Pergamon

TETRAHEDRON

Tetrahedron 58 (2002) 5827–5836

X=Y–ZH Systems as potential 1,3-dipoles. Part 54: Stereo- and facially-selective formation of bridged bicyclic *N*-heterocycles via a sequential one-pot electrophile induced oxime→nitrone→cycloaddition sequence. Multiplication of chirality

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Received 14 March 2002; revised 9 May 2002; accepted 30 May 2002

Abstract—Electrophile induced bridged-ring forming cyclisations creating azabicyclo-[3.3.1]- and azabicyclo-[3.2.1]-nitrones, followed by cycloaddition, occur stereo-, regio- and facially specifically in good to excellent yield. Chiral bridged-ring systems have been synthesised that involve multiplication of chiral centres from one to six and one to seven in one pot reactions. © 2002 Elsevier Science Ltd. All rights reserved.

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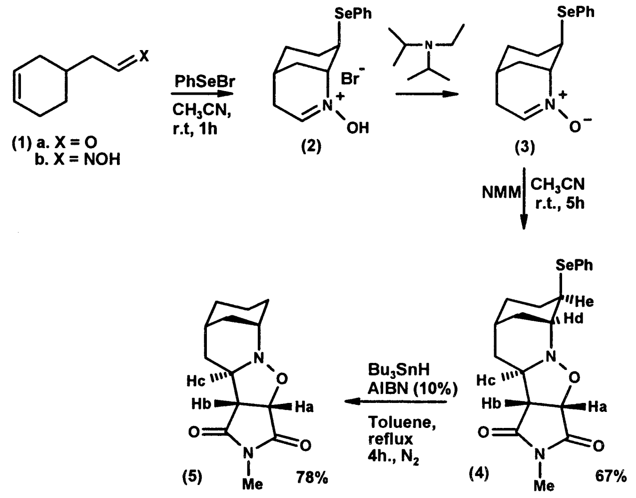
1. Introduction

We have recently reported a range of 1-pot sequential and cascade electrophile induced oxime→nitrone→cycloaddition reactions furnishing nitrones and their cycloadducts in good yield.[1–3] In a preliminary communication we reported that phenylselenyl bromide is an excellent reagent for effecting stereo- and regio-specific spiro- and bridged-ring forming cyclisation of oximes onto proximate alkenes.[4] In a recent paper we reported a related electrophile induced cyclisation of oxime *O*-allyl and *O*-benzyl ethers generating the corresponding oxime ether salts. These oxyiminium ions can, under appropriate conditions, be transformed into nitrones, imines or, by reduction, hydroxylamines.[5] Related oximinium ions have proved versatile intermediates in solid phase synthesis.[6] As part of an ongoing research program developing new cascade reaction we now report full details of our work on bridged-ring forming cyclisations of oximes and oxime ethers. Chiral bridged-ring systems have also been synthesised by this strategy and these processes involve multiplication of chiral centres from one to six and one to seven in one pot reactions.

2. Azabicyclo[3.3.1] systems

2.1. Cyclisation onto cyclohexenes

Formation of bridged ring nitrones was first evaluated with oxime (**1b**) prepared as a 1:1 *E*/*Z*-isomer mixture in 93% yield from the known aldehyde **1a**.[7,8] Aldoxime (**1b**) was treated with phenylselenyl bromide in acetonitrile at ambient temperature for 1 h to afford the corresponding azabicyclo[3.3.1]nonane nitrone salt (**2**) which, upon treatment with Hunig's base afforded nitrone (**3**) (Scheme 1).



Scheme 1.

Keywords: facially-selective; *N*-heterocycles; chirality.

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PII: S0040-4020(02)00564-1

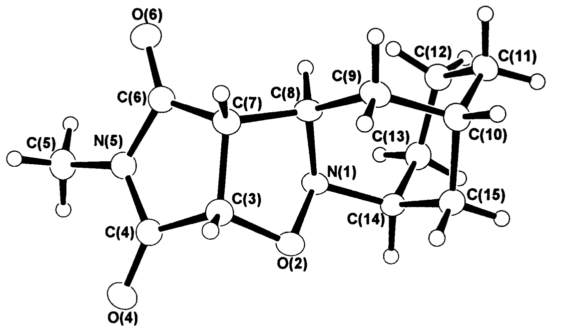


Figure 1. X-Ray crystal structure of (**5**).

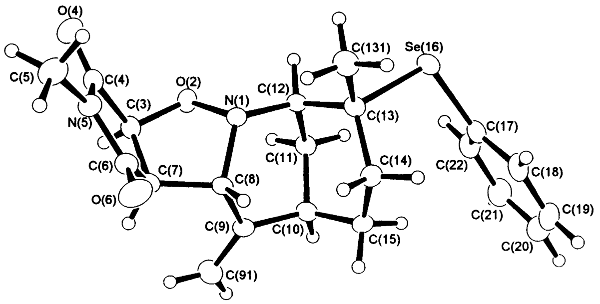


Figure 2. X-Ray crystal structure of (**9**).

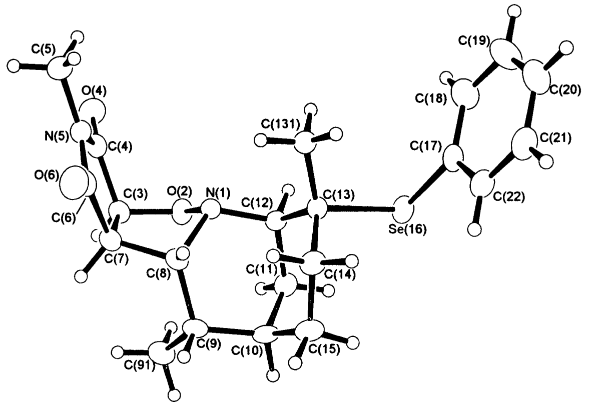


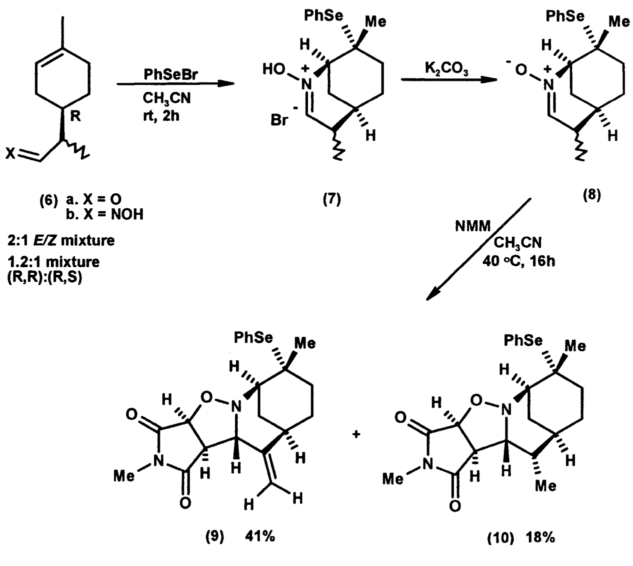
Figure 3. X-Ray crystal structure of (**10**).

Nitrone (**3**) underwent to 1,3-dipolar cycloaddition with *N*-methylmaleimide (NMM) in acetonitrile at room temperature over 5 h. Cycloadduct (**4**) was obtained as a 4:1 mixture of isomers (^{1}H NMR) in 67% overall yield from oxime (**1b**) (Scheme 1). The minor isomer appears to possess an equatorial SePh moiety (^{1}H NMR). The stereochemistry of the major isomer (**4**) was determined by n.O.e and 2D-COSY studies. Cycloadduct (**4**) arises via an *exo*-transition state which is dictated by the array of axial protons hindering *endo*-transition states on both faces of the nitrone. Steric hindrance to the *exo*-transition state *syn* to the 3-carbon bridge is significantly greater than that *syn* to the 1-carbon bridge (see Fig. 4). Hence *exo*-cycloaddition *syn* to the 1-carbon bridge is observed.

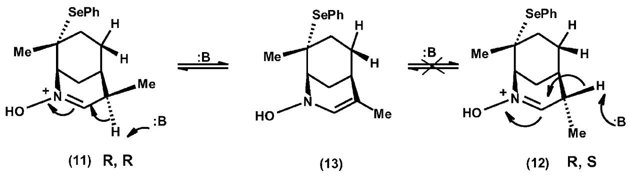
Reductive removal of the PhSe group from the 4:1 mixture using Bu$_3$SnH (1 mol equiv.)/AIBN (10 mol%) gave the expected product (**5**) in 78% yield as a single isomer indicating that the observed 4:1 mixture of isomers of (**4**) arises from the PhSe group and that both isomers are *exo*-cycloadducts. The stereochemistry of (**5**) was assigned from n.O.e. data, 2D-COSY studies and X-ray crystallography (Fig. 1).

The synthesis of a further azabicyclo[3.3.1]nonane system was investigated using oxime (**6b**). Aldehyde (**6a**), synthesised[9] from commercially available (+)-menth-1-en-9-ol, which comprised a 2:1 mixture of (*R*,*R*) and (*R*,*S*) isomers, was converted to aldoxime (**6b**) with hydroxylamine hydrochloride—sodium acetate in 96% yield. The aldoxime (**6b**) comprised a mixture of four isomers. Thus each isomer in the 2:1 mixture of *E*- and *Z*-oximes was a 1.2:1 mixture of (*R*,*R*) and (*R*,*S*) isomers. This oxime (**6b**) mixture reacted with phenylselenyl bromide to give a mixture of (*R*,*R*) and (*R*,*S*) nitrone salts (**7**) (Scheme 2). Liberation of the nitrones (**8**) using potassium carbonate, and subsequent cycloaddition with NMM gave a 2:1 mixture of cycloadducts (**9**) and (**10**) in 59% combined yield from **6b**. The stereochemistry of products (**9**) and (**10**) was determined from n.O.e data, 2D-COSY studies and X-ray crystallography (Figs. 2 and 3). The oxime cyclisation is regioselective and gives exclusively the bicyclo[3.3.1]nitrone salt. No bicyclo[3.2.2]nitrone salt, which would arise from attack at the more substituted carbon of the alkene, was detected.

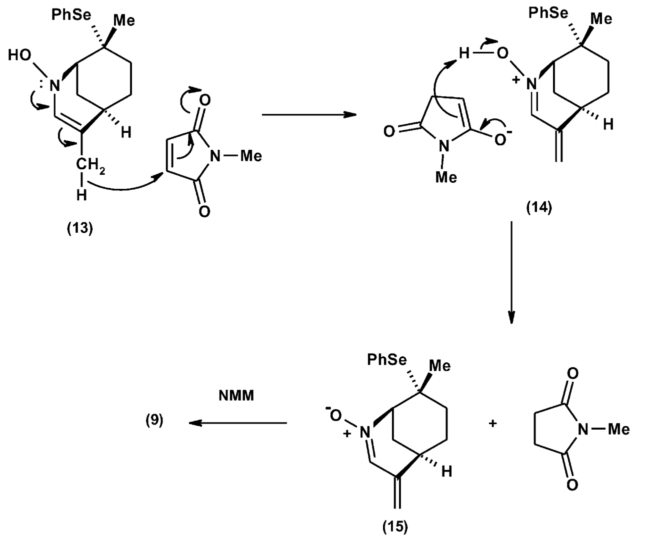
Formation of cycloadduct (**9**) requires generation of a dehydrogenated nitrone (Scheme 4). This can be rationalised by initial selective deprotonation of the *R*,*R*-salt (**11**) to generate the ene-hydroxylamine (**13**) (Scheme 3). Molecular models show that pseudo-axial deprotonation of salt *R*,*R*-(**11**) can be easily achieved whilst the



Scheme 2.



Scheme 3.



Scheme 4.

pseudo-equatorial deprotonation of the *R*,*S*-salt (**12**) is stereoelectronically disfavoured resulting in inhibition of deprotonation.

Conversion of (**13**) into (**15**) could occur via hydride transfer from the ene-hydroxylamine (**13**) to *N*-methylmaleimide (Scheme 4). Assuming deprotonation is chemoselective for (**11**) (Scheme 3) the operation of both Schemes 3 and 4 would require 1.5 mol equiv. of NMM. In Scheme 2, 1.4 mol equiv. of NMM was employed which indicates, within experimental error, that chemoselective deprotonation of (**11**) is occurring. This concurs with the *S*-stereochemistry at C of (**10**) established by X-ray crystallography (Fig. 3).

The cycloaddition reactions of the two nitrones (**15**) and (**12**) occurs with high facial selectivity via *exo*-transition states (**16**) and (**17**) (Fig. 4) to afford the *exo*-cycloadducts (**9**) and (**10**). The top face of the dipole remains more sterically hindered even in the presence of the additional pseudo axial methyl group on the bottom face of (**17**) (Fig. 4). Consequently, *exo*-cycloaddition syn to the 1-carbon bridge is observed, as previously discussed for (**3**), affording *endo*-cycloadducts (**9**) and (**10**). These bicyclo[3.3.1]nitrone cycloaddition transition states are analogous to that for formation of (**5**).

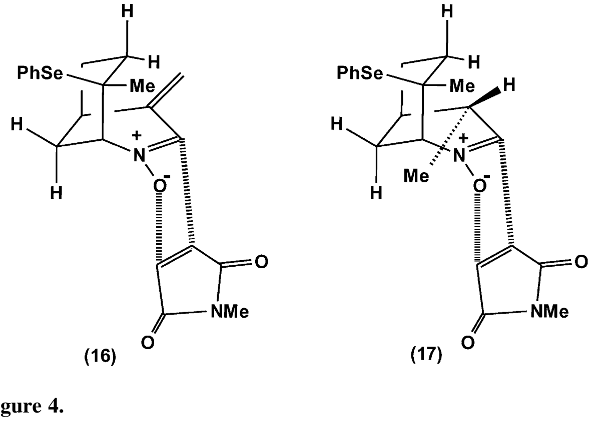
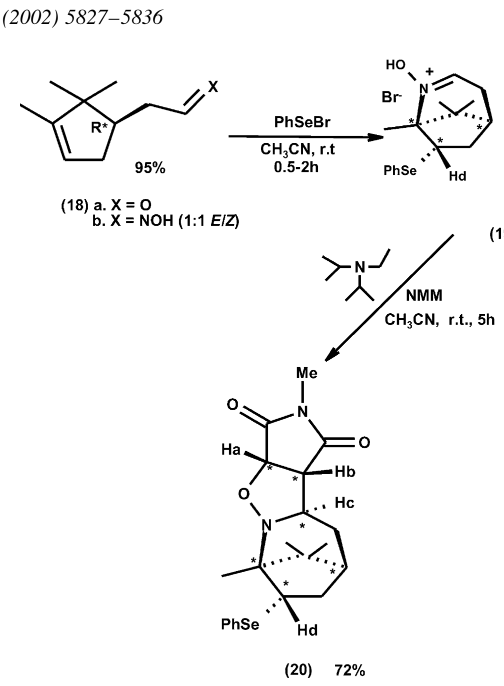


Figure 4.



Scheme 5.

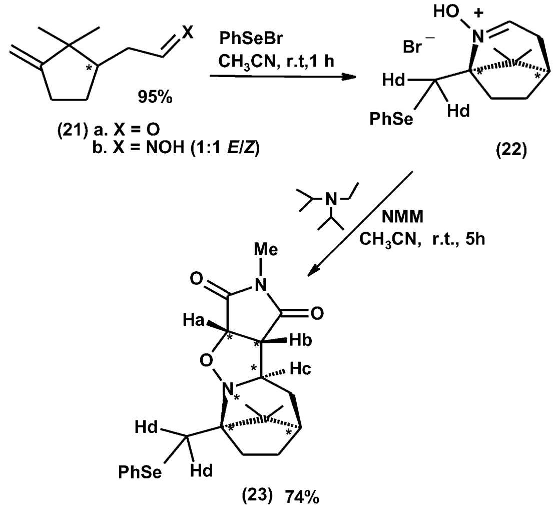
2.2. Cyclisation onto cyclopentenes

Syntheses of optically active bridged-ring systems involving multiplication of stereocentres from one to six or one to seven in high yielding one pot reactions have also been achieved by analogous sequences involving cyclopentenes. Thus the known literature rearrangement of (−)-α-pinene epoxide[10] was used to prepare *R*-(**18a**) which was converted to its oxime (**18b**). The chiral oxime was a colourless liquid which comprised a 1:1 mixture of *E*- and *Z*-isomers. The versatility of the electrophile induced cyclisation process is demonstrated by the cyclisation of (**18b**) to (**19**) despite the potential for steric inhibition by the gem-dimethyl group. Cycloaddition of (**19**) with NMM in the presence of Hunig's base afforded a single cycloadduct formulated as (**20**), $[\alpha]_D^{20}=+67$ (c=0.8, $CHCl_3$) in 72% overall yield from (**18b**) (Scheme 5). The stereochemistry of (**20**) was determined from n.O.e. data, 2D-COSY studies and X-ray crystallography.[4] This sequence results in the multiplication of one chiral centre in (**18b**) to seven in (**20**).

3. Azabicyclo[3.2.1] systems

3.1. Cyclisation onto an *exo*-cyclic alkenes

Bridged-ring formation via cyclisation of a chiral oxime onto an *exo*-methylene group was studied with (1*R*)-(2,2-dimethyl-3-methylenecyclopentyl)-1-acetaldehyde (**21a**), prepared according to the literature procedure[10], which was converted to oxime (**21b**) (1:1 *E*/*Z*-isomer mixture). The oxime reacted (MeCN, rt, 1 h) with PhSeBr to give the nitrone salt (**22**) which was not isolated but was treated with Hunig's base followed by addition of NMM (MeCN, rt). After stirring the mixture for 10 h work up gave a single



Scheme 6.

exo-cycloadduct (**23**), $[\alpha]_D^{20}=-64.0$ (c=0.2, CHCl$_3$), (74%, from (**21b**)) (Scheme 6). In this sequence multiplication of one chiral centre in (**21b**) to six chiral centres in (**23**) has been achieved in a one pot process. The stereochemistry of the cycloadduct was determined from n.O.e data, 2D-COSY studies and X-ray crystallography (Fig. 5).

3.2. Cyclisation onto an *endo*-cyclic alkene

E-Oxime (**24**) was synthesised from 4-acetyl-1-methylcyclohexene and hydroxylamine hydrochloride in 86% yield. Only a trace amount of *Z*-isomer was detected in the ^{1}H nmr spectrum. *E*-Oxime (**24**) was then treated with phenylselenyl bromide in acetonitrile at ambient temperature for 20 h to afford the bicyclic salt (**24**). Neutralisation of the nitrone salt with potassium carbonate liberated the nitrone (**26**) and cycloaddition to NMM afforded a 1.2:1 mixture of cycloadducts (**27**) and (**28**) as in 54% combined yield together with 22% of recovered oxime (**24**) (Scheme 7). The stereochemistry of cycloadducts (**27**) and (**28**) was determined on the basis of n.O.e data and 2D-COSY studies.

The cyclisation reaction in this case is slow and incomplete.

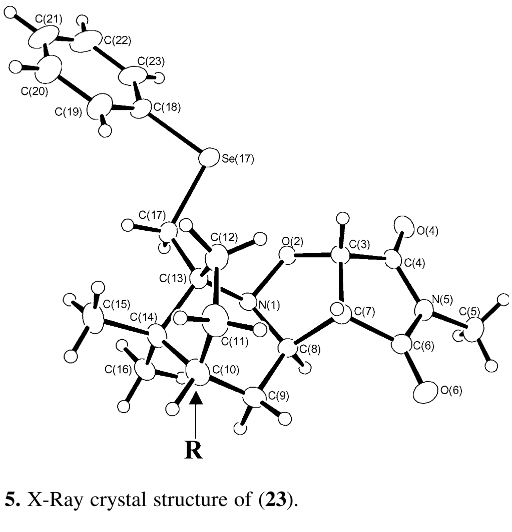
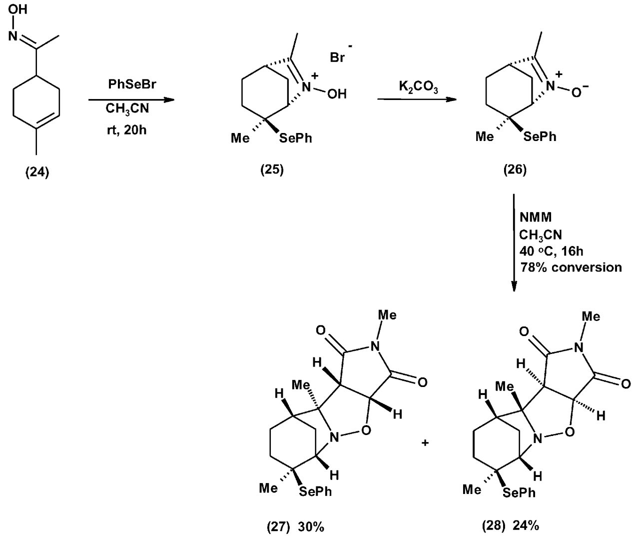


Figure 5. X-Ray crystal structure of (**23**).



Scheme 7.

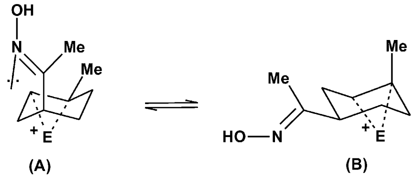


Figure 6.

The conformation of the intermediate onium species derived from oxime (**24**) is crucial in the cyclisation. Oxime (**24**) needs to access conformation (**A**), as opposed to conformation (**B**) to enable cyclisation (Fig. 6). However the required trajectory angle of the nitrogen lone pair necessary for cyclisation is reached with difficulty and imposes angle strain in the transition state. It is also noteworthy that this cyclisation is highly regioselective and gives (**25**) exclusively.

Both (**27**) and (**28**) arise via *exo*-transition states (Fig. 7) which is dictated by the steric impediment to *endo*-cycloaddition posed by the bicyclic framework of the nitrone. The top face of the dipole is less sterically hindered than the bottom face. Consequently, the approach of the dipolarophile from the top face of the dipole affords the major cycloadduct (**27**) and approach of the dipolarophile from the bottom face of the dipole leads to cycloadduct (**28**).

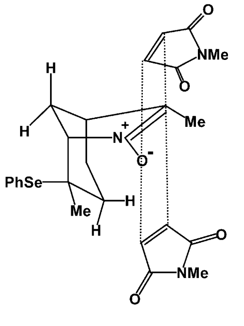
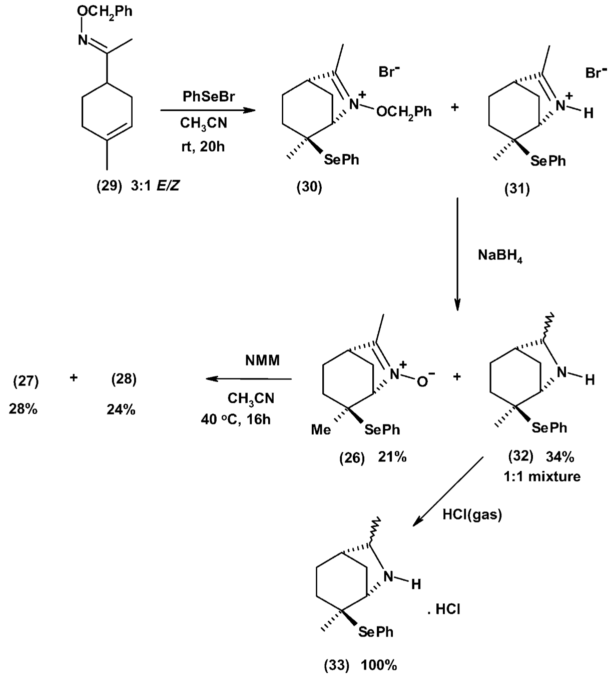


Figure 7.

4. Oxime *O*-benzyl ether cyclisation

Oxime *O*-benzyl ether (**29**) was synthesised as a 3:1 mixture of *E*- and *Z*-isomers from 4-acetyl-1-methyl-cyclohexene and *O*-benzylhydroxylamine in 82% yield (Scheme 8). Treatment of (**29**) with phenylselenyl bromide (1.0 equiv.) at rt for 16 h resulted in incomplete conversion (TLC). Additional phenylselenyl bromide (0.1 equiv.) was therefore added and the solution stirred at rt for additional 6 h. After work up the ^{1}H NMR spectrum of the crude product showed the presence of benzaldehyde, suggesting partial fragmentation of the oximinium salt (**30**) to iminium ion (**31**). A singlet at δ 4.5 ppm was diagnostic for the benzyl methylene protons of salt (**30**).



Scheme 8.

Reduction of this mixture with sodium borohydride afforded a 1:1.6 mixture of nitrone (**26**) (21%) and amine (**32**) (34%) from oxime ether (**29**). Amine (**32**) was converted quantitatively to its hydrochloride salt (**33**) using HCl (gas) in diethyl ether. Nitrone (**26**) was subjected to 1,3-dipolar cycloaddition reaction with NMM to produce a 1:1 mixture of *exo*-cycloadducts (**27**) and (**28**) in 52% combined yield.

In summary, the technically simple electrophile-induced nitrone generation from oximes followed by cycloaddition onto proximate alkenes constitutes a versatile and efficient method for the stereospecific formation of bridged bicyclic nitrogen heterocycles. The cyclisation step proceeds with high regioselectivity and follows Baldwin's rules.[11] The facial selectivity is rationalised on the basis of steric hindrance and the sequence occurs with high regio- and stereo-selectivity and provides a major increase in molecular complexity.

5. Experimental

5.1. General technical data

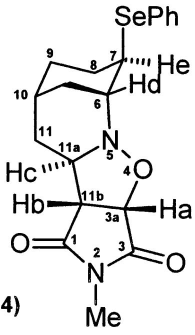
Nuclear magnetic resonance spectra and decoupling experiments were determined at 300 MHz on a QE 300 instrument and at 400 MHz on a Bruker AM400 spectrometer as specified. Chemical shifts are given in parts per million (δ) downfield from tetramethylsilane as internal standard. Spectra were determined in deuteriochloroform except where otherwise stated. The following abbreviations are used; s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad and brs=broad singlet.

Flash column chromatography was performed using silica gel 60 (230–400 mesh). Kieselgel columns were packed with silica gel GF$_{254}$ (Merck 7730). Petroleum ether refers the fraction with bp 40–60°C unless otherwise specified. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were obtained using a Carlo–Erba Model 1106 instrument. Mass spectra were recorded at 70 eV on a VG Autospec mass spectrometer. All calculations for selenium were based on its most abundant isotope ^{80}Se. Specific rotations were measured at ambient temperature with an Optical Activity Ltd., AA-1000 polarimeter. All solvents were purified according to procedures given in Purification of Laboratory Chemicals, D. D. Perrin, W. L. F. Armarego, D. R. Perrin, Permagon Press, 1980.

5.1.1. Cyclohex-3-enyl acetaldoxime (1b). A solution of cyclohex-3-enyl acetaldehyde (**1a**)[7] (0.9 g, 7.2 mmol) in acetonitrile (40 ml) was added to a solution of hydroxylamine hyrochloride (0.55 g, 1.1 equiv.) and sodium acetate (0.71 g, 1.2 equiv.) in water (40 ml). The resulting solution was stirred at ambient temperature for 3 h. and extracted with chloroform (2×100 ml). The combined organic layer was dried (MgSO$_4$) and concentrated under reduced pressure. The residue was subjected to column chromatography on silica eluting with 3:1 v/v petroleum ether–ether to afford the product (0.93 g, 93%) as a colourless liquid, bp 59–62°C/0.1 mm Hg which comprised a 1:1 mixture of *E*- and *Z*-isomers.

(Found: C, 69.15; H, 9.3; N, 9.9, $C_8H_{13}NO$ requires: C, 69.0; H, 9.4; N, 10.0%); δ_H (300 MHz, CDCl$_3$): 9.81 and 9.03 (br, 1H, OH, isomers), 7.48 (t, 1H, *E*-CH=N), 6.78 (t, 1H, *Z*-CH=N), 5.65 (brs, 2H, CH=CH, isomers) and 2.40–1.69 (m, 9H); *m/z* (%): 139 (M^+, 10), 120 (17), 93 (18), 80 (100), 67 (19), 59 (72), 53 (34) and 41 (40).

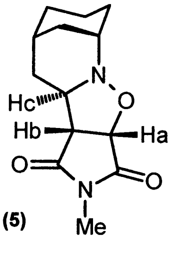
5.1.2. (3a*S*,6*S*,7*R*,11a*R*,11b*R*)-2-Methyl-7-(phenylseleno)-octahydro-6,10-methanopyrrolo[3′,4′:4,5]isoxazolo[2,3-*a*]-azocine-1,3(3a*H*)-dione (4). Phenylselenyl bromide (0.2 g, 0.86 mmol) was added to a solution of oxime (**1b**) (0.1 g, 0.72 mmol) in dry acetonitrile (5 ml). The resulting solution was stirred at ambient temperature for 1 h when NMM (0.079 g, 0.72 mmol) and diisopropylethylamine (Hunig's base) (0.11 g, 0.15 ml) were added. The resulting solution was stirred 25°C for 5 h and the solvent evaporated. The residue was subjected to column chromatography on silica eluting with 5:1 v/v petroleum ether–ether to afford the product (0.19 g, 67%) as a colourless solid, mp 53–54°C, that comprised 4:1 mixture of isomers.



(4)

(Found: C, 56.65; H, 5.75; N, 6.75; $C_{19}H_{22}N_2O_3Se$ requires: C, 56.3; H, 5.45; N, 6.90%); δ_H (300 MHz): 7.55 and 7.23 (m, 5H, ArH, isomers), 4.71 (d, 1H, *J*=7.22 Hz, Ha), 4.0 (m, 1H, Hc), 3.70 (m, 1H, He), 3.51 and 3.48 (m, 1H, Hd), 3.19 (d, 1H, *J*=7.28 Hz, Hb), 2.99 (s, 3H, NMe) and 2.36–1.41 (m, 9H); *m*/*z* (%): 406 (M^+, 24), 249 (100), 207 (62), 138 (61), 111 (49), 95 (52), 67 (42) and 41 (60).

5.1.3. (3a*S*,6*R*,11a*R*,11b*R*)-2-Methyloctahydro-6,10-methanopyrrolo[3′,4′:4,5]isoxazolo[2,3-*a*]azocine-1,3(3a*H*)-dione (5). Tri-*n*-butyltin hydride (0.11 g, 0.37 mmol) and 2,2′-azabis-(2-methyl propionitrile) (AIBN) (0.005 g, 10% mol) were added to a stirred solution of cycloadduct (**4**) (4:1 isomer mixture) (0.127 g, 0.31 mmol) in toluene (15 ml) at room temperature. The reaction mixture was stirred and boiled under reflux under N_2 for 4 h. After removing toluene under reduced pressure the residue was subjected to column chromatography on silica eluting with 1:3 v/v petroleum ether–ether to afford the product (0.061 g, 78%) as colourless prisms, mp 170–172°C.



(5)

(Found: C, 62.45; H, 7.25; N, 11.15; $C_{13}H_{18}N_2O_3$ requires: C, 62.30; H, 7.25; N, 11.19%); δ_H (400 MHz): 4.71 (d, 1H, *J*=7.3 Hz, Ha), 4.03 (m, 1H, Hc), 3.5 (m, 1H, Hd), 3.19 (d, 1H, *J*=7.3 Hz, Hb), 3.02 (s, 3H, NMe) and 2.2–0.91 (m, 11H, aliphatic); *m*/*z* (%): 250 (M^+, 38), 207 (89), 164 (100), 149 (23), 111 (21), 67 (21) and 41 (38); enhancement (%): (Table 1).

5.2. General procedure (A) for the preparation of oximes

A solution of aldehyde or ketone (1.0 equiv.) in acetonitrile (15 ml) was added to a solution of hydroxylamine hydrochloride (1.0–1.1 equiv.) and sodium acetate (1.2 equiv.) in water (7.5 ml). The resulting solution was stirred at ambient temperature for 4–16 h. then extracted with DCM (3× 20 ml). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was subjected to column chromatography on silica eluting with 1:1 v/v diethyl ether–hexane.

Table 1. n.O.e data: enhancement (%)

Signal irradiated	Ha	Hb	Hc
Ha		6.8	
Hb	9.8		2.8
Hc		2.3	

5.3. General procedure (B) for the PhSeBr induced nitrone formation–cycloaddition reactions of oximes

Phenylselenyl bromide (1.0 equiv.) was added to a stirred solution of oxime (1.0 equiv.) and stirring was continued at ambient temperature for 2 h. Anhydrous potassium carbonate (1.1 equiv.) was then added and the solution stirred at ambient temperature for an additional 1 h. *N*-Methylmaleimide (NMM) (1.2 equiv.) was then added and the resulting mixture was stirred at 40°C or boiled under reflux for 16 h. The solvent was then evaporated and the residue subjected to flash chromatography on silica.

5.3.1. 2-(4-Methyl-3-cyclohexen-1-yl)-propanal oxime (6b). Prepared from 2-(4-methyl-3-cyclohexen-1-yl)-propanal (1.02 g, 6.7 mmol), hydroxylamine hyrochloride (0.52 g, 7.4 mmol) and sodium acetate (0.68 g, 7.4 mmol) by general procedure (A). The oxime (1.08 g, 96%), obtained as a colourless oil, comprised a mixture of four isomers each of which was a 2:1 mixture of *E*- and *Z*-isomers, a 1.2:1 mixture of (*R*,*R*) and (*R*,*S*) isomers.

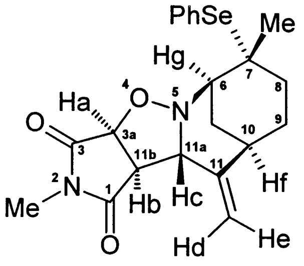
(Found: C, 71.75; H, 10.3; N, 8.1; $C_{10}H_{17}NO$ requires: C, 71.85; H, 10.15; N, 8.4%); δ_H (250 MHz): 8.38 and 8.13 (br, 1H, OH), 7.33 (2×d, 0.5H, *J*=7.7 Hz, *E*-CH=N), 6.58 (2×d, 0.5H, *J*=8.1 Hz, *Z*-CH=N), 5.34 (m, 1H, CH=C), 1.64 (s, 3H, Me–C=C), 3.09–1.16 (m, 8H), 1.08 (2×d, 3H, *J*=6.9 Hz, Me–CH) and 1.04 (2×d, 3H, *J*=6.9 Hz, Me–CH); *m*/*z* (%): 167 (M^+, 1), 149 (37), 134 (21), 95 (100), 79 (54) and 41 (25); ν_{max} (film): 3280 (br, 1H, OH), 2900 (CH), 1650 (C=C), 1440, 1380, 1310, 1155, 1070, 960 and 800 cm^{-1}.

5.4. Cycloadducts (9) and (10)

Prepared from oxime (**6B**) (0.36 g, 2.2 mmol), phenylselenyl bromide (0.57 g, 2.4 mmol), anhydrous potassium carbonate (0.36 g, 2.6 mmol) and NMM (0.36 g, 3.2 mmol) by general procedure (B) and purified by flash chromatography on silica eluting with 1:1 v/v diethyl ether–hexane to afford the (**9**) (0.38 g, 41%) and (**10**) (0.16 g, 18%).

5.4.1. (3a*S*,6*R*,7*R*,10*R*,11a*S*,11b*S*)-2,7-Dimethyl-11-methylene-7-(phenylseleno)octanydro-6,10-methanopyrrolo[3′,4′:4,5]isoxazolo[2,3-*a*]azocine-1,3(3a*H*)-dione (9). Crystallised from diethylether–hexane as pale yellow prisms, mp 119–120°C. $[\alpha]_D^{20}=-34.0$ (1.05 g/100 ml, $CHCl_3$).

(Found: C, 58.45; H, 5.75; N, 6.7; $C_{21}H_{24}N_2O_3Se$ requires: C, 58.35; H, 5.55; N, 6.5%); δ_H (500 MHz): 7.58–7.56 (m, 2H, ArH), 7.45–7.20 (m, 3H, ArH), 5.06 (d, 1H, *J*=2.4 Hz, He), 4.95 (d, 1H, *J*=2.4 Hz, Hd), 4.63 (d, 1H, *J*=7.2 Hz, Ha), 4.37 (br, 1H, Hc), 3.79 (d, 1H, *J*=7.2 Hz, Hb), 3.340



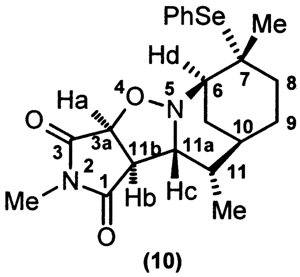
(9)

(br, 1H, Hg), 2.99 (s, 3H, NMe), 2.68 (br, 1H, Hf), 2.42–1.58 (m, 6H) and 1.38 (s, 3H, Me); δ_C (125 MHz): 176.5, 175.2, 138.3, 129.1, 129.0, 128.9, 126.8, 111.9, 73.4, 64.4, 60.5, 53.6, 49.7, 36.6, 34.1, 26.6, 28.2, 24.8 and 24.1; *m*/*z* (%) (FAB): 432 (M^+, 10), 275 (100), 219 (6), 188 (5), 164 (16), 148 (11), 107 (5) and 93 (8); enhancement (%): (Table 2).

Table 2. Enhancement (%)

Signal irradiated	Ha	Hb	Hc	Hd	He	Hf	Hg	Me	Ar
Ha		6.4							
Hb	9.0		2.3	10.7					
Hc		3.1		0.6					
Hd		16.9			21.5				
He				19.2		8.4			
Hf					7.0				
Hg								2.2	3.4
Me			1.1				2.3		2.6

5.4.2. (3a*S*,6*R*,7*R*,10*R*,11*S*,11a*R*,11b*R*)-2,7,11-Trimethyl-7-(phenylseleno)octahydro-6,10-methanopyrrolo[3′,4′:4,5]-isoxazolo[2,3-*a*]azocine-1,3(3a*H*)-dione (10). Crystallised from ethyl acetate–petroleum ether as pale yellow plates, mp 147–148°C. $[\alpha]_D^{20}=-22.0$ (1.07 g/100 ml, $CHCl_3$).



(10)

(Found: C, 57.95; H, 6.15; N, 6.4; $C_{21}H_{26}N_2O_3Se$ requires: C, 58.15; H, 6.0, N, 6.45%); δ_H (500 MHz): 7.57–7.55 (m, 2H, ArH), 7.39–7.24 (m, 3H, ArH), 4.55 (d, 1H, *J*=7.1 Hz, Ha), 3.95 (d, 1H, *J*=6.3 Hz, Hd), 3.51 (d, 1H, *J*=7.1 Hz, Hb), 3.27 (m, 1H. Hc), 2.98 (s, 3H, NMe), 2.29–1.62 (m, 8H), 1.32 (s, 3H, Me) and 1.18 (d, 3H, *J*=7.3 Hz, Me); δ_C (100 MHz): 177.3, 175.3, 138.3, 129.0, 128.9, 127.0, 74.0 62.1, 59.7, 53.3, 50.2, 35.3, 34.4, 33.4, 29.4, 28.4, 24.9, 19.2 and 17.8; *m*/*z* (%): 434 (M^+, 1), 166 (100), 93 (91), 77 (31), 54 (31) and 41 (24); enhancement (%): (Table 3).

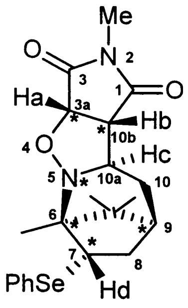
Table 3. Enhancement (%)

Signal irradiated	Ha	Hb	Hc	Hd	Me_a	Me_b
Ha		6.3	1.9		2.8	3.4
Hb	5.4			2.2		5.2
Hc						14.2
Hd		3.7				
Me_a		0.5	2.3	0.9		
Me_b	1.3	3.3				

5.4.3. (+)-(1*R*)-2,2-3-Trimethyl-3-ene-1-acetaldoxime (18b). A solution of aldehyde (**18a**) (2 g, 13 mmol) in acetonitrile (75 ml) was added to a solution of hydroxylamine hydrochloride (1 g, 1.1 equiv.) and sodium acetate (1.29 g, 1.2 equiv.) in water (75 ml). The resulting solution was stirred at ambient temperature for 3 h. then extracted with chloroform (2×200 ml). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was subjected to column chromatography on silica eluting with 1:1 v/v petroleum ether–ether to afford the product (2.1 g, 95%) as a colourless liquid, bp 66–68°C/0.1 mm Hg which comprised a 1:1 mixture of *E*- and *Z*-isomers. $[\alpha]_D^{20}=+11.2$ (*c* 1.5 g/100 ml, $CHCl_3$).

(Found: C, 71.6; H, 10.5; N, 8.4; $C_{10}H_{17}NO$ requires: C, 71.8; H, 10.25; N, 8.4%); δ_H (300 MHz): 9.86 and 9.32 (br, 1H, OH, isomers), 7.46 (t, 1H, *E*-CH=N), 6.75 (t, 1H, *Z*-CH=N), 5.21 (brs, 1H, C=CH, isomers), 2.54–1.66 (m, 5H, aliphatic-H, isomers), 1.66 and 1.60 (s, 3H, CH=CH–Me, isomers), 1.03 and 1.00 (s, 3H, Me, isomers) and 0.8 and 0.7 (s, 3H, Me, isomers); *m*/*z* (%): 167 (M^+, 6), 150 (7), 134 (21), 108 (100), 93 (52), 67 (11) and 41 (18).

5.4.4. (3a*S*,6*S*,7*S*,9*S*,10a*R*,10b*R*)-2,6,11,11-Tetramethyl-7-(phenylseleno)octahydro-1*H*-6,9-methanopyrrolo-[3′,4′:4,5]isoxazolo[2,3-*a*]azepine-1,3-dione (20). Phenylselenyl bromide (0.14 g, 1.2 equiv.) was added to a solution of oxime (**18b**) (0.1 g, 0.6 mmol) in dry acetonitrile (5 ml). The resulting solution was stirred at ambient temperature for 1 h when NMM (0.066 g, 1 equiv.) and diisopropylethylamine (Hunig's base) (0.0773 g, 0.1 ml, 1.2 equiv.) were added. The resulting solution was stirred 25°C for 5 h and the solvent evaporated. The residue was subjected to column chromatography on silica, eluting with 6:1 v/v petroleum ether–ether, to afford the product (0.19 g, 72%) which crystallized from petroleum ether (bp 60–80°C)-ether as colourless prisms of a single stereoisomer, mp 154–156°C; $[\alpha]_D^{20}=+67$ (*c* 0.8 g/100 ml, $CHCl_3$).



(20)

(Found: C, 58.0; H, 6.05; N, 6.45; $C_{21}H_{26}N_2O_3Se$ requires: C, 58.2; H, 6.0; N, 6.4%). δ_H (300 MHz, C_6D_6): 7.52–6.90 (m, 5H, ArH), 4.40 (d, 1H, *J*=8.1 Hz, Ha), 3.26 (m, 1H, Hc), 3.0 (m, 1H, Hd), 2.60 (m, 1H, Hb, 2.44s, 3H, NMe), 2.07–1.21 (m, 5H), 1.50 (s, 3H, NC–Me), 0.82 (s, 3H, Me) and 0.74 (s, 3H, Me); *m*/*z* (%): 434 (M^+, 2), 323 (40), 166 (50), 150 (38), 121 (41), 107 (100), 91 (48), 77 (58), 55 (34) and 41 (61); enhancement (%): (Table 4).

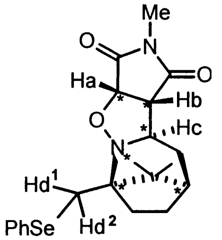
Table 4. Enhancement (%)

Signal irradiated	Ha	Hb	Hc	Hd
Ha		4.0		11.0
Hb	7.0			10.0
Hc		1.0		
Hd	17.0	10.0		

5.4.5. (1*R*)-2,2-Dimethyl-3-methylidene cyclopentane-1-acetaldoxime (21b). A solution of aldehyde (**21a**)[10] (0.1 g, 0.6 mmol) in acetonitrile (10 ml) was added to a solution of hydroxylamine hydrochloride (0.055 g, 1.1 equiv.) and sodium acetate (0.065 g, 1.2 equiv.) in water (10 ml). The resulting solution was stirred at ambient temperature for 3 h and extracted with chloroform (2×50 ml). The combined organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was subjected to column chromatography on silica eluting with 3:1 v/v petroleum ether–ether to afford the product (0.098 g, 89%) as a thick colourless oil which comprised a 1:1 mixture of *E*- and *Z*-isomers.

HRMS: 167.1310; $C_{10}H_{17}NO$ requires: 167.1312; δ_H (300 MHz): 9.05 (br, 1H, OH, isomers), 7.47 (t, 1H, *E*-CH=N), 6.74 (t, 1H, *Z*-CH=N) 4.79 (brs, 2H, C=CH_2, isomers), 2.60 −1.1 (m, 7H), and 1.08 and 0.85 (2×s, 6H, Me); *m*/*z* (%): 166 (M−1, 6), 107 (100), 92 (86), 78 (53) and 41 (51).

5.4.6. (3a*S*,6*R*,9*R*,10a*R*,10b*R*)-2,11,11-Trimethyl-6-[(phenylseleno)methyl]octahydro-1*H*-6,9-methanopyrrolo-[3′,4′:4,5]isoxazolo[2,3-*a*]azepine-1,3-dione (23). Phenylselenyl bromide (0.175 g, 0.63 mmol) was added to a solution of oxime (**21b**) (0.1 g, 0.59 mmol) in dry acetonitrile (10 ml). The resulting solution was stirred at ambient temperature for 1 h when NMM (0.066 g, 0.59 mmol) and diisopropylethylamine (Hunig's base) (0.093 g, 1.2 equiv.) were added. The resulting solution was stirred 25°C for 5 h and the solvent evaporated. The residue was subjected to column chromatography on silica eluting with 6:1 v/v petroleum ether–ether to afford a single cycloadduct (**23**) (0.192 g, 74%) as colourless needles, mp 161–163°C. $[\alpha]_D^{20}=-64.0$ (0.2 g/100 ml, $CHCl_3$).



(23)

(Found: C, 58.25; H, 5.80; N, 6.40; $C_{21}H_{26}N_2O_3Se$ requires: C, 58.20; H, 6.05; N, 6.45%); δ (400 MHz, C_6H_6): 7.55 and 7.01 (m, 5H, ArH), 4.57 (d, 1H, *J*=7.8 Hz, Ha), 3.30 and 3.15 (2×d, 2H, Hd^1 and Hd^2), 3.19 (t, 1H, *J*=9.1 Hz, Hc), 2.87 (t, 1H, *J*=9.2, Hb), 2.60 (s, 3H, NMe), 1.90–1.20 (m, 7H) and 0.98 and 0.60 (2×s, 6H, Me). *m*/*z* (%) (FAB): 435 (M+1, 87), 324 (6), 277 (100), 263 (10), 150 (9) and 109 (26); enhancement (%): (Table 5).

Table 5. Enhancement (%)

Signal irradiated	Ha	Hb	Hd^1	Hd^2	ArH
Ha		5.5			
Hb	9.6				
Hd^1				11.9	2.7
Hd^2			27.0		5.1

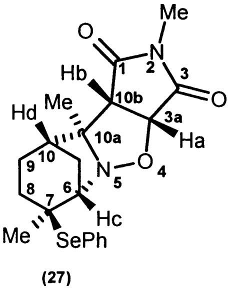
5.4.7. 1-(4-Methyl-3-cyclohexen-1-yl)-1-ethanone oxime (24). Prepared from 4-acetyl-1-methylcyclohexene (3.0 g, 21.7 mmol), hydroxylamine hydrochloride (1.66 g, 23.8 mmol) and sodium acetate (2.15 g, 26.2 mmol) by the general procedure (A) and purified by flash chromatography on silica eluting with 1:2 v/v diethyl ether–hexane to afford the *E*-oxime (2.84 g, 86%) as a colourless oil.

(Found: C, 70.8; H, 10.0; N, 9.1; $C_9H_{15}NO$ requires: C, 70.6; H, 9.8; N, 9.15%). δ (250 MHz): 9.79 (br, 1H, OH), 5.40 (m, 1H, CH=C), 1.89 (s, 3H, Me–C=N), 1.66 (s, 3H, Me–C=C) and 2.41–1.53 (m, 7H, cyclohexyl); *m*/*z* (%): 153 (M^+, 61), 136 (48), 121 (70), 108 (48), 95 (95), 79 (73), 67 (63), 55 (31) and 42 (100); ν_{max} (film): 3240 (br, 1H, OH), 2900 (CH), 1650 (C=C), 1440, 1370, 1150, 950, 790 and 700 cm^{-1}.

5.5. Cycloadducts (27) and (28)

Prepared from oxime (**24**) (0.50 g, 3.3 mmol), phenylselenyl bromide (0.79 g, 3.3 mmol), anhydrous potassium carbonate (0.55 g, 4 mmol) and NMM (0.53 g, 4.8 mmol) by general procedure (B) and purified by flash chromatography on silica eluting with 1:1 v/v diethyl ether–hexane to afford the products (**27**) (0.41 g, 30%) and (**28**) (0.33 g, 24%) (78% conversion).

5.5.1. (3a*R*,6*S*,7*S*,10*S*,10a*R*,10b*S*)-2,7,10a-Trimethyl-7-(phenylseleno)octahydro-1*H*-6,10-methanopyrrolo-[3′,4′:4,5]isoxazolo[2,3-*a*]azepine-1,3-dione (27). Crystallised from ethyl acetate–petroleum ether as colourless needles, mp 163–164°C.



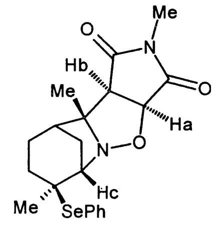
(27)

(Found: C, 57.4; H, 5.85; N, 6.85; $C_{20}H_{24}N_2O_3Se$ requires: C, 57.3; H, 5.75; N, 6.7%); δ_H (400 MHz): 7.60–7.57 (m, 2H, ArH), 7.39–7.26 (m, 3H, ArH), 4.85 (d, 1H, *J*=7.6 Hz, Ha), 3.36 (d, 1H, *J*=7.6 Hz, Hb), 3.20 (d, 1H, *J*=6.5 Hz, Hc), 2.97 (s, 3H, NMe), 2.62 (d, 1H, *J*=12.8 Hz), 2.45 (m, 1H, Hd), 1.91–1.83 (m, 2H), 1.69–1.49 (m, 3H), 1.46 (s, 3H, Me) and 1.37 (s, 3H, Me). δ_C (100 MHz): 174.0, 171.4, 137.9, 129.1, 128.8, 127.0, 80.8, 77.8, 74.1, 62.0, 51.9, 46.0, 33.3, 32.9, 29.1, 24.9, 23.9 and 17.1; *m*/*z* (%) (FAB): 420 (M^+, 9), 263 (100), 169.(11) and 95 (8); enhancement (%): (Table 6).

Table 6. Enhancement (%)

Signal irradiated	Ha	Hb	Hc	Hd	Ar
Ha		4.5	4.1		
Hb	11.8			9.0	
Hc	8.0				2.6
Hd		13.8			
Me	−0.2	0.8		4.8	

5.5.2. (3a*S*,6*S*,7*S*,10*S*,10a*R*,10b*R*)-2,7,10a-Trimethyl-7-(phenylseleno)octahydro-1*H*-6,10-methanopyrrolo-[3′,4′:4,5]isoxazolo[2,3-*a*]azepine-1,3-dione (28). Obtained as a colourless amorphous solid, mp 45–47°C. (Found: C, 57.6; H, 5.95; N, 6.5; $C_{20}H_{24}N_2O_3Se$ requires: C, 57.3; H, 5.75; N, 6.7%); δ_H (400 MHz): 7.61–7.51 (m, 2H, ArH), 7.38–7.24 (m, 3H, ArH), 4.88 (d, 1H, J=8.1 Hz, Ha), 3.43 (d, 1H, J=8.1 Hz, Hb), 3.19 (d, 1H, J=6.5 Hz, Hc), 3.00 (s, 3H, NMe), 2.81 (d, 1H, J=3.3 Hz), 2.40 (d, 1H, J13.8 Hz), 2.02–1.49 (m, 3H), 1.47 (s, 3H, Me–C–N), 1.43 (s, 3H, Me–C–Se) and 1.38–1.21 (m, 2H). δ_C (125 MHz): 174.8, 173.9, 138.5, 134.3, 129.6, 129.2, 79.5, 77.7, 74.4, 62.5, 52.1, 40.4, 33.8, 33.4, 29.6, 25.4, 25.2 and 24.6; m/z (%) (FAB): 420 (M^+, 4), 363 (100), 159.(6), 133 (8) and 55 (78); enhancement (%): (Table 7).



(28)

Table 7. Enhancement (%)

Signal irradiated	Ha	Hb	Hc	Me–C–N	Me–C–Se	Ar
Ha		5.4				
Hb	6.2					
Hc				2.2	3.5	
Me–C–N	0.6	5.8	0.8			0.5
Me–C–Se		0.9	2.6			1.8

5.5.3. 1-(4-Methyl-3-cyclohexen-1-yl)-1-ethanone *O*-benzyl oxime ether (29). A solution of 4-acetyl-1-methylcyclohexene (2.0 g, 14.5 mmol), in acetonitrile was added to a asolution of *O*-benzylhydroxylamine hyrochloride (2.54 g, 15.9 mmol.) and sodium acetate (1.42 g, 17.3 mmol) in water. The mixture was stirred at room temperature for 8 h and then extracted with $CHCl_3$(×2). Work up followed by flash chromatography on silica eluting with 1:5 v/v diethyl ether–hexane to afford the oxime ether (2.89 g, 82%) as a colourless oil which comprised a 3:1 mixture of *E*- and *Z*-isomers.

(Found: C, 78.7; H, 8.65; N, 5.65; $C_{16}H_{21}NO$ requires: C, 79.0; H, 8.65; N, 5.75%); δ_H (300 MHz): 7.35–7.23 (m, 5H, ArH), 5.40 (m, 1H, CH=C), 5.07 and 5.05 (s, 2H, CH_2Ph), 2.35 (m, 1H, CH–C=N), 2.10–1.95 (m, 5H), 1.83 and 1.78 (s, 3H, *E*- and *Z*-Me–C=N), 1.64 (s, 3H, Me–C=C) and 1.57 (m, 1H, cyclaalkyl); m/z (%): 243 (M^+, 27), 152 (11), 121 (12), 108 (11), 95 (27), 91 (100), 79 (17), 77 (23), 55 (10) and 42 (19).

5.6. Cyclisation products (26) and (32)

Phenylselenyl bromide (0.48 g, 2.0 mmol) was added to a solution of oxime ether (**29**) (0.5 g, 2.0 mmol) in dry acetonitrile (20 ml). The resulting solution was stirred at room temperature for 16 h. Acetonitrile was removed under reduced pressure and the residue was taken up in 1:1 v/v DCM–MeOH (20 ml), $NaBH_4$ (0.15 g, 4.0 mmol) added and the mixture was stirred at room temperature for 2 h. The solvent was then evaporated under reduced pressure and the residue was subjected to column chromatography on silica, eluting with 95:5 v/v chloroform methanol to afford nitrone (**26**) (0.13 g, 21%) and amine (**32**) (0.2 g, 34%).

5.6.1. Nitrone (26). Obtained as a pale yellow oil δ (300 MHz): 7.64–7.53 (m, 2H, ArH), 7.28–7.22 (m, 3H, ArH), 3.50 (m, 1H, CH–N), 2.74–1.56 (m, 10H, cycloalkyl and Me–C=N), and 1.52 (s, 3H, Me); m/z (%): 309 (M^+, 3), 152 (91), 134 (14), 124 (44), 108 (68), 79 (100), 67 (29) and 55 (36).

5.6.2. Amine (32). Obtained as a colourless oil which comprised a 1:1 mixture of diastereoisomers. δ (300 MHz): 7.65–7.55 (m, 2H, ArH), 7.37–7.25 (m, 3H, ArH), 5.96 (br, 1H, NH), 3.75 (m, 1H, CH–N), 3.46 (m, 1H, CH–Me), 2.56–1.52 (m, 7H, cycloalkyl) and 1.32–1.23 (m, 6H, 2×Me); m/z (%): 2.95 (M^+, 1), 157 (6), 138 (100), 96 (33), 67 (15) and 55 (20). This compound was characterised as its hydrochloride salt (**33**).

5.6.3. Amine hydrochloride (33). HCl gas was bubbled through a solution of amine (**32**) (0.2 g, 0.67 mmol) in diethylether (5 ml) for 5 min. The solution was concentrated under reduced pressure and diethyl ether (10 ml) was added to precipitate the hydrochloride salt, which after filtration afforded amine hydrochloride (0.22 g, 100%) as a colourless amorphous solid, mp 181–182°C, which comprised a 1:1 mixture of diastereoisomers.

(Found: C, 54.35; H, 6.7; N, 4.5; $C_{15}H_{22}NSeCl$ requires: C, 54.5; H, 6.65; N, 4.25%).; δ (300 MHz): 7.59–7.54 (m, 2H, ArH), 7.29–7.26 (m, 3H, ArH), 4.05 (dd, 0.5H, J=2.1 and 6.5 Hz, CH–C–Se), 3.93 (dd, 0.5H, J=6.9 and 10.1 Hz, CH–C–Se), 3.64 (m, 1H, CH–Me), 2.62–1.67 (m, 7H, cycloalkyl) and 1.55–1.42 (m, 6H, 2×Me); m/z (%): 295 (M−HCl, 1), 157 (6), 138 (100), 96 (33), 67 (15) and 55 (20).

5.7. Single crystal X-ray analysis of (5) and (23)

Crystallographic measurements for these compounds were carried out on a Stoe STADI 4 diffractometer at ambient temperature using graphite monochromated Cu Kδ X-radiation (λ=1.54184 Å). Data for both were collected in the ranges $4.0<\theta<65°$ using ω/θ scans. No significant variation was observed in the intensity of three 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[12] and were refined by full-matrix least squares (based on F^2) using SHELXL-93[13] which uses all data for refinement.

5.8. Single crystal X-ray analysis of (9) and (10)

Crystallographic data for these compounds were measured on a Nonius Kappa CCD area-detector diffractometer using a mixture of area detector ω- and Φ-scans and graphite monochromated Mo Kα radiation (λ=0.71073 Å). Both structures were solved by direct methods using SHELXS-86[12] and were refined by full-matrix least-squares (based on F^2) using SHELXL-97.[13] The weighting scheme used was $w=[\sigma^2(F_o^2)+(xP)^2+yP]^{-1}$ where $P=(F_o^2+2F_c^2)/3$. All non-hydrogen atoms of both structures were refined with anisotropic displacement parameters whilst hydrogen atoms were constrained to predicted positions using a riding model. The residuals wR_2 and R_1, given below, are defined as $wR_2=(\Sigma[w(F_o^2F_c^2)^2]/\Sigma[wF_o^2]^2)^{1/2}$ and $R_1=\Sigma\|F_o\|F_c\|/\Sigma|F_o|$.

Crystal data for (5): $C_{13}H_{18}N_2O_3$, 0.48×0.35×0.20 mm^3, M=250.29, monoclinic, space group $P2_1/n$.

a=9.3342(5) Å, b=6.4093(4) Å), c=20.0230(12) Å, α=90°, β=103.076(5)°, γ=90°, U=1166.83(11) Å^3, Z=4, D_x=1.425 g cm^{-3}, μ=0.836 mm^{-1}, F(000)=536.

*Crystal data for **9***: $C_{21}H_{24}N_2O_3Se$, 0.35×0.35×0.28 mm^3, M=431.40, orthorhombic, space group $P2_12_12_1$, a=7.5349(1), b=14.0844(2), c=17.9728(3) Å, U=1907.36(5) Å^3, Z=4, D_c=1.51 Mg m^{-3}, μ=1.99 mm^{-1}, F(000)=896, T=190 K.

Data collection: 1.0<2θ<52.0°; 3733 unique data were collected [R_{int}=0.0231]; 3668 reflections with F_o>4.0 $\sigma(F_o)$.

Structure refinement: Number of parameters=247, goodness of fit, s=1.053; wR_2=0.0544, R_1=0.0199.

*Crystal data for **10***: $C_{21}H_{26}N_2O_3Se$, 0.4×0.35×0.1 mm^3, M=433.40, monoclinic, space group $P2_1$ a=6.6744(7), b=22.571(3), c=6.6555(5) Å, β=100.943(6)°, U=984.4(8) Å^3, Z=2, D_c=1.46 Mg m^{-3}, μ=1.93 mm^{-1}, F(000)=448, T=190 K.

Data collection: 1.0<2θ<52.0°; 3434 unique data were collected [R_{int}=0.037]; 3296 reflections with F_o>4.0$\sigma(F_o)$.

Structure refinement: Number of parameters=247, goodness of fit, s=1.023; wR_2=0.0921, R_1=0.357.

Crystal data for (23): $C_{21}H_{26}N_2O_3Se$, 0.50×0.38×0.22 mm, M=433.40, monoclinic, space group $P2_1/a$

a=8.8640(3) Å, b=12.5682(5) Å), c=17.6878(6) Å, α=90°, β=91.209(3)°, γ=90°, U=1970.06(12) Å^3, Z=4, D_x=1.461 g cm^{-3}, μ=2.774 mm^{-1}, F(000)=896.

Full supplementary crystallographic data-sets for all four structures, which include hydrogen co-ordinates, thermal parameters and complete bond lengths and angles, have been deposited at the Cambridge Crystallographic Data Centre (**5**: CCDC180875; **9**: CCDC167659; **10**: CCDC167660; **23**: CCDC180876) and are available on request.

Acknowledgements

One of us (H. A. D.) thanks Mersin University, Turkey for leave of absence. We thank Leeds University and the EPSRC for support and Dr Christian Chapuis (Firmenich) for carrying out the pyrolysis generating **21a**.

References

1. (a) Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Thomas, W. A.; Kennewell, P. *Tetrahedron* **2000**, *56*, 10087–10096. (b) Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Kennewell, P.; Thornton-Pett, M. *Tetrahedron* **2001**, *57*, 1119–1128. (c) Dondas, H. A.; Grigg, R.; Thibault, S. *Tetrahedron* **2001**, *57*, 7035–7045. (d) Dondas, H. A.; Cummins, J. E.; Grigg, R.; Thorton-Pett, M. *Tetrahedron* **2001**, *57*, 7951–7964.
2. For a review see: Frederickson, M.; Grigg, R. *Org. Prep. Proced.* **1997**, *29*, 33–62 see also pp 63–115.
3. (a) Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J.; Thornton-Pett, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1388–1389. (b) Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J. *J. Chem. Soc., Chem. Commun.* **1992**, 1537–1538. (c) Dondas, H. A.; Frederickson, M.; Grigg, R.; Markandu, J.; Thornton-Pett, M. *Tetrahedron* **1997**, *53*, 14339–14354. (d) Markandu, J.; Dondas, H. A.; Frederickson, M.; Grigg, R.; Thornton-Pett, M. *Tetrahedron* **1997**, *53*, 13165–13176.
4. Preliminary communication: Dondas, H. A.; Grigg, R.; Frampton, C. S. *Tetrahedron Lett.* **1997**, *38*, 5719–5722.
5. Dondas, H. A.; Grigg, R.; Markandu, J.; Perrior, T.; Suziki, T.; Thibault, S.; Thomas, W. A.; Thornton-Pett, M. *Tetrahedron* **2002**, *58*, 161–173.
6. (a) Blaney, P.; Grigg, R.; Rankovic, Z.; Thoroughgood, M. *Tetrahedron Lett.* **2000**, *41*, 6635–6638. (b) Blaney, P.; Grigg, R.; Rankovic, Z.; Thoroughgood, M. *Tetrahedron Lett.* **2000**, *41*, 6639–6642.
7. Sato, F.; Sato, S.; Kodama, H.; Sato, M. *J. Organomet. Chem.* **1977**, *142*, 71–79.
8. Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.
9. Ohloff, G.; Giersch, W.; Schulte-Elte, K. H.; Kovats, E. *Helv. Chim. Acta* **1969**, *52*, 1531.
10. Chapuis, C.; Brauchli, R. *Helv. Chim. Acta* **1992**, *75*, 1527–1546.
11. Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.
12. Sheldrick, G. M. *Acta Crytallogr. Sect. A* **1990**, *46*, 467–473.
13. Sheldrichk, G. M. *SHELXL 93, Program for Refinement of Crystal structures*; University of Gottingen: Gottingen, 1993.