Pergamon

Tetrahedron 57 (2001) 7035–7045

TETRAHEDRON

X=Y–ZH Systems as potential 1,3-dipoles. Part 52: Fused-ring forming electrophile induced oxime→nitrone→cycloaddition cascades☆

H. Ali Dondas, Ronald Grigg* and Sylvie Thibault

School of Chemistry, The University of Leeds, Woodhouse Lane, Leeds LS2 9JT, UK

Received 24 April 2001; revised 24 May 2001; accepted 14 June 2001

Abstract—Electrophile induced cyclisation of oximes onto endocyclic alkenes and *exo*-methylene cycloalkanes occurs stereo- and regio-specifically generating *cis*-fused bicyclic nitrones in good yield. Subsequent facially selective cycloaddition with *N*-methylmaleimide occurs in good yield. The sequence may be carried out as a one-pot procedure and results in the formation of 4 bonds, 2 rings and 6 stereocentres.

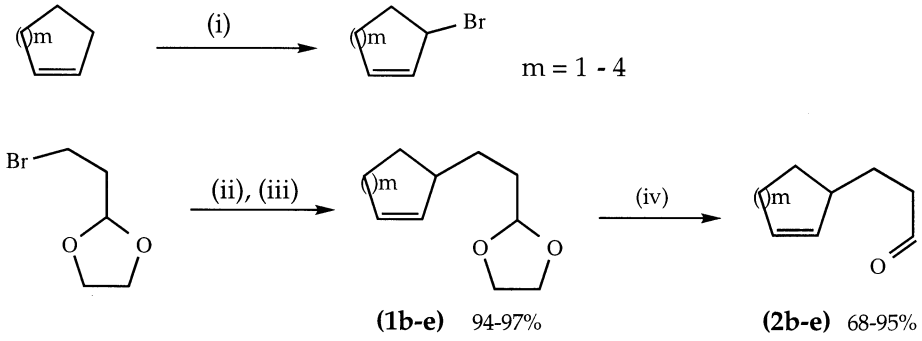
1. Background

As part of an ongoing research program developing new cascade reactions we have recently reported a range of electrophile induced oxime→nitrone→cycloaddition cascades[2] involving stereo- and regio-specific spiro- and bridged-ring forming cyclisation of oximes onto proximate alkenes.[3,4]

We now report that oximes cyclise onto endocyclic alkenes and *exo*-methylene cycloalkanes in the presence of electrophiles such as PhSeBr and *N*-bromosuccinimide (NBS) to generate *cis*-fused bicyclic nitrones which can be trapped in 1,3-dipolar cycloaddition reactions.

2. Cyclisation of oximes onto endocyclic alkenes

Aldehyde (**2a**) was prepared by the literature procedure[5] whilst aldehydes (**2b**–**e**) were prepared as outlined in Scheme 1.[6] Aldehydes (**2a**–**e**) were converted to their oximes (**3a**–**e**) which were obtained as 1:1 mixtures of *E*/*Z*-isomers (Scheme 2). The reaction of (**3a**) with PhSeBr (MeCN, rt, 1 h.) gave the nitrone salt (**4a** E=PhSe). The nitrone was liberated from the salt by treatment with Hunig's base and trapped in situ in a 1,3-dipolar cycloaddition reaction with *N*-methylmaleimide (NMM) (MeCN, rt, 10 h). The cycloaddition occured with high facial selectivity and the product comprised a separable 1:1 mixture (70%) of the *exo*-(**5a**) and *endo*-(**6a**) cycloadducts whose stereochemistry

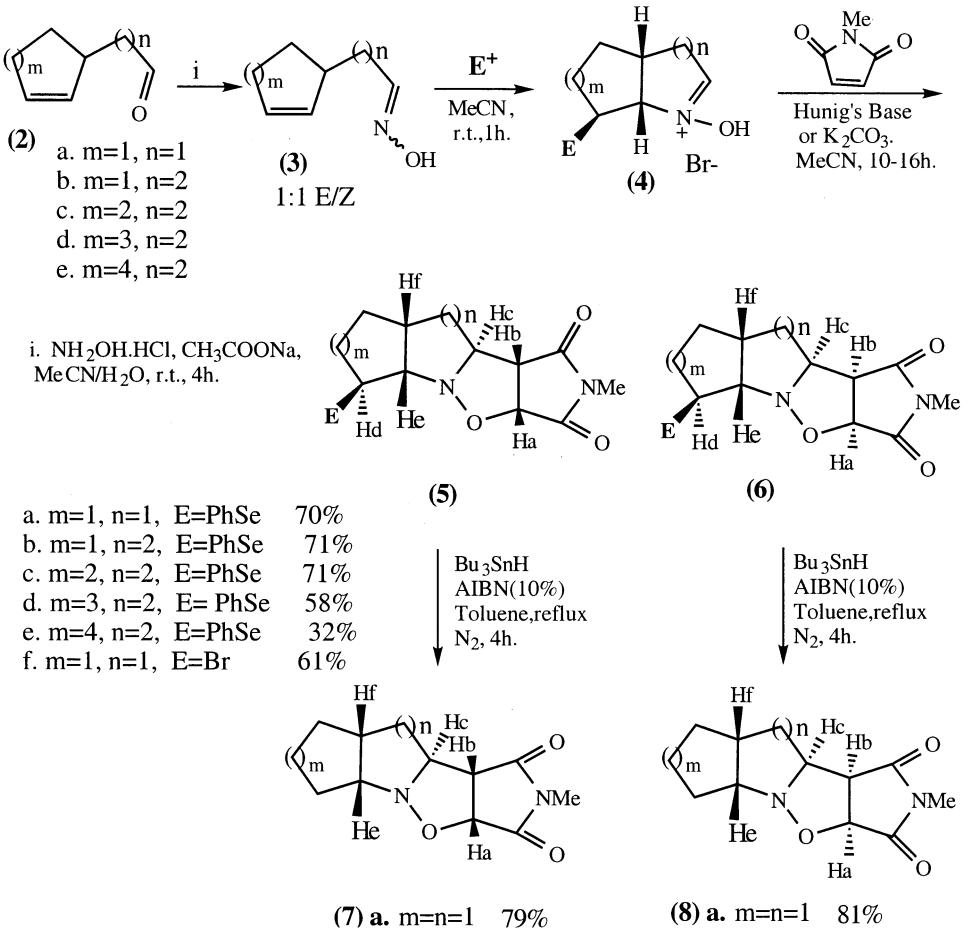


Scheme 1. (i) NBS/AIBN; (ii) Mg/THF; (iii) 3-bromocycloalkene/rt/3 h; (iv) 2N H_2SO_4/3:1 v/v CH_3CN–H_2O/rt/20 h.

☆ See Ref. 1 for Part 51.

Keywords: cycloalkenes; *exo*- and *endo*-trig cyclisation; onium ions; cyclic nitrones; 1,3-dipolar cycloaddition; facial selectivity.
* Corresponding author. Tel./fax: +44-113-2336501; e-mail: r.grigg@chem.leeds.ac.uk

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00661-5



Scheme 2.

was assigned from n.O.e data and 2D-COSY studies. Both cycloadducts arise from cycloaddition to the less hindered outer surface of the bowl-shaped nitrone i.e. *syn* to the ring junction H-atoms. The PhSe groups of the cycloadducts (**5a**) and (**6a**) were removed using Bu_3SnH/AIBN affording (**7a**) and (**8a**) in 79–81% yield (Scheme 2).

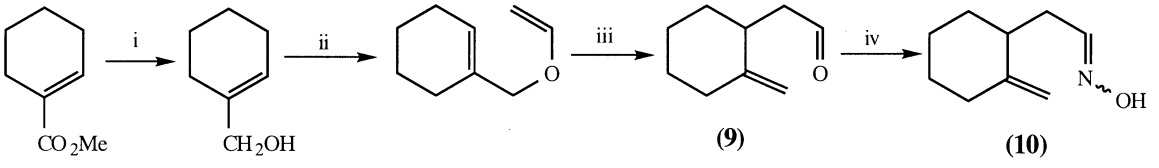
Oximes (**3b–e**) reacted with PhSeBr under same reaction conditions to give the nitrone salts (**4b–e**, E=PhSe) from which the nitrones were liberated with K_2CO_3 and similarly trapped in situ in 1,3-dipolar cycloaddition reactions using NMM as the dipolarophile (MeCN, 80°C, 16 h) to produce *exo*-cycloadducts (**5b–e**) in moderate to good yield (Scheme 2) together, in the case of (**3b**) and (**3d**), with a trace amount (<5%) of (**6b**) and (**6d**). The stereochemistry of (**5b–e**) was determined on the basis of n.O.e data and 2D-COSY studies. Thus the longer tether in these latter cases imposes high *exo*-selectivity on the facially selective cycloaddition.

2.1. Br^+ as electrophile

The reaction of (**3a**) with NBS (CH_2Cl_2, 25°C, 2 h) afforded the nitrone free base of (**4a**, E=Br) in essentially quantitative yield with the succinimide acting as a proton scavenger. Cycloaddition (NMM, benzene, 60°C, 13 h) furnished a 1:1 mixture (61%) of *exo*-(**5f**) and *endo*-(**6f**) cycloadducts as a separable mixture. Their respective stereochemistries were assigned from n.O.e data and 2D-COSY studies.

3. Cyclisation of oximes onto *exo*-methylene cycloalkanes

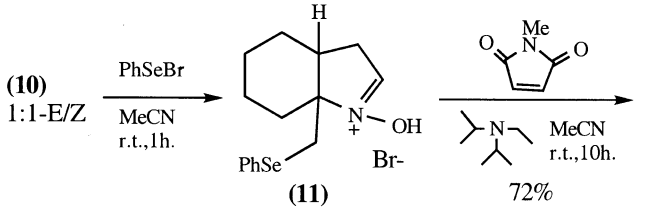
(2-Methylenecyclohexyl) acetaldehyde (**9**) was prepared from methyl cyclohexen-1-carboxylate via hydride reduction, vinyl transeterification and Claisen rearrangement as outlined in Scheme 3[7] and was converted into oxime (**10**) which comprised a 1:1 *E*/*Z*-mixture of isomers.

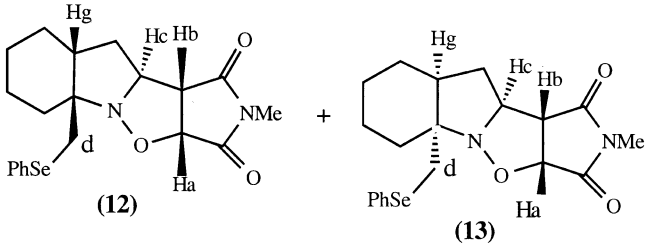


Scheme 3. (i) $NaAlH_2(OCH_2CH_2OCH_3)_2$, benzene, N_2, rt, 24 h; (ii) $CH_2{=}CHOCH_2CH_3$, $Hg(Oac)_2$, N_2, reflux, 6 h; (iii) Sealed tube, 200°C, N_2, 1 h; (iv) $NH_2OH{\cdot}HCl$, CH_3CO_2Na, $MeCN/H_2O$, rt, 6 h.

3.1. $PhSe^+$ as electrophile

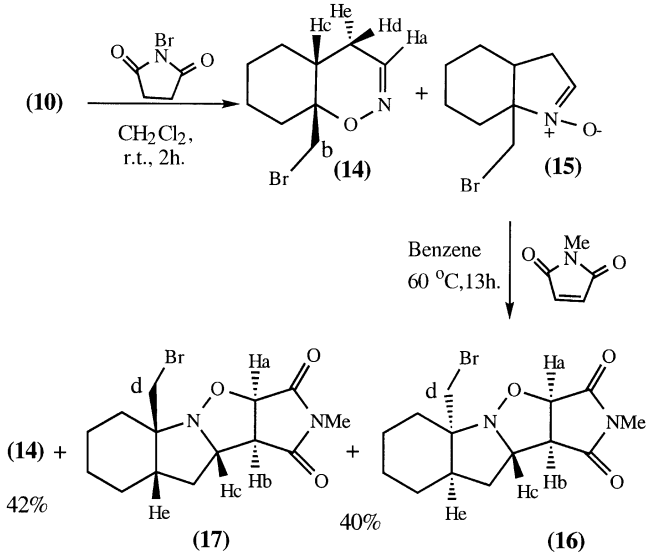
The reaction of *E*/*Z*-(**10**) with PhSeBr (MeCN, rt, 1 h) gave the nitrone salt (**11**). The free nitrone was liberated in situ and trapped in a 1,3-dipolar cycloaddition reaction with NMM (MeCN, rt, Hunig's base, 10 h) to produce a 1:1 mixture (72%) of diastereoisomeric *exo*-cycloadducts (**12**) and (**13**), in 37 and 35% overall yield from (**10**), respectively. The stereochemistries of (**12**) and (**13**) were assigned from n.O.e data and 2D-COSY studies.





3.2. Br^+ as electrophile

The reaction of the 1:1 mixture of *E*/*Z*-isomers (**10**) with NBS (CH_2Cl_2, 25°C, 2 h) afforded a 1:1 mixture of oxazine (**14**) and nitrone (**15**) reflecting the *E*/*Z*-ratio of the starting oxime (**3**). In this case the succinimide acts as the proton scavenger. Treating the mixture with NMM (C_6H_6, 60°C, 13 h) afforded a 1:1 mixture of diastereoisomeric cycloadducts (**16**) and (**17**) in 73% yield relative to *E*-(**10**) together with unchanged (**14**), [42% relative to *Z*-(**10**)]. The stereochemistries of the cycloadducts were assigned from n.O.e data and 2D-COSY studies.



In summary, the electrophile-induced cyclisation of oximes onto proximate endocyclic alkenes or *exo*-methylene cycloalkenes creates *cis*-fused bicyclic nitrones which undergo facially selective 1,3-dipolar cycloaddition to *N*-methylmaleimide. The sequence may be carried out as a one-pot procedure and results in a considerable increase in molecular complexity with the formation of four bonds, two rings and six stereocentres.

4. Experimental

4.1. General

Nuclear magnetic resonance spectra and decoupling experiments were determined at 300 MHz on a Q.E 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. Solvents were purified according to procedures given in Purification of Laboratory Chemicals, D. D. Perrin, W. L. F. Armanego, D. R. Perrin, Pergamon Press, 1980.

4.1.1. 2-(2-Cyclopent-2-enylethyl)-1,3-dioxolane (1b). A solution of 2-(2-bromoethyl)-1,3-dioxolane (1.81 g, 1.3 equiv.) in THF (2 mL) was added dropwise to a suspension of magnesium turnings (0.244 g, 1.3 equiv.) in THF (10 mL). After dissolution of all the magnesium, a solution of 3-bromocyclopentene (1.17 g, 8.0 mmol) in THF (2 mL) was slowly added to the Grignard reagent over 20 min. The solution was stirred at room temperature for 3 h, poured into ice-water (50 mL) and the product extracted with diethyl ether (3×50 mL). The combined organic layers were washed with saturated aq. NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated to afford the product (1.26 g, 94%) as a colourless oil, bp 45°C/0.1 mmHg. (Found (HRMS): 168.1141, $C_{10}H_{16}O_2$ requires: 168.1150); δ (300 MHz): 5.68 (m, 2H, CH=CH), 4.85 (t, 1H, J= 5.0 Hz, CH–O), 4.00–3.82 (m, 4H, 2×CH_2–O) and 2.69–1.35 (m, 9H, cyclopentyl and alkyl); *m*/*z* (%): 168 (M^+, 1), 106 (19), 99 (27), 80 (79), 73 (100), 67 (37), 45 (34) and 41 (19).

4.1.2. 2-(2-Cyclohex-2-enylethyl)-1,3-dioxolane (1c). A solution of 2-(2-bromoethyl)-1,3-dioxolane (9.05 g, 1.2 equiv.) in THF (15 mL) was added dropwise to a suspension of magnesium turnings (1.22 g, 1.2 equiv.) in THF (40 mL). After dissolution of all magnesium, a solution of 3-bromocyclohexene (6.44 g, 40.0 mmol) in THF (5 mL) was slowly added to the Grignard reagent over 45 min. The solution

was stirred at room temperature for 3 h, poured into ice-water (200 mL) and the product extracted with diethyl ether (3×200 mL). The combined organic layers were washed with saturated aq. NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated to afford the product (6.82 g, 94%) as a colourless oil, bp 50°C/0.1 mmHg. (Found: C, 72.3; H, 9.85, $C_{11}H_{18}O_2$ requires: C, 72.55; H, 9.9%); δ (300 MHz): 5.66 (dt, 1H, J=3.0 and 10.0 Hz, CH_2–*CH*═), 5.57 (dd, 1H, J=1.5 and 10.0 Hz, CH–*CH*═), 4.85 (t, 1H, J=4.5 Hz, CH–O), 3.99–3.82 (m, 4H, 2×CH_2–O), 2.07 (m, 1H, CH) and 1.98–1.17 (m, 10H, cyclohexyl and alkyl); *m*/*z* (%): 182 (M^+, 4), 121 (51), 99 (29), 94 (62), 81 (100), 73 (97), 67 (19), 57 (21), 45 (44) and 41 (33).

4.1.3. 2-(2-Cyclohept-2-enylethyl)-1,3-dioxolane (1d). A solution of 2-(2-bromoethyl)-1,3-dioxolane (1.84 g, 1.2 equiv.) in THF (2 mL) was added dropwise to a suspension of magnesium turnings (0.244 g, 1.2 equiv.) in THF (10 mL). After dissolution of all magnesium, a solution of 3-bromocycloheptene (1.41 g, 8.0 mmol) in THF (2 mL) was slowly added to the Grignard reagent over 20 min. The solution was stirred at room temperature for 3 h, poured into ice-water (50 mL) and the product extracted with diethyl ether (3×50 mL). The combined organic layers were washed with saturated aq. NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated to afford the product (1.51 g, 96%) as a colourless oil, bp 60°C/0.1 mmHg. (Found HRMS: 196.1457, $C_{12}H_{20}O_2$ requires: 196.1463); δ (300 MHz): 5.77 (m, 1H, CH_2–*CH*═), 5.54 (dd, 1H, J=3.0 and 11.0 Hz, CH–*CH*═), 4.85 (t, 1H, J=4.5 Hz, CH–O), 3.98–3.81 (m, 4H, 2×CH_2–O) and 2.28–1.21 (m, 13H, cycloheptyl and alkyl); *m*/*z* (%): 196 (M^+, 4), 134 (16), 108 (79), 99 (55), 93 (39), 86 (22), 79 (28), 73 (100), 67 (19), 45 (31) and 41 (20).

4.1.4. 2-(2-Cyclooct-2-enylethyl)-1,3-dioxolane (1e). A solution of 2-(2-bromoethyl)-1,3-dioxolane (5.44 g, 1.2 equiv.) in THF (5 mL) was added dropwise to a suspension of magnesium turnings (0.731 g, 1.2 equiv.) in THF (20 mL). After dissolution of all magnesium, a solution of 3-bromocyclooctene (4.53 g, 24.0 mmol) in THF (5 mL) was slowly added to the Grignard reagent over 30 min. The solution was stirred at room temperature for 3 h, poured into ice-water (100 mL) and the product extracted with diethyl ether (3×100 mL). The combined organic layers were washed with saturated aq. NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated to afford the product (4.89 g, 97%) as a colourless oil, bp 74°C/0.1 mmHg. (Found HRMS: 210.1614, $C_{13}H_{22}O_2$ requires: 210.1620); δ (300 MHz): 5.65 (q, 1H, J=8.5 Hz, CH_2–*CH*═), 5.20 (t, 1H, J=8.5 Hz, CH–*CH*═), 4.85 (t, 1H, J=4.5 Hz, CH–O), 3.99–3.81 (m, 4H, 2×CH_2–O) and 2.50–1.08 (m, 15H, cyclooctyl and alkyl); *m*/*z* (%): 210 (M^+, 2), 181 (3), 148 (5), 122 (22), 109 (11), 99 (73), 73 (100), 67 (34), 55 (20), 45 (40) and 41 (34).

4.1.5. 3-(Cyclopent-2-enyl)-propionaldehyde (2b). 2N H_2SO_4 (10 mL) was added to a stirred solution of acetal (**1b**) (0.51 g, 3.0 mmol) in a 3:1 v/v mixture of acetonitrile–water (30 mL) and stirring was continued at room temperature for 20 h. 8% Aq. $NaHCO_3$ (50 mL) was then added, the product extracted with diethyl ether (3×50 mL), the combined organic layers dried ($MgSO_4$) and concentrated to afford the product (0.25 g, 68%) as a colourless oil. δ (300 MHz): 9.78 (t, 1H, J=2.0 Hz, CHO), 5.77–5.62 (m, 2H, CH═CH) and 2.78–1.38 (m, 9H, cyclopentyl and alkyl); *m*/*z* (%): 124 (M^+, 5), 107 (16), 80 (68), 67 (100), 55 (26) and 41 (12).

4.1.6. 3-(Cyclohex-2-enyl)-propionaldehyde (2c). 2N H_2SO_4 (10 mL) was added to a stirred solution of acetal (**1c**) (0.55 g, 3.0 mmol) in a 3:1 v/v mixture of acetonitrile–water (30 mL) and stirring was continued at room temperature for 6 h. 8% Aq. $NaHCO_3$ (50 mL) was then added, the product extracted with diethyl ether (3×50 mL), the combined organic layers dried ($MgSO_4$) and concentrated to afford the product (0.36 g, 88%) as a colourless oil. δ (300 MHz): 9.78 (t, 1H, J=1.5 Hz, CHO), 5.69 (m, 1H, CH_2–*CH*═), 5.52 (dd, 1H, J=2.0 and 10.0 Hz, CH–*CH*═), 2.48 (dt, 2H, J=1.5 and 7.5 Hz, *CH*$_2$–CHO) and 2.14–1.16 (m, 9H, cyclohexyl and alkyl); *m*/*z* (%): 138 (M^+, 3), 94 (100), 81 (93), 79 (99), 67 (27), 53 (26) and 41 (39).

4.1.7. 3-(Cyclohept-2-enyl)-propionaldehyde (2d). 2N H_2SO_4 (10 mL) was added to a stirred solution of acetal (**1d**) (0.61 g, 3.1 mmol) in a 3:1 v/v mixture of acetonitrile–water (30 mL) and stirring was continued at room temperature for 20 h. 8% Aq. $NaHCO_3$ (50 mL) was then added, the product extracted with diethyl ether (3×50 mL), the combined organic layers dried ($MgSO_4$) and concentrated to afford the product (0.45 g, 95%) as a colourless oil. (Found HRMS: 152.1203, $C_{10}H_{16}O$ requires: 152.1201); δ (300 MHz): 9.78 (t, 1H, J=1.5 Hz, CHO), 5.80 (m, 1H, CH_2–*CH*═), 5.51 (dd, 1H, J=3.5 and 11.0 Hz, CH–*CH*═) and 2.50–1.22 (m, 13H, cycloheptyl and alkyl); *m*/*z* (%): 152 (M^+, 3), 108 (100), 93 (69), 79 (48), 67 (45) and 55 (22); ν_{max} (film): 2910 (C–H), 2830 (CHO), 2710 (CHO), 1720 (C═O), 1440 (*CH*2–CHO), 735 and 690 cm^{-1}.

4.1.8. 3-(Cyclooct-2-enyl)-propionaldehyde (2e). 2N H_2SO_4 (10 mL) was added to a stirred solution of acetal (**1e**) (0.65 g, 3.0 mmol) in a 3:1 v/v mixture of acetonitrile–water (30 mL) and stirring was continued at room temperature for 20 h. 8% Aq. $NaHCO_3$ (50 mL) was then added, the product extracted with diethyl ether (3×50 mL), the combined organic layers dried ($MgSO_4$) and concentrated to afford the product (0.43 g, 84%) as a colourless oil. (Found HRMS: 166.1360, $C_{11}H_{18}O$ requires: 166.1358); δ (300 MHz): 9.78 (t, 1H, J=1.7 Hz, CHO), 5.70 (q, 1H, J=9.5 Hz, CH_2–*CH*═), 5.16 (t, 1H, J=9.5 Hz, CH–*CH*═) and 2.52–1.12 (m, 15H, cyclooctyl and alkyl); *m*/*z* (%): 166 (M^+, 11), 122 (100), 107 (39), 93 (57), 79 (61), 67 (91), 55 (52) and 41 (83); ν_{max} (film): 2920 (C–H), 2850 (CHO), 1720 (C═O), 1445 (*CH*2–CHO), 750 and 710 cm^{-1}.

4.1.9. 2-(Cyclopent-2-en)-1-acetaldoxime (3a). A solution of aldehyde (**2a**) (10 g, 90.9 mmol) in acetonitrile (200 mL) was added to a solution of hydroxylamine hydrochloride (6.95 g, 1.1 equiv.) and sodium acetate (8.95 g, 1.2 equiv.) in water (100 mL). The resulting solution was stirred at ambient temperature for 6 h and then extracted with chloroform (2×300 mL). The combined organic layer was dried ($MgSO_4$), concentrated under reduced pressure and the

residue subjected to column chromatography on silica, eluting with 1:1 v/v petroleum ether–ether. The product (9.8 g, 86%) was obtained as a colourless thick oil, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 66.7; H, 8.55; N, 10.95, $C_7H_{11}NO$ requires: C, 67.15; H, 8.85, N, 11.2%); δ (300 MHz): 9.8 and 9.47 (br, 1H, OH, isomers), 7.43 (t, 1H, *E*-CH═N), 6.77 (t, 1H, *Z*-CH═N), 5.77 (brs, 1H, CH═C, isomers), 5.66 (brs, 1H, CH═C, isomers) and 2.88–1.44 (m, 7H). *m/z* (%); 125 (M^+, 2), 108 (14), 91 (6), 80 (14), 67 (100), 59 (12), 41 (14) and 39 (10).

4.1.10. 3-(Cyclopent-2-enyl)-propionaldoxime (3b). A solution of aldehyde (**2b**) (0.17 g, 1.3 mmol) in acetonitrile (15 mL) was added to a solution of hydroxylamine hydrochloride (0.10 g, 1.1 equiv.) and sodium acetate (0.13 g, 1.2 equiv.) in water (7.5 mL). The resulting solution was stirred at ambient temperature for 4 h and then extracted with dichloromethane (3×20 mL). The combined organic layer was dried ($MgSO_4$), concentrated under reduced pressure and the residue subjected to column chromatography on silica, eluting with 1:2 v/v ether–hexane. The product (0.12 g, 65%) crystallised from ether–hexane as colourless needles, mp 65–67°C, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 68.9; H, 9.4; N, 10.0, $C_8H_{13}NO$ requires: C, 69.1; H, 9.35, N, 10.05%); δ (300 MHz): 9.2 and 8.8 (br, 1H, OH, isomers), 7.44 (t, 1H, *J*=6.0 Hz, *E*-CH═N), 6.74 (t, 1H, *J*=5.5 Hz, *Z*-CH═N), 5.75 (m, 1H, CH═C, isomers), 5.64 (m, 1H, CH═C, isomers) and 2.72–1.36 (m, 9H); *m/z* (%): 139 (M^+, 10), 122 (13), 106 (10), 93 (23), 79 (54), 67 (100) and 53 (12).

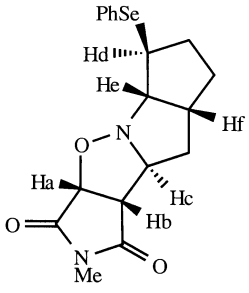
4.1.11. 3-(Cyclohex-2-enyl)-propionaldoxime (3c). A solution of aldehyde (**2c**) (1.04 g, 7.5 mmol) in acetonitrile (50 mL) was added to a solution of hydroxylamine hydrochloride (0.58 g, 1.1 equiv.) and sodium acetate (0.75 g, 1.2 equiv.) in water (25 mL). The resulting solution was stirred at ambient temperature for 4 h and then extracted with dichloromethane (3×50 mL). The combined organic layer was dried ($MgSO_4$), concentrated under reduced pressure and the residue subjected to column chromatography on silica, eluting with 1:2 v/v ether–hexane. The product (0.91 g, 79%) crystallised from ether–hexane as colourless needles, mp 60–62°C, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 70.65; H, 10.1; N, 9.25, $C_9H_{15}NO$ requires: C, 70.6; H, 9.8, N, 9.15%); δ (300 MHz): 8.82 and 8.38 (br, 1H, OH, isomers), 7.43 (t, 1H, *J*=6.0 Hz, *E*-CH═N), 6.73 (t, 1H, *J*=5.5 Hz, *Z*-CH═N), 5.69 (m, 1H, CH═C, isomers), 5.56 (m, 1H, CH═C, isomers) and 2.47–1.17 (m, 11H); *m/z* (%): 153 (M^+, 2), 135 (18), 120 (10), 107 (26), 95 (60), 81 (100), 67 (55) and 53 (31).

4.1.12. 3-(Cyclohept-2-enyl)-propionaldoxime (3d). A solution of aldehyde (**2d**) (0.30 g, 2.0 mmol) in acetonitrile (15 mL) was added to a solution of hydroxylamine hydrochloride (0.15 g, 1.1 equiv.) and sodium acetate (0.19 g, 1.2 equiv.) in water (7.5 mL). The resulting solution was stirred at ambient temperature for 4 h and then extracted with dichloromethane (3×20 mL). The combined organic layer was dried ($MgSO_4$), concentrated under reduced pressure and the residue subjected to column chromatography on silica, eluting with 1:2 v/v ether–hexane. The product (0.25 g, 75%) was obtained as a colourless viscous oil, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 71.75; H, 10.0; N, 8.35, $C_{10}H_{17}NO$ requires: C, 71.85; H, 10.15, N, 8.4%); δ (300 MHz): 8.92 and 8.47 (br, 1H, OH, isomers), 7.44 (t, 1H, *J*=6.0 Hz, *E*-CH═N), 6.74 (t, 1H, *J*=5.5 Hz, *Z*-CH═N), 5.77 (m, 1H, CH═C, isomers), 5.55 (m, 1H, CH═C, isomers) and 2.47–1.19 (m, 13H); *m/z* (%): 167 (M^+, 4), 150 (49), 135 (19), 121 (14), 109 (96), 95 (45), 93 (47), 79 (62), 67 (100), 59 (38) and 55 (37).

4.1.13. 3-(Clooct-2-enyl)-propionaldoxime (3e). A solution of aldehyde (**2e**) (0.53 g, 3.2 mmol) in acetonitrile (20 mL) was added to a solution of hydroxylamine hydrochloride (0.24 g, 1.1 equiv.) and sodium acetate (0.32 g, 1.2 equiv.) in water (10 mL). The resulting solution was stirred at ambient temperature for 4 h and then extracted with dichloromethane (3×20 mL). The combined organic layer was dried ($MgSO_4$), concentrated under reduced pressure and the residue subjected to column chromatography on silica, eluting with 1:2 v/v ether–hexane. The product (0.53 g, 92%) was obtained as a colourless oil, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 72.8; H, 10.7; N, 7.75, $C_{11}H_{19}NO$ requires: C, 72.95; H, 10.05, N, 7.75%); δ (300 MHz): 8.82 and 8.43 (br, 1H, OH, isomers), 7.43 (t, 1H, *J*=6.0 Hz, *E*-CH═N), 6.73 (t, 1H, *J*=5.5 Hz, *Z*-CH═N), 5.67 (q, 1H, *J*=9.0 Hz, CH═C, isomers), 5.17 (q, 1H, *J*=9.0 Hz, CH═C, isomers) and 2.53–1.09 (m, 15H); *m/z* (%): 181 (M^+, 3), 164 (88), 149 (11), 123 (23), 107 (18), 93 (32), 81 (77), 67 (100), 55 (54) and 41 (96).

4.1.14. *exo*-2-Methyl-7-phenylselenyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (5a) and *endo*-2-methyl-7-phenylselanyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (6a). Phenylselenyl bromide (1.32 g, 1.2 equiv.) was added to a solution of oxime (**3a**) (0.5 g, 4.0 mmol) in dry acetonitrile (50 mL). The resulting solution was stirred at ambient temperature for 1 h and NMM (0.48 g, 1 equiv.) and diisopropylethylamine (Hunig's base) (0.84 mL, 1.2 equiv.) were added. The resulting mixture was stirred at 25°C for 10 h. The solvent was then evaporated and the residue was subjected to column chromatography on silica, eluting with 3:1 v/v petroleum ether–ether to afford the product (1.12 g, 70%) as a 1:1 mixture of *endo*- and *exo*-isomers (**5a**) and (**6a**).

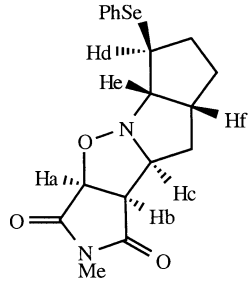
Compound (**5a**): Obtained (35%) as colourless prisms from ether–petroleum ether, mp 119–121°C. (Found: C, 55.35; H, 5.1; N, 7.0, $C_{18}H_{20}N_2O_3Se$ requires: C, 55.25; H, 5.15; N, 7.15%); δ (400 MHz): 7.52–7.19 (m, 5H, ArH), 4.70 (d, 1H, *J*=7.0 Hz, Ha), 4.0 (dd, 1H, *J*=5.5 and 8.0 Hz, He), 3.72 (dd, 1H, *J*=6.5 and 10.5 Hz, Hc), 3.43 (d, 1H, *J*=7.0 Hz, Hb), 3.23 (m, 1H, Hd), 2.97 (s, 3H, NMe), 2.80 (m, 1H, Hf) and 2.24–1.211 (m, 6H); *m/z* (%): 392 (M^+, 28), 281 (12), 264 (34), 235 (99), 233 (54), 207 (5) and 184 (13).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		9.6					
Hb	12.8		4.0				
Hc		4.4		3.9			
Hd			5.3		4.7		6.2
He	2.3			2.7		8.2	2.6

Compound (**6a**): Obtained (35%) as colourless needles from ether–petroleum ether, mp 117–119°C. (Found: C, 55.35; H, 5.2; N, 7.15, $C_{18}H_{20}N_2O_3Se$ requires: C, 55.25; H, 5.15; N, 7.15%); δ (400 MHz): 7.47–7.19 (m, 5H, ArH), 4.75 (d, 1H, J=8.5 Hz, Ha), 3.90 (m, 1H, Hc), 3.61 (t, 1H, J=8.5 Hz, Hb), 3.57–3.54 (m, 1H, Hd), 3.48 (dd, 1H, J=4.0 and 8.0 Hz, He), 2.82 (s, 3H, NMe), 2.65 (m, 1H, Hf), 2.35 (m, 1H, CH2) and 1.98–1.27 (m, 5H); *m/z* (%): 392 (M^+, 34), 264 (49), 235 (100), 223 (78), 157 (44), 143 (54), 108 (60), 67 (69), 54 (64) and 41 (54).

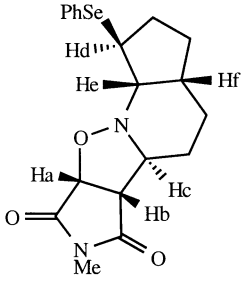


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		11.1					
Hb	15.1		11.7				
Hc		16.9					
Hd	2.5		4.2				8.6
He	1.7					7.7	4.5

4.1.15. *exo*-7-Methyl-1-phenylselenyl-octahydro-9-oxa-7,9a-diaza-cyclopenta[*b*]-as-indacene-6,8-dione (5b). Phenylselenyl bromide (0.14 g, 1.0 equiv.) was added to a stirred solution of oxime (**3b**) (0.08 g, 0.5 mmol) in dry acetonitrile (10 mL) and stirring was continued at ambient temperature for 2 h. Anhydrous potassium carbonate (0.09 g, 1.1 equiv.) was then added and the solution stirred at ambient temperature for an additional 1 h. NMM (0.08 g, 1.2 equiv.) was added and the resulting mixture was boiled under reflux for 16 h. The solvent was then evaporated and the residue subjected to column chromatography on silica, eluting with 2:1 v/v ether–hexane to afford the *exo*-cycloadduct (**5b**) (0.16 g, 71%) contaminated with trace amount (<5%) of *endo*-isomer (**6b**).

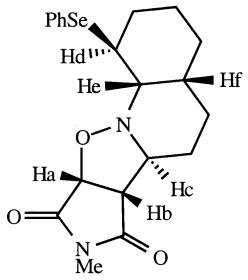
Compound (**5b**): Obtained as colourless amorphous solid, mp 104–106°C. (Found: C, 56.3; H, 5.7; N, 6.7, $C_{19}H_{22}N_2O_3Se$ requires: C, 56.3; H, 5.45; N, 6.9%); δ (400 MHz), (C_6D_6): 7.59–7.02 (m, 5H, ArH), 4.07 (d, 1H, J=7.5 Hz, Ha), 3.53 (dt, 1H, J=6.0 and 9.2 Hz, Hd), 3.23 (dt, 1H, J=5.0 and 7.5 Hz, Hc), 3.09 (t, 1H, J=6.0 Hz, He), 2.59 (s, 3H, NMe), 2.42 (dd, 1H, J=5.0 and 7.5 Hz, Hb), 2.05 (m, 2H, Hf and aliphatic) and 1.80–0.72 (m, 7H); *m/z* (%): 406 (M^+, 19), 284 (100), 249 (65), 221 (57), 198 (55), 157 (60), 111 (42), 79 (85), 67 (68), 54 (59) and 41 (67).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		7.0			4.6		2.4
Hb	11.7		5.4		4.9		
Hc		3.2		5.0			
Hd			4.1		2.2		8.5
He	9.3	3.4		3.9		7.0	3.1

4.1.16. *exo*-8-Methyl-1-phenylselenyl-decahydro-10-oxa-8,10a-diaza-pentaleno[2,1-*a*]-naphthalene-7,9-dione (5c). Phenylselenyl bromide (0.21 g, 1.0 equiv.) was added to a stirred solution of oxime (**3c**) (0.14 g, 0.9 mmol) in dry acetonitrile (10 mL) and stirring was continued at ambient temperature for 2 h. Anhydrous potassium carbonate (0.14 g, 1.1 equiv.) was then added and the solution stirred at ambient temperature for an additional 1 h. NMM (0.13 g, 1.2 equiv.) was added and the resulting mixture was boiled under reflux for 16 h. The solvent was then evaporated and the residue subjected to column chromatography on silica, eluting with 2:1 v/v ether–hexane to afford the *exo*-cycloadduct (**5c**) (0.27 g, 71%) which crystallised from ether–hexane as colourless needles, mp 162–164°C. (Found: C, 57.2; H, 5.85; N, 6.45, $C_{20}H_{24}N_2O_3Se$ requires: C, 57.3; H, 5.75; N, 6.7%); δ (400 MHz), (DMSO, 37.3°C): 7.63–7.38 (m, 5H, ArH), 4.86 (d, 1H, J=7.0 Hz, Ha), 3.84 (dt, 1H, J=4.0 and 8.0 Hz, Hd), 3.67 (m, 1H, Hc), 3.55 (dd, 1H, J=4.0 and 7.0 Hz, Hb), 3.20 (dd, 1H, J=4.0 and 8.0 Hz, He), 2.97 (s, 3H, NMe), 2.31 (m, 1H, Hf) and 2.35–1.49 (m, 10H); *m/z* (%): 420 (M^+, 30), 309 (13), 292 (25), 263 (78), 250 (23), 221 (100), 212 (20), 169 (13), 157 (49), 134 (50), 111 (46), 91 (61), 79 (70), 77 (75), 67 (50) and 54 (60).

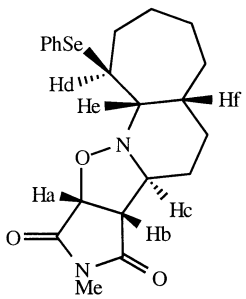


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		6.7			4.0		
Hb	15.7						
Hc				5.8			
Hd			4.3				7.8
He	8.5	4.3				8.5	

4.1.17. Cycloadducts (5d) and (6d). Phenylselenyl bromide (0.17 g, 1.1 equiv.) was added to a stirred solution of oxime (**3d**) (0.11 g, 0.6 mmol) in dry acetonitrile (10 mL) and stirring was continued at ambient temperature for 2 h. Anhydrous potassium carbonate (0.11 g, 1.2 equiv.) was then added and the solution stirred at ambient temperature for an additional 1 h. NMM (0.09 g, 1.3 equiv.) was added and the resulting mixture was boiled under reflux for 16 h. The solvent was then evaporated and the residue subjected to column chromatography on silica, eluting with 2:1 v/v ether–hexane to afford the *exo*-cycloadduct (**5d**) (0.16 g, 58%) contaminated with trace amount (<5%) of *endo*-isomer (**6d**).

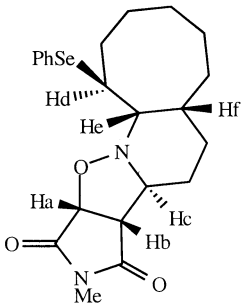
Compound (**5d**): Obtained as a colourless amorphous solid, mp 52–54°C. (Found: C, 58.05; H, 6.05; N, 6.45, $C_{21}H_{26}N_2O_3Se$ requires: C, 58.25; H, 6.0; N, 6.45%); δ (400 MHz), (C_6D_6): 7.53–6.95 (m, 5H, ArH), 4.05 (d, 1H, J=7.0 Hz, Ha), 3.70 (m 1H, Hc), 3.60 (m, 1H, Hd), 3.29 (m, 1H, He), 2.70 (s, 3H, NMe), 2.52 (dd, 1H, J=3.0 and 7.0 Hz, Hb), 2.14 (m, 1H), 1.99 (m, 1H, Hf) and 1.59–0.86 (m, 11H); *m/z* (%): 434 (M^+, 29), 306 (48), 277 (100), 226 (88), 221 (92), 157 (44), 132 (61), 119 (28), 111 (55), 106 (56), 91 (48), 79 (53), 78 (68), 77 (65), 67 (52), 54 (60) and 41 (55).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		7.6					
Hb	12.4		6.2		4.6		
Hc		2.8					3.1
Hd			4.6				12.0
He	7.2	1.5				6.8	3.6

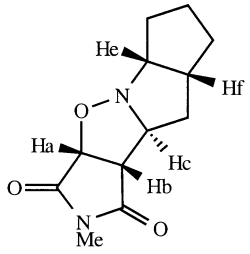
4.1.18. Cycloadduct (5e). Phenylselenyl bromide (0.14 g, 1.0 equiv.) was added to a stirred solution of oxime (**3e**) (0.11 g, 6.0 mmol) in dry acetonitrile (10 mL) and stirring was continued at ambient temperature for 2 h. Anhydrous potassium carbonate (0.09 g, 1.1 equiv.) was then added and the solution stirred at ambient temperature for an additional 1 h. NMM (0.08 g, 1.2 equiv.) was added and the resulting mixture was boiled under reflux for 16 h. The solvent was then evaporated and the residue subjected to column chromatography on silica, eluting with 2:1 v/v ether–hexane to afford the *exo*-cycloadduct (**5e**) (0.08 g, 32%) as a colourless amorphous solid, mp 192–194°C. (Found: C, 59.1; H, 6.2; N, 6.05, $C_{22}H_{28}N_2O_3Se$ requires: C, 59.1; H, 6.25; N, 6.25%); δ (400 MHz), (DMSO, 60°C): 7.59–7.37 (m, 5H, ArH), 4.87 (d, 1H, J=7.0 Hz, Ha), 4.08 (m, 1H, Hd), 3.92 (m, 1H, Hc), 3.75 (dd, 1H, J=10.0 and 4.5 Hz, He), 3.41 (d, 1H, J=7.0 Hz, Hb), 2.97 (s, 3H, NMe), 2.21 (m, 1H, Hf) and 1.95–1.41 (m, 14H); *m/z* (%): 448 (M^+, 34), 320 (8), 291 (63), 221 (100), 208 (27), 180 (7), 157 (40), 91 (21), 77 (33), 67 (41) and 55 (36).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	He	Hf	Ph
Ha		7.3					
Hb	16.3		4.6				
Hc		-0.4		4.1			
Hd			7.5				9.8
He	2.6	-3.5		0.9		7.7	2.1

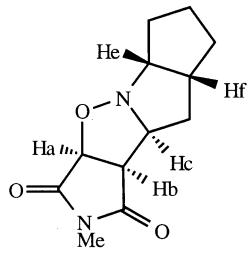
4.1.19. *exo*-2-Methyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (7a). Tri-*n*-butyltin hydride (Bu_3SnH) (0.57 mL, 1.2 equiv.) and 2,2′-azobis-(2-methylpropionitrile) (AIBN) (0.0294 g, 10 mol%) were added to a stirred solution of cycloadduct (**5a**) (0.7 g, 1.79 mmol) in toluene (70 mL) at room temperature. The reaction mixture was stirred and heated at 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–diethyl ether to afford the product (0.337 g, 79%) as colourless prisms. mp 124–126°C. (Found: C, 61.15; H, 6.85; N, 11.85, $C_{12}H_{16}N_2O_3$ requires: C, 61.0; H, 6.85; N, 11.85%) δ (400 MHz): 4.69 (d, 1H, J=7.0 Hz, Ha), 4.0 (dd, 1H, J=14.5 and 8.0 Hz, He), 3.70 (t, 1H, J=8.5 Hz, Hc), 3.44 (d, 1H, J=7.0 Hz, Hb), 2.94 (s, 3H, NMe), 2.73 (m, 1H, Hf) and 2.05–1.17 (m, 8H); *m*/*z* (%): 236 (M^+, 61), 125 (74), 112 (17), 108 (38), 67 (100), 59 (25), 54 (25) and 41 (39).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	He	Hf
Ha		7.7			
Hb	11.7		3.3		
Hc		3.4			
He					6.2
Hf				8.3	

4.1.20. *endo*-2-Methyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (8a). Tri-*n*-butyltin hydride (Bu_3SnH) (0.32 mL, 1.2 equiv.) and 2,2′-azobis-(2-methyl propionitrile) (AIBN) (0.017 g, 10 mol%) were added to a stirred solution of cycloadduct (**6a**) (0.4 g, 1.02 mmol) in toluene (40 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 (0.34 g, 81%) as colourless prisms, mp 121–123°C. (Found: C, 60.95; H, 6.8; N, 11.75, $C_{12}H_{16}N_2O_3$ requires: C, 61.0; H, 6.85; N, 11.85%); δ (400 MHz): 4.78 (d, 1H, J=8.0 Hz, Ha), 3.86 (m, 1H, Hc), 3.67 (t, 1H, J=8.0 Hz, Hb), 3.48 (m, 1H, He), 2.92 (s, 3H, NMe), 2.46 (m, 1H, Hf) and 2.26–1.39 (m, 8H); *m*/*z* (%): 236 (M^+, 29), 125 (79), 108 (38), 95 (16), 86 (17), 80 (38), 67 (100), 54 (41), 53 (30) and 41 (48).

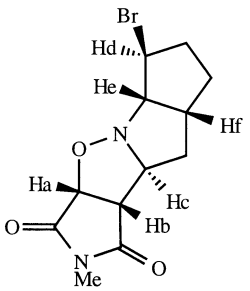


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	He	Hf
Ha		8.1			
Hb	11.8		8.3		
Hc		11.0			
He					5.4
Hf				7.4	

4.1.21. *exo*-7-Bromo-2-methyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (5f) and *endo*-7-bromo-2-methyl-octahydro-8-oxa-2,7b-diaza-dicyclopenta[*a*,*e*]pentalene-1,3-dione (6f). A solution of oxime (**3a**) (0.4 g, 3.2 mmol) and NBS (recrystallised) (0.57 g, 3.2 mmol) in dry DCM (40 mL) was stirred at room temperature for 3 h. The DCM was removed under reduced pressure and the residue was taken up in benzene (40 mL), NMM (0.35 g, 3.2 mmol) added and the mixture heated at 60°C for 13 h. After cooling the benzene was evaporated under reduced pressure to leave a yellow brown oil which comprised a 1:1 mixture of (**5f**) and (**6f**). Flash column chromatography eluting with 1:1 v/v ethyl acetate–hexane afforded the separated *exo*- and *endo*-isomers (**5f**) and (**6f**) (0.61 g, 61% combined yield).

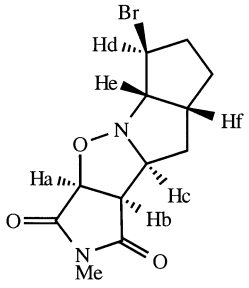
Compound (**5f**): Obtained as a pale yellow solid, mp 163–165°C. (Found: C, 45.7; H, 4.55; N, 8.7; Br, 25.55, $C_{12}H_{15}N_2O_3Br$ requires: C, 45.7; H, 4.8; N, 8.85, Br, 25.4%); δ (400 MHz): 4.78 (d, 1H, J=7.5 Hz, Ha), 4.19 (dd, 1H, J=8.0 and 3.5 Hz, He), 4.10 (m, 1H, Hd), 3.67 (m, 1H, Hc), 3.46 (d, 1H, J=7.5 Hz, Hb), 3.05 (m, 1H, Hf), 3.02 (s, 3H, NMe) and 2.23–1.34 (m, 6H); *m*/*z* (%): 316 (M^+, 87), 314 (89), 235 (100), 203 (50), 123 (30), 108 (41), 79 (62), 67 (92), 53 (60) and 41 (89).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	He	Hf
Ha		7.7		1.6	
Hb	7.9		3.5		
Hc		1.7			
He		2.9			5.2
Hf				5.4	

Compound (**6f**): Obtained as colourless colourless prisms, mp 159–161°C. (Found: C, 45.9; H, 4.5; N, 8.6, Br; 25.45, $C_{12}H_{15}N_2O_3Br$ requires: C, 45.7; H, 4.8; N, 8.85, Br; 25.4%); δ (400 MHz): 4.88 (d, 1H, J=8.0 Hz, Ha), 4.31 (brs, 1H, He), 3.95 (m, 1H, Hc), 3.65–3.61 (m, 2H, Hb and Hd), 3.02 (s, 3H, NMe) and 2.73–1.04 (m, 7H); *m/z* (%): 316 (M^+, 53), 314 (55), 235 (73), 203 (56), 155 (61), 145 (36), 112 (30), 108 (35), 67 (92) and 41 (100).



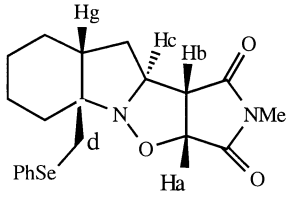
Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	He	Hf
Ha		9.5			
Hb	7.1		6.4	4.0	
Hc		18.7		2.7	6.5
Hd					
He				5.4	7.0

4.1.22. 2-Methylenecyclohexyl acetaldoxime (10). A solution of aldehyde (**9**) (5 g, 36.2 mmol) in acetonitrile (130 mL) was added to a solution of hydroxylamine hydrochloride (2.77 g, 1.1 equiv.) and sodium acetate (3.56 g, 1.2 equiv.) in water (50 mL). The resulting solution was stirred at ambient temperature for 6 h, and 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. The product (4.81 g, 87%) was obtained as a colourless thick oil, which comprised a 1:1 mixture of *E*- and *Z*-isomers. (Found: C, 70.3; H, 9.9; N, 9.05, $C_9H_{15}NO$ requires: C, 70.55; H, 9.9; N, 9.1%); δ (300 MHz): 9.92 (br, 1H, OH, isomers), 7.44 (t, 1H, *E*-CH=N), 6.72 (t, 1H, *Z*-CH=N) 4.69 and 4.57 (2×brs, 2H, vinyl-H, isomers) and 2.66–1.20 (m, 11H); *m/z* (%): 153 (M^+, 8), 136 (12), 121 (42), 95 (100), 67 (57), 55 (29) and 41 (32).

4.1.23. Cycloadducts (12) and (13). Phenylselenyl bromide (0.462 g, 1.2 equiv.) was added to a solution of oxime (**10**) (0.25 g, 1.63 mmol) in dry acetonitrile (25 mL). The resulting solution was stirred at ambient temperature for 1 h when NMM (0.181 g, 1 equiv.) and diisopropylethylamine (Hunig's base) (0.34 mL, 1.2 equiv.) were added. The resulting mixture was stirred at 25°C for 10 h, then the solvent was evaporated. The residue was subjected to column chromatography on silica, eluting with 3:2 v/v petroleum ether–diethyl ether to afford the product (0.49 g, 72%) as a 1:1 mixture of diastereoisomers (**12**) and (**13**) in 35% and 37% yield respectively.

4.1.24. 2-Methyl-7a-phenylselanylmethyl-octahydro-8-oxa-2,7b-diaza-cyclopenta[*a*,*e*]-pentalene-1,3-dione (12). Obtained as pale yellow thick oil. (Found: C, 57.05; H, 5.8; N, 6.55 $C_{20}H_{24}N_2O_3Se$ requires: C, 57.25; H, 5.75; N, 6.7%); δ (400 MHz): 7.50–7.15 (m, 5H, ArH), 4.84 (d, 1H, J=7.5 Hz Ha), 3.99–3.94 (m, 1H, Hc), 3.43 (dd, 1H, J=3.0 and 7.5 Hz, Hb), 3.04 (2×d, 2H, J=12.0 Hz, Hd), 2.93 (s, 3H, NMe) and 2.35–1.27 (m, 11H); *m/z* (%): 421 (M+1, 37), 263 (23), 249 (100), 171 (3), 137 (44), 134 (6), 93 (8) and 79 (5).

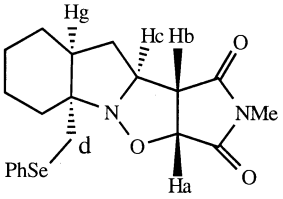


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hd	Hg	Ph
Ha		7.2			
Hb	12.1				
Hc		4.6			
Hd			25.0	7.6	3.5

4.1.25. *exo*-2-Methyl-7a-phenylselanylmethyl-octahydro-8-oxa-2,7b-diaza-cyclopenta[*a*,*e*]-pentalene-1,3-dione (13). Obtained as colourless prisms from ether–petroleum ether (60–80°C), mp 194–196°C. (Found: C, 57.45; H, 5.5; N, 6.55 $C_{20}H_{24}N_2O_3Se$ requires: C, 57.25; H, 5.75; N, 6.7%); δ (300 MHz), (C_6D_6): 7.62–6.96 (m, 5H, ArH), 4.11 (d, 1H, J=7.4 Hz, Ha), 3.89–3.84 (m, 1H, Hc), 3.52 (d, 1H, J=12.0 Hz, Hd), 3.14 (d, 1H, J=12.0 Hz, Hd), 2.66 (d, 1H, J=7.4 Hz, Hb), 2.49 (s, 3H, NMe) and 2.31–0.51 (m,

11H); *m/z* (%): 421 (M+1, 49), 263 (21), 249 (100), 134 (8), 109 (13), 95 (20) and 67 (21).

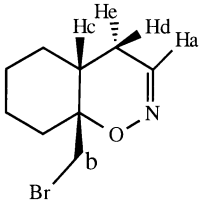


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd	Hg	Ph
Ha		7.6				
Hb	11.5		4.4			
Hc		2.5				
Hd			5.5		3.1	6.4
Hg			7.9	2.4		

4.1.26. 8a-Bromomethyl-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*e*][1,2]oxazine(14), *exo*-7a-bromomethyl-2-methyl-octahydro-8-oxa-2,7b-diaza-cyclopenta[*a*,*e*]-pentalene-1,3-dione(16) and 7a-bromomethyl-2-methyl-octahydro-8-oxa-2,7b-diaza-cyclopenta[*a*,*e*]-pentalene-1,3-dione (17). A solution of oxime (**10**) (0.25 g, 1.63 mmol) and NBS (recrystallised) (0.29 g, 1.63 mmol) in dry DCM (30 mL) was stirred at room temperature for 4 h. Then DCM was removed under reduced pressure, the residue taken up in benzene (30 mL), NMM (0.181 g, 1.63 mmol) added and the mixture heated at 60°C for 13 h. After cooling, the benzene was evaporated under reduced pressure to leave a yellow-brown oily mixture which was separated by flash column chromatography eluting with 1:1 v/v ethyl acetate–hexane, to give (**14**), (**16**) and (**17**).

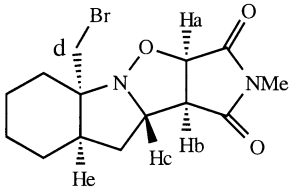
Compound (**14**): Obtained (42%) as a pale yellow thick oil (Found: C, 46.8; H, 6.2; N, 6.1; Br, 34.35 $C_9H_{14}BrNO$ requires: C, 46.55; H, 6.1; N, 6.05; Br, 34.4%); δ 7.26 (d, 1H, *J*=4.0 Hz, Ha), 3.48 (d, 1H, *J*=10.7 Hz, Hb), 3.24 (d, 1H, *J*=10.7 Hz, Hb), 2.40 (m, 1H, He), 2.15 (m, 1H, Hc), 1.68 (m, 1H, Hd) and 1.83–0.88 (m, 8H); *m/z* (%): 232 (M+1, 3), 151 (90), 137 (88), 106 (75), 92 (93), 67 (70), 55 (100) and 41 (86).



Enhancement (%)

Irradiated hydrogen	Ha	Hb1	Hb2	Hd	He
Ha				8.7	7.2
Hb1			16.5		
Hb2		17.3			
Hc		1.8	1.1		
He	3.8			21.8	

Compound (**16**): Obtained (18%) as colourless prisms from ether–petroleum ether, mp 197–199°C. (Found: C, 49.2; H, 5.6; N, 8.2, $C_{14}H_{19}BrN_2O_3$ requires: C, 40.0; H, 5.6; N, 8.15%); δ (400 MHz): 4.86 (d, 1H, *J*=7.5 Hz, Ha), 3.14–4.09 (m, 1H, Hc), 3.84 (d, 1H, *J*=11.0 Hz, Hd1), 3.62 (d, 1H, *J*=11.0 Hz, Hd2), 3.47 (d, 1H, *J*=7.5 Hz, Hb), 3.02 (s, 3H, NMe), 2.60 (m, 1H, He), 2.35 (m, 1H, CH_2), 1.90 (m, 1H, CH_2) and 2.32–0.95 (m, 8H); *m/z* (%): 344 (M^+, 4), 249 (100), 152 (21), 138 (11), 111 (10), 95 (22) and 41 (21).

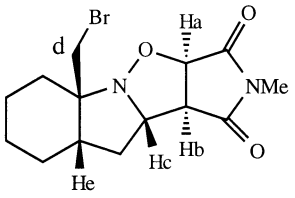


Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc	Hd1	He
Ha		8.3			
Hb	12.8		3.9		
Hc		3.9			
Hd				29.4	7.3
He	1.9			6.6	

Compound (**17**): Obtained (22%) as a pale yellow thick oil which solidified from petroleum ether–ether as an amorphous solid, mp 169–171°C. (Found: C, 48.85; H, 5.55; N, 7.9. $C_{14}H_{19}BrN_2O_3$ requires: C, 49.0, H, 5.6; N, 8.15%); δ (400 MHz), (C_6D_6): 4.18 (d, 1H, *J*=7.5 Hz, Ha), 3.74–3.70 (m, 1H, Hc), 2.94 and 2.91 (2d, 2H, *J*=11.0 Hz, Hd), 2.65 (dd, 1H, *J*=7.5 and 2.0 Hz, Hb), 2.54 (s, 3H, NMe) and 1.85–0.88 (m, 11H); *m/z* (%): 344 (M^+,

5), 279 (2), 262 (3), 249 (100), 149 (10), 122 (7), 108 (5) and 41 (8).



Enhancement (%)

Irradiated hydrogen	Ha	Hb	Hc
Ha		6.1	
Hb	7.5		4.0
Hc		2.7	
Hd			5.6

Acknowledgements

We thank Mersin University (Turkey) (H. A. D.) for leave of absence and Leeds University for support.

References

1. Part 51: Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Kennewell, P.; Thornton-Pett, M. *Tetrahedron* **2001**, *57*, 1119–1128.
2. Frederickson, M.; Grigg, R.; Markandu, J.; Redpath, J. *J. Chem. Soc., Chem. Commun.* **1994**, 2225–2226. Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J.; Thornton-Pett, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1388–1389. Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1340–1342. Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J. *J. Chem. Soc., Chem. Commun.* **1992**, 1537–1538.
3. Dondas, H. A.; Grigg, R.; Frampton, C. S. *Tetrahedron Lett.* **1997**, *38*, 5719–5722.
4. Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Thomas, W. A.; Kennewell, P. *Tetrahedron* **2000**, *56*, 10 087–10 096.
5. Oppolzer, W.; Siles, S.; Snowden, R. L.; Bakker, B. H.; Petrzilka, M. *Tetrahedron* **1985**, 3497–3509. Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660. Collins, I.; Fox, M. E.; Holmes, A. B.; Williams, S. F.; Baker, R.; Forbes, I. J.; Thompson, M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 175–182. Howard, C.; Newton, R. F.; Reynolds, D. P.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2049–2054.
6. Bordwell, F.; Kern, R. *J. Am. Chem. Soc.* **1955**, *77*, 1141–1150. Cope, A.; Esters, L. *J. Am. Chem. Soc.* **1950**, *72*, 1128–1132. Cope, A.; Liss, T.; Wood, G. *J. Am. Chem. Soc.* **1957**, *79*, 6287–6292. Bergbreiter, D. E.; Whitesides, G. M. *J. Org. Chem.* **1975**, *40*, 779–782.
7. McAndrew, B. A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1837–1846. Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1957**, *79*, 2828–2833. Cresson, P. *Bull. Soc. Chim. Fr.* **1964**, 2629–2635. Larock, R. C.; Oertle, K.; Potter, G. F. *J. Am. Chem. Soc.* **1980**, *102*, 190–197.