Cyclic nitronic esters from highly diastereoselective cycloaddition of 2-(4-morpholinyl)norbornene to conjugated nitroolefins

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Dedicated with warm regards to Miha Tišler on the occasion of his 75th birthday

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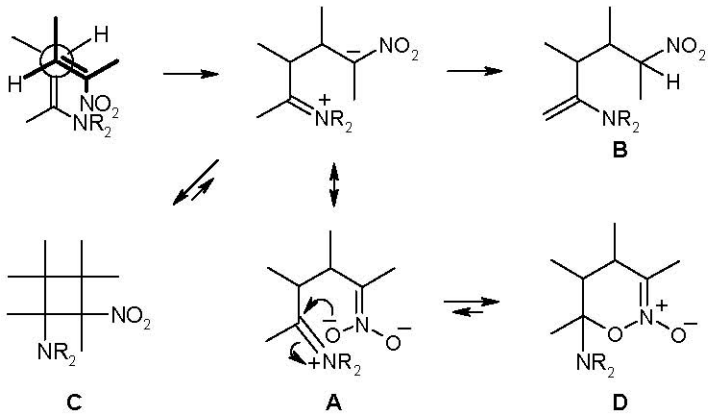
Abstract

The reactions of the morpholino enamine of 2-norbornanone towards a series of cyclic and acyclic conjugated nitroolefins resulted in the formation of the corresponding 1,2-oxazine N-oxides through an exo approach of the electrophiles. The stability of the heterocycles was strongly influenced by the nature of the substituents and in some cases it has been found to be unexpectedly high. Differently from analogous systems, opening of the heterocyclic ring to the corresponding enamine systems was not observed.

Keywords: Enamines, nitroolefins, 1,2-oxazine N-oxides, nitroalkylated norbornanones, 1,4-dicarbonyl compounds

Introduction

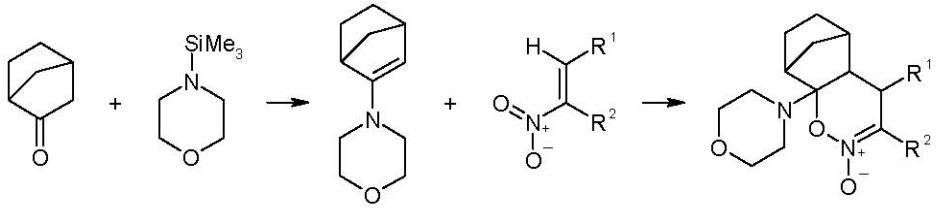
The versatility of the conjugated nitroalkenes as synthetic tools in their reactions with nucleophilic olefins is known.[1-9] In the particular case in which the reacting centres are prochiral, the approach of the two reactants can be either *like* or *unlike*[8] and the first step involves the diastereoselective formation of a new carbon-carbon bond in the resulting dipolar intermediate **A**. The fate of this species does depend on the nature of the reactants and it may lead to different products. The most common is a Michael-type adduct **B** whose formation derives from abstraction of a proton by the carbanion. Alternatively, the carbanion can collapse onto the iminium carbon atom producing a cyclic compound, which can be either a cyclobutane **C** or a 1,2-oxazine N-oxide **D**, through the nitronate form the betaine **A**, as a result of a formal [2+2] and a [4+2] cycloaddition reaction respectively. In most cases the cycloadducts were not stable and converted eventually to the system **B**, usually as the less substituted nitroalkylated enamine.[1,2,3]



The 1,2-oxazine N-oxide systems are of particular interest as this type of heterocycles are highly reactive reagents for 1,3-dipolar cycloadditions[4,8,9] and also as intermediates for the obtainment of γ-nitroketones[1,3,7,8] and γ-diketones[7] which are formed by hydrolysis under different reaction conditions. In this paper we present the synthesis, characterization and reactivity of interesting 1,2-oxazine N-oxides in which the heterocyclic ring is fused to the norbornane ring.

Results and Discussion

The enamine substrate used as a 2π component in this study was 2-(4-morpholinyl)bicyclo [2.2.1]heptene (**3**). It was prepared by condensation of 2-norbornanone (**1**) with trimethylsilyl morpholine (**2**) in the presence of *p*-toluenesulfonic acid as a catalyst, under gentle heating.[10]



1 **2** **3** **4a-k** **5b-k**

The 4π components were a series of cyclic and acyclic nitroolefins **4a-k** which are listed in Table 1 together with their geometry. The disubstituted nitroolefins were in *E* configuration with the exception of **4e** and **4i** which were mixtures of *E* and *Z* isomers in the ratio of 7:3 and 9:1 respectively.

Table 1. Cyclic and acyclic olefines

	R^1	R^2	$R^1CH=CR^2NO_2$ 4
a	H	H	Nitroethylene[11]
b	H	CH_3	2-Nitropropene[11]
c	H	Ph	α-Nitrostyrene[12]
d	CH_3	H	1-Nitropropene[11]
e	CH_3	CH_3	(*E*),(*Z*)-2-Nitro-2-butene[13]
f	CH_3	Ph	(*E*)-1-Nitro-1-phenylpropene[14]
g	Ph	H	(*E*)-β-Nitrostyrene
h	Ph	CH_3	(*E*)-2-Nitro-1-phenylpropene[15]
i	Ph	Ph	(*E*),(*Z*)-α-Nitrostilbene[16]
j	$(CH_2)_3$		1-Nitrocyclopentene[17]
k	$(CH_2)_4$		1-Nitrocyclohexene[17]

The reactions between **3** and **4a-k** were carried out at low temperatures in order to trap the heterocyclic intermediates. Actually the desired compounds **5** were isolated in all cases with the exception of the reaction of **3** with nitroethylene **4a** for which the corresponding nitroketones were obtained directly, although classically anhydrous conditions were used. The 1,2-oxazine N-oxide derivatives systems **5** showed in their IR spectra an intense $C=N^+-O^-$ stretching band in the region 1630-1570 cm^{-1},[18] the low frequency range being characteristic of those compounds, such as **5c**, **5f**, **5i** in which a phenyl group was in conjugation with the C=N double bond, while the higher frequency value was observed for **5j** and **5k** in which the double bond was external to a ring. All heterocycles were pure diastereomers. The only exception was the product derived from α-nitrostilbene, which was a 9:1 mixture of two diastereomers, **5i** and **5'i**. In all the cases examined the configuration of the heterocyclic ring was always *exo* with respect to the bicyclic ring, as proved by nOe difference spectroscopy measurements performed on **5g**, **5h**, **5i** and **5'i** (Figure 1). Prior to these measurements, proton decoupling experiments and two dimensional spectra allowed the correct assignments to all protons and carbon atoms (Experimental Section).

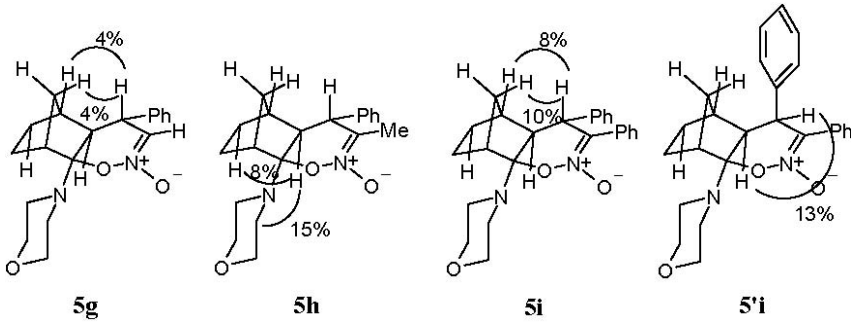


Figure 1

The configurational assignments for the other 1,2-oxazine N-oxide derivatives were then made by comparing the carbon shifts of the respective bicyclic rings, whose carbon atoms would have been particularly affected by a change in stereochemistry. The values of ^{13}C shifts of all compounds **5b-k** are listed in Table 2, which also includes the value found for **5'i**. Although numbering for **5j** and **5k** is different from that of **5b-i**, the carbon atoms occupying the same positions in the rings are listed in the same column for a better understanding.

From a comparison of these data it is evident that there is practically no difference in the absorption values of the bicyclic carbom atoms for all **5b-k**. This is particularly true for C-6, C-7 and C-9 which would have been shifted upfield if the configuration were *endo* and not *exo*. This observation also holds for **5'i** although its steric situation seems more crowded than that present in its isomer. A reason for this feature might be the $A^{1,2}$ strain between the two phenyl groups.[19] The nOe difference experiments performed on **5'i** accounted for a *cis* relationship of H-4 and H-4a (Figure 1). Also the value of J_{44a} (9.76 Hz) is in agreement with a *quasi* eclipsed situation of the protons in question as it is the upfield shift observed for the bridge protons H-9 when compared with those of **5i** (1.40, 0.82 ppm *vs* 2.35, 1.35 ppm) caused by the presence of the phenyl ring at C-4 facing the bridge.

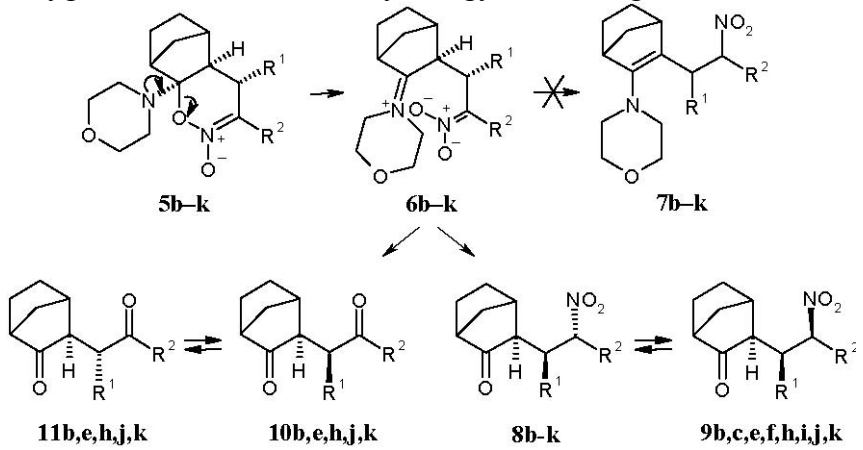
Table 2. The ^{13}C shifts for the 1,2-N-oxide derivatives 5b-k

	C-3	**C-4**	**C-4a**	**C-5**	**C-6**	**C-7**	**C-8**	**C-8a**	**C-9**
5b	124.9	31.9	46.7	42.7	28.0	23.5	45.0	112.4	34.8
5c	125.4	29.8	47.2	42.7	28.0	23.9	45.2	112.2	34.8
5d	120.5	32.9	55.3	41.7	28.0	23.6	44.8	113.2	35.4
5e	128.9	34.9	55.8	41.6	28.2	23.6	44.9	111.2	35.3
5f	128.7	35.6	55.9	41.9	28.2	24.0	45.4	111.5	35.5
5g	119.6	45.3	56.8	41.0	27.9	23.8	45.6	112.3	35.2
5h	128.7	48.4	55.7	41.2	28.1	23.7	45.5	110.6	35.1
5i	126.8	48.7	56.9	41.7	27.9	24.0	46.0	110.9	35.2
5'i	128.4	45.3	49.2	40.1	28.7	24.0	43.1	113.0	35.3
	C-3a	**C-9b**	**C-9a**	**C-9**	**C-8**	**C-7**	**C-6**	**C-5a**	**C-10**
5j	133.7	42.8	55.0	43.1	28.4	23.6	44.4	112.8	35.6
	C-6a	**C-10a**	**C-10b**	**C-1**	**C-2**	**C-3**	**C-4**	**C-4a**	**C-11**
5k	127.6	36.7	55.0	41.5	28.3	23.4	44.8	110.7	35.4

Finally, it should be mentioned that the steric encumbrance suffered by the morpholine ring in these systems is such that no rotation and no conformational change is possible, as demonstrated by the broadness of the proton and carbon signals as well as by the fact that nearly each proton and carbon atom of the morpholine ring showed a distinct resonance value.

The thermodynamic stability of the 1,2-oxazine N-oxides **5b-k** was much higher than that observed for other analogous systems fused to monocyclic rings. In fact most of them could be stored unaltered in the solid state at –20°C for long periods and some of them even in chloroform

solution at room temperature. Furthermore, differently from all the other systems previously studied, compounds **5b-k** did not open into the corresponding enamines **7b-k**, through the zwitterion intermediates **6b-k**, but this latter underwent hydrolysis to the corresponding nitroketones **8a-k**, **9a-k**. This is probably due to the fact that abstraction of the proton from C-3 by the nitronate oxygen would have been very energy demanding.



When the heterocycles having R^2 other than H were hydrolysed at pH 4-5, a mixture of the corresponding nitroketones **8** and **9** was obtained, in which however the less stable ketone prevailed. Evidently protonation of the nitronate carbon atom in the dipolar intermediate **6** was more or less diastereoselective. Only in a few cases it was possible to assign the correct geometry to the nitromethine carbon atom in the nitroketones (essentially by means of ^{13}C NMR spectroscopy, see Experimental Section) and hence to determine the preferite side of protonation. This was particularly evident in the case of the hydrolysis of **5k** for which the firstly formed mixture of diastereomeric nitroketones **8k** (nitromethine proton: W_H = 8.0 Hz) and **9k** completely equilibrated into **9k** having the nitro group equatorially oriented (nitromethine proton: W_H = 28.0 Hz).

Incidentally, it can be observed that hydrolysis of the 1,2-oxazine N-oxide **5e** carried out in acidic medium, albeit moderate, lead to the elimination of the nitro group, via a Nef-type reaction[7] and therefore its opening was accomplished by dissolution in CCl_4 and hydrolysis was then performed by the humidity of the air.

Hydrolyses of the 1,2-oxazine N-oxides **5b**,**e**,**h**,**j**,**k**, carried out at very low pH values, allowed the isolation of the corresponding *exo* diketones **10b**,**e**,**h**,**j**,**k** and **11b**,**e**,**h**,**j**,**k** through a Nef-type reaction. These latters differed in the configuration of C-1' because of a rapid epimerization of the stereocentre.

The *exo-endo* equilibration of the diastereomeric mixtures of the nitroketones and those of the diketones could be performed only on heating in refluxing toluene in the presence of *p*-toluenesulfonic acid as a catalyst. However, although the products were not separated, the *exo* isomers were always the major components in the mixtures. Equilibration under basic conditions could not be used owing to the presence of the nitro group in **8**, **9** and that of two carbonyl groups in **10**, **11** which would have lead to condensation products.

Conclusions

The reactivity of the enamine from norbornanone with conjugated nitroolefins showed an *exo* stereoselectivity, as a consequence of a less steric demand. In the case of nitroethylene a small amount (12%) of the *endo* nitroketone was detected. (The assignment followed from a comparison with the carbon shifts of 3-methyl-2-norbornanone,[20] see Experimental Section). When the nitroolefins were substituted, in their approach to the the enamine **3** the R^1 and R^2 substituents assumed preferably an *exo* orientation with respect to the bridge, in accordance with the topological rule by Seebach.[21] Therefore this type of attack can be defined *exo-exo*. The only exception to this rule was just the more hindered nitroolefin, namely **4i**, which approached the enamine also in an *exo-endo* fashion (10%).

Experimental Section

General Procedures. Melting points were determined with a Büchi SHP-20 apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$, unless otherwise stated, on a JASCO FT/IR-200 spectrometer. ^{1}H NMR spectra were run on a Jeol EX-400 (400 M Hz) spectrometer using deuterochloroform as a solvent and tetramethylsilane as internal standard; J value and WH are given in Hz. ^{13}C NMR spectra were recorded on a Jeol EX-400 (100.4 M Hz) instrument. GLC analyses were obtained on a Carlo Erba GC 8000 instrument, the capillary column being OV 1701 25 m x 0.32 mm (carrier gasHe 40KPa, split 1:50, 2 min at 100°C, 3°C/min, 200 °C), Mass spectra were run by the electron impact mode (20 eV and 70 eV) on a VG 7070 spectrometer. TLC were performed on Whatman K6F silica gel plates (eluant: light petroleum/ethyl acetate). Flash chromatography was run on silica gel 230-400 mesh ASTM (Kieselgel 60, Merck) (Eluant: light petroleum/ethyl acetate, gradient from 100/0 to 90:10). Light petroleum refers to the fraction with b.p. 40-70 °C and ether to diethyl ether.

The enamine 2-(4-morpholinyl)bicyclo[2.2.1]heptene **3** was prepared in accordance with the literature.[10] B. p. 95-6 °C, 1.5 Torr (55% yield); IR, ν cm-1: 1598 (N-C=C), 1110 (C-O-C); ^{1}H-NMR δ 4.53 (1H, d, *J* = 3.1 Hz, H-3), 3.68 (4H, t, CH_2OCH_2), 2.88 (1H, m, H-1), 2.86-2.80 (2H, m, CH_2N), 2.76 (3H, m, CH_2N, H-4), 1.66 (1H, m, H 5), 1.57 (1H, m, H-6), 1.34 (1H, m, H-7), 1.07 (3H, m, H-5, H-6, H-7); ^{13}C NMR, δ 158.1 (s, C-2), 102.5 (d, C-3), 66.5 (t, CH_2OCH_2), 48.9 (t, CH_2NCH_2), 47.0 (d, C-7), 41.5 (d, C-1), 40.9 (d, C-4), 28.1 (t, C-5), 25.1 (t, C-6).

The nitroolefins **4a-k** were prepared by the procedures indicated in Table 1. β-Nitrostyrene was purchased from Aldrich.

Reactions with the nitroolefins

To a solution of the enamine **3** (1.0 g, 5.6 mmoles) in anhydrous ether was added dropwise a solution of the nitroolefin (5.6 mmoles) in the same solvent, at -45°C, under argon. The reaction mixture was kept at -30°C for 12 h. When a precipitate was formed it was filtered off.

Hydrolyses of the 1,2-oxazine N-oxide derivatives. The pH value of a methanol-water solution of the 1,2-oxazine N-oxides was adjusted to 4-5 (or 2) by adding 1N HCl. The resulting mixture was extracted three times with ether, the organic extracts washed with dilute sodium bicarbonate and water. After removal of the solvent the residue was purified either by column chromatography or by crystallization. In the case of **5e**, the heterocycle underwent rapid Nef reaction even at pH 5 and therefore opening was achieved by dissolution in carbon tetrachloride.

Reaction of the enamine 3 with nitroethylene 4a

The ^{1}H NMR spectrum of the oily crude reaction mixture showed the presence of two diastereomers, **8a** and **8'a** in the ratio of 88:12 (HRGC: **8a**: RT = 25.3 min; **8'a**: RT = 25.4 min) which were separated by flash chromatography. Anal. Calcd. for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 58.63; H, 7.01; N, 7.80.

***exo*-3-(2-Nitroethyl)bicyclo[2.2.1]heptan-2-one (8a).** Oil; IR, ν 1735 (C=O), 1540, 1375 (NO_2) cm^{-1}; 1H NMR, δ 4.50 (2H, t, J = 7.3 Hz, CH_2NO_2), 2.53 (1H, bd, H-1), 2.35 (1H, bd, H-4), 2.06 (2H, m, C*H*$_2$CH$_2$NO$_2$), 1.80 (3H, m, H-5, H-6, H-7), 1.71 (1H, dt, J_1 = 8.3, J_2 = 3.4 Hz, H-3), 1.44 (3H, m, H-5, H-6, H-7); ^{13}C NMR, δ 218.0 (s), 73.5 (t, CH_2NO_2), 49.7 (d, C-3), 49.3 (d, C-1), 39.7 (d, C-4), 34.7 (t, C-7), 27.8 (t, C-5), 26.8 (t, *C*H$_2$CH$_2$NO$_2$), 23.4 (t, C-6).

***endo*-3-(2-Nitroethyl)bicyclo[2.2.1]heptan-2-one (8'a).** Oil; IR, ν 1738 (C=O), 1550, 1378 (NO_2) cm^{-1}; ^{1}H NMR δ 4.50 (2H, t, J = 6.8 Hz, CH_2NO_2), 2.58, 2.56 (2H, bd, H-1, and bs, H-4), 2.19 (1H, m, C*H*CH$_2$NO$_2$), 1.97 (1H, m, H-3), 1.92 (1H, m, C*H*CH$_2$NO$_2$), 1.86 (1H, m, H-6), 1.65 (2H, m, H-5, H-7), 1.50 (2H, m, H-5, H-7), 1.39 (1H, m, H-6); ^{13}C NMR , δ 217.9 (s), 73.9 (t, CH_2NO_2), 50.1 (2d, C-3, C-1), 38.7 (d, C-4), 36.8 (t, C-7), 25.3 (t, C-6), 24.6 (t, *C*H$_2$CH$_2$NO$_2$), 21.1 (t, C-5).

Reaction of the enamine 3 with 2-nitropropene 4b

(4aR*,5S*,8R*,8aS*)-3-Methyl-8a-(4-morpholinyl)-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine *N*-oxide (5b). The heterocycle **5b** was isolated as a white crystalline product, mp 125-127 °C (72%); IR, ν: 1610 (C=N$^+$-O$^-$), 1110 (C-O-C) cm^{-1}, ^{1}H NMR, δ 3.69 (2H, 2 b signals, CHOCH), 3.40 (2H, 2 b signals, CHOCH), 3.04, 2.82, 2.59 (4H, 4 b signals, CH_2NCH_2), 2.47 (1H, d, J = 2.2 Hz, H-8), 2.34 (1H, dd, J_1 = 7.8 Hz, J_2 = 15.6 Hz, H-4), 2.20 (1H, ddd, J_1 = 15.6, J_2 = 9.8, J_3 = 1.5 Hz, H-4), 2.10 (2H, m, H-4a, and d, J = 9.8 Hz, H-9), 2.02 (1H, d, J = 2.2 Hz, H-5), 1.93 (3H, d, J = 1.5 Hz, CH3), 1.60 (2H, m, H-6, H-7), 1.32 (1H, m, H-7), 1.23 (2H, m, H-6, and d, J = 9.8 Hz, H-9); ^{13}C NMR δ 124.9 (s, C-3), 112.4 (s, C-8a), 67.6 (t, CH_2O), 66.8 (t, CH_2O), 46.8 (t, CH_2NCH_2), 46.7 (d, C-4a), 45.0 (d, C-8), 42.7 (d, C-5), 34.8 (t, C-9), 31.9 (t, C-4), 28.0 (t, C-6), 23.5 (t, C-7), 17.5 (q, CH_3). Anal. Calcd. for $C_{14}H_{22}N_2O_3$: C 63.14, H 8.33, N 10.52. Found: C 63.17, H 8.36, N 10.46.

***exo*-3-(2-Nitropropyl)bicyclo[2.2.1]heptan-2-one (8b) and (9b).** An inseparable mixture of two diastereomers in the ratio of 55:45 were isolated from the hydrolysis carried out at pH 4-5. Oil; IR (neat) ν 1725 (C=O), 1545, 1370 (NO_2) cm^{-1}; Although they were not separated, their NMR data are given separately for sake of clarity. ^{1}H NMR, δ **major isomer**: 4.76 (1H, m, $CHNO_2$), 2.55 (1H, b signal, H-1), 2.44 (1H, bd, H-4), 2.22 (1H, m, H-1'), 1.82 (3H, m, H-5,

H.6, H-7), 1.69 (2H, m, H-1', H-3), 1.5 (5H, m H-6, H-7 and at 1.52, d, J = 6.7 Hz, CH_3), 1.44 (1H, m, H-5); ^{13}C NMR δ 217.6 (s,), 81.2 (d, $CHNO_2$), 49.5 (d, C-3), 49.2 (d, C-1), 39.7 (d, C-4), 34.70 (t, C-7), 34.5 (t, CH_2CHNO_2), 27.86 (t, C-5), 23.39 (t,), 19.8 (q, CH_3); **minor isomer**: 1H NMR, δ 4.85 (1H, m, $CHNO_2$), 2.55 (1H, b signal, H-1), 2.32 (1H, bd, H-4), 2.05 (1H, ddd, H-1'), 1.82 (4H, m, H-1', H-5, H.6, H-7), 1.70 (1H, m, H-3), 1.52 (5H, m H-6, H-7 and at 1.57, d, J = 6.7 Hz, CH_3), 1.44 (1H, m, H-5); ^{13}C NMR, δ 218.2 (s,), 82.3 (d, $CHNO_2$), 50.0 (d, C-3), 49.3 (d, C-1), 39.7 (d, C-4), 34.66 (t, C-7), 34.2 (t, CH_2CHNO_2), 27.82 (t, C-5), 23.45 (t, C-6), 19.0 (q, CH_3). Anal. Calcd. for its 2,4-dinitrophenylhydrazone, m.p. 171-173 °C: $C_{16}H_{19}N_5O_6$: C 50.93, %H 5.08, %N 18.56. Found: C 50.87, %H 5.07, %N 18.30.

***exo*-3-(2-Oxopropyl)bicyclo[2.2.1]heptan-2-one (10b).** Yellow oil (HRGC: RT = 15.8 min); IR, ν: 1710, 1730 (C=O) cm^{-1}; ^{1}H NMR δ 2.68 (1H, dd, J_1 = 3.4 Hz, J_2 = 17.1 Hz, CHCO), 2.55 (1H, bd, H-1), 2.39 (1H, bd, H-4), 2.30 (1H, dd, J1 = 10.7, J2 = 17.1, CHCO), 2.27 (1H, dt, J_1 = 3.4 Hz, J_2 = 3.4 Hz, J3 = 10.7 Hz, H-3), 2.17 (3H, s, $COCH_3$), 1.83 (2H, m, H-5, H-6), 1.75 (1H, bd, J = 10.7 Hz, H-7), 1.57 (2H, m, H-5, H-6), 1.51 (1H, bd, J = 10.7 Hz, H-7); ^{13}C NMR δ 219.2 (s), 206.1 (s), 49.3 (d, C-1), 48.6 (d, C-3), 42.6 (t, CH_2COCH_3), 39.4 (d, C-4), 34.4 (t, C-7), 29.8 (q, CH_3), 27.8 (t, C-5), 23.2 (t, C-6). Anal. Calcd. for $C_{10}H_{14}O_2$: C 72.26, H 8.49. Found: C 71.83, H 8.14.

Reaction of the enamine 3 with α-nitrostyrene 4c

(4aR*,5S*,8R*,8aS*)-8a-(4-Morpholinyl)- 3-phenyl-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine N-oxide (5c). mp 115 °C (41% yield).; IR, ν 1570 (C=N$^+$-O$^-$), 1110 (C-O-C), 1590, 760 (Ph) cm^{-1}; ^{1}H NMR δ 7.96 (2H, d, J = 7.8 Hz, *o*-ArH), 7.36 (3H, m, *m*-, *p*-ArH), 3.83, 3.66 (2H, 2 bd, CHOCH), 3.46, 3.37 (2H, 2 bt, CHOCH), 3.26, 3.14 (2H, 2 bt, CHNCH), 3.05 (1H, dd, J1 = 7.3 Hz, J2 = 14.6 Hz, H-4), 2.93 (1H, bd, CHN), 2.82 (1H, bd, CHN), 2.64 (1H, d, J = 3.4 Hz, H-8), 2.48 (1H, dd, J_1 = 10.5, J_2 = 14.6 Hz, H-4), 2.26 (2H, dd, J1 = 10.5, J_2 = 7.3 Hz, H-4a, and d, J = 9.4 Hz, H-9), 2.21 (1H, d, J = 3.4 Hz, H-5), 1.70 (2H, m, H-6, H-7), 1.46 (1H, m, H-7), 1.33 (2H, m, H-6$_{ax}$, and d, J = 9.4 Hz, H-9,); ^{13}C NMR δ 131.0 (s), 128.9 (d), 128.3 (2d), 127.3 (2d), 125.4 (s, C-3), 112.2 (s, C-8a), 67.6 (t, CH_2O), 66.9 (t, CH_2O), 47.2 (d, C-4a), 47.2, 47.0 (t, CH_2NCH_2), 45.2 (d, C-8), 42.7 (d, C-5), 34.8 (t, C-9), 29.8 (t, C-4), 28.0 (t, C-6), 23.9 (t, C-7). Anal. Calcd. for $C_{19}H_{24}N_2O_3$: C, 69.49; H, 7.37; N, 8.53. Found: C, 70.01; H, 7.41; N 8.45.

***exo*-3-(2-Nitroethyl-2-phenyl)bicyclo[2.2.1]heptan-2-one (8c) and (9c).** The hydrolysis product from **5c** was isolated as a 55:45 mixture of two diastereomers. Pale yellow oil. Although they were not separated, their spectra are given separately for sake of clarity. **Major isomer:** ^{1}H NMR, δ 7.42 (1H, m, *o*-ArH), 7.26 (3H, m, *m*-, *p*-ArH), 5.73 (1H, m, $CHNO_2$), 2.49 (2H, m and bs, C*H*$CHNO_2$, H-1), 2.27 (1H, bd, H-4), 2.10 (1H, m, C*H*$CHNO_2$), 1.72 (3H, m, H-5, H-6, H-7), 1.55 (1H, dt, J1 = 7.6 Hz, J2 = 7.6 Hz, J3 = 3.0 Hz, H-3), 1.40 (2H, m, H-6, H-7), 1.25 (1H, m, H-5); ^{13}C NMR, δ 217.8 (s), 133.9 (s), 129.8 (2d), 128.9 (2d), 127.8 (2d), 127.4 (2d), 88.4 (d, $CHNO_2$), 49.2 (d, C-3), 49.0 (d, C-1), 39.7 (d, C-4), 34.7 (t, C-7), 33.3 (t, C-1'), 27.7 (t, C-5), 23.3 (t, C-6); **minor isomer**: ^{1}H NMR δ 7.36 (2H, m, *o*-ArH), 7.26 (3H, m, *m*-, *p*-ArH), 5.73 (1H, m, $CHNO_2$), 2.49 (2H, m and bs, C*H*$CHNO_2$, H-1), 2.34 (1H, bd, H-4), 2.10 (1H, m,

C*H*CHNO$_2$), 1.72 (3H, m, H-5, H-6, H-7), 1.38 (3H, m, H-3, H-5, H-6); ^{13}C NMR, δ 218.0 (s), 134.2 (s), 129.8 (2d), 129.0 (2d), 127.8 (2d), 127.3 (2d), 89.2 (d, CHNO$_2$), 49.6 (d, C-3), 49.4 (d, C-1), 39.5 (d, C-4), 34.8 (t, C-7), 33.4 (t, C-1'), 27.7 (t, C-5), 23.4 (t, C-6). Anal. Calcd. for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 68.83; H, 6.71; N 5.48.

Reaction of the enamine (3) with 1-nitropropene 4d

(4S*,4aS*,5S*,8R*,8aS*)-4-Methyl-8a-(4-morpholinyl)-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine *N*-oxide (5d). It was isolated as a white solid, m.p 56-58 °C (63% yield). In spite of its instability in chloroform, the 1,2-oxazine N-oxide **5d** was identified spectroscopically as a single diastereomer. IR, ν 1610 (C=N$^+$-O$^-$), 1110 (C-O-C) cm^{-1}; ^{1}H NMR δ 6.18 (1H, d, *J* = 3.4 Hz, H-3), 3.80, 3.73 (2H, 2 bd, CHOCH), 3.54, 3.44 (2H, 2 bt, CHOCH), 3.18 (2H, 2 bt, CHNCH), 3.03, 2.76 (2H, 2 bd, CHNCH), 2.55 (1H, d, *J* = 2.9 Hz, H-8), 2.39 (1H, m, H-4), 2.23 (1H, d, *J* = 2.9 Hz, H-5), 2.13 (1H, d, *J* = 9.8 Hz, H-9), 1.73 (2H, m, H-4a, H-7), 1.55 (1H, m, H-6), 1.44 (1H, m, H-7), 1.32 (2H, m, H-6, and d, *J* = 9.8 Hz, H-9), 1.21 (3H, d, *J* = 7.3 Hz, CH$_3$); ^{13}C NMR δ 120.5 (d, C-3), 113.2 (s, C-8a), 67.0 (t, CH$_2$O), 66.8 (t, CH$_2$O), 55.3 (d, C-4a), 47.2 (t, CH$_2$N), 46.7 (t, CH$_2$N), 44.8 (d, C-8), 41.7 (d, C-5), 35.4 (t, C-9), 32.9 (d, C-4), 28.0 (t, C-6), 23.6 (t, C-7), 17.1 (q, CH$_3$). Anal. Calcd. for $C_{14}H_{22}N_2O_3$: C, 63.14; H, 8.33; N, 10.52. Found: C, 63.03; H 8.11; N 10.42.

(1R*,3S*,4S*,1'S*)-*Exo*-3-(1-methyl-2-nitroethyl)bicyclo[2.2.1]heptan-2-one (8d). A single diastereomer was isolated from hydrolysis of **5d** at pH 4-5. Colorless crystalline product, m.p. 36 °C (HRGC: RT = 26.0 min); IR, ν 1720 (C=O), 1545, 1370 (NO$_2$) cm^{-1}; ^{1}H NMR δ 4.92 (1H, dd, *J*1 = 4.7, *J*2 = 12.7 Hz, CHNO$_2$), 4.26 (1H, dd, J_1 = 9.0, J_2 = 12.7 Hz, CHNO$_2$), 2.60 (2H, m, H-1, H-4), 2.40 (1H, m, C*H*CH$_3$), 1.87 (3H, m, H-5, H-6, H-7), 1.57 (3H, m, H-3, H-6, H-7), 1.42 (1H, m, H-5), 1.07 (3H, d, *J* = 6.7 Hz, CH$_3$); ^{13}C NMR δ 218.0 (s), 79.45 (t, CH$_2$NO$_2$), 55.5 (d, C-3), 49.6 (d, C-1), 38.1 (d, C-4), 34.8 (t, C-7), 31.8 (d, *C*HCH$_3$), 28.0 (t, C-5), 24.2 (t, C-6), 16.7 (q, CH$_3$). Anal. Calcd. for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.57; H, 7.70; N, 6.96.

Reaction of the enamine 3 with 2-nitro-2-butene 4e

(4S*,4aS*,5S*,8R*,8aS*)-3,4-Dimethyl-8a-(4-morpholinyl)-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine *N*-oxide (5e). The heterocycle **5e** was isolated as a white crystalline product, mp 119-121 °C (63%); IR, ν cm^{-1}: 1610 (C=N$^+$-O$^-$), 1110 (C-O-C); ^{1}H NMR δ 3.82 (1H, bd, CHO), 3.73 (1H, bd, CHO), 3.51 (1H, bt, CHO), 3.41 (1H, bt, CHO), 3.18, 3.10 (2H, 2 bt, CH$_2$N), 2.84 (1H, bd, CHN), 2.76 (1H, bd, CHN), 2.55 (1H, d, *J* = 2.9 Hz, H-8), 2.40 (1H, dqq, J_1 = 9.7 Hz, J_2 = 7.3, J_3 = 2.2, Hz, H-4), 2.23 (1H, d, *J* = 2.9 Hz, H-5), 2.18 (1H, bd, *J* = 9.7 Hz, H-9,), 2.00 (3H, d, *J* = 2.2 Hz, CH$_3$ at C-4), 1.69 (3H, m, , H-6, H-7), 1.41 (1H, m, H-7), 1.33-1.4 (2H, m, H-6, and bd, *J* = 10.6 Hz, H-9), 1.21 (3H, d, *J* = 7.3 Hz, CH$_3$ at C-3); ^{13}C NMR δ 128.9 (s, C-3), 111.2 (s, C-8a), 67.7 (t, CH$_2$O), 66.8 (t, CH$_2$O), 55.8 (d, C-4a), 46.8 (t, CH$_2$NCH$_2$), 44.9 (d, C-8), 41.6 (d, C-5), 35.3 (t, C-9), 34.9 (t, C-4), 28.2 (t, C-6), 23.6 (t, C-7), 16.1 (q, CH$_3$ at C-3), 16.1 (q, CH$_3$ at C-4). Anal. Calcd. for $C_{15}H_{24}N_2O_3$: C 64.26, H 8.63, N 9.99. Found: C 63.87, H 8.16, N 10.16.

***exo*-3-(1-Methyl-2-nitropropyl)bicyclo[2.2.1]heptan-2-one (8e) and (9e).** Opening of the heterocycle **5e** was accomplished by dissolving it in CCl_4: a 7:3 mixture of **8e** and **9e** was obtained. Oil; IR ν 1739, (C=O), 1543, 1391, 1370 (NO_2) cm^{-1}.. Although they were not separated, the NMR data of the diastereomers are given separately. Compound **8e**, **major component**: ^{1}H NMR, δ 5.04 (0.3H, dq, J_1 = 6.9, J_2 = 4.0 Hz, $CHNO_2$), 2.52 (1H, bd, H-1), 2.45 (1H, bs, H-4), 2.35 (1H, m, C*H*CH_3), 1.94 (1H, dd, J_1 = 8.6, J_2 = 3.1 Hz, H-3), 1.89 (1H, bd, *J* = 9.2 Hz, H-7), 1.80 (2H, m, H-5, H-6), 1.46 (5H, m, H-6, H-7 and d, *J* = 6.2 Hz, C*H*$_3$$CHNO_2$), 1.39 (1H, m, H-5), 0.92 (3H, d, *J* = 6.9 Hz, C*H*$_3$CH); ^{13}C NMR δ 217.9 (s), 84.0 (t, CH_2NO_2), 53.8 (d, C-3), 49.2 (d, C-1), 37.1 (d, C-4), 36.9 (d, *C*HCH3), 34.9 (t, C-7), 28.5 (t, C-5), 23.02 (t, C-6), 17.0 (q, *C*$H_3$$CHNO_2$), 12.6 (q, CH*C*$H_3$). Compound **9e**, **minor component**: ^{1}H NMR δ 4.95 (1H, dq, J_1 = 6.9, J_2 = 4.8 Hz, $CHNO_2$), 2.55 (1H, bd, H-1), 2.48 (2H, bs H-4), 2.42 (1H, m, C*H*CH_3), 1.89 (1H, bd, *J* = 9.2 Hz, H-7), 1.80 (2H, m, H-5, H-6), 1.44 (6H, m, H-3, H-6, H-7 and d, *J* = 6.6 Hz, C*H*$_3$$CHNO_2$), 1.39 (1H, m, H-5), 0.88 (3H, d, *J* = 7.0 Hz, C*H*$_3$CH); ^{13}C NMR δ 218.3 (s), 84.5 (t, CH_2NO_2), 55.2 (d, C-3), 49.8 (d, C-1), 38.1 (d, C-4), 36.7 (d, *C*HCH_3), 35.0 (t, C-7), 28.0 (t, C-5), 24.0 (t, C-6), 12.8 (q, CH*C*H_3), 12.2 (q, *C*$H_3$$CHNO_2$). Anal. Calcd. for $C_{11}H_{17}$NO3: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.70; H, 8.15; N, 6.80. The composition of the mixture changed from 7:3 to 3:7 on standing in $CDCl_3$ for 96 h.

(1R*,3S*,4S*,1'S*)-*exo*-3-(1-Methyl-2-oxopropyl)bicyclo[2.2.1]heptan-2-one (10e) and **(1R*,3S*,4S*,1'R*)-*exo*-3-(1-Methyl-2-oxopropyl)bicyclo[2.2.1]heptan-2-one (11e)**

Compound **10e**: oil; IR, ν 1710, 1730 (C=O) cm^{-1}: ^{1}H NMR δ 2.53 (3H, m, H-1, H-4, C*H*CH_3), 2.18 (3H, s, COC*H*$_3$), 2.16 (1H, dd, H-3), 1.90-1.72 (3H, m, H-5, H-6, H-7), 1.49 (3H, m, H-5, H-6, H-7). ^{13}C NMR δ 218.5 (s), 210.4 (s), 55.2 (d, C-3), 49.1 (d, C-1), 45.7 (d, C-4), 36.9 (d, *C*HCH_3), 34.9 (t, C-7), 28.9 (q, CO*C*H3), 28.8 (t, C-5), 23.3 (t, C-6), 15.1 (q, CH*C*H3). Anal. Calcd. for $C_{11}H_{16}O_2$: C 73.30 , H 8.95. Found: C 72.98 , H 8.64. On standing in $CDCl_3$, an equilibration occurred and a 55:45 mixture of **10e** and **11e** were obtained. Compound **11e** was identified only spectroscopically: ^{1}H NMR, δ 2.23 (0.45H, bs, H-4), 2.12 (1.35H, s, $COCH_3$), 1.94 (0.45H, dd, H-3), 1.22 (1.35H, d, J = 6.9 Hz, $CHCH_3$) (The other signals overlapped with those of **10e**); ^{13}C NMR, δ 217.9 (s), 211.9 (s), 54.8 (d, C-3), 50.1 (d, C-1), 46.7 (d, C-4), 39.5 (d, *C*HCH_3), 34.7 (t, C-7), 28.6 (t, C-5), 28.3 (q, CO*C*H_3), 23.7 (t, C-6), 15.2 (q, CH*C*H_3).

Reaction of the enamine (3) with 1-nitro-1-phenylpropene 4f

(4S*,4aS*,5S*,8R*,8aS*)-4-Methyl-8a-(4-morpholinyl)-3-phenyl-4a,5,6,7,8,8a-hexahydro-5,8-methano-4*H*-1,2-benzoxazine *N*-oxide (5f). Yellow solid; m.p. 153-155 °C (62% yield); IR, ν 1590 (C=N$^+$-O$^-$), 1110 (C-O-C), 705 (Ph) cm^{-1}; ^{1}H NMR, δ 7.38 (5H, m, Ph), 3.82 (2H, 2 bd, CHOCH), 3.55 (2H, 2 bt, CHOCH), 3.40 (1H, bt, CHN), 3.20 (2H, bd, CHNCH), 2.80 (1H, bd, CHN), 2.76 (1H, dq, *J* = 6.9 Hz, 8.8 Hz, H-4), 2.65 (1H, d, *J* = 2.9 Hz, H-8), 2.28 (1H, d, *J* = 4.4 Hz, H-5), 2.25 (1H, bd, *J* = 10.7 Hz, H-9), 1.90 (1H, bd, *J* = 8.8, H-4a), 1.71 (2H, m, H-6, H-7), 1.44 (1H, tt, H-7), 1.35 (2H, m, H-6 and bd, *J* = 10.7 Hz, H-9), 1.04 (3H, d, *J* = 6.9 Hz, CH_3); ^{13}C NMR, δ 130.9 (s), 128.7 (s, C-3 and d, *p*-ArH), 128.3 (2d), 128.2 (2d), 111.5 (s, C-8a), 67.7 (t, CH_2O), 66.9 (t, CH_2O), 55.8 (d, C-4a), 47.9 (t, CH_2N), 46.9 (t, CH_2N), 45.4 (d, C-8), 41.9 (d, C-5), 35.6 (d, C-4), 35.5 (t, C-9), 28.2 (t, C-6), 24.0 (t, C-7), 17.8 (q, CH_3). Anal. Calcd. for

$C_{20}H_{26}N_2O_3$: C, 70.15; H, 7.65; N, 8.18. Found: C, 69.88; H, 7.48; N, 8.31.

***exo*-3-(1-Methyl-2-nitro-2-phenylethyl)bicyclo[2.2.1]heptan-2-one *(*8f) and (9f).** Hydrolysis of the 1,2-oxazine N-oxide **5f** carried out at pH 4-5 furnished a 1:3 mixture of the corresponding diastereomeric nitroalkylated ketones **8f** and **9f** (HRGC: RT_1 = 26.4 min, RT_2 = 27.3 min). Crystalline product, m.p. 110 °C; IR, ν, 1730 (C=O), 1550, 1370 (NO2) cm-[1]; Although they were not separated, their NMR data are given separately for sake of clarity. **Major isomer**: ^{1}H NMR δ 7.47, 7.41 (5H, 2 m, ArH), 5.50 (1H, d, *J* = 9.8 Hz, CHNO2), 3.02 (1H, m, C*H*CH_3), 2.60 (1H, bd, H-4), 2.46 (1H, bd, H-1), 1.94 (1H, bd, *J* = 10.8 Hz, H-7), 1.84 (2H, m, H-5, H-6), 1.66 (1H, dd, J_1 = 6.0 Hz, J_2 = 3.3 Hz, H-3), 1.54 (2H, m, H-6, H-7), 1.39 (1H, m, H-5), 0.72 (3H, d, *J* = 7.0 Hz, CH_3); 13C NM δ, 217.5 (s), 133.1 (s), 129.8 (d), 129.2 (d), 128.9 (2d), 128.6 (2d), 94 0 (d, CHNO2), 54.4 (d, C-3), 48.9 (d, C-1), 36.7 (d, C-4, *C*HCH_3), 35.6 (t, C-7), 29.3 (t, C-5), 23.7 (t, C-6), 14.1 (q, CH_3); **minor isomer**: ^{1}H NMR δ 7.47, 7.41 (5H, 2 m, ArH), 5.33 (1H, d, *J* = 11.0 Hz, $CHNO_3$), 3.02 (1H, m, C*H*CH_3), 2.51 (1H, bd, H-1), 2.48 (1H, bs, H-4), 1.82 (1H, bd, *J* = 11.1 Hz, H-7), 1.72 (2H, m, H-5, H-6), 1.50 (1H, bd, *J* = 11.1 Hz, H-7), 1.40 (1H, m, H-3), 1.32 (1H, m, H-6), 1.02 (3H, d, *J* = 6.7 Hz, CH_3); ^{13}C NMR δ 217.1 (s), 133.2 (s), 130.1 (d), 129.2 (2d), 128.0 (2d), 96.2 (d, $CHNO_2$), 52.3 (d, C-3), 48.3, (d, C-1), 37.3 (d, *C*HCH_3), 35.7 (t, C-7), 35.2 (d, C-4), 29.6 (t, C-5), 23.1 (t, C-6), 13.9 (q, CH_3); Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H 7.01; N, 5.12. Found: C, 69.18; H, 6.95; N 5.06. On standing in $CDCl_3$ the composition of the mixture changed from 1:3 to 1:1.

Reaction of the enamine 3 with β-nitrostyrene 4g

(4R*,4aS*,5S*,8R*,8aS*)-8a-(4-Morpholinyl)-4-phenyl-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine *N*-oxide (5g). White crystalline product, m. p 101 °C (65% yield); IR, ν 1600 (C=N^+-O^-), 1110 (C-O-C), 770, 700 (Ph) cm^{-1}; ^{1}H NMR δ 7.35 (3H, m, *m*-, *p*-ArH), 7.21 (2H, d, *o*-ArH), 6.46 (1H, d, *J* = 3.9 Hz, H-3), 3.84 (2H, bm, CHOCH), 3.48 (4H, m, CHOCH, CHN, H-4), 3.25 (2H, m, C*H*NCH, CHNC*H*), 2.84 (1H, m, CHN), 2.65 (1H, d, *J* = 2.4 Hz, H-8), 2.29 (1H, d, J = 10.7 Hz, H-9), 2.25 (1H, d, *J* = 3.9 Hz, H-5), 2.16 (1H, d, *J* = 9.8 Hz, H-4a), 1.68 (1H, m, H-7ax), 1.59 (1H, m, H-6eq), 1.43 (1H, m, H-7eq), 1.39 (1H, d, *J* = 10.7 Hz, H-9), 1.19 (1H, m, H-6eq); ^{13}C NMR δ 139.7 (s), 129.2 (2d), 128.0 (2d), 127.7 (d), 119.6 (d, C-3), 112.3 (s, C-8a), 67.6 (t, CH_2O), 66.8 (t, CH_2O), 56.8 (d, C-4a), 47.4 (t, CH_2N), 47.0 (t, CH_2N), 45.6 (d, C-8), 45.3 (d, C-4), 41.0 (d, C-5), 35.2 (t, C-9), 27.9 (t, C-6), 23.8 (t, C-7). Anal. Calcd. for $C_{19}H_{24}N_2O_3$: C, 69.49; H, 7.37; N, 8.53. Found: C, 69.28; H, 7.40; N, 8.61.

(1R*,3S*,4S*,1'R*)-*exo*-3-(2-Nitro-1-phenylethyl)bicyclo[2.2.1]heptan-2-one (8g). Yellow solid, m.p. 60-62 °C; IR, ν 1730 (C=O), 1550, 1370 (NO_2) cm^{-1}; ^{1}H NMR δ 7.31 (3H, m, *m*-, *p*-ArH), 7.17 (2H, d, *J* = 7.6 Hz, *o*-ArH), 5.31 (1H, dd, J_1 = 4.6, J_2 = 13.1 Hz, $CHNO_2$), 4.64 (1H, dd, J_1 = 11.3, J_2 = 13.1 Hz, $CHNO_2$), 3.50 (1H, dt, J_1 = 11.3, J_2 = 4.6 Hz, C*H*Ph), 2.68 (1H, d, *J* = 4.6 Hz, H-1), 2.04 (1H, d, J = 3.1 Hz, H-4), 1.97 (2H, dd, J_1 = 3.1, J_2 = 11.3 Hz, H-3, and bd, *J* = 9.8 Hz, H-7), 1.82 (1H, tt, H-6), 1.72 (1H, tt, H-5), 1.55 (1H, m, H-5, H-6), 1.45 (1H, bd, J = 9.8 Hz, H-7), 1.33 (1H, m, H-5); ^{13}C NMR δ 217.6 (s), 138.0 (s), 129.1 (2d), 128.0 (d), 127.7 (2d), 79.0 (t), 55.0 (d), 50.0 (d), 43.3 (d), 38.8 (d), 34.6 (t), 27.8 (t), 24.3 (t). Anal. Calcd. for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.10; H, 6.65; N, 5.57.

Reaction of the enamine 3 with 2-nitro-1-phenylpropene 4h

(4S*,4aS*,5S*,8R*,8aS*)-3-Methyl-8a-(4-morpholinyl)-4-phenyl-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2- benzoxazine *N*-oxide (5h). White crystalline product, m.p. 176 °C (81% yield); IR, ν 1590 (C=N^+-O^-), 1110 (C-O-C) cm^{-1}; ^{1}H-NMR δ 7.37 (3H, m, *m*-, *p*-ArH), 7.25 (2H, m, *o*-ArH), 3.84 (2H, b signal, CHOCH), 3.55 (3H, bm, CHOCH and dd, J_1 = 10.2, J_2 = 2.0 Hz, H-4), 3.28 (2H, bm, CHNCH), 3.15 (1H, bd, CHN), 2.81 (1H, bd, CHN), 2.64 (1H, d, *J* = 2.7 Hz, H-8), 2.35 (1H, d, *J* = 10.2 Hz, H-4a), 2.32 (1H, d, *J* = 9.5 Hz, H-9), 2.04 (1H, d, *J* = 3.7 Hz, H-5), 1.72 (4H, m, H-7ax, and d, *J* = 2.0 Hz, CH_3), 1.57 (1H, tt, H-6eq), 1.41 (1H, tt, H-7eq), 1.34 (1H, d, *J* = 9.8 Hz, H-9), 1.19 (1H, m, H-6ax); ^{13}C-NMR δ 138.1 (s), 129.0 (4d), 127.9 (d), 127.8 (d, C-3), 110.6 (s, C-8a), 67.8 (t, CH_2O), 66.9 (t, CH_2O), 55.7 (d, C-4a), 48.4 (d, C-4), 47.0 (2t, CH_2NCH_2), 45.5 (d, C-8), 41.2 (d, C-5), 35.1 (t, C-9), 28.1 (t, C-6), 23.7 (t, C-7), 15.4 (q, CH_3); Anal. Calcd. for $C_{20}H_{26}N_2O_3$, requires: C, 70.15; H, 7.65; N, 8.18. Found: C, 70.12; H, 7.66; N, 8.12.

***exo*-3-(2-Nitro-1-phenylpropyl)bicyclo[2.2.1]heptan-2-one (8h) and (9h).** A single isomer, **8h**, was obtained by opening of the heterocycle **5h** in the air, m.p. 104-105 °C, from cyclohexane; IR, ν 1733 (C=O), 1538, 1388, 1376 (NO2), 1605, 1582, 1495, 770, 730, 706 (Ph) cm^{-1}; ^{1}H NMR δ 7.30, 7.06 (5H, 2 m, ArH), 5.21 (1H, dq, J_1 = 6.8 Hz, J_2 = 5.9 Hz, $CHNO_2$), 3.58 (1H, dd, J_1 = 5.9 Hz, J_2 = 10.7 Hz, C*H*Ph), 2.50 (1H, bs, H-1), 2.17 (1H, bs, H-4), 2.09 (1H, dd, J_1 = 3.4 Hz, J_2 = 10.7 Hz, H-3), 1.70 (2H, m, H-5, H-6), 1.61 (1H, bd, *J* = 11.9 Hz, H-7), 1.45 (1H, m, H-6), 1.33 (4H, m, H-5 and d, *J* = 6.6 Hz, CH_3), 1.29 (1H, bd, *J* = 11.9 Hz, H-7); 217.5 (s), 135.6 (s), 128.8 (2d), 128.7 (2d), 128.0 (d), 83.9 (d, $CHNO_2$), 53.9 (d, C-3), 49.7 (d, C-1), 48.1 (d, CHPh), 38.9 (d, C-4), 34.7 (t, C-7), 28.2 (t, C-5), 24.3 (t, C-6), 14.1 (q, CH_3). On standing in acidic medium at room temperature, **8h** isomerized into a 7:3 mixture of **8h** and **9h** (HRGC: RT_1 = 26.4 min, RT_2 = 27.3 min). Compound **9h**: ^{1}H NMR δ 7.30, 7.06 (5H, 2 m, ArH), 5.39 (1H, dq, J_1 = 6.7 Hz, J_2 = 4.9 Hz, $CHNO_2$), 3.16 (1H, dd, J_1 = 4.9 Hz, J_2 = 10.0 Hz, C*H*Ph), 2.49 (2H, m, H-1, H-3), 2.08 (1H, bd, H-4), 1.78-1.64 (2H, m, H-5, H-6), 1.60 (1H, m, H-6), 1.48 (5H, m, H-5, H-7 and d, *J* = 6.7 Hz, CH_3), 1.22 (1H, bd, *J* = 9.1 Hz, H-7);^{13}C NMR δ 217.9 (s),135.9 (s), 128.8 (2d), 128.7 (2d), 128.1 (d), 83.1 (d, $CHNO_2$), 52.3 (d, C-3), 49.6 (d, C-1), 49.0 (d, CHPh), 38.3 (t, C-4), 28.3 (t, C-5), 24.0 (t, C-6), 17.4 (q, CH_3). Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N 5.12. Found: C, 69.96; H, 7.14; N 5.24.

***exo*-3-(2-Oxo-1-phenylpropyl)bicyclo[2.2.1]heptan-2-one (8h).** Oil; IR, ν 1720, 1700 (C=O), 1600, 690 (Ph) cm^{-1}; ^{1}H NMR δ 7.33 (3H, m, *m*-, *p*-ArH), 7.20 (2H, m, *o*-ArH), 3.69 (1H, d, *J* 9.9 Hz, C*H*Ph), 2.83 (1H, dd, *J*1 3.3 Hz, *J*2 9.8 Hz, H-3), 2.54 (1H, m, H-1), 2.15 (3H, s, $COCH_3$), 2.10 (1H, m, H-4), 1.75 (2H, H-5, H-6), 1.53 (3H, m, H-5, H-6 and bd, *J* = 9.2 Hz, H-7), 1.33 (1H, bd, J = 9.2 Hz, H-7); ^{13}C NMR δ 217.6 (s), 206.5 (s), 136.0 (s), 128.9 (2d), 128.6 (2d), 127.6 (d), 57.5 (d, CHPh), 54.0 (d, C-3), 49.1 (d, C-1), 37.4 (d, C-4), 34.5 (t, C-7), 28.4 (t, C-5), 23.2 (t, C-6). Anal. Calcd. for $\mathbf{C}_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.85; H, 7.45.

Reaction of the enamine 3 with α-nitrostilbene 4I

(4S*,4aS*,5S*,8R*,8aS*)-3,4-Diphenyl-8a-(4-morpholinyl)-4a,5,6,7,8,8a-hexahydro-5,8-

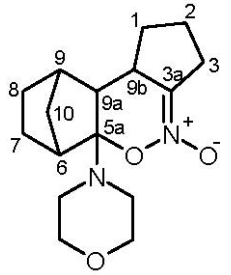
methano-4H-1,2-benzoxazine N-oxide (5i) and **(4R*,4aS*,5S*,8R*,8aS*)-3,4-Diphenyl-8a-(4-Morpholinyl)-4a,5,6,7,8,8a-hexahydro-5,8-methano-4H-1,2-benzoxazine *N*-oxide (5'i).** The reaction between the enamine **3** and the nitroolefin **4i** furnished the corresponding heterocyclic compound as a 9:1 mixture of diastereomers **5i** and **5'i** (44%). Crystalline product, mp 165-166 °C; IR, ν 1590 (C=N^+-O^-), 1110 (C-O-C), 720, 700 (Ph) cm^{-1}; For sake of clarity the NMR data are given separately although the diastereomers were not separated. Compound **5i**, major isomer: ^{1}H NMR δ 7.16 (8H, m, ArH), 7.03 (2H, *J* = 6.3 Hz, *o*-ArH at C-4), 4.00 (1H, d, *J* = 8.3 Hz, H-4), 3.70 (2H, b signal, CHOCH), 3.60-3-20 (4H, b signals, CHOCH, CHNCH), 3.10, 2.85 (2H, b signals, CHNCH), 2.77 (1H, d, *J* = 1.9 Hz, H-8), 2.36 (2H, 2 overlapping doublets, *J* = 9.8 Hz, H-4a, H-9), 2.21 (1H, d, *J* = 3.9 Hz, H-5), 1.73 (1H, m, H-7), 1.58 (1H, m, H-6), 1.42 (1H, m, H-7), 1.35 (1H, d, *J* = 10.7 Hz, H-9), 1.19 (1H, m, H-6); When the spectrum was registered in a 4:1 mixture of $CDCl_3$ and C_6D_6, the two signals relative to H-4a and H-9 were split, allowing the nOe measurements to be performed: 2.25 (d, *J* = 10.7 Hz, H-9), 2.22 (d, *J* = 8.8 Hz, H-4a); ^{13}C NMR δ 139.1 (s), 130.6 (s), 129.1 (2d), 128.6 (2d), 128.3 (2d), 128.3 (2d), 128.1 (d), 127.4 (2d), 126.9 (d), 126.7 (, C-3), 110.9 (s, C-8a), 67.6 66.8 (t, CH2O), 56.9 (d, C-4a), 48.7 (d, C-4), 47.6 (t, CH_2N), 46.9 (t, CH_2N), 46.0 (d, C-8), 41.7 (d, C-5), 35.1 (t, C-9), 27.9 (t, C-6), 24.0 (t, C-7). Compound **5'i**, **minor isomer:** ^{1}H NMR, δ ppm: 7.84 (2H, d, *J* = 6.8 Hz, *o*-ArH at C-4), 7.16 (8H, m, ArH), 4.50 (1H, d, *J* = 9.8 Hz, H-4), 3.70 (2H, b signal, CHOCH), 3.60-3-20 (4H, b signals, CHOCH, CHNCH), 3.10, 2.85 (2H, b signals, CHNCH), 2.50 (2H, d, *J* = 1.9 Hz, H-8, and d, *J* = 9.8 Hz, H-4a), 2.21 (1H, d, *J* = 3.9 Hz, H-5), 1.73 (1H, m, H-7), 1.68 (1H, d, H-9), 1.58 (1H, m, H-6), 1.42 (1H, m, H-7), 1.19 (1H, m, H-6), 0.84 (1H, d, *J* = 10.3 Hz, H-9); ^{13}C NMR δ 137.6 (s), 130.3 (s), 128.8 (d), 128.6 (2d), 128.4 (s, C-3), 128.2 (2d), 128.1 (2d), 127.1 (d), 127.1 (2d), 113.0 (s, C-8a), 66.9 (t, CH_2O), 65.1 (t, CH_2O), 49.2 (d, C-4a), 47.6 (t, CH_2N), 46.7 (t, CH_2N), 45.3 (d, C-4), 43.1 (d, C-8), 40.1 (d, C-5), 35.3 (t, C-9), 28.7 (t, C-6), 24.0 (t, C-7). Anal. Calcd. for $C_{25}H_{28}N_2O_3$: C, 74.26; H, 6.98; N, 6.93. Found: C, 73.97; H, 6.89; N 6.94.

***exo*-3-(1,2-Diphenyl-2-nitroethyl)bicyclo[2.2.1]heptan-2-one (8i) and (9i).** A white crystalline product was isolated as an 85:15 mixture of two diastereomers, which were separated by fractional crystallization from carbon tetrachloride and *n*-hexane Anal. Calcd. for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.51; H, 6.34; N 4.22. Major isomer: m.p. 146-148 °C; IR ($CDCl_3$), ν 1743 (C=O), 1559, 1550, 1382 (NO_2), 1602, 1497 (Ph) cm^{-1}; ^{1}H NMR δ 7.60 (2H, m, o-ArH), 7.42 (3H, m, m-, p-ArH), 7.22 (5H, m, Ph), 6.08 (1H, d, *J* = 12.2 Hz, $CHNO_2$), 4.38 (1H, dd, J_1 = 2.9, J_2 = 12.2 Hz, CHPh), 2.53 (1H, bd, H-4), 2.22 (1H, bs, H-1), 1.60 (2H, m, H-5, H-6), 1.58 (1H, dd, J_1 = 2.9, J_2 = 3.4 Hz, H-3), 1.12 (1H, m, H-6), 1.00 (2H, m, H-5, H-7), 0.45 (1H, d, *J* = 10.7 Hz, H-7). ^{13}C NMR δ 216.1 (s), 135.8 (s), 133.0 (s), 130.4 (d), 129.4 (2d), 128.0 (6d), 127.9 (d), 93.2 (d, $CHNO_2$), 53.1 (d, C-3), 47.8 (d, C-1), 47.7 (d, CHPh), 36.0 (d, C-4), 34.6 (t, C-7), 29.3 (t, C-5), 23.3 (t, C-6). Minor isomer: m.p. 165-166 °C; IR ($CDCl_3$), ν cm-1: 1739 (C=O), 1555, 1380 (NO_2), 1602, 1497 (Ph); ^{1}H NMR δ 7.15 (2H, bd, *o*-ArH), 7.22-7.10 (6H, m, Ar-H), 6.92 (2H, d, *o*-ArH), 6.20 (1H, d, *J* = 9.8 Hz, $CHNO_2$), 4.28 (1H, dd, J_1 = 7.3, J_2 = 9.8 Hz, CHPh), 2.49 (2H, bd, H-1, H-4), 2.00 (1H, dd, J_1 = 2.4, *J*2 = 7.3 Hz, H-3), 1.75 (2H, bs, H-5, H-6), 1.53 (1H, m, H-6), 1.40-1.20 (3H, m, H-5, 2 H-7). ^{13}C NMR δ 217.0 (s), 135.9

(s), 132.6 (s), 129.4 (d), 129.1 (2d), 128.4 (6d), 127.5 (d), 92.2 (d, $CHNO_2$), 55.3 (d, C-3), 49.1 (d, C-1), 47.6 (d, CHPh), 38.0 (d, C-4), 34.7 (t, C-7), 28.7 (t, C-5), 24.2 (t, C-6).

Reaction of the enamine 3 with 1-nitrocyclopentene 4j

(5aS*,6R*,9S*,9aS*,9bS*)-6,9-Methano-5a-(4-morpholinyl)-1,2,3,5a,6,7,8,9,9a,9b-decahydrocyclopenta[c][1,2]benzoxazine N-oxide (5j).



Pinky crystalline solid, mp 155-157 °C (61%); IR, ν 1630 ($C=N^+-O^-$), 1370, 1110 (C-O-C) cm^{-1}; ^1H NMR δ 3.72 (2H, b signal, CHOCH), 3.42 (2H, b signal, CHOCH), 3.08 (2H, b signal, CH_2N), 2.72 (2H, b signal, CH_2N), 2.63 (1H, m, H-1), 2.46 (1H, d, *J* = 2.2 Hz, H-6), 2.38 (2H, m, H-1, H-9b), 2.25 (1H, m, H-3), 2.12 (1H, d, *J* = 3.7 Hz, H-9), 2.03 (1H, d, *J* = 10.4 Hz, H-10), 1.90 (1H, m, H-7), 1.74 (1H, d, *J* = 7.6 Hz, H-9a), 1.62 (3H, m, H-2, H-7, H-8), 1.40 (2H, m, H-2, H-3), 1.27 (2H, m, H-8, and d, *J* = 10.4 Hz, H-10); ^{13}C NMR δ 133.7 (s, C-3a), 112.8 (s, C-5a), 67.6 (t, CH_2O), 66.8 (t, CH_2O), 55.0 (d, C-9a), 47.1 (t, CH_2NCH_2), 44.4 (d, C-6), 43.1 (d, C-9), 42.8 (d, C-9b), 35.6 (t, C-10), 33.5 (t, C-3), 28.5 (t, C-1), 28.4 (t, C-8), 23.6 (2t, C-2, C-7). Anal. Calcd. for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 66.77; H, 8.42; N, 9.48.

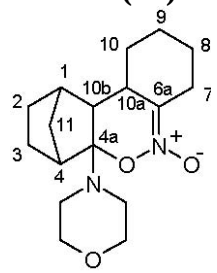
***exo, trans*-3-(2-Nitrocyclopentyl)bicyclo[2.2.1]heptan-2-one (8j).** White solid, mp 70 °C; IR, ν 1725 (C=O), 1545, 1370 (NO_2) cm^{-1}; ^1H NMR δ 5.17 (1H, dt, J_1 = 4.9, J_2 = 8.3 Hz, $CHNO_2$), 2.73 (1H, ddt, J_1 = 8.3, J_2 = 5.4, J_3 = 10.7 Hz, H-1'), 2.58 (1H, d, *J* = 3.4 Hz, H-4), 2.49 (1H, bd, H-1), 2.22 (2H, m, 2 H-3'), 2.15 (1H, m, H-5'), 1.95 (1H, dt, J_1 = 10.7, J_2 = 1.0, Hz, H-7), 1.85 (2H, m, H-5, H-6), 1.75 (2H, m, 2 H-4'), 1.57 (1H, dd, J_1 = 3.0, *J*2 = 10.7, H-3), 1.52 (2H, m, H-6, H-7), 1.40 (2H, m, H-5', H-5); ^{13}C NMR δ 217.7 (s), 88.4 (d, $CHNO_2$), 55.9 (d, C-3), 49.2 (d, C-4), 44.0 (d, C-1'), 39.1 (d, C-1), 34.3 (d, C-7), 32.7 (t, C-3'), 31.5 (t, C-5'), 27.7 (t, C-5), 24.0 (t, C-6), 23.4 (t, C-4'). Anal. Calcd. for $\mathbf{C}_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.80; H, 7.83; N, 6.17. On standing in $CDCl_3$, the nitroketone **8j** partially converted into its diastereoisomer **9j**. The final mixture was a 9:1 mixture of **8j** and **9j.**

***exo, cis*-3-(2-Nitrocyclopentyl)bicyclo[2.2.1]heptan-2-one (9j).** Of the ^1H NMR spectrum only the signal at 4.98 ppm relative to the nitromethine proton was visible, the other signals being submerged by other signals. ^{13}C NMR δ 217.5 (s), 89.2 (d, $CHNO_2$), 52.4 (d, C-3), 48.9 (d, C-4), 44.8 (d, C-1'), 38.1 (d, C-1), 34.8 (d, C-7), 32.7 (t, C-3'), 31.8 (t, C-5'), 28.2 (t, C-6), 23.1 (t, C-5), 22.1 (t, C-4').

***exo*-3-(2-Oxocyclopentyl)bicyclo[2.2.1]heptan-2-one (10j) and (11j).** Two diastereomers in the ratio of 3:2 (HRGC: RT_1 = 25.1 min, RT_2 = 26.0 min) were isolated from the hydrolysis of the heterocycle **5j** carried out at pH 2. Yellow oil; IR, ν 1725 (C=O) cm^{-1}; ^1H NMR δ 2.75 (0.6H, bs), 2.52 (1.4H, m), 2.37 (0.4H, m), 2.29 (1.6H, m), 2.15 (2H, m), 2.05 (2H, m), 1.84 (2.4H, m), 1.74 (2H, m), 1.59 (0.6H, m), 1.54 (3H, m); ^{13}C NMR δ **major component**: 218.4 (s), 217.7 (s), 52.3 (d), 49.3 (d), 48.6 (d), 39.0 (d), 37.2 (t), 34.3 (t), 28.1 (t), 27.2 (t),23.2 (t), 20.3 (t); **minor**

component: 218.9 (s), 218.3 (s), 50.5 (d), 49.6 (d), 47.8 (d), 36.9 (d), 36.8 (t), 35.4 (t), 28.8 (t), 26.2 (t), 22.9 (t), 20.2 (t). Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.07; H, 8.45. On standing in $CDCl_3$, the composition of the mixture changed to 1:1.

Reaction of the enamine (3) with 1-nitrocyclohexene 4k (1S*,4R*,4aS*10aS*,10bS*)-1,4-Methano-4a-(4-morpholinyl)-2,3,4,4a,7,8,9,10,10a,10b-decahydro-1H-dibenz[c,e][1,2]oxazine 6-oxide (5k).



White crystals (68% yield), m.p. 167 °C; IR, ν 1630 (C=N^+-O^-), 1110 (C-O-C) cm^{-1}; ^{1}H NMR, δ 3.80 (2H, b signal, CHOCH), 3.50 (2H, b signal, CHOCH), 3.10 (2H, b signal, CHNCH), 2.90 (1H, b signal, CHN), 2.80 (1H, b signal, CHN), 2.62 (1H, m, H-7), 2.52 (1H, bd, H-4), 2.35 (2H, m, H-47, H-10a), 2.22 (1H, bd, H-1), 2.16 (1H, d, J = 10.7 Hz, H-11), 2.07 (1H, m, H-10), 1.87 (1H, m, H-8 or H-9), 1.69 (4H, m, H-2, H-3, H-8 or H-9, and d, J = 9.3 Hz, H-10b), 1.45 (2H, m, H-3, H-8 or H-9), 1.87 (4H, m, H-2, H-8 or H-9, H-10, H-11); ^{13}C NMR δ 127.6 (s, C-6a), 110.7 (s, C-4a), 67.5 (t, CH2O), 66.8 (t, CH2O), 55.0 (d, C-10b), 47.0 (2t, CH_2NCH_2), 44.8 (d, C-4), 41.5 (d, C-1), 36.7 (d, C-10a), 35.4 (t, C-11), 29.6 (t, C-10), 28.3 (t, C-2), 25.1 (t, C-7), 23.4 (t, C-3), 22.1 (t, C-8 or C-9), 21.9 (t, C-9 or C-8). Anal. Calcd. for $C_{17}H_{26}N_2O_3$: C, 66.64; H, 8.55; N, 9.14. Found: C, 66.65; H, 8.57; N 9.11.

***exo,cis*-3-(2-Nitrocyclohexyl)bicyclo[2.2.1]heptan-2-one *(*8k).** Opening of the heterocycle **5k** in $CDCl_3$ lead to the less thermodynamically stable nitroketone **8k** which was identified only through its ^{13}C NMR spectrum. ^{1}H NMR δ 4.96 (q, J = 4.0 Hz, W_H 8.0 Hz, $CHNO_2$); ^{13}C NMR δ 218.3 (s), 83.6 (d, $CHNO_2$), 54.4 (d, C-3), 49.4 (d, C-1), 38.8 (d, C-4), 37.6 (t, C-1'), 35.0 (t, C-7), 30.9 (t,), 28.4 (, C-5), 25.0 (t,), 24.8 (t, C-6), 20.1 (t, C-4'). Ketone **8k** equilibrated into its isomer **9k.**

***exo,trans*-3-(2-Nitrocyclohexyl)bicyclo[2.2.1]heptan-2-one (9k).** White solid, mp 79 °C, (HRGC: RT = 38.4 min); IR, ν 1720 (C=O), 1545, 1370 (NO_2) cm^{-1}; ^{1}H NMR δ 4.50 (1H, dt, J_1 = 10.7 Hz, J_2 = 10.7 Hz, J_3 = 4.0 Hz, H-2'), 2.59 (1H, bd, H-4), 2.52 (1H, bd, H-1), 2.46 (1H, m, W_H 30.5 Hz, H-1'), 2.26 (1H, m, H-3'), 1.87 (1H, m, H-3'), 1.81 (4H, m, H-5, H-7, 2 CH), 1.68 (2H, m, 2 CH), 1.58 (1H, dd, J_1 = 5.2 Hz, J_2 = 3.7 Hz, H-3), 1.50 (2H, m, H-7, CH), 1.43-1.25 (3H, m, H-5, 2 CH) 1.17 (1H, m, CH); ^{13}C NMR δ 217.6 (s), 88.0 (d, C-2'), 53.8 (d, C-3). 48.7 (d, C-1), 40.6 (d, C-1'), 36.6 (d, C-4), 35.7 (t, C-7), 31.5 (t, C-3'), 29.3 (t, C-5), 27.9 (t), 24.4 (t), 23.9 (t), 23.6 (t). Anal. Calcd. for $C_{13}H_{19}NO_3$: C, 65.82; H, 8.02; N, 5.91. Found: C, 65.80; H, 8.18; N 5.84.

***exo*-(2-Oxocyclohexyl)bicyclo[2.2.1]heptan-2-one (10k) and (11k).** Oil, 55:45 mixture of diastereomers (HRGC: RT_1 = 28.0 min, RT_2 = 30.2 min); IR, ν 1700, 1725 (C=O) cm^{-1}; ^{1}H NMR δ 2.69 (0.55H, dt, J_1 = 11.2 Hz, J_2 = 5.4 Hz, H-1'), 2.48 -2.20 (5.45H, m, H-1, H-1' (0.45H), H-3

(0.55H), 2 H-3', H-4', H-5 (0.45H)), 1.99 (0.45 H, dd, J_1 = 10.2 Hz, J_2 = 2.9 Hz, H-3), 1.95-1.35 (11.55H, m, 2 H-4', H-5 (1.55H), 2 H-5', 2 H-6, 2 H-6', 2 H-7); ^{13}C NMR δ **major isomer**: 219.6 (s), 211.1 (s), 51.2 (d, C-3), 50.5 (d, C-1'), 48.6 (d, C-1), 41.8 (t, C-3'), 37.3 (d, C-4), 35.5 (t, C-7), 30.5 (t), 29.2 (t), 27.7 (t), 24.6 (t), 23.4 (t); **minor isomer:** 219.4 (s), 211.1 (s), 52.4 (d, C-3), 50.6 (d, C-1'), 50.1 (d, C-1), 42.2 (t, C-3'), 40.1 (d, C-4), 34.5 (t, C-7), 32.0 (t), 28.3 (t), 27.6 (t), 24.5 (t), 24.4 (t). Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.13; H, 8.68.

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