (3R*,5R*,1'R*)-5-*Acetoxy*-2-*methyl*-3-(η^6-2-*trimethylsilylphenyl*)*isoxazolidine*(*tricarbonyl*)*chromium*(0) **12c** *and* **14c** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **12c** had m.p. 117–119 °C (from diethyl ether) as yellow solids (Found: M^+, 429.0727. $C_{18}H_{23}CrNO_6Si$ requires *M*, 429.0698); ν_{max}/cm^{-1} 1990, 1910 and 1750 (CO); δ_H 6.36 (1 H, dd, *J* 1.5 and 6.4, 5-H), 5.86 (1 H, d, *J* 6.4, aromatic-H), 5.52–5.49 (1 H, m, aromatic-H), 5.34–5.30 (2 H, m, aromatic-H), 3.79 (1 H, dd, *J* 5.9 and 9.3, 3-H), 3.10 (1 H, ddd, *J* 6.4, 9.3 and 13.7, 4-H), 2.95 (3 H, s, CH_3), 2.23 (1 H, ddd, *J* 1.5, 5.9 and 13.7, 4-H), 2.05 (3 H, s, CH_3) and 0.41 (9 H, s, TMS); *m/z* 429 (M^+, 1), 302 (20), 243 (11), 176 (100), 73 (14) and 52 (4). The chromium complexed isoxazolidine **14c** had m.p. 114–115 °C (from hexane–methylene dichloride) as yellow needles (Found: M^+, 429.0759. $C_{18}H_{23}CrNO_6Si$ requires *M*, 429.0698); ν_{max}/cm^{-1} 1990, 1910 and 1750 (CO); δ_H 6.40 (1 H, d, *J* 4.9, 5-H), 5.58–5.56 (2 H, m, aromatic-H), 5.38 (1 H, d, *J* 6.8, aromatic-H), 5.23 (1 H, t, *J* 6.8, aromatic-H), 4.06 (1 H, br s, 3-H), 2.86 (1 H, dd, *J* 6.4 and 13.7, 4-H), 2.76–2.64 (4 H, m, N-CH_3 and 4-H), 2.11 (3 H, s, CH_3) and 0.45 (9 H, s, TMS); *m/z* 429 (M^+, 3), 302 (17), 243 (7), 176 (100), 73 (12) and 52 (4).

(3R*,5S*)-5-*Acetoxy*-2-*methyl*-3-*phenylisoxazolidine* **17c**.—The isoxazolidine **17c** (28 mg, 85%) was obtained from the reaction of **9** (41 mg, 0.15 mmol) with **4c** (4 cm^3) (conditions: heated at 75 °C for 24 h, chromatography with benzene–acetone, 10:1). The isoxazolidine **17c** had m.p. 66.5–67 °C (from hexane) as colourless needles (Found: C, 65.2; H, 7.1; N, 6.3. $C_{12}H_{15}NO_3$ requires C, 65.14; H, 6.83; N, 6.33%); ν_{max}/cm^{-1} 1740 (CO); δ_H 7.43–7.31 (5 H, m, aromatic-H), 6.34 (1 H, dd, *J* 3.0 and 6.5, 5-H), 3.54 (1 H, dd, *J* 8.0 and 10, 3-H), 3.06 (1 H, ddd, *J* 6.5, 8.0 and 14.5, 4-H), 2.64 (3 H, s, CH_3), 2.46 (1 H, ddd, *J* 3.0, 10 and 14.5, 4-H) and 2.15 (3 H, s, CH_3); *m/z* 221 (M^+, 27), 179 (27), 105 (100) and 43 (36). (3R*,5S*,1'R*)-5-*Acetoxy*-2-*methyl*-3-(η^6-*phenyl*)*isoxazolidine*(*tricarbonyl*)*chromium*(0) **13c** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **13c** was a yellow oil (Found: M^+, 357.0233. $C_{15}H_{15}CrNO_6$ requires *M*, 357.0302); ν_{max}/cm^{-1} 1970, 1900 and 1745 (CO); δ_H 6.33 (1 H, dd, *J* 1.8 and 6.4, 5-H), 5.50 (2 H, t-like, *J* 6.4, aromatic-H), 5.40–5.29 (3 H, m, aromatic-H), 3.38 (1 H, t, *J* 8.5, 3-H), 3.15 (1 H, ddd, *J* 6.4, 8.5 and 14, 4-H), 2.79 (3 H, s, CH_3), 2.40 (1 H, ddd, *J* 1.8, 8.5 and 14, 4-H) and 2.10 (3 H, s, CH_3); *m/z* 357 (M^+, 0.3), 230 (100), 171 (31) and 52 (11).

(3R*,5S*)- *and* (3R*,5R*)-2-*Methyl*-5-*trimethylsilyl*-3-(2-*trimethylsilylphenyl*)*isoxazolidines* **16d** *and* **18d**.—The isoxazolidines **16d** and **18d** (7 mg, 15%) were obtained from the reaction of **2** (51 mg, 0.15 mmol) with **4d** (1.5 cm^3) (conditions: heated in benzene (0.5 cm^3) in a sealed tube at 80 °C for 24 h, chromatography with hexane–benzene–ethyl acetate, 10:10:1). The isoxazolidines **16d** and **18d** were obtained as an inseparable colourless oil (Found: M^+, 307.1778. $C_{16}H_{29}NOSi_2$ requires *M*, 307.1786); δ_H 7.73 (0.14 H, d, *J* 7.8, aromatic-H), 7.62 (0.86 H, d, *J* 7.8, aromatic-H), 7.47 (0.14 H, dd, *J* 1.5 and 7.3, aromatic-H), 7.44 (0.86 H, d, *J* 7.8, aromatic-H), 7.39 (1 H, t, *J* 7.3, aromatic-H), 7.25–7.19 (1 H, m, aromatic-H), 4.01 (0.86 H, br s, 5-H), 3.92–3.86 (1 H, m, 3-H), 3.66 (0.14 H, t, *J* 8.8, 5-H), 2.78–2.72 (0.86 H and 2.58 H, m, 4-H and CH_3), 2.60 (0.42 H, s, CH_3), 2.52 (0.14 H, td, *J* 8.8 and 12.2, 4-H), 2.23 (0.14 H, ddd, *J* 7.8, 8.8 and 12.2, 4-H), 2.06 (0.86 H, dt, *J* 8.3 and 12.2, 4-H), 0.36 (7.74 H, s, TMS), 0.35 (1.26 H, s, TMS), 0.11 (1.26 H, s, TMS) and 0.10 (7.74 H, s, TMS); *m/z* 307 (M^+, 58), 264 (3), 190 (25), 176 (100), 73 (50) and 28 (59).

(3R*,5S*)- *and* (3R*,5R*)-2-*Methyl*-3-*phenyl*-5-*trimethylsilylisoxazolidines* **17d** *and* **19d**.—The isoxazolidines **17d** (14.9 mg, 34%) and **19d** (3.7 mg, 8%) were obtained from the reaction of **9** (51 mg, 0.19 mmol) with **4d** (1.5 cm^3) (conditions: heated in benzene (0.5 cm^3), in a sealed tube at 80 °C for 24 h, chromatography with hexane–benzene–ethyl acetate, 13:7:1). The isoxazolidine **17d** was a colourless oil (Found: M^+, 235.1372. $C_{13}H_{21}NOSi$ requires *M*, 235.1390); δ_H 7.36–7.35 (2 H, m, aromatic-H), 7.32–7.29 (2 H, m, aromatic-H), 7.24–7.21 (1 H, m, aromatic-H), 3.88 (1 H, dd, *J* 6.3 and 11.7, 3-H), 3.80 (1 H, m, 5-H), 2.76 (1 H, td-like, *J* 6.3 and 11.7, 4-H), 2.70 (3 H, s, CH_3), 2.11 (1 H, dt, *J* 8.3 and 11.7, 4-H) and 0.07 (9 H, s, TMS); *m/z* 235 (M^+, 49), 118 (80), 104 (41) and 73 (60). The isoxazolidine **19d** was also a colourless oil (Found: M^+, 235.1387. $C_{13}H_{21}NOSi$ requires *M*, 235.1390); δ_H 7.40–7.38 (2 H, m, aromatic-H), 7.34–7.31 (2 H, m, aromatic-H), 7.28–7.25 (1 H, m, aromatic-H), 3.80 (1 H, t, *J* 9.3, 3-H), 3.42–3.35 (1 H, m, 5-H), 2.60 (3 H, s, CH_3), 2.52 (1H, td-like, *J* 9.3 and 12.2, 4-H), 2.34–2.28 (1 H, m, 4-H) and 0.09 (9 H, s, TMS); *m/z* 235 (M^+, 61), 118 (100), 104 (43) and 73 (76). (3R*,5S*,1'R*)- *and* (3R*,5R*,1'R*)-*Tricarbonyl*[2-*methyl*-3-(η^6-*phenyl*)-5-*trimethylsilyl*)*isoxazolidine*]*chromium*(0) **13d** *and* **15d** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidines **13d** and **15d** were obtained as an inseparable yellow oil (Found: M^+, 371.0664. $C_{16}H_{21}CrNO_4Si$ requires *M*, 371.0644); ν_{max}/cm^{-1} 1970 and 1890 (CO); δ_H 5.66 (0.80 H, d, *J* 6.8, aromatic-H), 5.61 (0.20 H, d, *J* 6.8, aromatic-H), 5.38–5.30 (2.4 H, m, aromatic-H), 5.24 (0.80 H, t-like, *J* 6.8, aromatic-H), 5.18 (0.80 H, d, *J* 6.8, aromatic-H), 3.84 (0.80 H, dd, *J* 6.8 and 12.0, 3-H), 3.68 (0.80 H, dd, *J* 5.9 and 8.0, 5-H), 3.58 (0.20 H, dd, *J* 6.8 and 12.0, 3-H), 3.39 (0.20 H, dd, *J* 5.9 and 9.3, 5-H), 2.88 (0.80 H, ddd-like, *J* 6.8, 8.0 and 12.0, 4-H), 2.76 (2.4 H, s, CH_3), 2.75 (0.6 H, s, CH_3), 2.55 (0.20 H, dt, *J* 9.3 and 12.0, 4-H), 2.21 (0.2 H, ddd, *J* 5.9, 6.8 and 12.0, 4-H), 1.94 (0.8 H, dt, *J* 5.9 and 12.0, 4-H), 0.08 (1.8 H, s, TMS) and 0.04 (7.2 H, s, TMS); *m/z* 371 (M^+, 2), 287 (13), 187 (17), 171 (100), 73 (14) and 52 (33).

(3R*,5S*)- *and* (3R*,5R*)-5-*Cyano*-2-*methyl*-3-(2-*trimethylsilylphenyl*)*isoxazolidines* **16e** *and* **18e**.—The isoxazolidine **16e** (10.5 mg, 20%) and **18e** (24.5 mg, 46%) were obtained from the reaction of **2** (70 mg, 0.20 mmol) with **4e** (2 cm^3) (conditions: refluxed for 30 min., chromatography with hexane–ethyl acetate, 25:1). The isoxazolidine **16e** was a colourless oil (Found: M^+, 260.1346. $C_{14}H_{20}N_2OSi$ requires *M*, 260.1344); ν_{max}/cm^{-1} 2350 (CN); δ_H 7.57 (1 H, d, *J* 7.8, aromatic-H), 7.51 (1 H, dd-like, *J* 1.5 and 7.8, aromatic-H), 7.39 (1 H, dt, *J* 1.5 and 7.8, aromatic-H), 7.29 (1 H, dt, *J* 1.5 and 7.8, aromatic-H), 4.85 (1 H, dd, *J* 3.9 and 8.8, 5-H), 4.18 (1 H, t, *J* 8.8, 3-H), 2.92 (1 H, ddd, *J* 3.9, 8.8 and 12.7, 4-H), 2.72 (3 H, s, CH_3), 2.67 (1 H, td, *J* 8.8 and 12.7, 4-H) and 0.40 (9 H, s, TMS); δ_C 142.77, 139.14, 134.73, 130.03, 127.58, 126.51, 118.21, 70.97, 63.66, 45.93, 43.67 and 0.92; *m/z* 260 (M^+, 74), 192 (100), 111 (37) and 73 (59). The isoxazolidine **18e** had m.p. 142–143 °C (from hexane) as colourless cubes (Found: C, 64.65; H, 7.7; N, 10.7. $C_{14}H_{20}N_2OSi$ requires C, 64.57; H, 7.74; N, 10.76%); ν_{max}/cm^{-1} 2350 (CN); δ_H 7.80 (1 H, d, *J* 7.8, aromatic-H), 7.49–7.43 (2 H, m, aromatic-H), 7.29 (1 H, dt, *J* 1.0 and 7.3, aromatic-H), 4.84 (1 H, dd, *J* 3.9 and 8.3, 5-H), 3.78 (1 H, t, *J* 8.3, 3-H), 3.07 (1 H, td, *J* 8.3 and 12.2,

Table 2 Crystal data

Empirical formula	$C_{22}H_{24}NO_4BrCrSi$
Formula weight	526.42
Crystal system	Orthorhombic
Recrystallistion solvent	Ethanol
Melting point	178–179.5 °C
Lattice parameters	
	a = 12.662 (2)A
	b = 19.344 (3)A
	c = 9.741 (3)A
	V = 2386.0 (8)A^3
Space group	$P212121$ (#19)
Z Value	4
D_c	1.465 g cm^{-3}

Table 3 Data collection

Diffractometer	Rigaku AFC5S
Radiation	Mo-Kα (λ = 0.710 69A)
No. refls used cell determ. (range)	25 (25.0–28.0°)
μ(Mo-Kα)/cm^{-1}	22.01
Crystal colour, habit	Yellow, prism
Crystal dimensions (mm)	0.3 × 0.3 × 0.3
Scan type	ω–2θ
Scan rate (° min^{-1})	32.0 (in omega)
Scan width (°)	(1.47 + 0.30 tan θ)
$2\theta_{max}$ (°)	45.1
No. of independent reflections	1838
$F(000)$	1072
Corrections	Lorentz-polarization

Table 4 Structure Analysis and Refinements

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Function minimized	$\Sigma w(1 F_0 1-1 F_c 1)^2$
Least-squares weights	$4F_02/\sigma^2(F_02)$
p-Factor	0.03
Anomalous dispersion	All non-hydrogen atoms
No. observations [1 > 3.00σ(1)]	1027
No. Variables	271
Residuals: R; R_w	0.042; 0.043
Goodness of fit indicator	1.42
Max shift/error in final cycle	0.21
Maximum peak in final diff. map (e/A^3)	0.32
Minimum peak in final diff. map (e/A^3)	−0.26
Programmes used	TEXSAN

4-H), 2.65 (3 H, s, CH_3) and 2.53 (1 H, ddd, J 3.9, 8.3 and 12.2, 4-H); δ_C 143.11, 138.93, 134.46, 130.38, 127.49, 127.19, 119.68, 70.84, 63.91, 45.92, 42.31 and 0.94; m/z 260 (M$^+$, 45), 192 (100), 111 (22) and 73 (31). (3R*,5R*,1'R*)-*Tricarbonyl*[5-*cyano*-2-*methyl*-3-(η^6-2-*trimethylsilylphenyl*)]*isoxazolidinechromium*(0) **14e** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **14e** had m.p. 159–161 °C (from MeOH) as yellow needles (Found: C, 51.2; H, 5.1; N, 7.05. $C_{17}H_{20}CrN_2O_4Si$ requires C, 51.50; H, 5.09; N, 7.07%); ν_{max}/cm^{-1} 2350 (CN), 1970 and 1890 (CO); δ_H 5.86 (1 H, d, J 6.4, aromatic-H), 5.56 (1 H, m, aromatic-H), 5.32 (2 H, m, aromatic-H), 4.83 (1 H, dd, J 2.9 and 9.3, 5-H), 3.79 (1 H, dd, J 5.4 and 9.3, 3-H), 3.16 (1 H, td, J 9.3 and 13.2, 4-H), 2.95 (3 H, s, CH_3), 2.42 (1 H, ddd, J 2.9, 5.4 and 13.2, 4-H) and 0.40 (9 H, s, TMS); m/z 396 (M$^+$, 10), 312 (14), 244 (19), 176 (100) and 73 (12).

(3R*,5S*)- *and* (3R*,5R*)-5-*Cyano*-2-*methyl*-3-*phenylisoxazolidines* **17e** *and* **19e**.—The isoxazolidines **17e** and **19e** (38 mg, 64%) were obtained from the reaction of **9** (86 mg, 0.32 mmol) with **4e** (3 cm^3) (conditions: refluxed for 30 min., chromatography with hexane–ethyl acetate, 10:2). The isoxazolidines **17e** and **19e** were obtained as an inseparable colourless oil (Found: M$^+$, 188.0950. $C_{11}H_{12}N_2O$ requires M, 188.0949); ν_{max}/cm^{-1} 2350 (CN); δ_H 7.43–7.32 (5 H, m, aromatic-H), 4.86–4.82 (1 H, m, 5-H), 3.94 (0.23 H, br s, 3-H), 3.47 (0.77 H, t, J 8.3, 3-H), 3.08 (0.77 H, td, J 8.3 and 12.7, 4-H), 2.97 (0.23 H, ddd, J 4.4, 6.8 and 11.2, 4-H), 2.80–2.73 (0.23 H and 0.69 H, m, 4-H and CH_3) and 2.64–2.58 (0.77 H and 2.31 H, m, 4-H and CH_3); m/z 188 (M$^+$, 83), 134 (100) and 115 (21).

(3R*,5S*)- *and* (3R*,5R*)-5-(4-*Bromophenyl*)-2-*methyl*-3-(2-*trimethylsilylphenyl*)*isoxazolidines* **16f** *and* **18f**.—The isoxazolidines **16f** (36.8 mg, 45%) and **18f** (3.2 mg, 4%) were obtained from **2** (72 mg, 0.16 mmol) with **4f** (1 cm^3) (conditions: heated in a sealed tube at 80 °C for 6 h, chromatography with hexane–ethyl acetate, 50:1). The isoxazolidine **16f** had m.p. 108–109 °C (from MeOH) as colourless needles (Found: C, 58.4; H, 6.1; N, 3.6. $C_{19}H_{24}BrNOSi$ requires C, 58.45; H, 6.20; N, 3.59%); δ_H 7.56 (1 H, d, J 7.8, aromatic-H), 7.50–7.46 (3 H, m, aromatic-H), 7.38–7.33 (3 H, m, aromatic-H), 7.25–7.22 (1 H, m, aromatic-H), 5.20 (1 H, t, J 7.5, 5-H), 4.02 (1 H, dd, J 6.8 and 9.2, 3-H), 3.13 (1 H, ddd, J 6.8, 7.5 and 12.5, 4-H), 2.68 (3 H, s, CH_3), 2.27 (1 H, ddd, J 7.5, 9.2 and 12.5, 4-H) and 0.39 (9 H, s, TMS); δ_C 144.76, 142.98, 138.53, 134.34, 131.54, 129.94, 127.55, 126.94, 120.97, 77.40, 72.99, 50.28, 43.31 and 0.99; m/z 391 (M$^+$ + 1, 31), 390 (M$^+$, 9), 389 (M$^+$ − 1, 31), 206 (20), 192 (100), 134 (21) and 73 (61). The isoxazolidine **18f** was a colourless oil (Found: M$^+$ − 1, 389.0809. $C_{19}H_{24}BrNOSi$ requires M − 1, 389.0809); δ_H 7.76 (1 H, d, J 7.8, aromatic-H), 7.51–7.48 (3 H, m, aromatic-H), 7.44–7.41 (1 H, m, aromatic-H), 7.31–7.27 (3 H, m, aromatic-H), 5.23 (1 H, dd, J 6.4 and 8.6, 5-H), 3.99 (1 H, t, J 8.6, 3-H), 2.70 (3 H, s, CH_3), 2.63 (1 H, td, J 8.6 and 12.7, 4-H), 2.54 (1 H, ddd, J 6.4, 8.6 and 12.7, 4-H) and 0.34 (9 H, s, TMS); δ_C 145.36, 140.04, 138.65, 134.39, 131.68, 129.99, 128.19, 126.99, 121.73, 78.19, 72.20, 49.29, 43.16 and 1.01; m/z 391 (M$^+$ + 1, 48), 390 (M$^+$, 17), 389 (M$^+$ −1, 46), 206 (29), 192 (100), 134 (36) and 73 (100). (3R*,5S*,1'R*)-5-(4-*Bromophenyl*)-2-*methyl*-3-(η^6-2-*trimethylsilylphenyl*)*isoxazolidine*(*tricarbonyl*)-*chromium*(0) **12f** could be isolated by chromatography before treatment with CAN. The chromium complexed isoxazolidine **12f** had m.p. 178–179.5 °C (from EtOH) as yellow prisms (Found: C, 50.1; H, 4.75; N, 2.5. $C_{22}H_{24}BrCrNO_4Si$ requires C, 50.02; H, 4.60; N, 2.66%); ν_{max}/cm^{-1} 1970 and 1880 (CO); δ_H 7.45 (2 H, d, J 8.3, aromatic-H), 7.18 (2 H, d, J 8.3, aromatic-H), 5.72 (1 H, d, J 6.2, aromatic-H), 5.65 (1 H, t-like, J 6.2, aromatic-H), 5.39 (1 H, dd, J 1.0 and 6.2, aromatic-H), 5.30 (1 H, t, J 7.8, 5-H), 5.14–5.11 (1 H, m, aromatic-H), 4.08 (1 H, dd, J 5.9 and 8.8, 3-H), 3.27 (1 H, ddd, J 7.8, 8.8 and 12.7, 4-H), 2.97 (3 H, s, CH_3), 2.04 (1 H, ddd, J 5.9, 7.8 and 12.7, 4-H) and 0.40 (9 H, s, TMS); m/z 527 (M$^+$ + 1, 6), 526 (M$^+$, 2), 525 (M$^+$ − 1, 5), 441 (67), 244 (33), 176 (100), 73 (61) and 52 (65).

X-ray Analysis of **12f**.—Details of the X-ray crystallographic study are presented in tabular form (see Tables 2–4). Details of the atomic coordinates, bond lengths and bond angles have been deposited with the Cambridge Crystallographic Data Centre.*

Removal of the TMS Group of **12a** *with TBAF*.—To a solution of **12a** (27.6 mg, 0.06 mmol) in THF (2 cm^3) was added dropwise a solution of TBAF in THF (1 mol dm^{-3} solution; 0.1 cm^3, 0.1 mmol) at −10 °C. The solution was stirred at −10 °C for 10 min after which THF was evaporated off and the residue was

* See Instructions for Authors (1993), *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

treated with CAN in methanol. Work-up and chromatography of the residual oil afforded **17a** (11.5 mg, 78%).

General Procedure for 1,3-*Dipolar Cycloaddition of the Nitrones* **10** *and* **11** *with the Dipolarophiles* **4**.—A mixture of the nitrone and the dipolarophile **4** was heated to the temperature indicated for the corresponding complexed nitrones **2** and **9**. Removal of excess of dipolarophile and chromatographic purification of the residue afforded the isoxazolidines. The ratios and yields are summarised in Table 1.

Reaction of **10** *with* **4a**.—(3R*,5R*)-2-*Methyl*-5-*phenyl*-3-(2-*trimethylsilylphenyl*)*isoxazolidine* **18a** (28 mg, 79%) was obtained from the reaction of **10** (23.7 mg, 0.11 mmol) with **4a** (3 cm^3) along with **16a** (6 mg, 17%) (conditions: heated in a sealed tube at 110 °C for 11 h, chromatography with hexane–ethyl acetate, 45:1). The isoxazolidine **18a** was a colourless oil (Found: M^+, 311.1697. $C_{19}H_{25}NOSi$ requires *M*, 311.1704); δ_H 7.80 (1 H, d, *J* 7.8, aromatic-H), 7.49 (1 H, d, *J* 7.8, aromatic-H), 7.44–7.36 (5 H, m, aromatic-H), 7.32–7.24 (2 H, m, aromatic-H), 5.28 (1 H, t, *J* 7.8, 5-H), 4.03 (1 H, t, *J* 7.8, 3-H), 2.71 (3 H, s, CH_3), 2.63 (2 H, t, *J* 7.8, 4-H), and 0.36 (9 H, s, TMS); δ_C 145.66, 140.81, 138.62, 134.32, 129.96, 128.55, 127.91, 127.04, 126.88, 126.63, 78.96, 72.35, 49.31, 43.16 and 0.99; *m/z* 311 (M^+, 49), 206 (18), 192 (81), 176 (5) and 73 (100).

Reaction of **11** *with* **4a**.—The isoxazolidines **17a** (40 mg, 44%) and **19a** (18 mg, 20%) were obtained from the reaction of **11** (51 mg, 0.38 mmol) with **4a** (3 cm^3) (conditions: heated in a sealed tube at 100 °C for 6 h, chromatography with hexane–ethyl acetate, 20:1). The isoxazolidine **19a**; δ_H 7.45–7.25 (10 H, m, aromatic-H), 5.25 (1 H, dd, *J* 6.3 and 8.3, 5-H), 3.72 (1 H, t, *J* 8.3, 3-H), 2.77–2.71 (4 H, m, CH_3 and 4-H), 2.62 (1 H, ddd, *J* 6.3, 8.3 and 12.7, 4-H).

Reaction of **10** *with* **4b**.—(3R*,5R*)-5-*Ethoxy*-2-*methyl*-3-(2-*trimethylsilylphenyl*)*isoxazolidine* **18b** (379 mg, 66%) was obtained from the reaction of **10** (430 mg, 2.08 mmol) with **4b** (7 cm^3) along with **16b** (147 mg, 25%) (conditions: heated in a sealed tube at 80 °C for 140 h, chromatography with hexane–ethyl acetate, 20:1). The isoxazolidine **18b** was a colourless oil (Found: M^+, 279.1652. $C_{15}H_{25}O_2NSi$ requires *M*, 279.1653); δ_H 7.69 (1 H, d, *J* 7.5, aromatic-H), 7.47 (1 H, dd-like, *J* 1.5 and 7.5, aromatic-H), 7.38 (1 H, dt, *J* 1.5 and 7.5, aromatic-H), 7.27–7.21 (1 H, m, aromatic-H), 5.21 (1 H, d, *J* 4.6, 5-H), 4.33 (1 H, dd, *J* 6.3 and 10.2, 3-H), 3.86 (1 H, qd, *J* 6.9 and 9.6, OCH_2CH_3), 3.50 (1 H, qd, *J* 6.9 and 9.6, OCH_2CH_3), 2.81 (3 H, s, CH_3), 2.58 (1 H, dd, *J* 6.3 and 12.5, 4-H), 2.34 (1 H, ddd, *J* 4.6, 10.2 and 12.5, 4-H), 1.25 (3 H, t, *J* 6.9, CH_3) and 0.38 (9 H, s, TMS); δ_C 145.80, 138.44, 134.24, 129.75, 126.87, 126.80, 102.20, 69.73, 62.65, 48.25, 46.68, 15.23 and 0.84; *m/z* 279 (M^+, 13), 233 (19), 192 (20), 115 (100) and 73 (25).

Reaction of **11** *with* **4b**.—The isoxazolidines **17b** (22 mg, 32%) and **19b** (26 mg, 38%) were obtained from the reaction of **11** (44.7 mg, 0.33 mmol) with **4b** (3 cm^3) (conditions: heated in a sealed tube at 80 °C for 72 h, chromatography with hexane–ethyl acetate, 10:1). The isoxazolidine **19b**; δ_H 7.40 (2 H, d, *J* 7.4, aromatic-H), 7.35–7.32 (2 H, m, aromatic-H), 7.29–7.25 (1 H, m, aromatic-H), 5.20 (1 H, d, *J* 4.9, 5-H), 4.05 (1 H, dd, *J* 6.4 and 10.3, 3-H), 3.88 (1 H, qd, *J* 7.3 and 14.2, OCH_2CH_3), 3.52 (1 H, qd, *J* 7.3 and 14.2, OCH_2CH_3), 2.82 (3 H, s, CH_3), 2.59 (1 H, dd, *J* 6.4 and 12.7, 4-H), 2.46 (1 H, ddd, *J* 4.9, 10.3 and 12.7, 4-H) and 1.26 (3 H, t, *J* 7.3, CH_3).

Reaction of **10** *with* **4c**.—The isoxazolidines **16c** (11.2 mg, 17%) and **18c** (31.8 mg, 49%) were obtained from the reaction of **10** (46 mg, 0.22 mmol) with **4c** (3 cm^3) (conditions: heated in a sealed tube at 105 °C for 24 h, chromatography with benzene–ethyl acetate, 50:1).

Reaction of **11** *with* **4c**.—The isoxazolidines **17c** (40 mg, 47%) and **19c** (20 mg, 24%) were obtained from the reaction of **11** (52 mg, 0.39 mmol) with **4c** (3 cm^3) (conditions: heated in a sealed tube at 105 °C for 24 h, chromatography with benzene–acetone, 10:1). The isoxazolidine **19c** had m.p. 73–74.5 °C (from hexane) as colourless needles (Found: C, 65.1; H, 7.1; N, 6.4. $C_{12}H_{15}NO_3$ requires C, 65.14; H, 6.83; N, 6.33%); ν_{max}/cm^{-1} 1740 (CO); δ_H 7.40–7.26 (5 H, m, aromatic-H), 6.40 (1 H, t, *J* 2.9, 5-H), 4.02 (1 H, t, *J* 8.3, 3-H), 2.79 (3 H, s, CH_3), 2.65 (2 H, dd, *J* 2.9 and 8.3, 4-H) and 2.12 (3 H, s, CH_3); *m/z* 221 (M^+, 38), 174 (35), 105 (100) and 43 (26).

Reaction of **10** *with* **4d**.—A mixture of **16d** and **18d** (29 mg, 88%) was obtained from the reaction of **10** (23 mg, 0.11 mmol) with **4d** (0.5 cm^3) [conditions: heated in benzene (0.5 cm^3) in a sealed tube at 80 °C for 24 h, chromatography with hexane–benzene–ethyl acetate, 10:10:1].

Reaction of **11** *with* **4d**.—The isoxazolidine **17d** (24.4 mg, 22%) and **19d** (36.6 mg, 32%) were obtained from the reaction of **11** (65 mg, 0.48 mmol) with **4d** (0.8 cm^3) [conditions: heated in benzene (1 cm^3) in a sealed tube at 80 °C for 24 h, chromatography with hexane–benzene–ethyl acetate = 13:7:1].

(+)-*Tricarbonyl*[η^6-(Z)-N-(2-*trimethylsilylphenylmethylene*)*methylamine* N-*oxide*]*chromium*(0) (+)-**2**.—According to the procedure described for the racemic compound, the nitrone (+)-**2** (134 mg, 87%) was obtained from (+)-**1** (141 mg, 0.45 mmol) as red needles, m.p. 105–106 °C (from hexane–benzene) (Found: M^+, 343.0377. $C_{14}H_{17}CrNO_4Si$ requires *M*, 343.0311); $[\alpha]_D^{22}$ + 1574 (*c* 0.45, $CHCl_3$).

(−)-*Tricarbonyl*[η^6-(Z)-N-(2-*trimethylsilylphenylmethylene*)*methylamine* N-*oxide*]*chromium*(0) (−)-**2**.—According to the procedure for the racemic compound, the nitrone (−)-**2** (86 mg, 90%) was obtained from (−)-**1** (88 mg, 0.28 mmol) as red needles, m.p. 104–105 °C (from hexane–benzene) (Found: M^+, 343.0371. $C_{14}H_{17}CrNO_4Si$ requires *M*, 343.0311); $[\alpha]_D^{25}$ −1527 (*c* 0.44, $CHCl_3$).

Asymmetric 1,3-*Dipolar Cycloaddition of the Chromium Complexed Nitrone* **2**.—Asymmetric 1,3-dipolar cycloadditions were carried out as described for the racemates.

(−)-(3S,5R)-2-*Methyl*-5-*phenyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine*(−)-**16a**. The isoxazolidine (−)-**16a** (45 mg, 65%) was obtained from (+)-**2** (76 mg, 0.22 mmol) as a colourless oil (Found: M^+, 311.1753. $C_{19}H_{25}NOSi$ requires *M*, 311.1704); $[\alpha]_D^{20}$ − 210 (*c* 0.26, $CHCl_3$). (>98% e.e.).

(+)-(3R,5S)-2-*Methyl*-5-*phenyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine* (+)-**16a**. The isoxazolidine, (+)-**16a** (40 mg, 68%) was obtained from (−)-**2** (65 mg, 0.19 mmol) as a colourless oil (Found: M^+, 311.1741. $C_{19}H_{25}NOSi$ requires *M*, 311.1704); $[\alpha]_D^{16}$ +222 (*c* 0.29, $CHCl_3$). (>98% e.e.).

(−)-(3S,5R)-5-*Ethoxy*-2-*methyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine*(−)-**16b**. The isoxazolidine, (−)-**16b** (38 mg, 62%) was obtained from (+)-**2** (75 mg, 0.22 mmol) as a colourless oil (Found: M^+, 279.1626. $C_{15}H_{25}NO_2Si$ requires *M*, 279.1653); $[\alpha]_D^{21}$ − 220 (*c* 0.30, $CHCl_3$) (97% e.e.).

(+)-(3R,5S)-5-*Ethoxy*-2-*methyl*-3-(2-*trimethylsilylphenyl*)-*isoxazolidine* (+)-**16b**.—The isoxazolidine, (+)-**16b** (37 mg, 61%) was obtained from (−)-**2** (75 mg, 0.22 mmol) as a colourless oil (Found: M^+, 279.1702. $C_{15}H_{25}NO_2Si$ requires *M*, 279.1653); $[\alpha]_D^{27}$ + 206 (*c* 0.17, $CHCl_3$) (96% e.e.).

(−)-(1S,3R)-3-*Acetoxy*-1-(N-*methylacetamido*)-3-*phenyl*-1-(2-*trimethylsilylphenyl*)*propane* (−)-**20**.—A solution of (−)-**16a** (13 mg, 0.04 mmol) in ethanol (2 cm^3) was stirred at room temperature in the presence of Raney-Ni (W-7) under a hydrogen atmosphere for 1 h. Raney-Ni was filtered off by suction and washed with acetone several times. The filtrate and washings were combined and concentrated to dryness. The crude N–O bond cleavage product was dissolved in methylene dichloride (1 cm^3) to which acetic anhydride (1 drop) and 4-(*N*,*N*-dimethylamino)pyridine (5 mg) were then added at 0 °C. The reaction mixture was allowed to stand at the same temperature for 1 h. The methylene dichloride solution was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–acetone, (5:1) gave (−)-**20** (12.5 mg, 74%) as a colourless oil (Found: M^+, 397.2125. $C_{23}H_{31}NO_3Si$ requires *M*, 397.2071); $[\alpha]_D^{27}$ −44.2 (*c* 0.23, $CHCl_3$); ν_{max}/cm^{-1} 1730 and 1640 (CO); δ_H (in C_6D_6) 7.68 (1 H, d, *J* 7.3, aromatic-H), 7.58 (2 H, d, *J* 7.3, aromatic-H), 7.32–7.17 (6 H, m, aromatic-H), 6.32 (1 H, t, *J* 7.3, 3-H), 6.02 (1 H, dd, *J* 5.2 and 7.3, 1-H), 2.83 (1 H, m, 2-H), 2.30 (4 H, m, 2-H and N-CH_3), 1.87 (3 H, s, CH_3), 1.83 (3 H, s, CH_3) and 0.44 (9 H, s, TMS); *m*/*z* 397 (M^+, 2), 324 (96), 248 (87), 192 (84), 117 (23), 73 (18) and 56 (17).

(+)-(1R,3S)-3-*Acetoxy*-1-(N-*methylacetamido*)-3-*phenyl*-1-(2-*trimethylsilylphenyl*)*propane* (+)-**20**.—Following the method described for the preparation of (−)-**20**, (+)-**20** (12 mg, 72%) was obtained from (+)-**16a** (13 mg, 0.04 mmol) as a colourless oil (Found: M^+, 397.2062. $C_{23}H_{31}NO_3Si$ requires *M*, 397.2071); $[\alpha]_D^{27}$ +47.9° (*c* 0.24, $CHCl_3$).

Determination of Enantiomeric Excess of (+)- *and* (−)-**20**.—To a solution of (±)-**20** (5.0 mg, 1.25 × 10^{-2} mmol) in C_6D_6 (0.5 cm^3) was added a solution of [Eu(tfc)$_3$] (12 mg, 1.25 × 10^{-2} mmol) in C_6D_6 (0.1 cm^3). The ^1H NMR spectrum of (±)-**20** in the presence of [Eu(tfc)$_3$] indicated that the peak of TMS group (occurred at 0.44 ppm in the absence of the shift reagent) was shifted downfield and split in two singlets at 0.85 and 0.98 ppm in a ratio of 1:1. The ^1H NMR spectrum of (+)-**20** under the same conditions described for (±)-**20** showed only a singlet at 0.85 ppm, the signal at 0.98 ppm due to the enantiomer not being detected (> 98% e.e.). The TMS signal of (−)-**20** appeared at 0.98 ppm as a singlet and the peak of TMS group due to (+)-**20** was not recognised (> 98% e.e.).

(−)-(S)-3-[(N-*Benzyl*)*methylamino*]-3-(2-*trimethylsilylphenyl*)*propan*-1-*ol* (−)-**21**.—A mixture of (−)-**16b** (60 mg, 0.22 mmol) and benzyl bromide (376 mg, 2.22 mmol) in methylene dichloride (0.5 cm^3) was heated in a sealed tube at 80 °C for 24 h. Excess of benzyl bromide was removed by passage through a short pad of silica gel. To a solution of the quaternary ammonium salts in THF (1.5 cm^3) was added LAH (17 mg, 0.44 mmol). The reaction mixture was refluxed for 2 h. After addition of a small amount of water to the reaction mixture it was passed through a short pad of Celite. The filtrate was dried, and concentrated to dryness. Chromatography of the residue with hexane–acetone (20:1) provided (−)-**21** (20 mg, 33%) as a colourless oil (Found: M^+, 327.2051. $C_{20}H_{29}NOSi$ requires *M*, 327.2017); $[\alpha]_D^{27}$ −8.9 (*c* 0.40, $CHCl_3$); ν_{max}/cm^{-1} 3300 (OH); δ_H (1 H, d, *J* 7.5, aromatic-H), 7.55 (1 H, dd, *J* 1.0 and 7.3, aromatic-7.67 H), 7.44–7.40 (1 H, m, aromatic-H), 7.31–7.21 (6 H, m, aromatic-H), 4.10 (1 H, t, *J* 4.9, 3-H), 3.89 (1 H, ddd, *J* 4.9, 8.3 and 11.0, 1-H), 3.75 (1 H, ddd, *J* 4.9, 5.9 and 11.0, 1-H), 3.70 (1 H, d, *J* 13.3, CH_2Ph), 3.36 (1 H, d, *J* 13.3, CH_2Ph), 2.36 (1 H, dddd, *J* 4.9, 5.9, 8.3 and 14.7, 2-H), 2.25 (3 H, s, CH_3), 1.86 (1 H, qd, *J* 4.9 and 14.7, 2-H) and 0.42 (9 H, s, TMS); δ_C 146.47, 139.10, 138.65, 135.22, 128.99, 128.61, 128.34, 127.62, 126.99, 126.56, 68.32, 60.59, 59.70, 39.59, 33.91 and 1.47; *m*/*z* 327 (M^+, 1), 283 (29), 178 (11) and 73 (12).

(+)-(R)-3-[(N-*Benzyl*)*methylamino*]-3-(2-*trimethylsilylphenyl*)*propan*-1-*ol* (+)-**21**.—Following the method described for the preparation of (−)-**21**, the amino alcohol, (+)-**21** (14 mg, 28%) was obtained from (+)-**16b** (42 mg, 0.15 mmol) as a colourless oil (Found: M^+, 327.2011. $C_{20}H_{29}NOSi$ requires *M*, 327.2017); $[\alpha]_D^{27}$ +10.8 (*c* 0.40, $CHCl_3$).

Determination of Enantiomeric Excess of (+)- *and* (−)-**21**.—To a solution of (±)-**21** (5.0 mg, 1.52 × 10^{-2} mmol) in C_6D_6 (0.5 cm^3) was added a solution of [Eu(hfc)$_3$] (54.4 mg, 4.56 × 10^{-2} mmol) in C_6D_6 (0.3 cm^3). The ^1H NMR spectrum of (±)-**21** in the presence of [Eu(hfc)$_3$] indicated that the signal of the TMS group (occurred at 0.42 ppm in the absence of the shift reagent) was shifted downfield and split in two singlets at 2.03 and 2.15 ppm in a ratio of 1:1. The ^1H NMR spectrum of (+)-**21** under the same condition described for (±)-**21** showed two singlets at 2.03 and 2.15 ppm in a ratio of 98:2 (96% e.e.), whereas that of (−)-**21** revealed two singlets at 2.03 and 2.15 in a ratio of 1.5:98.5 (97% e.e.).

References

1 A part of this work was published in a preliminary communication: C. Mukai, W.-J. Cho, I. J. Kim and M. Hanaoka, *Tetrahedron Lett.*, 1990, **31**, 6893.

2 (*a*) C. Mukai, I. J. Kim and M. Hanaoka, *Tetrahedron: Asymmetry*, 1992, **3**, 1007; (*b*) C. Mukai, M. Miyakawa, A. Mihira and M. Hanaoka, *J. Org. Chem.*, 1992, **57**, 2034; (*c*) C. Mukai, A. Mihira and M. Hanaoka, *Chem. Pharm. Bull.*, 1991, **39**, 2863; (*d*) C. Mukai, W.-J. Cho, I. J. Kim, M. Kido and M. Hanaoka, *Tetrahedron*, 1991, **47**, 3007.

3 Recent Reviews: (*a*) S. G. Davies, T. J. Donohoe and J. M. J. Williams, *Pure & Appl. Chem.*, 1992, **64**, 379; (*b*) J. P. Collman, L. S. Hegedus, J. R. Norton and R. G. Finke, in *Principles and Applications of Organotransition Metal Chemistry*, University Science Books, Mill Valley, CA, 1987, p. 921; (*c*) A. J. Pearson, in *Metallo-Organic Chemistry*, John Wiley & Sons, New York, 1985, p. 348; (*d*) S. G. Davies, *Organotransition Metal Chemistry, Application to Organic Synthesis*, Pergamon Press, Oxford, 1982.

4 Recent Reviews: (*a*) P. DeShong, S. W. Lander, Jr., J. M. Leginus and C. M. Dicken, in *Advances in Cycloaddition*, ed. D. P. Curran, JAI Press Inc., London, 1988, p. 87; (*b*) P. N. Confalone and E. M. Huie, *Org. React.*, 1988, **36**, 1; (*c*) K. B. G. Torssell, *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis*, VCH Publishers, New York, 1987; (*d*) J. J. Tufariello, in *1,3-Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley Interscience, New York, 1984, vol. 2, p. 83.

5 J. J. Tufariello, *Acc. Chem. Res.*, 1979, **12**, 396.

6 P. DeShong and J. M. Leginus, *J. Org. Chem.*, 1984, **49**, 3421.

7 M. F. Semmelhack, H. T. Hall, Jr., R. Farina, M. Yoshifuji, G. Clark, T. Bargar, K. Hirotsu and J. Clardy, *J. Am. Chem. Soc.*, 1979, **101**, 3535.

8 R. Huisgen, R. Grashey, H. Hauck and H. Seidl, *Chem. Ber.*, 1968, **101**, 2548.

9 C. M. Dicken and P. DeShong, *J. Org. Chem.*, 1982, **47**, 2047.

10 (*a*) A. Padwa, L. Fisera, K. F. Koehler, A. Rodriguez and G. S. K. Wong, *J. Org. Chem.*, 1984, **49**, 276; (*b*) R. Huisgen, H. Hauck, R. Grashey and H. Seidl, *Chem. Ber.*, 1968, **101**, 2568.

11 S. G. Davies and C. L. Goodfellow, *J. Chem. Soc., Perkin Trans. 1*, 1990, 393.

12 W. Carruthers, P. Coggins and J. B. Weston, *J. Chem. Soc., Chem. Commun.*, 1991, 117.

13 A. Solladie-Cavallo, G. Solladie and E. Tsamo, *J. Org. Chem.*, 1979, **44**, 4189.

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