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X=Y-ZH Systems as Potential 1,3-Dipoles. Part 48.[1] Enantiopure Cycloadducts from Oxime-Nitrone-Isoxazolidine Cascades

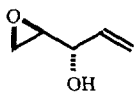
H. Ali Dondas, Martyn Frederickson, Ronald Grigg,* Jasothara Markandu, and Mark Thornton-Pett

School of Chemistry, The University of Leeds, Leeds, LS2 9JT.

Abstract: Enantiopure cycloadducts have been prepared in good yield *via* oxime-nitrone-isoxazolidine cascade reactions involving the nucleophilic opening of enantiopure epoxides with oximes followed by 1,3-dipolar cycloaddition reactions with suitable dipolarophiles. © 1997 Elsevier Science Ltd.

In a recent paper[1] we described the use of epoxides as suitable electrophiles with which to effect the *N*-substitution of oximes, thereby generating nitrones, which subsequently underwent *in situ* 1,3-dipolar cycloaddition reactions to afford a wide variety of isoxazolidine based heterocycles. We also provided examples of all four broad synthetic variants of these cascade processes (Classes 1-4) which depend on the inter- or intra-molecular nature of both the initial epoxide cleavage and the subsequent cycloaddition steps. Our interest in the synthesis of complex isoxazolidines in optically active forms[2] led us to investigate the use of enantiopure epoxides in these cascades and in this paper we report on these studies.

Epoxides **1-6** were prepared for use in these studies. Epoxide **1**, containing the dipolarophile necessary for the cycloaddition step, allowed the investigation of intermolecular epoxide cleavage-intramolecular cycloaddition cascades (Class 2, Type 2),[1] whereas epoxyoximes **2-6** were used to investigate intramolecular epoxide cleavage followed by intermolecular cycloaddition (Class 3 processes).



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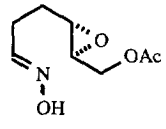

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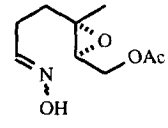

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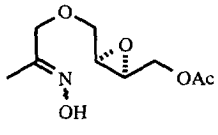

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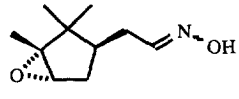

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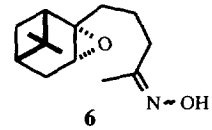


6

(2*R*,3*S*)-Epoxide **1**[3] was treated with the sodium salt of (*Z*)-benzaldoxime (1·00 mol equiv) at room temperature to afford a single (*Z*)-nitrone **7** (51%) which when heated in xylene (140°C, 18 h) underwent smooth intramolecular cycloaddition to afford a 2:1 mixture of the regioisomeric cycloadducts **8** and **9** (84%). The stereochemistry of **8** was determined from 2D-COSY and n.O.e data (see Experimental section) whilst the

stereochemistry of **9** was established by X-ray crystallography (*Figure 1*).[4] Notably neither of the other two possible alternative diastereomers **10** and **11** were formed thus implying that cycloaddition occurs (in both regiochemical senses) in essentially a facially specific manner. The origin of the facial selectivity apparently resides in the destabilising steric effects that develop between an axial hydroxy group and the constituents of the putative two atom bridge (-CH_2O- in **10** and -CH_2CHPh- in **11**) in the pre-transition state conformers. These dominant destabilising interactions are absent in the corresponding pre-transition state conformers leading to **8** and **9** and are responsible for the switch in facial selectivity between **8** and **9** (*Figure 2*).

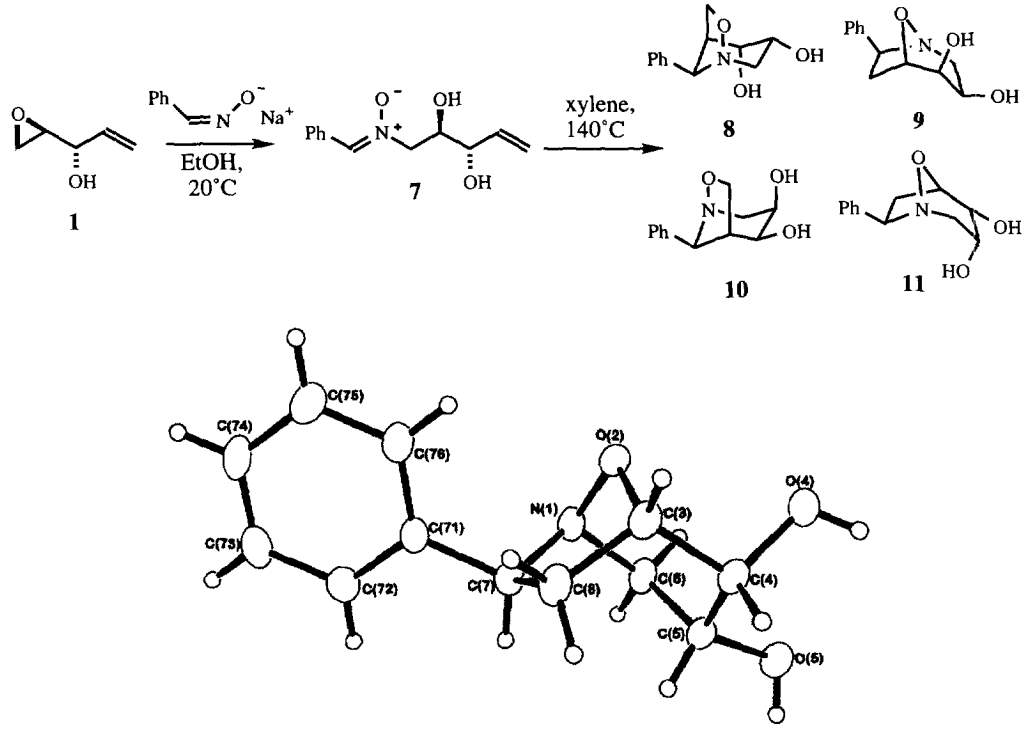


Figure 1: X-ray crystallographic structure of **9**

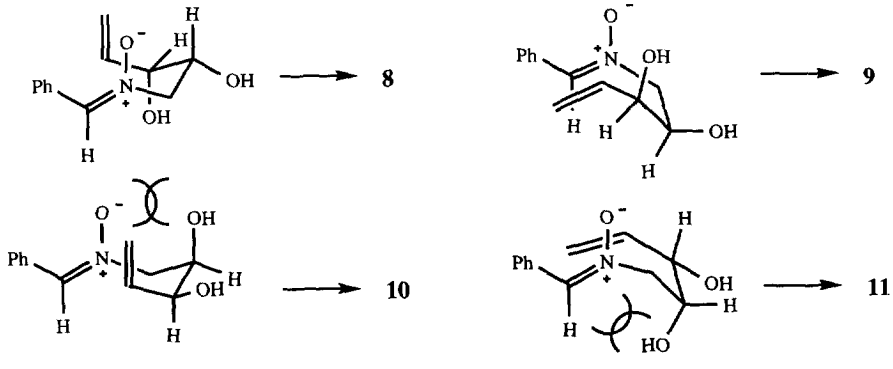
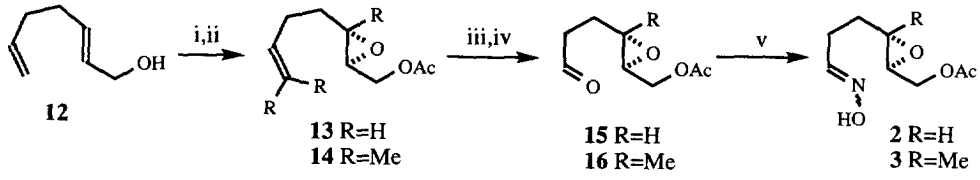
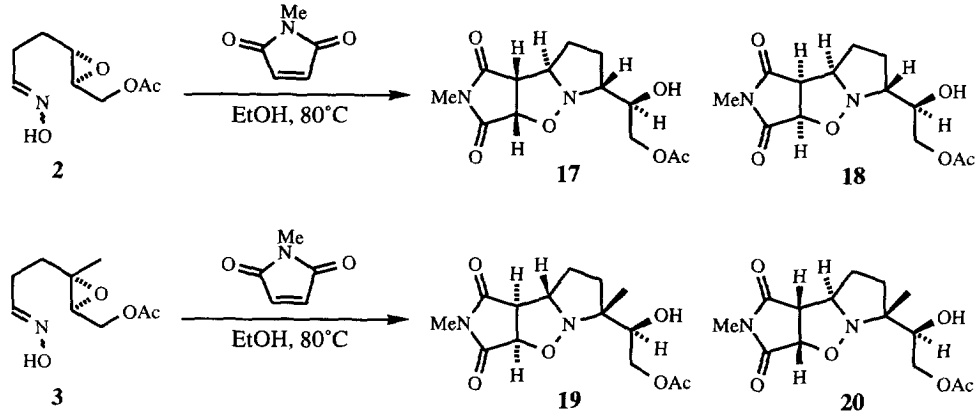


Figure 2: Pre-transition state conformers leading to **8**, **9**, **10** and **11**

Epoxyoximes **2** and **3** were prepared *via* similar asymmetric epoxidation,[5] acetylation, ozonolysis and oximation sequences. Thus asymmetric epoxidation followed by *in situ* acetylation of dienol **12**[6] afforded the epoxy ester **13** (83%). Ozonolysis of epoxyacetates **13** and **14**[5] afforded aldehydes **15** and **16** which were oximated to yield the required epoxyoximes **2** and **3** (56-64%).



i, L-(+)-diethyl tartrate, $Ti(O^iPr)_4$, ^tBuOOH, 4Å molecular sieves, CH_2Cl_2, -20°C; ii, Et_3N, Ac_2O, DMAP, CH_2Cl_2, -20°C; iii, O_3, EtOAc, -78°C; iv, Et_3N, 20°C; v, $NH_2OH{\cdot}HCl$, NaOAc, MeCN, H_2O, 20°C



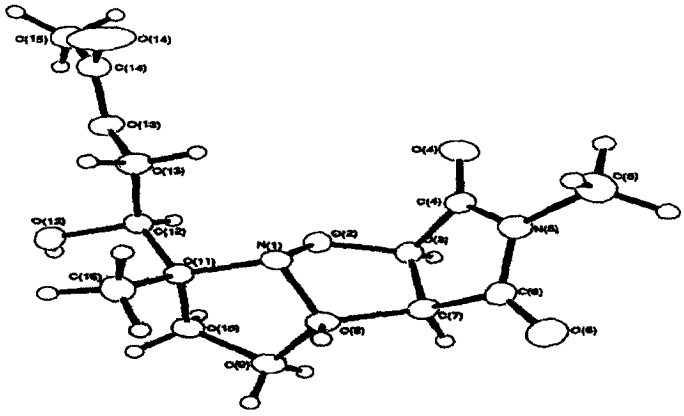
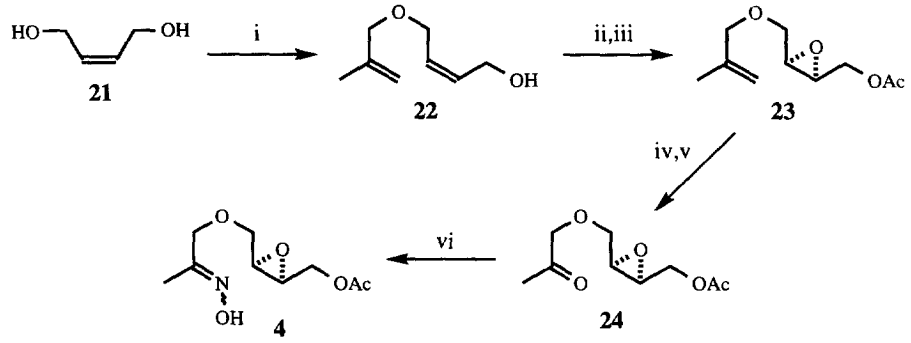


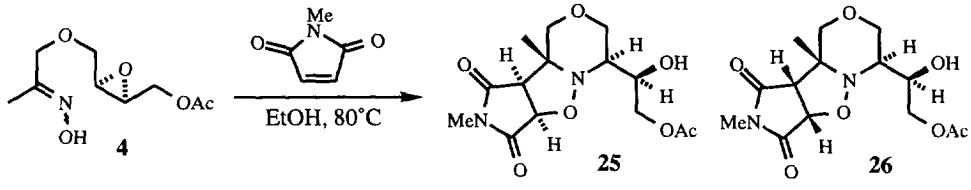
Figure 3: X-ray crystallographic structure of **19**

Heating epoxyoxime **2** in ethanol (80°C) in the presence of *N*-methylmaleimide (NMM) resulted in 5-*exo*-tet epoxide cleavage followed by *in situ* cycloaddition to afford a 1:1 mixture of *exo*- and

endo cycloadducts **17** and **18** (73%). Thus two products arise by facially selective cycloaddition *anti* to the bulky $CH(OH)CH_2OAc$ substituent. When subjected to identical conditions, epoxyoxime **3** afforded a 2:1 mixture of *exo*-adducts **19** and **20**. In this case the geminal $C(Me)CH(OH)CH_2OAc$ substitution α to the nitrone precludes *endo*-cycloaddition from either face and hence two *exo*-cycloadducts result. The stereochemistries of **17**, **18** and **20** were determined using the combined data from 2D-COSY and n.O.e. experiments (see Experimental section) whilst that of **19** was established by X-ray crystallography (*Figure 3*).[4]



i, C_4H_7Cl, NaH, DMF, 0°C; ii, L-(+)-diethyl tartrate, $Ti(O^iPr)_4$, ^tBuOOH, 4Å molecular sieves, CH_2Cl_2, -20°C; iii, Et_3N, Ac_2O, DMAP, CH_2Cl_2, -20°C; iv, O_3, EtOAc, -78°C; v, Et_3N, 20°C; vi, $NH_2OH{\cdot}HCl$, NaOAc, MeCN, H_2O, 20°C



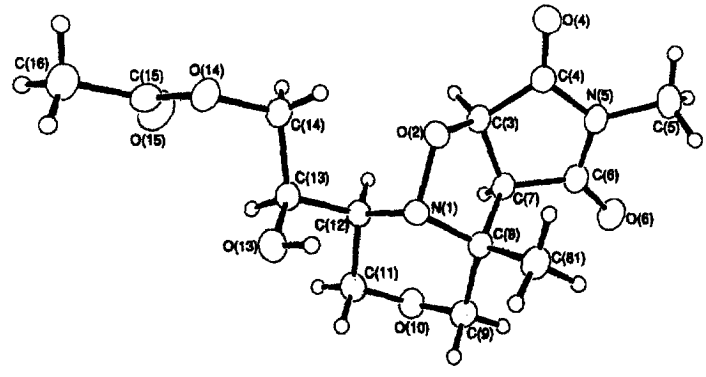
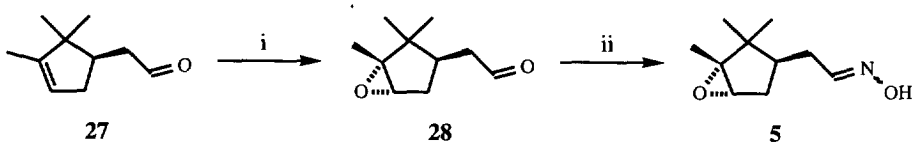


Figure 4: X-ray crystallographic structure of **25**

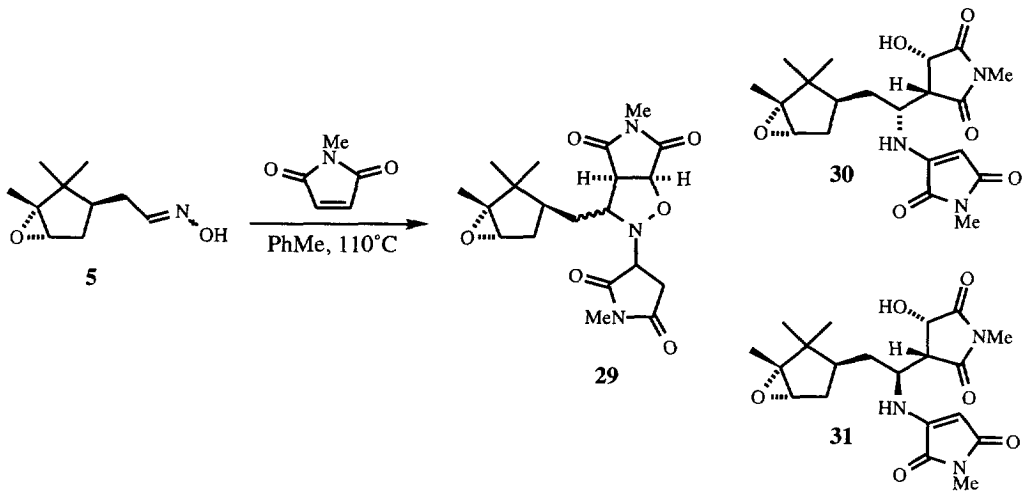
Epoxyketoxime **4** was readily prepared from commercially available (Z)-2-butene-1,4-diol **21**. Mono methallylation afforded the dienol **22** (81%) which was epoxidized and acetylated to yield the

enantiopure acetate **23** (50%). Ozonolysis gave ketone **24** which was readily oximated to yield **4**. Reaction between oxime **4** and *N*-methylmaleimide occured in boiling ethanol to afford a 3:1 mixture of *exo*- and *endo*-cycloadducts **25** and **26**. The stereochemistry of the former was determined by X-ray crystallography (*Figure 4*)[4] and that of the latter from 2D COSY and n.O.e. data (see Experimental section).



27 **28** **5**

i, MCPBA, CH_2Cl_2, 20°C; ii, NH_2OH·HCl, NaOAc, MeCN, H_2O, 20°C



5 **29** **30** **31**

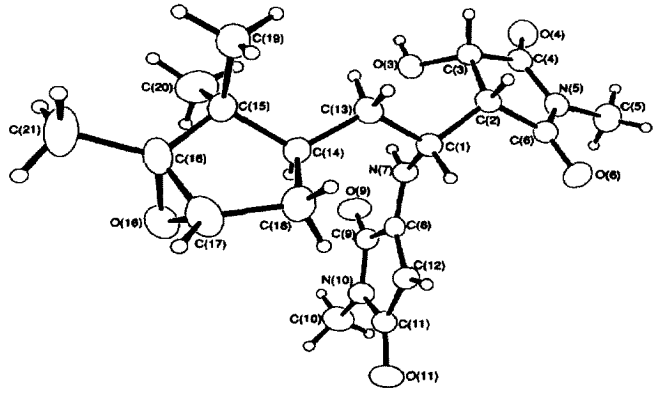
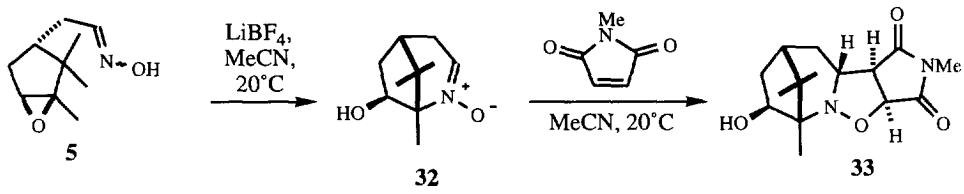


Figure 5: X-ray crystallographic structure of **30**

Epoxide **5** was prepared in two steps from the known aldehyde **27**.[7] Epoxidation of **27** occurred *anti* to the acetaldehyde sidechain to afford **28** which was readily oximated to yield **5**. When oxime **5** was treated

with *N*-methylmaleimide in toluene at 110°C none of the desired 1:1 cycloadducts were obtained. Instead a 2:1 mixture of two isomeric adducts **30** and **31** resulting from the incorporation of two equivalents of NMM resulted. Repetition of the reaction in the presence of excess NMM afforded **30** (52%) and **31** (26%). Clearly in this case, steric effects slow the epoxide ring opening by the internal oxime nucleophile and the alternative 1,3-azaprotio cyclotransfer (APT)[8]-cycloaddition cascades occur with the resulting isoxazolidines **29** subsequently undergoing rearrangement with N-O bond cleavage to afford the products **30** and **31**. The structure of **30** was established by X-ray crystallographic analysis (*Figure 5*)[4] whilst **31** is tentatively assigned as its epimer.



Intramolecular epoxide cleavage of **5** was induced using sub-stoichiometric quantities of lithium salts.[1] Treatment of epoxide **5** with $LiBF_4$ (30 mol%) in acetonitrile (20°C, 24 h) resulted in formation of nitrone **32** which underwent cycloaddition with NMM at 20°C to afford a single 1:1 cycloadduct **33** albeit in moderate yield (34%). The stereochemistry of **33** was established by X-ray crystallography (*Figure 6*).[4] This reaction sequence (**27**→**28**→**5**→**32**→**33**) thus results in the amplification of chirality, with six stereocentres in the product **33** being generated from only one in the terpenoid starting material **27**.

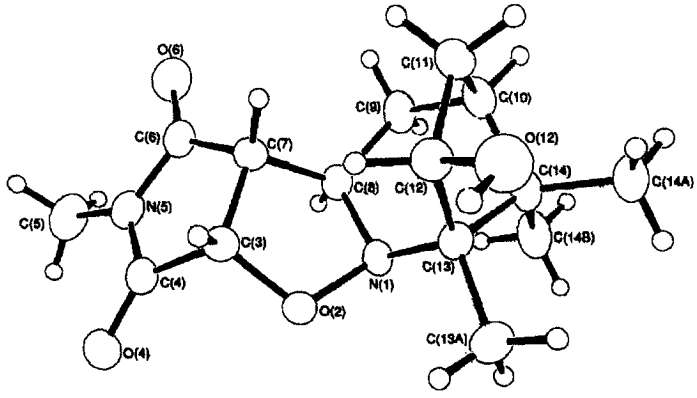
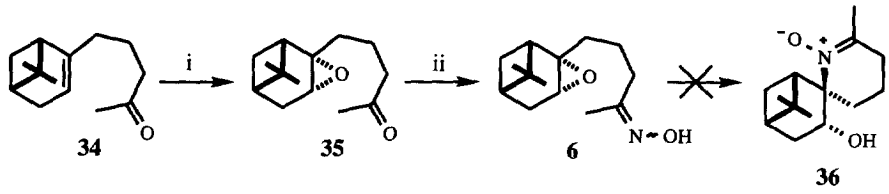


Figure 6: X-ray crystallographic structure of **33**

Adverse steric interactions also proved to be problematic in cascades involving the β-pinene derived epoxyoxime **6**. Treatment of the known ketone **34**[9] with MCPBA resulted in stereospecific epoxidation *anti* to the CMe_2 bridge to afford epoxyketone **35** from which ketoxime **6** was prepared under standard conditions. Unfortunately, nitrone **36** could not be prepared from oxime **6** either under thermal (xylene, 140°C, 16 h) or Lewis acid catalysed conditions (LiCl, THF or xylene, 20°C, 66°C or 140°C). In this case the CMe_2 group effectively shields the epoxide moiety from cleavage by the internal oxime nucleophile in either the 6-*exo*-tet sense or in the alternative 7-*endo*-tet manner.



i, MCPBA, CH_2Cl_2, 20°C; ii, NH_2OH·HCl, NaOAc, MeCN, H_2O, 20°C

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Specific rotations were measured at ambient temperature with an Optical Activity Ltd., AA-1000 polarimeter. Microanalyses were obtained using a Carlo Erba MOD 1106 instrument. Mass spectra were recorded at 70 ev on a VG Autospec mass spectrometer. ^1H Nuclear magnetic resonance spectra were recorded using either a General Electric QE300 spectrometer (300 MHz) or a Bruker AM-400 spectrometer (400 MHz) in the solvents specified. Flash column chromatography was performed using silica gel 60 (Merck 9385). Petroleum ether (b.p. 40-60°C) and ethyl acetate were distilled prior to use. Acetonitrile was dried by distillation from calcium hydride, *N,N*-dimethylformamide was dried by distillation from barium oxide and ethanol was dried by distillation from magnesium and iodine prior to use.

(4*S*,5*S*)-6-Acetoxy-4,5-epoxyhexanaldoxime 2. A solution of (4*S*,5*S*)-6-acetoxy-4,5-epoxyhexanal **15** (344 mg, 2·00 mmol) in acetonitrile (10 ml) was added to a solution of hydroxylamine hydrochloride (154 mg, 2·20 mmol) and sodium acetate (198 mg, 2·40 mmol) in water (10 ml). The resulting solution was stirred at room temperature for 8 h and then extracted with chloroform (2 x 20 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 2:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **2** (292 mg, 78%, 1:1 *E/Z* mixture), as a colourless oil. $[\alpha]_D$ +14·4 (*c* 0·5, $CHCl_3$); (Found: C, 50·75; H, 6·95; N, 7·7. $C_8H_{13}NO_4$ requires C, 51·3; H, 7·0; N, 7·5%); *m/z* (%) 188 (MH^+, 100), 170 (34), 127 (61), 114 (52), 85 (78), 68 (72), 41(65); δ_H ($CDCl_3$) 8·75 and 8·68 (1H, 2 x broad s, OH), 7·46 and 6·78 (1H, 2 x t, *J* 5·5 Hz, CH=N), 4·36 (1H, d, *J* 12 Hz, C*H*HOAc), 3·95 (1H, dd, *J* 12 and 6 Hz, CH*H*OAc), 3·00 and 2·93 (2 x 1H, 2 x m, OCH), 2·62-2·21 (2H, m, CH_2CH=N), 2·10 (3H, s, OAc), 1·86-1·71 (2H, m, CH_2).

(4*S*,5*S*)-6-Acetoxy-4,5-epoxy-4-methylhexanaldoxime 3. A solution of (4*S*,5*S*)-6-acetoxy-4,5-epoxy-4-methylhexanal **16** (700 mg, 3·76 mmol) in acetonitrile (15 ml) was added to a solution of hydroxylamine hydrochloride (280 mg, 4·10 mmol) and sodium acetate (370 mg, 4·50 mmol) in water (5 ml). The resulting solution was stirred at room temperature for 3 h and then extracted with dichloromethane (2 x 30 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **3** (660 mg, 70%, 1:1 *E/Z* mixture), as a colourless oil. (Found: C, 53·9; H, 7·7; N, 6·7. $C_9H_{15}NO_4$ requires C, 53·75; H, 7·45; N, 6·95%); *m/z* (%) 201 (M^+, 1), 183 (1), 158 (1), 142 (5), 98(35), 82 (57), 43 (100); δ_H ($CDCl_3$) 7·42 and 6·72 (1H, 2 x t, *J* 6 and 5·5 Hz, CH=N), 4·22 (1H, m, C*H*HOAc), 4·05 (1H, dd, *J* 12 and 6·5 Hz, CH*H*OAc),

3·00 (1H, m, OCH), 2·48 and 2·30 (2H, m, CH_2CH=N), 2·10 (3H, s, OAc), 1·75 (2H, m, CH_2), 1·35 and 1·33 (3H, 2 x s, Me).

(6*R*,7*S*)-8-Acetoxy-6,7-epoxy-4-oxa-2-octanone oxime 4. A solution of (6*R*,7*S*)-8-acetoxy-6,7-epoxy-4-oxa-2-octanone **24** (0·69 g, 3·40 mmol) in acetonitrile (15 ml) was treated with hydroxylamine hydrochloride (0·26 g, 3·80 mmol) and sodium acetate (0·34 g, 4·10 mmol) in water (5 ml). The resulting solution was stirred at room temperature for 3 h and then extracted with dichloromethane (2 x 30 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **4** (0·65 g, 61% 2:1 *E*/*Z* mixture), as a colourless oil. (Found: C, 49·5, H, 7·05; N, 6·25. $C_9H_{15}NO_5$ requires C, 49·75; H, 6·9; N, 6·45 %); *m*/*z* (%) 217 (M^+, 3), 200 (1), 175 (10), 144 (14), 98 (20), 43 (100); δ_H ($CDCl_3$) 4·39 (1H, m, C*H*HOAc), 4·10 (3H, m, CH*H*OAc and OCH_2), 3·70 (1H, m, OC*H*H), 3·55 (1H, m, OCH*H*), 3.26 (2H, m, 2 x OCH), 2·10 (3H, s, OAc), 1·94 (3H, s, 3H, Me).

Epoxycampholenaldoxime 5. A stirred solution of epoxycampholenal **28** (1·00 g, 5·95 mmol) in acetonitrile (50ml) was treated with a solution of hydroxylamine hydrochloride (0·45 g, 6·55 mmol) and sodium acetate (0·59 g, 7·41 mmol) in water (50 ml). The resulting solution was stirred at room temperature for 3 h and then extracted with chloroform (2 x 100 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **5** (0·99 g, 91%, 1:1 *E*/*Z* mixture), as a colourless oil. $[\alpha]_D$ -6·8 (*c* 1·0, $CHCl_3$); (Found: C, 65·5; H, 9·05; N, 7·3. $C_{10}H_{17}NO_2$ requires C, 65·5; H, 9·3; N, 7·6%); *m*/*z* (%) 183 (M^+, 15), 166 (18), 124 (21), 109 (39), 72 (39), 55 (53), 43 (100), 41 (83); δ_H ($CDCl_3$) 9·84 and 9·28 (1H, broad s, OH), 7·32 and 6.62 (1H, 2 x t, *J* 5·5 Hz, CH=N), 3·23 (1H, s, OCH), 2·31-1·34 (5H, m, CH and 2 x CH_2), 1·29, 0·98 and 0·87 (3 x 3H, 3 x s, 3 x Me).

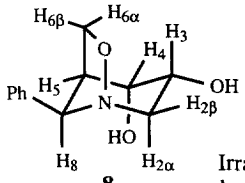
Epoxyketoxime 6. A stirred solution of epoxyketone **35** (1·40 g, 6·30 mmol) in acetonitrile (75 ml) was treated with a solution of hydroxylamine hydrochloride (482 mg, 6·93 mmol) and sodium acetate (0·62 g, 7·56 mmol) in water (50 ml) and the resulting solution was stirred at room temperature for 6 h and then extracted with chloroform (2 x 100 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **6** (1·33 g, 89%), as a colourless oil. $[\alpha]_D$ -129·2 (*c* 1·0, $CHCl_3$); (Found: C, 70·55; H, 9·65; N, 5·85. $C_{14}H_{23}NO_2$ requires: C, 70·85 H, 9.75; N, 5·9%); *m*/*z* (%) 237 (M^+, 2), 220 (49), 122 (87), 107 (25), 67 (48), 55 (60), 43 (42), 41 (100); δ_H ($CDCl_3$) 9·58 (1H, broad s, OH), 3·12 (1H, broad s, OCH), 2·40-1·41 (12H, m, 2 x CH and 5 x CH_2), 1·87 (3H, s, C=NMe), 1·29 and 0·91 (2 x 3H, 2 x s, 2 x Me).

***C*-Phenyl,*N*-[(2*R*,3*S*)-2,3-dihydroxy-4-pentenyl]nitrone 7**. A solution of (Z)-benzaldoxime (1·22 g, 10·00 mmol) in dry ethanol (40 ml) was added to a solution of sodium ethoxide [prepared by reaction of sodium (0·23 g, 10·00 mmol) with dry ethanol (10 ml)] and the solution was stirred at room temparature for 20 min whereupon (2*R*,3*S*)-1,2-epoxy-4-penten-3-ol **1**[3] (1·00 g, 10·00 mmol) was added and the mixture was stirred at room temperature for a further 24 h. After removal of the solvent *in vacuo*, water (20 ml) was added, and the mixture extracted with dichloromethane (4 x 50 ml). The combined organic layers were dried over

anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 1:1 v/v diethyl ether-ethyl acetate afforded the *product* **7** (1·13 g, 51%), as a colourless solid, m.p. 137-139°C; $[\alpha]_D$ -35·6 (*c* 1·0, $CHCl_3$); (Found: C, 65·0; H, 6·7; N, 6·3. $C_{12}H_{15}NO_3$ requires C, 65·15; H, 6·85; N, 6·35%); *m/z* (%) 221 (M^+, 6), 204 (12), 164 (29), 122 (37), 118 (77), 91 (100), 83 (35), 77 (30); δ_H ($CDCl_3$) 8·21 (2H, m, ArH), 7·43 (4H, m, PhC*H*=N and ArH), 5·95 (1H, m, C*H*=CH_2), 5·42 and 5·21(2H, 2 x d, CH=CH_2), 4·23 (1H, broad s, C*H*OH), 4·05 (3H, broad s, C*H*OH and NCH_2).

(1*R*,3*R*,4*S*,5*S*,8*R*)-3,4-Dihydroxy-8-phenyl-1-aza-7-oxabicyclo[3.2.1]octane 8 and **(1*S*,3*R*,4*R*,5*S*,7*S*)-3,4-dihydroxy-7-phenyl-1-aza-8-oxabicyclo[3.2.1]octane 9**. A solution of *C*-phenyl,*N*-[(2*R*,3*S*)-2,3-dihydroxy-4-pentenyl]nitrone **7** (100 mg, 0·45 mmol) in degassed xylene (3 ml) was held at reflux under a nitrogen atmosphere for 18 h. After cooling the solvent was removed *in vacuo* and the residue subjected to column chromatography. Elution with 2:1 v/v ethyl acetate-diethyl ether afforded the *products* **8** and **9** in the ratio of 2:1 (84 mg, 84%).

8: Colourless prisms. m.p. 145-147°C; $[\alpha]_D$ -3·2 (*c* 0·5, $CHCl_3$); (Found: C, 64·35; H, 6·5; N, 6·0. $C_{12}H_{15}NO_3 \cdot {}^1/_8H_2O$ requires C, 64·5; H, 6·85; N, 6·25%); *m/z* (%) 221 (M^+, 25), 204 (9), 176 (9), 162 (43), 118 (66), 105 (100), 91 (72), 77 (37); δ_H ($CDCl_3$) 7·45-7·21 (5H, m, ArH), 4·79 (1H, s, H-8), 4·20 (2H, m, 2H, H-3 and H-4), 3·77 (1H, d, *J* 7.5 Hz, H-6α), 3·72 (1H, dd, *J* 13 and 6 Hz, H-2β), 3·55 (1H, dd, *J* 7·5 and 5 Hz, H-6β), 3·10 (1H, t, *J* 5 Hz, H-5), 2·86 (1H, dd, *J* 13 and 9·5 Hz, H-2α), 2·50 (2H, broad s, OH).



8

Irradiated hydrogen

Enhancement (%)

	H-2α	H-2β	H-3,4	H-5	H-6α	H-6β	H-8
H-2α		10·1					5·4
H-2β	7·5						
H-3,4		1·4		1·1			
H-5			2·6			2·8	1·6
H-6α			2·7			12·5	
H-6β					11·2		
H-8	2·4						

9: Colourless prisms. m.p. 160-162°C; $[\alpha]_D$ +62·0 (*c* 0·5, $CHCl_3$); (Found: C, 64·85; H, 6·65; N, 6·05. $C_{12}H_{15}NO_3$ requires C, 65·15; H, 6·85; N, 6·35%); *m/z* (%) 221 (M^+, 7), 204 (7), 162 (62), 133 (53), 105 (100), 91 (61), 77 (32); δ_H ($CDCl_3$) 7·29-7·16 (5H, m, ArH), 4·62 (1H, d, *J* 7·5 Hz, H-5), 4·28 (1H, dd, *J* 9 and 4·5 Hz, H-8), 3·82 (1H, m, H-3), 3·73 (1H, t, *J* 3·5 Hz, H-4), 3·20-3·10 (2H, m, H-2α and H-2β), 2·60 (2H, broad s, OH), 2·59 (1H, dd, *J* 13 and 9 Hz, H-6α), 2·30 (1H, m, H-6β).

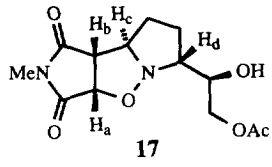
(2*S*,3*S*)-1-Acetoxy-2,3-epoxy-6-heptene 13. A mixture of powdered activated 4Å molecular sieves (600 mg) and dichloromethane (100 ml) was cooled to 0°C. L-(+)-Diethyl tartrate (3·48 g, 16·90 mmol) and titanium tetraisopropoxide (4·15 ml, 14·00 mmol) were added sequentially. After the mixture was cooled to

-20°C, *tert*-butyl hydroperoxide (7·0 ml, 21·00 mmol) was added and the resulting mixture was stirred for 20 min, whereupon (*E*)-2,6-heptadien-1-ol **12**[6] (1·57 g, 14·00 mmol) was added and the mixture was kept in the freezer at -25°C for 6 d. Triethylamine (3·9 ml, 28·00 mmol), acetic anhydride (2·6 ml, 28·00 mmol) and 4-(dimethylamino)pyridine (0·10 g, 0·84 mmol) were then added at -20°C with stirring and the reaction was allowed to warm to room temperature. After 1 h the mixture was filtered through celite, the solvent evaporated *in vacuo*, diethyl ether (50 ml) added and the solution washed with 5% sulphuric acid (3 x 15 ml) and 3M pH 7 sodium potassium phosphate buffer (15 ml) to afford a clear solution that was dried over anhydrous magnesium sulphate. After removal of solvent *in vacuo* the residue was subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **13** (1·40 g, 83%), as a colorless liquid. (Found: C, 63·4; H, 8·45. $C_9H_{14}O_3$ requires: C, 63·5; H, 8·3%); *m/z* (%) 171 (MH^+, 1), 127 (12), 115 (90), 111 (12), 86 (30), 67 (100), 57 (84) and 53 (32); δ_H ($CDCl_3$) 5·80 (1H, m, C*H*=CH_2), 5·00 (2H, m, CH=C*H*$_2$), 4.37 (1H, dd, *J* 12 and 2 Hz, C*H*HOAc), 3.92 (1H, dd, *J* 12 and 6 Hz, CH*H*OAc), 2·98 and 2·88 (2 x 1H, 2 x broad s, 2 x OCH), 2·30 (2H, m, CH_2), 2·09 (3H, s, OAc), 1·68 (2H, m, CH_2).

(4*S*,5*S*)-6-Acetoxy-4,5-epoxyhexanal 15. A solution of (2*S*,3*S*)-1-acetoxy-2,3-epoxy-6-heptene **13** (0·80 g, 4·70 mmol) in ethyl acetate (20 ml) at -78°C was treated with ozone until a blue colour persisted. Excess ozone was removed by flushing with nitrogen and the mixture was treated with triethylamine (1·30 ml, 9·43 mmol), stirred at -78°C for 1 h and allowed to warm to room temperature over 16 h. The solvent was removed *in vacuo* to afford the crude *product* **15** (0·65 g, 80%), that was used without further purification. δ_H ($CDCl_3$) 9·80 (1H, broad s, CHO), 4·40 and 3·90 (2 x 1H, 2 x m, C*H*$_2$OAc), 3·15 (2H, m, 2 x OCH), 2·62 (2H, t, *J* 7 Hz, C*H*$_2$CHO), 2·05 (4H, m, C*H*H and OAc), 1·80 (1H, m, CH*H*).

(4*S*,5*S*)-6-Acetoxy-4,5-epoxy-4-methylhexanal 16. A solution of (2*S*,3*S*)-1-acetoxy-2,3-epoxy-3,7-dimethyl-7-octene **14**[5] (1·00 g, 4·70 mmol) in ethyl acetate (20 ml) at -78°C was treated with ozone until a blue colour persisted. Excess ozone was removed by flushing with nitrogen and the mixture was treated with triethylamine (1·30 ml, 9·43 mmol), stirred at -78°C for 1 h and allowed to warm to room temperature over 16 h. The solvent was removed *in vacuo* to afford the crude *product* **16** (0·70 g, 79%), that was used without further purification. δ_H ($CDCl_3$) 9·80 (1H, broad s, CHO), 4·30 (1H, dd, *J* 12 and 4·5 Hz, C*H*HOAc), 4·03 (1H, dd, *J* 12 and 7 Hz, CH*H*OAc), 3·00 (1H, dd, *J* 7 and 4·5 Hz, OCH), 2·42 (2H, t, *J* 8 Hz, C*H*$_2$CHO), 2·10 (3H, s, OAc), 1·90 (2H, t, *J* 8 Hz, CH_2), 1·35 (3H, s, Me).

Cycloadducts 17 and 18. A solution of (4*S*,5*S*)-6-acetoxy-4,5-epoxyhexanaldoxime **2** (0·20 g, 1·07 mmol) and *N*-methylmaleimide (119 mg, 1·07 mmol) in dry ethanol (10 ml) was held at reflux for 15 h. After cooling the solvent was removed *in vacuo* and the residue subjected to column chromatography. Elution with 3:2 v/v ethyl acetate-diethyl ether afforded the *products* **17** and **18** (232 mg, 73%) in a 1:1 ratio. **17**: Pale yellow prisms, m.p. 78-80°C; $[\alpha]_D$ + 88·6 (*c* 1·0, $CHCl_3$); (Found: C, 52·4; H, 5·8; N, 9·1. $C_{13}H_{18}N_2O_6$ requires C, 52·35; H, 6·0; N, 9·35 %); *m/z* (%) 298 (M^+, 1), 238 (1), 225 (1), 195 (100), 111 (5), 82 (18), 68 (23), 43(41); δ_H ($CDCl_3$) 4·78 (1H, d, *J* 7·5 Hz, H_a), 4·10-3·98 (2H, m, C*H*$_2$OAc), 3·90 (1H, m, C*H*OH), 3·73 (1H, m, H_c), 3·52 (2H, m, H_b and H_d), 2·98 (3H, s, NMe), 2·76 (1H, broad s, OH), 2·04 (3H, s, OAc), 2·22-1·72 (4H, m, 2 x CH_2).

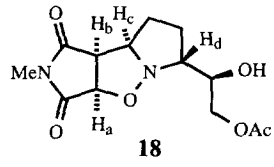


17

Enhancement (%)

Irradiated hydrogen	H_a	H_b,H_d	H_c
H_a		10·9	
H_b,H_d	8·2		2·9
H_c		3·2	

18: Pale yellow oil. $[\alpha]_D$ +136·4 (*c* 1·0, $CHCl_3$); (Found: C, 52·25; H, 6·05; N, 9·2. $C_{13}H_{18}N_2O_6$ requires C, 52·35 ; H, 6·0; N, 9·35 %); *m/z* (%) 299 (MH^+, 3), 283 (13), 239 (7), 225 (10), 195 (100), 179 (72), 112 (12), 84 (46), 68 (27), 43 (97); δ_H ($CDCl_3$) 4·85 (1H, d, *J* 8 Hz, H_a), 4·20-4·00 (2H, m, CH_2OAc), 3·92 (1H, m, H_c), 3·81 (1H, m, *CH*OH), 3·69 (1H, t, *J* 8 Hz, H_b), 2·98 (1H, m, H_d), 2·96 (3H, s, NMe), 2·80 (1H, broad s, OH), 2·05 (3H, s, OAc), 2·14-1·78 (4H, m, 2 x CH_2).



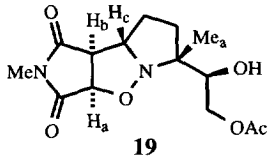
18

Enhancement (%)

Irradiated hydrogen	H_a	H_b	H_c
H_a		10·3	
H_b	12·6		10·3
H_c		18·9	

Cycloadducts 19 and **20**. A solution of (4*S*,5*S*)-6-acetoxy-4,5-epoxy-4-methylhexanaldoxime **3** (0·50 g, 2·50 mmol) and *N*-methylmaleimide (0·27 g, 2·50 mmol) in dry ethanol (10 ml) was held at reflux for 24 h. After cooling the solvent was removed *in vacuo* and the residue subjected to column chromatography. Elution with 3:2 v/v ethyl acetate-diethyl ether afforded the *products* **19** and **20** (468 mg, 60%) in a 2:1 ratio.

19: Colourless prisms from petroleum ether (b.p. 40-60°C)-diethyl ether, m.p. 221-222°C; $[\alpha]_D$ -41° (*c* 0·4, $CHCl_3$); (Found: C, 53·7; H, 6·6, H, 9·0. $C_{14}H_{20}N_2O_6$ requires C, 53·85; H, 6·4; N, 8·95%); *m/z* (%) 312 (M^+, 2), 239 (2), 209 (100), 43 (65); δ_H ($CDCl_3$) 4·80 (1H, d, *J* 7·5 Hz, H_a), 4·30 (1H, d, *J* 9·5 Hz, *CH*HOAc), 4·20 (2H, m, *CH*OH and CH*H*OAc), 4·00 (1H, t, *J* 7·5 Hz, H_c), 3·45 (1H, d, *J* 7·5 Hz, H_b), 3·00 (3H, s, NMe), 2·50 (1H, broad s, OH), 2·25 (2H, m, CH_2), 2·10 (3H, s, OAc), 1·78 (2H, m, CH_2), 1·00 (3H, s, Me_a).

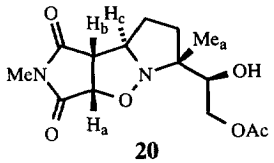


19

Enhancement (%)

Irradiated hydrogen	H_a	H_b	H_c	Me_a
H_a		7·1		
H_b	10·0			
H_c		3·8		5·6
Me_a			4·2	

20: Colourless wax, $[\alpha]_D$ +61° (*c* 0·48, $CHCl_3$); (Found: C, 54·0; H, 6·35, H, 8·8. $C_{14}H_{20}N_2O_6$ requires C, 53·85; H, 6·4; N, 8·95%); δ_H ($CDCl_3$) 4·24 (1H, dd, *J* 11·5 and 2·5 Hz, C*H*HOAc), 4·05 (1H, d, *J* 7·5 Hz, H_a), 3·94 (1H, dd, *J* 11·5 and 4 Hz, CH*H*OAc), 3·80 (1H, t, *J* 8 Hz, H_c), 3·30 (1H, dd, *J* 4 and 2·5 Hz, C*H*OH), 2·67 (1H, d, 1H, *J* 7·5 Hz, H_b), 2·60 (3H, s, OAc), 2·00 (1H, m, C*H*H), 1·67 (2H, m, CH_2), 1·60 (3H, s, Me_a), 1·54 (1H, m, CH*H*).



20

Enhancement (%)

Irradiated hydrogen	H_a	H_b	H_c
H_a		8·5	
H_b	10·7		4·8
H_c		4·7	

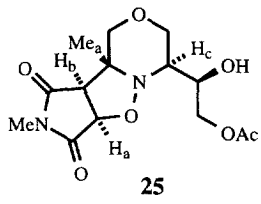
(*Z*)-7-Methyl-5-oxa-2,7-octadienol 22. A solution of (*Z*)-2-butene-1,4-diol **21** (1·76 g, 20·00 mmol) in dry *N*,*N*-dimethylformamide (10 ml) was added dropwise over 30 min to a stirred suspension of sodium hydride (60 wt%, 1·00 g, 25·00 mmol) in dry *N*,*N*-dimethylformamide (10 ml) at -20°C. The resulting mixture was stirred at 0°C for 30 min and methallyl chloride (2·26 g, 25·00 mmol) was added dropwise while keeping the temperature below 0°C. The reaction mixture was stirred at 0°C for 1 h and at room temperature for 16 h. The solvent was removed *in vacuo*, the residue taken up into dichloromethane (100 ml), washed with water (2 x 100 ml), dried over anhydrous magnesium sulphate and the solvent removed *in vacuo* to afford a residual oil which was distilled to afford the *product* **22** (2·30 g, 81%), as a colourless oil, b.p. 44°C/0·1 mm Hg; (Found: C, 67·6; H, 10·3. $C_8H_{14}O_2$ requires C, 67·6, H, 9·85%); *m/z* (%) 142 (M^+, 1), 124 (3), 72 (33), 55 (100), 41 (83); δ_H ($CDCl_3$) 5·76 (2H, m, CH=CH), 4·96 and 4·91 (2 x 1H, 2 x s, C=CH_2), 4·20 (2H, d, *J* 5 Hz, CH_2OH), 4·00 (2H, d, *J* 6 Hz, OCH_2), 3·90 (2H, s, OCH_2), 2·70 (1H, broad s, OH), 1·70 (3H, s, Me).

(2*S*,3*R*)-1-Acetoxy-2,3-epoxy-7-methyl-5-oxa-7-octene 23. A mixture of powdered activated 4Å molecular sieves (600 mg) and dichloromethane (100 ml) was cooled to 0°C. L-(+)-Diethyl tartrate (3·48 g, 16·90 mmol) and titanium tetraisopropoxide (4·15 ml, 14·00 mmol) were added sequentially, the mixture cooled to -20°C, *tert*-butyl hydroperoxide (7·0 ml, 21·00 mmol) added and the resulting mixture stirred for 20 min. (Z)-7-Methyl-5-oxa-2,7-octadienol **22** (2·00 g, 14·00 mmol) was then added and the mixture was kept in the freezer at -25°C for 6 d. Triethylamine (3·9 ml, 28·00 mmol), acetic anhydride (2·6 ml, 28·00 mmol) and 4-(dimethylamino)pyridine (0·10 g, 0·84 mmol) were added at -20°C with stirring and the reaction was allowed to warm to room temperature. After 1 h the mixture was filtered through celite, the solvent evaporated *in vacuo*, diethyl ether (50 ml) added and the solution washed with 5% sulphuric acid (3 x 15 ml) and 3M pH 7 buffer (sodium potassium phosphate, 15 ml) to afford a clear solution that was dried over anhydrous magnesium sulphate. After removal of solvent *in vacuo* the residue was subjected to column chromatography. Elution with 1:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **23** (1·40 g, 50%), as a colourless oil. (Found: C, 59·7; H, 8·3. $C_{10}H_{16}O_4$ requires C, 60·0, H, 8·0%); *m/z* (%) 200 (M^+, 2), 157 (5), 129 (30), 129 (15), 115 (23), 43 (100); δ_H ($CDCl_3$) 4·98 and 4·92 (2 x 1H, 2 x s, C=CH_2), 4·35 (1H, dd, *J* 12 and 1·5 Hz, OC*H*H) 4·00 (3H, m, OCH*H* and OCH_2), 3·67 and

3·53 (2 x 1H, 2 x dd, *J* 11 and 4·5 Hz, CH_2OAc), 3·30 (2H, m, 2 x OCH), 2·10 (3H, s, OAc), 1·75 (3H, s, Me).

(6*R*,7*S*)-8-Acetoxy-6,7-epoxy-4-oxa-2-octanone 24. A solution of (2*S*,3*R*)-1-acetoxy-2,3-epoxy-7-methyl-5-oxa-7-octene **23** (1·00 g, 5·00 mmol) in ethyl acetate (20 ml) at -78°C was treated with ozone until a blue colour persisted. Excess ozone was removed by flushing with nitrogen and the mixture was treated with triethylamine (1·4 ml, 10·00 mmol), stirred at -78°C for 1 h and allowed to warm to room temperature over 16 h. The solvent was removed *in vacuo* to afford the crude *product* **24** (0·68 g, 68%), that was used without further purification. δ_H ($CDCl_3$) 4·29 (1H, dd, *J* 12·5 and 4 Hz, C*H*HOAc), 4·11 (3H, m, CH*H*OAc and OCH_2), 3·80 (1H, dd, *J* 11·5 and 3·5 Hz, OC*H*H), 3·55 (1H, dd, *J* 11·5 and 7 Hz, OCH*H*), 3·20 (2H, m, 2 x OCH), 2·13 (3H, s, OAc), 2·08 (3H, s, COMe).

Cycloadducts 25 and **26**. A solution of (6*R*,7*S*)-8-acetoxy-6,7-epoxy-4-oxa-2-octanone oxime **4** (0·50 g, 2·30 mmol) and *N*-methylmaleimide (0·26 g, 2·30 mmol) in dry ethanol (10 ml) was held at reflux for 24 h. After cooling the solvent was removed *in vacuo* and the residue subjected to column chromatography. Elution with 3:2 v/v ethyl acetate-diethyl ether afforded the *products* **25** and **26** (0·45 g, 60%) in a 3:1 ratio.
25: Colourless solid, m.p. 205-206°C; $[\alpha]_D$ -33° (*c* 0·4, $CHCl_3$); *m/z* (%) 328 (M^+, 1), 269 (1), 225 (100), 98 (15), 43 (51); δ_H (C_6D_6) 4·34 (1H, d, *J* 8·5 Hz H_a), 4·23 (1H, dd, *J* 11·5 and 4 Hz, C*H*HOAc), 4·15 (1H, dd, *J* 11·5 and 7·5 Hz, CH*H*OAc), 3·80 (1H, dd, *J* 12·5 and 1·5 Hz, OC*H*H), 3·70 (2H, m, C*H*OH and OC*H*H), 3·38 (1H, d, *J* 8·5 Hz, H_b), 3·07 (1H, t, *J* 11 Hz, OCH*H*), 2·90 (1H, d, *J* 12·5 Hz, OCH*H*), 2·69 (1H, m, H_c), 2·50 (4H, s, NMe and OH), 1·70 (3H, s, OAc), 0·76 (3H, s, Me_a).

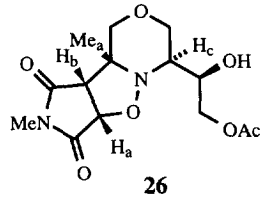


25

Enhancement (%)

Irradiated hydrogen	H_a	H_b	H_c
H_a		8·7	8·0
H_b	6·5		5·2
H_c	12·4	12·3	

26: Colourless solid, m.p. 185-187°C; $[\alpha]_D$ -51° (*c* 0·3, $CHCl_3$); *m/z* (%) 328 (M^+, 1), 269 (3), 225 (100), 43 (37); δ_H ($CDCl_3$) 4·90 (1H, d, *J* 8 Hz, H_a), 4·57 (1H, dd, *J* 12·5 and 1·5 Hz, OC*H*H), 4·20 (2H, m, CH_2OAc), 3·80 (1H, m, OC*H*H), 3·60 (1H, m, C*H*OH), 3·50 (1H, d, *J* 12·5 Hz, OCH*H*), 3·35 (1H, t, *J* 11 Hz, OCH*H*), 3·30 (1H, d, *J* 8 Hz, H_b), 3·00 (3H, s, NMe), 2·86 (1H, d, *J* 9 Hz, OH), 2·82 (1H, m, H_c), 2·10 (3H, s, OAc), 1·30 (3H, s, Me_a).



26

Enhancement (%)

Irradiated hydrogen	H_a	H_b	Me_a
H_a		10·0	
H_b	15·1		4·9
Me_a	0·9	6·1	

Epoxycampholenal 28. *m*-Chloroperbenzoic acid (60%, 946 mg, 3·29 mmol) in dichloromethane (10 ml) was added dropwise over 15 min to a stirred solution of (+)-campholenal **27**[7] (0·50 g, 3·29 mmol) in dichloromethane (5 ml) and the reaction mixture was stirred at room temperature for a further 10 h. After dilution with dichloromethane (25 ml) the mixture was washed with saturated aqueous sodium bicarbonate solution (30 ml), the organic layer dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 3:2 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **28** (340 mg, 62%), as a colourless oil. (Found: C, 70·95; H, 9·45. $C_{10}H_{16}O_2$ requires C, 71·3; H, 9·6 %); *m/z* (%) 168 (M^+, 15), 150 (7), 139 (12), 123 (51), 108 (62), 98 (13), 943 (34), 90 (18), 41 (93); δ_H ($CDCl_3$) 9·71 (1H, t, *J* 2 Hz, CHO), 3·27 (1H, s, OCH), 2·42-1·97 (5H, m, CH and 2 x CH_2), 1·34, 1·02 and 0·77 (3 x 3H, 3 x s, 3 x Me).

Cycloadducts 30 and 31. A solution of epoxycampholenaldoxime **5** (0·50 g, 2·73 mmol) and *N*-methylmaleimide (0·72 g, 6·55 mmol) in toluene (100 ml) was stirred and held at reflux for 12 h. After cooling the solvent was removed *in vacuo* and the residue subjected to column chromatography. Elution with 4:1 v/v hexane-ethyl acetate afforded the *products* **30** (0·57 g, 52%) and **31** (0·29 g, 26%).

30: Pale yellow prisms from hexane-dichloromethane, m.p. 129-131°C; $[\alpha]_D$ +21·8 (*c* 1·1, $CHCl_3$); (Found: C, 59·0; H, 6·9; N, 10·5. $C_{20}H_{27}N_3O_6$ requires C, 59·2; H, 6·7; N, 10·3%); *m/z* (%) 405 (M^+, 3), 387 (4), 267 (83), 249 (100), 191 (44), 155 (39), 41 (82); δ_H ($CDCl_3$) 6·11 (1H, *J* 10·5 Hz, NH), 4·85 (1H, s, C=CH), 4·76 (1H, *J* 8 Hz, OCH), 3·90 (1H, m, C*H*NH), 3·17 (1H, dd, *J* 8 and 2·5 Hz, OCH), 2·94 and 2·89 (2 x 3H, 2 x s, 2 x NMe), 2·10-1·90 (4H, m, CHCO, CH_2 and OH), 1·29 and 0·94 (2 x 3H, 2 x s, 2 x Me), 1·30-1·10 (3H, m, CH and CH_2), 0·76 (3H, s, Me).

31: Pale yellow prisms from hexane-dichloromethane, m.p. 131-133°C; (Found: C, 59·5; H, 6·8; N, 10·1. $C_{20}H_{27}N_3O_6$ requires C, 59·2; H, 6·7; N, 10·3%); *m/z* (%) 405 (M^+, 3), 362 (6), 267 (68), 249 (94), 191 (40), 139 (25), 41 (100); δ_H ($CDCl_3$) 5·89 (1H, *J* 9·5 Hz, NH), 4·83 (1H, s, C=CH), 4·78 (1H, *J* 8 Hz, OCH), 3·94 (1H, dm, *J* 10·5 Hz, C*H*NH), 3·26 (1H, s, OH), 3·12 (1H, dd, *J* 8 and 2·5 Hz, OCH), 2·94 and 2·89 (2 x 3H, 2 x s, 2 x NMe), 2·10-1·70 (6H, m, CHCO, CH and 2 x CH_2), 0·94, 0·72 and 0·28 (3 x 3H, 3 x s, 3 x Me).

Cycloadduct 33. A stirred solution of epoxycampholenaldoxime **5** (350 mg, 1·91 mmol) in dry acetonitrile (35 ml) was treated with a solution of $LiBF_4$ (54 mg, 0.57 mmol) in dry acetonitrile (15 ml). The resulting solution was stirred at room temperature for 24 h, *N*-methylmaleimide (212 mg, 1·91 mmol) added and stirring continued for a further 24 h at room temperature. The acetonitrile was then removed *in vacuo*, water (20 ml) added and the mixture extracted with chloroform (2 x 40 ml). The combined organic layers were washed with brine, dried over anhydrous magnesium sulphate, the solvent removed *in vacuo* and the residue subjected to column chromatography. Elution with 2:3 v/v hexane-ethyl acetate afforded the *product* **33** (0·39 g, 34%) which crystallized from petroleum ether (b.p. 60-80°C)-dichloromethane as colourless prisms. m.p. 142-144°C; $[\alpha]_D$ -35·0 (*c* 0.4, $CHCl_3$); (Found: C, 55·1; H, 6·9; N, 8·2. $C_{15}H_{22}N_2O_4 \cdot {}^1/_2CH_2Cl_2$ requires C, 55·2; H, 6·85; N, 8·3 %); *m/z* (%) 294 (M^+, 3), 279 (20), 166 (23), 149 (100), 83 (32), 71 (40), 57 (66), 43 (78); δ_H (C_6H_6) 4·65 (1H, d, *J* 9 Hz, OCHCO), 3·70 (1H, m, C*H*OH), 3·21 (1H, t, *J* 9 Hz, NCH), 2·91 (1H, t, *J* 9 Hz, CHCO), 2·55 (3H, s, NMe), 2·02-1·50 (5H, m, CH and 2 x CH_2), 1·34, 1·02 and 0·87 (3 x 3H, 3 x s, 3 x Me).

Epoxyketone 35. *m*-Chloroperbenzoic acid (60%, 1·40 g, 4·85 mmol) in dichloromethane (15 ml) was added dropwise over 15 min to a solution of ketone **34**[9] (0·50 g, 3·29 mmol) in dichloromethane (10 ml). The reaction mixture was stirred at room temperature for 10 h, diluted with dichloromethane (30 ml), washed with saturated aqueous sodium bicarbonate solution (50 ml) and the organic layer dried over anhydrous magnesium sulphate. The solvent was then removed *in vacuo* and the residue subjected to column chromatography. Elution with 2:1 v/v petroleum ether (b.p. 40-60°C)-diethyl ether afforded the *product* **35** (0·86 g, 80%), as a colourless oil. $[\alpha]_D$ -151·6 (*c* 1·0, $CHCl_3$); (Found: C, 75·4; H, 10·0. $C_{14}H_{22}O_2$ requires: C, 75·6; H, 10·0%); *m/z* (%) 222 (M^+, 3), 207 (8), 95 (66), 85 (13), 79 (25), 67 (33), 55 (32), 43 (100); δ_H ($CDCl_3$) 3·10 (1H, broad s, OCH), 2·49-1·45 (12H, m, 2 x CH and 5 x CH_2), 2·13 (3H, s, COMe), 1·29 (3H, s, Me), 0·91(3H, s, Me).

Single crystal X-ray analysis of 9, 19, 25, 30 and **33**.[4] All crystallographic measurements were carried out on a Stoe STADI 4 diffractometer at 293(2) K (for **9**), 293(2) K (for **19**), 473(2) K (for **25**), 200(2) K (for **30**) and 200(2) K (for **33**) using graphite monochromated copper K_α X-radiation (λ=1·54184 Å). Two equivalent sets of data were collected in the ranges $3{\cdot}68 \leq \theta \leq 64{\cdot}43^\circ$ (for **9**), $4{\cdot}34 \leq \theta \leq 64{\cdot}56^\circ$ (for **19**), $3{\cdot}86 \leq \theta \leq 64{\cdot}49^\circ$ (for **25**), $4{\cdot}33 \leq \theta \leq 64{\cdot}48^\circ$ (for **30**) and $3{\cdot}35 \leq \theta \leq 64{\cdot}49^\circ$ (for **33**) using ω/θ scans. No significant variation was observed in the intensity of five standard reflections. Lorentz and polarization corrections were applied to the data sets together with a semi-empirical absorption correction based on azimuthal ψ-scans. The structures were solved by direct methods using SHELXS-86[10] and were refined by full-matrix least squares (based on F^2) using SHELXS-93[11] which uses all data for refinement.

Crystal data for **9**:[4] $C_{12}H_{15}NO_3$, 0·45 x 0·33 x 0·20 mm, M = 221·25, triclinic, space group $P\bar{1}$, a = 5·55130(11) Å, b = 8·2622(2) Å, c = 12·2663(2) Å, α = 84·2990(14)°, β = 79·005(2)°, γ = 82·088(2)°, U = 545·47(2) Å^3, Z = 2, D_x = 1·347 gcm^{-3}, μ = 0·797 mm^{-1}, F(000) = 236.

Crystal data for **19**:[4] $C_{14}H_{20}N_2O_6$, 0·58 x 0·51 x 0·44 mm, M = 312·32, orthorhombic, space group $P2_12_12_1$, a = 6·23550(11) Å, b = 11·7893(2) Å, c = 20·2967(4) Å, α = 90°, β = 90°, γ = 90°, U = 1492·05(5) Å^3, Z = 4, D_x = 1·390 gcm^{-3}, μ = 0·923 mm^{-1}, F(000) = 664.

Crystal data for **25**:[4] $C_{14}H_{20}N_2O_7$, 0·45 x 0·345 x 0·24 mm, M = 328·32, orthorhombic, space group $P2_12_12_1$, a = 5·753(3) Å, b = 11·558(5) Å, c = 22·902(12) Å, α = 90·00(4)°, β = 90·00(4)°, γ = 90·00(4)°, U = 1522·9(13) Å^3, Z = 4, D_x = 1·432 gcm^{-3}, μ = 0·984 mm^{-1}, F(000) = 696.

Crystal data for **30**:[4] $C_{20}H_{27}N_3O_6$, 0·60 x 0·49 x 0·38 mm, M = 405·45, monoclinic, space group $P2_12_12_1$, a = 9·8680(4) Å, b = 12·9729(4) Å, c = 16·5207(5) Å, α = 90°, β = 90°, γ = 90°, U = 2114·92(12) Å^3, Z = 4, D_x = 1·273 gcm^{-3}, μ = 0·787 mm^{-1}, F(000) = 864.

Crystal data for **33**:[4] $C_{15}H_{22}N_2O_4 \cdot {}^1/_2CH_2Cl_2$, 0·45 x 0·28 x 0·10 mm, M = 336·81, monoclinic, space group $P2_1/c$, a = 7·5236(4) Å, b = 26·3590(14) Å, c = 9·0005(6) Å, α = 90°, β = 102·047(6)°, γ = 90°, U = 1745·6(2) Å^3, Z = 4, D_x = 1·221 gcm^{-3}, μ = 2·041 mm^{-1}, F(000) = 684.

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