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1-NITRO-1-PHENYLPROPENE. 1,2-OXAZINE N-OXIDES FROM AMINOCYCLO-ALKENES. †

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SUMMARY.- The reactions between the nitroolefin with enamines from cycloalkanones have been studied. No ring-chain tautomerism between the title heterocycles and the nitroalkylated enamines has been found, in contrast with the case of the isomeric 2-nitro 1-phenylpropene.

Nitroalifatic compounds are very important tools in organic synthesis.[1,2] Among the various methods available for their synthesis, one of the most used is the Michael-type addition of conjugated nitroolefins to enamine systems.[3,4,5]

Besides the open-chain products,[3,4,5] either carbocyclic[6,7] or heterocyclic compounds[4,8] can be easily formed depending on the structure of the reagents and the conditions used.

As for the heterocycles formed, the product is a 1,2-oxazine N-oxide derivative which undergoes nucleophilic ring fission to the corresponding Michael-type adduct.

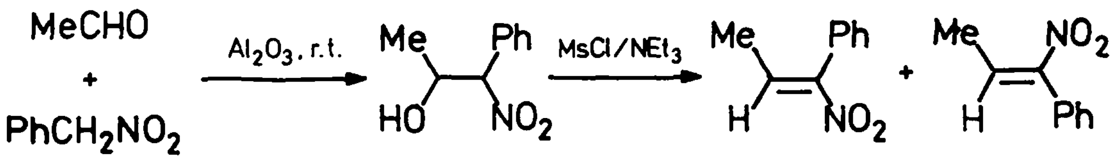
Continuing our studies on this subject we have taken into account 1-nitro-1-phenylpropene[9] as the electrophilic reagent, also to make a comparison with the reactivity of its isomer 2-nitro-1-phenylpropene.[4]

1-Nitro-1-phenyl-propene (2) was prepared by dehydration of the corresponding nitroalcohol 1, obtained from acetaldehyde and phenyl nitromethane by nitroaldol Henry condensation, following the method of G. Rosini.[10]

Dehydration of the diastereoisomeric pair of 1 has been performed by treating the previously formed methanesulphonate derivatives of 1, in accordance with Mc Murray.[11]

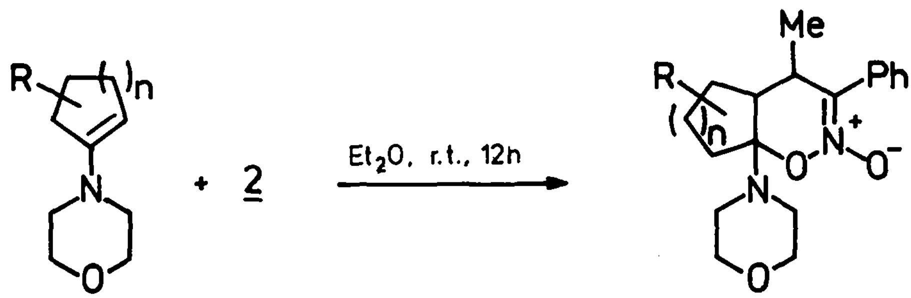
The nitroolefin was a mixture of (E)- and (Z)- diastereoisomers in ratio 9 to 1, as determined by ^{1}H NMR, with the aid of a lanthanide shift reagent, to avoid signal overlapping.

† Dedicated to Professor Amerigo Risaliti on the occasion of his 65th birthday.



1 (E)-2 (Z)-2

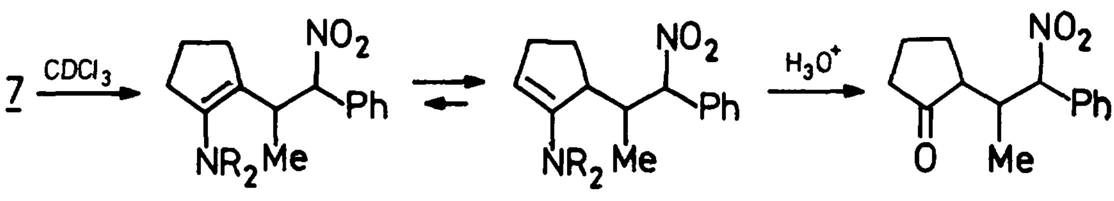
With all the aminocycloalkenes used as nucleophiles, 3, 4, 5, and with 2-morpholino-cyclohexen-1-one (6), the products of kinetic formation were the corresponding bicyclic 1,2-oxazine N-oxide derivatives, 7-11, respectively.



n=1, R=H: 3
n=2, R=H: 4
n=2, R=4-Bu^t: 5
n=2, R=1-oxo: 6

n=1, R=H: 7
n=2, R=H: 8
n=2, R=6-Bu^t: 9, 10
n=2, R=8-oxo: 11

It is known how these systems are not stable and undergo nucleophilic ring fission with pathways which depend on the size of the fused ring and on the substituents at the rings.[4,12]



12 a,b 13 a,b 14 a,b,c,d

The 1,2-oxazine N-oxide 7 in fact opened into the corresponding tetrasubstituted enamines 12a, b, as a pair of diastereoisomers (the two systems differing for the configuration around the nitromethine carbon atom). However an equilibrium was rapidly settled between the systems 12 and the trisubstituted enamines 13, in ratio 1:4 respectively. The trisubstituted enamines are in number of four, as a result of a lack of stereoselectivity in the protonation of the β-enamine carbon atom of 12.[4] These transformations have been followed by ^1H NMR spectroscopy. The following Table summarizes the values of the main signals for the six isomers.

Table 1

	δ $CHNO_2$, ppm (d, J=12.0 Hz)	δ C=CH, ppm	δ Me, ppm (d, J=6.75 Hz)
12 a	5.75	-	1.2(0.8)
12 b	5.50	-	0.8(1.2)
13 a	6.05	4.90	hidden
13 b	5.80	4.90	hidden
13 c	5.40	4.65	0.6
13 d	5.35	4.65	1.0

No significant difference was found in the behaviour of compound 7 with respect to the analogous derivative of 2-nitro-1-phenylpropene.[4]

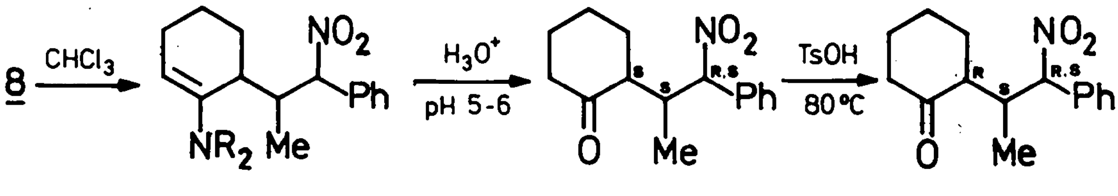
Crystallization of the equilibration mixture from benzene-light petroleum lead to the isolation of the single isomer 13 d.

Hydrolysis of the enamine mixture, carried out at pH 5-6, furnished a mixture of two pairs of diastereoisomeric ketones 14 a, b and 14 c, d, in ratio 9:1. It is likely that the pair 14 a, b differs from their isomers 14 c, d in the configuration around C-2. In fact an acidic equilibration of the hydrolysis mixture lead to a new ratio of the two pairs, namely 7:3, always in favour of the pair 14 a, b. Table 2 lists the main ^{1}H NMR values for all the ketones.

Also in this case, fractional crystallization from methanol allowed a single isomer to be separated, namely 14 b.

Table 2

	δ $CH-NO_2$, ppm (d, J=12.0 Hz)	δ Me, ppm (d, J=7.5 Hz)
14 a	5.35	1.0
14 b	5.45	0.6
14 c	6.25	1.1
14 d	6.25	0.7



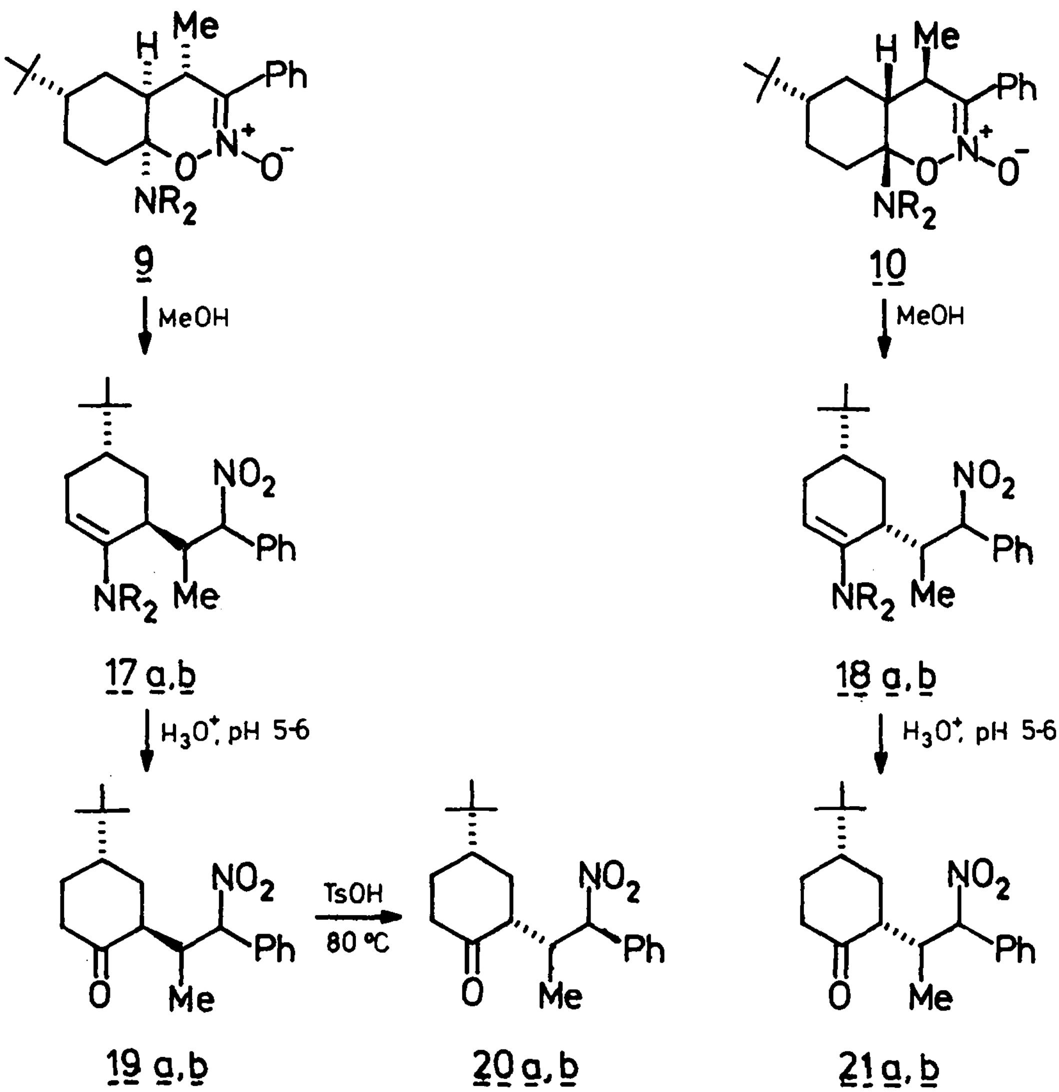
Opening of the heterocycle 8 furnished quantitatively the corresponding trisubstituted enamine 15 as a pair of diastereoisomers a and b, in ratio 1:1.† It is worth noting, however, that a single isomer was formed initially in $CDCl_3$ solution, which subsequently underwent equilibration, owing to the isomerization of the nitromethine carbon atom. Treatment of the mixture 15 a, b with methanol allowed the single isomer 15 a to be isolated. Hydrolysis of the enamine pair under non epimerizing conditions gave a mixture of diastereoisomeric ketones 16 a,

† The relative configurations of C-6 and C-α were determined by the Re*-Re* approach of the reagents which lead to the heterocycle 8.[3]

b, from which 16 a was separated by fractional crystallization. The same ketone 16 a was formed as a single isomer by hydrolysis in the air of the 1,2-oxazine N-oxide system 8. Treatment of the pure isomer 16 a with TsOH in refluxing toluene caused epimerization of both C-2 and C-β with formation of a mixture of diastereoisomers 16 a, b and 16 c, d. The ratio 16 a, b:16 c, d was about 1:1.

Table 3

	δ $CH-NO_2$, ppm (d, J=12.0 Hz)	δ Me, ppm (d, J=7.5 Hz)
16 a	5.40	0.7
16 b	5.35	1.0
16 c	6.1	0.8
16 d	6.0	1.2



The reaction of 1-nitro-1-phenylpropene with the biased enamine 5 was somewhat more complex, the substrate presenting two possible sites of attack by the nitro-olefin. Actually two 1,2-oxazine N-oxide systems were separated, 9 and 10, the deriving from the α-attack and the latter from the β-attack of the nitro olefin on the substrate. The ratio of the two types of attack was 55:45 in favour of the antiparallel β one.

In chloroform, both heterocycles 9 and 10 opened quantitatively into the corresponding trisubstituted enamines 17 and 18 with trans and cis configuration respectively.

A comparison between the two isomeric nitroolefins shows that they differ in two important features. The first one is the stereoselectivity of the attack: 2-nitro-1-phenylpropene in fact attacks exclusively from the β side.[13] The second remarkable difference is that the 1,2-oxazine N-oxide thus formed is in equilibrium with the open chain enamine system,[13] whereas in the present case no equilibrium is observed.

The two diastereoisomeric enamines 17 and 18 were formed at different rates, as a consequence of the higher energy of the dipolar intermediate bearing the nitro alkyl chain equatorial ($A^{1,3}$ strain),[14] which was formed by nucleophilic ring fission of the oxazine 10.

For the same reason, also hydrolyses of the respective enamines occurred at different rates, that of enamine 17 being higher.

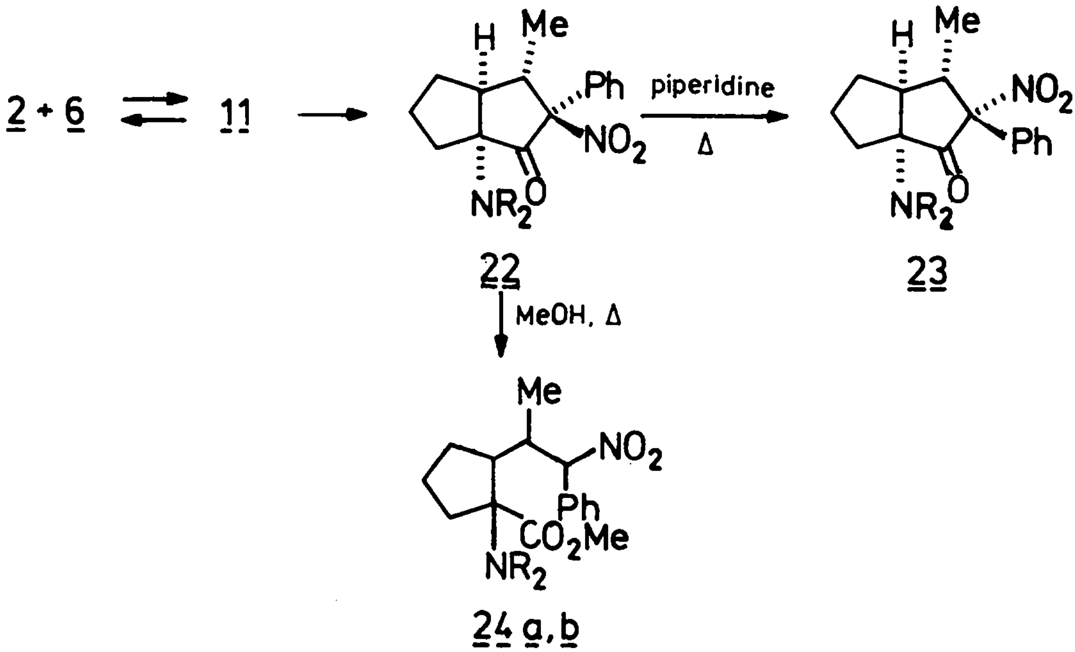
The resulting ketones, 19 and 21 respectively, had the same trans and cis configuration as the enamines from which they derived. Both were a pair of diastereoisomers a and b.

Whereas ketones 21 a, b did not undergo equilibration in acidic medium and under heating, ketones 19 a, b epimerized into their corresponding cis isomers 20 a, b under the same conditions. Although ketones 20 and 21 are both cis, they are diastereoisomers, as it can be inferred from the following Table which reports the ^{1}H NMR values of the signals of interest for the ketones in question.

Table 4

	δ $CHNO_2$, ppm (d, J=12.0 Hz)	δ Bu^t, ppm (s)	δ Me, ppm (d, J=6.75 Hz)
19 a	5.5	0.75	1.0 (0.65)
19 b	5.5	0.90	0.65 (1.0)
21 a	6.3	1.05	0.95
21 b	6.4	0.90	1.20
20 a	5.55	1.00	0.70
20 b	5.5	0.92	1.10

The reaction of 1-nitro-1-phenylpropene with the enamine 6 derived from cyclohexan-1,2-dione was slightly different, first for the conditions used, i. e. absence of solvent, and second for the fate of the 1,2-oxazine N-oxide formed. The absence of solvent was necessary, otherwise the reaction did not proceed, as the equilibrium reagents-products laid by far towards the reagents.



When the heterocycle 11 was heated in acetonitrile, it partially reverted into its components and partially rearranged into the pentalenone derivative 22, whose formation followed the route already found for the analogous reaction with 2-nitro-1-phenylpropene.[15] Differently from this latter case in which two diastereoisomeric pentalenones were formed, in this case only one isomer was formed under kinetic control. In fact its isomerization with piperidine under heating, lead to the more stable pentalenone 23. The two isomers were assigned the configurations shown in the scheme on the basis of their ^{13}C NMR. The methyl resonance of 22 is at higher field than that of 23 (13.5 ppm vs 18.5 ppm), thus indicating a more compressed steric situation, and hence a cis relationship with the phenyl group. Difficult was the ring fission of the pentalenone 22 by means of methanol to yield the substituted cyclopentane carboxylic esters 24.[12] This reaction required prolonged heating to be performed. Evidently, the nucleophilic attack of the alcohol to the carbonyl group is hindered by the steric incumbrance of the phenyl group on one side and of that of the base on the other side.

In conclusion, 1-nitro-1-phenylpropene is by far more reactive than its isomer 2-nitro-1-phenylpropene, its reactivity being much more similar to α-nitrostyrene,[8] as shown by the lack of stereoselectivity in the attack to anancomeric systems.

EXPERIMENTAL

General: IR spectra were obtained on a Perkin-Elmer 1320 double beam spectrophotometer, as Nujol mulls. ^{1}H NMR were obtained on a Jeol-C-60 HL or on a Bruker W-80 spectrometer. ^{13}C NMR were registered on a Bruker WP-80 (20.1 MHz) spectrometer. Chemical shifts are in ppm relative to tetramethylsilane. All samples were run in deuterochloroform unless otherwise indicated.

Melting points were determined on a Büchi 510 apparatus and are uncorrected. Analytical thin layer chromatography (TLC) was performed on precoated silica gel plates (250 μm) with a fluorescent indicator supplied by Whatman. Flash column chromatography was performed on Merck silica gel 60 (230-400 mesh).

Preparation of the reactants.-All enamines 3-6 were prepared by Stork condensation of the appropriate ketone and secondary amine, followed by distillation.

1-Nitro-1-phenyl-2-propanol(1).-Phenylnitromethane (10 g, 73 mmol) was added to acetaldehyde (6.26 g, 142 mmol) in an ice bath and under stirring. After 5 min, basic alluminium oxide (14.6 g) was added and the mixture stirred for further 1 h. The mixture was left in the ice bath for 4 h and at room temperature for further 20 h. The alluminium oxide was washed with dichloromethane (5x40 ml) and the solvent eliminated. The crude oily residue was an about 1:1 mixture of the two diastereoisomers 1 a and 1 b. IR (neat): 3550, 3450 (OH), 1550, 1370 (NO_2), 1600, 1500, 720, 700 cm^{-1} (Ph). ^1H NMR, δ : 7.5 (m, 5H, Ph), 5.5 (d, J=10.5 Hz, 1H, $CHNO_2$), 4.8 (m, 1H, CHOH), 3.0 (bs, 1H, OH), 1.2 (d, J=6.75 Hz, 1.5H, Me), 1.0 (d, J=6.75 Hz, 1.5 Me). By standing in the refrigerator for some time, one of the two diasteroisomers separated as white crystals, m.p. 86-7°C. (Found: C, 59.5; H, 5.87; N, 7.55. $C_9H_{11}NO_3$ requires: C, 59.66; H, 6.11; N, 7.55%). IR: 3200 (OH), 1560 (NO_2), 730, 700 cm^{-1} (Ph); ^1H NMR, δ : 7.7 (m, 5H, Ph), 5.5 (d, J=10.5 Hz, 1H, $CHNO_2$), 4.8 (dq, J =10.5 Hz, J = 6.75 Hz, 1H, CHOH), 3.95 (br signal, 1H, OH), 1.0 (d, J=6.75 Hz, 3H, Me).

1-Nitro-1-phenylpropene(2).-Methansulphonylchloride (4.6 g, 40 mmol) was added to a solution of the nitroalcohol 1 (7.25 g, 40 mmol) in dichloromethane, in an ice bath and under nitrogen. Triethylamine (16 g, 160 mmol) was then added dropwise. After 45 min, the mixture was washed with water, 5% hydrochloride and brine. Elimination of the solvent left an oil which was purified by flash chromatography (eluent: ethyl acetate:light petroleum 5:95). The yellow liquid thus separated was a 9:1 mixture of the E and Z diastereoisomers. IR (neat): 1665 (C=C); 1520, 1335 (NO_2); 1600, 1490, 775, 730, 705 cm^{-1} (Ph); ^1H NMR, δ : 7.5 (m and q, 5.9H, Ph, (E)-C=CH); 6.3 (q, J=7.5 Hz, 0.1 H, (Z)-C=CH), 2.0 (d, J= 7.5 Hz, (Z)-Me), 1.9 (d, J=7.5 Hz, (E)-Me); ^1H NMR (with Eu(fod)$_3$ added), δ : 7.9 (q, J=7.5 Hz, (E)-C=CH), 7.7 (m, Ph), 6.3 (q, J=7.5 Hz, (Z)-C=CH), 2.15 (d, J=7.5 Hz, (Z)-Me), 1.9 (d, J=7.5 Hz, (E)-Me); ^{13}C NMR (multiplicity): 150.6 (s), 132.1 (d), 128.7 (d), 127.9 (d), 126.8 (d), 126.2 (s), 12.3 ppm (q).

General Procedure for the Reactions between Enamines 3-5 and 1- Nitro-1-phenylpropene (2).-A solution of the nitroolefin either in anhydrous ether (3) or benzene-n-hexane (4-5) was added to the enamine dissolved in the same solvent, cooled to 0°C. The reaction mixture was then kept either at 5°C for further 48 h or at room temperature for 12 h. The reaction between enamine 6 and the nitroolefin was carried out in the absence of solvent and at room temperature. The solid formed in each case was then filtered off and the mother liquors hydrolyzed.

Reaction of 4-(1-cyclopentenyl)-morpholine (3) with 1-nitro-1-phenylpropene. |4S*-(4α,4aα,7aα)|-4,4a,5,6,7,7a-hexahydro-4-methyl-7a-(4-morpholinyl)-3-phenylcyclopenta|e|-1,2-oxazine N-oxide (7).-M.p. 85-7°C. IR: 1580, 1565 (Ph-C=N), 1600, 770, 750, 720, 700 (Ph), 1120 cm^{-1} (C-O-C); ^1H NMR, δ : 8.0 (m, 2H, o-ArH), 7.6 (m, 3H, m- and p-ArH), 3.9 (m, 4H, CH_2OCH_2), 1.35 (d, J=7.25 Hz, 3H, Me).

4-|5-(1-methyl-2-nitroethyl-2-phenyl)-1-cyclopentenyl|-morpholine (13 d).-M.p. 128-30°C, from benzene-light petroleum (Found: C, 68.4; H, 7.77; N, 8.75. $C_{18}H_{14}N_2O_3$ requires: C, 68.33; H, 7.65; N, 8.85%). IR: 1640 (N-C=C), 1550 (NO_2), 1120 (C-O-C), 880, 735, 700 cm^{-1} (Ph); ^1H NMR, δ : 7.6 (m, 5H, Ph), 5.35 (d, J=12.0 Hz, 1H, $CHNO_2$), 4.65 (bm, 1H, C=CH), 3.8 (t, 4H, CH_2OCH_2), 3.2-1.4 (m, 10H), 1.0 (d, J=6.75 Hz, Me).

2-(1-methyl-2-nitroethyl-2-phenyl)-cyclopentanone (14 b).-Hydrolysis of the enamine mixture with 3N HCl in methanol-water at pH 5 followed by treatment with methanol gave the ketone 14 b, m.p. 121-3°C, from methanol. (Found: C, 68.8; H, 6.85 ;N, 5.57. $C_{14}H_{17}NO_3$ requires: C, 68.00; H, 6.93; N, 5.66%). IR: 1735 (C=O), 1550 (NO_2), 730 (Ph); ^1H NMR, δ : 7.6 (m, 5H, Ph), 5.45 (d, J=11.25 Hz, 1H, $CHNO_2$), 3.4 (m, 1H, CHMe), 0.6 (d, J=6.75 Hz, 3H, Me); ^{13}C NMR (multiplicity): 218.5 (s), 130.4 (s), 130.0 (d), 129.0 (d), 128.4 (d), 95.1 (d), 50.6 (d), 38.3 (t), 35.6 (d), 22.8 (t), 20.0 (t), 11.3 ppm (q).

Reaction of 4-(1-cyclohexenyl)-morpholine (4) with 1-nitro-1-phenylpropene.-|4S*-(4α,4aα,8aα)|-4,4a,5,6,7,8,8a-hexahydro-4-methyl-(4-morpholinyl)-3-phenylbenz|e|-1,2-oxazine N-oxide (8).-M.p. 117-8°C, from benzene-n-hexane (Found: C, 69.18 ; H, 7.85 ; N, 8.50. $C_{19}H_{26}N_2O_3$ requires: C, 69.06; H, 7.93, N, 8.48%). IR: 1555 (Ph-C=N), 1595, 1575, 1490, 770, 700 (Ph), 1120 (C-O-C); ^1H NMR, δ : 7.75 (m, 2H, o_-ArH), 7,57 (m, 3H, m- and p-ArH), 3.8 (t, 4H, CH_2OCH_2), 1.16 (d, J=7.5 Hz, 3H, Me).

4-|6-(1-methyl-2-nitroethyl-2-phenyl)-1-cyclohexenyl|-morpholine (15 a)-The heterocycle 8 was kept in chloroform at room temperature for 24 h. The enamine mixture formed was then treated with methanol, from which the isomer 15 a was separated, m.p. 103-4°C, from methanol. (Found: C, 69.1; H, 7.68; N, 8.37.

$C_{19}H_{26}N_2O_3$ requires: C, 69.06; H, 7.93; N, 8.48%). IR: 1640 (N-C=C), 1550 (NO_2), 1120 (C-O-C), 880, 735, 700 cm^{-1} (Ph); ^1H NMR, δ : 7.6 (m, 5H, Ph), 5.5 (d, J=12.0 Hz, 1H, $CHNO_2$), 5.1 (t, 1H, C=CH), 3.8 (m, 4H, CH_2OCH_2), 0.5 (d, J=6.5 Hz, 3 H, Me). ^1H NMR for the mixture 15 a, b, δ: 7.6 (m, 5H, Ph), 5.5 (d, J=12.0 Hz, 0.5 H, $CHNO_2$), 5.4 (d, J=12.0 Hz, 0.5 H, $CHNO_2$), 3.8 (m, 4H, CH_2OCH_2), 0.9 (d, J=6.5 Hz, 1.5 H, Me), 0.5 (d, J=6.5 Hz, 1.5 H, Me).

2-(1-methyl-2-nitroethyl-2-phenyl)-cyclohexanone (16 a).-Hydrolysis of the enamine 15 a with 3N HCl in methanol-water at pH 5 gave the ketone 16 a, m.p. 156-7°C from methanol. (Found: C, 69.4; H, 7.01; N, 5.07. $C_{15}H_{19}NO_3$ requires: C, 68.94; H, 7.33; N 5,36%). IR: 1700 (C=O), 1550 (NO_2), 1500, 740, 700 cm^{-1} (Ph); ^1H NMR, δ : 7.5 (m, 5H, Ph), 5.4 (d, part A of the $AMXY_3$ spin system, J_{AM}=12.0 Hz, J_{AX}=J_{AY}=0 Hz, 1H, $CHNO_2$), 3.5 (2 dq, part M of $AMXY_3$, J_{AM}=12.0 Hz, J_{MX}=2.0 Hz, J_{MY}=7.5 Hz, 1H, CHMe), 0.7 (d, part Y of $AMXY_3$, J_{MY}=7.5 Hz, J_{AY}=J_{XY}=0 Hz, 3H, Me). ^{13}C NMR (multiplicity): 209.6 (s), 134.2 (s), 129.8 (d), 128.8 (d), 128.1 (d), 93.6 (d), 50.4 (d), 41.5 (t), 34.5 (d), 26.2 (t), 25.8 (t), 24.1 (t), 11.6 (q).

Reaction of 4-(4-t-butyl-1-cyclohexenyl)-morpholine (5) with 1- nitro-1-phenyl-propene

|4S*-(4α,4aα,6α,8aα)|-4,4a,5,6,7,8,8a-hexahydro-6-t-butyl-4-methyl-8a-(4-morpholinyl)-3-phenyl-benzo|e|-1,2-oxazine N-oxide (9).-M.p. 125-6°C, from benzene-n-pentane (Found: C, 70.8; H, 8.57; N, 7.12. $C_{23}H_{34}N_2O_3$ requires: C, 71.47; H, 8.87; N, 7.25). IR: 1585, 1570 (Ph-C=N), 1500, 700 (Ph), 1120 cm^{-1} (C-O-C); ^1H NMR, δ: 7.8 (m, 2H, o-ArH), 7.6 (m, 3H, m- and p-ArH), 3.8 (m, 4H, CH_2OCH_2), 1.1 (d, J=6.75 Hz, Me), 0.95 (s, 9H, Bu^t).

|4R*-(4α,4aα,6β,8aα)|-4,4a,5,6,7,8,8a-hexahydro-6-t-butyl-4-methyl-8a-(4-morpholinyl)-3-phenyl-benzo|e|-1,2-oxazine N-oxide (10).-M.p. 128-9°C, from benzene-n-pentane. (Found: C, 71.1; H, 8.48; N, 7.18. $C_{23}H_{34}N_2O_3$ requires: C, 71.47; H, 8.87; N, 7.25%). IR: 1590-1580 (Ph-C=N), 1500, 710 (Ph), 1120 cm^{-1} (C-O-C); ^1H NMR, δ : 8.0-7.4 (bm, 5H, Ph), 3.85 (t, 4H, CH_2OCH_2), 1.25 (d, J=7.5 Hz, 3H, Me), 0.95 (s, 9H, Bu^t).

4-|trans-4-t-butyl-6-(1-methyl-2-nitroethyl-2-phenyl)-1-cyclohexenyl|-morpholine (17 a,b).-The heterocycle 9 was opened in chloroform and it furnished the corresponding enamine 17, as a pair of diastereoisomers a and b, IR ($CDCl_3$): 1650 (N-C=C), 1550, 1370 (NO_2), 1120 (C-O-C); ^1H NMR, δ : 7.6 (m, 5H, Ph), 5.65 (d, J=12.0 Hz, 0.5 H, $CHNO_2$), 5.60 (d, J=11.25 Hz, 0.5H, $CHNO_2$), 5.5 (bt, C=CH), 5.10 (bdd, C=CH), 3.95, 3.90 (2 t, 4H, CH_2OCH_2), 1.1 (d, J=7.5 Hz, Me), 0.95, 0.90 (2 s, 9H, Bu^t), 0.65 (d, J=7.5 Hz, 1.5H, Me).

4- |cis-4-t-butyl-6-(1-methyl-2-nitroethyl-2-phenyl)-1-cyclohexenyl|-morpholine (18 a, b).-The heterocycle 10 was opened in chloroform into the corresponding enamines 18 a, b, m.p. 146°C, from methanol. (Found: C, 71.6; H 8.58; N, 7.17. $C_{23}H_{34}N_2O_3$ requires: C, 71.47; H, 8.87; N, 7.25%). IR ($CDCl_3$): 1650 (N-C=C), 1600 (Ph), 1550, 1370 (NO_2), 1120 cm^{-1} (C-O-C); ^1H NMR, δ: 7.6 (m, 5H, Ph), 5.60 (d, J=12.0 Hz, 0.5 H, $CHNO_2$), 5.50 (d, J=12.0 Hz, 0.5 H, $CHNO_2$), 5.2 (bm, 1H, C=CH), 3.85 (m, 4H, CH_2OCH_2), 1.3 (d, J=7.5 Hz, 1.5 H, Me), 0.95, 0.90 (2 s, 9H, Bu^t), 0.5 (d, J=6.75 Hz, 1.5 H, Me).

|2S*-(2α,4β)|-trans-4-t-butyl-2-(1-methyl-2-nitroethyl-2-phenyl)-cyclohexanone (19 a,b).-Hydrolysis of the heterocycle 9 gave the 1:1 mixture of ketones 19 a and 19 b, oil (Analysis of 2,4-dinitrophenylhydrazone: found: C, 60.5; H, 6.18; N, 13.96. $C_{25}H_{31}N_5O_6$ requires: C, 60.35; H, 6.28; N, 14.08). IR (neat): 1715 (C=O), 1550, 1360 cm^{-1} (NO_2). ^1H NMR, δ: 7.5 (m, 5H, Ph), 5.5 (d, J=11.25 Hz, $CHNO_2$), 3.5 (m, 1H, CHMe), 1.0, 0.65 (2d, J =J =6.75 Hz, Me), 0.9 (s, 4.5H, Bu^t), 0.75 (s, 4.5H, Bu^t).

|2R*-(2α,4α)|-cis-4-t-butyl-2-(1-methyl-2-nitroethyl-2-phenyl)-cyclohexanone (20 a, b).-Equilibration of the mixture of ketones 19 a and 19 b lead to a 1:1 mixture of the diastereoisomers 20 a and 20 b, which were separated by flash chromatography (eluent: light petroleum:ether 9:1). Ketone with major Rf, m.p. 106-8°C. (Found: C, 72.0; H, 8.72; N,4.30. $C_{19}H_{27}NO_3$ requires: C, 71.89; H, 8.57; N, 4.1%). IR ($CHCl_3$): 1710 (C=O), 1545, 1365 (NO_2), 1600, 1500 cm^{-1} (Ph); ^1H NMR, δ: 7.7 (m, 5H, Ph), 6.3 (d, J=11.25 Hz, 1H, $CHNO_2$), 1.05 (s, 9H, Bu^t), 0.95 (d, J=6.75 Hz, 3H, Me). Ketone with minor Rf, m.p. 68-70°C. (Found: C, 71.6; H, 8.63; N, 4.40. $C_{19}H_{27}NO_3$ requires: C, 71.89; H, 8.57; N, 4.41%). IR ($CHCl_3$): 1710 (C=O), 1545, 1370 (NO_2), 1600, 1500 cm^{-1} (Ph); ^1H NMR, δ : 7.6 (m, 5H, Ph), 6.4 (d, J=11.25 Hz, 1H, $CHNO_2$), 1.2 (d, J=6.75 Hz, 3H, Me), 0.9 (s, 9H,Bu^t).

|2 R*-(2α,4α)|-cis-4-t-butyl-2-(1-methyl-2-nitroethyl-2-phenyl)-cyclohexanone (21 a, b).-Hydrolysis of the heterocycle 10 carried out at room temperature for 24 h furnished a 1:1 mixture of the corresponding ketones 21 a and 21 b, which were separated by flash chromatography (eluent: light petroleum:ether 9:1). Ketone with major Rf m.p. 135-7°C. (Found: C, 72.0; H, 8.41; N, 4.23. $C_{19}H_{27}NO_3$ requires: C,

71.89; H, 8.57; N, 4.41%). IR ($CHCl_3$): 1710 (C=O), 1545, 1365 (NO_2), 1600, 1500 cm^{-1} (Ph); ^1H NMR, δ: 7.6 (m, 5H, Ph), 5.55 (d, J=10.5 Hz, 1H, $CHNO_2$), 3.55 (bm, 1H, CHMe), 1.0 (s, 9H, Bu^t), 0.7 (d, J=6.75 Hz, 3H, Me). Ketone with minor Rf m.p. 100-103°C. (Found: C, 72.2; H, 8.32; N, 4.56. $C_{19}H_{27}NO_3$ requires: C, 71.89; H, 8.57; 4.41%). IR ($CHCl_3$): 1710 (C=O), 1555, 1370 cm^{-1} (NO_2); ^1H NMR, δ: 7.7 (m, 5H, Ph), 5.5 (d, J=12.0 Hz, 1H, $CHNO_2$), 3.55 (m, 1H, CHMe), 1.1 (d, J=6.75 Hz, 3H, Me), 0.92 (s, 9H, Bu^t).

Reaction of 4-(1-oxo-2-cyclohexenyl)-morpholine (6) with 1-nitro-1-phenylpropene

|4S*-(4α,4aα,8aα)|-4a,5,6,7,8,8a-hexahydro-4-methyl-8a-(4-morpholinyl)-8-oxo-3-phenyl-4H-1,2-benz|e|oxazine N-oxide (11).-M.p. 129-130°C, from benzene. (Found: C, 65.8; H, 6.78; N, 8.10. $C_{19}H_{24}N_2O_4$ requires: C, 66.26; H, 7.02; N, 8.13%). IR: 1725 (C=O), 1595, 1575, 1565 (Ph-C=N), 1120 cm^{-1} (C-O-C); ^1H NMR, δ: 7.5 (m, 5H, Ph), 3.8 (t, 4H, CH_2OCH_2), 1.1 (d, J=6.75 Hz, 3H, Me).

|2S*-(2α,3β,3aβ,6aβ)|-hexahydro-3-methyl-6a-(4-morpholinyl)-2-nitro-2-phenyl-1(2H)-pentalenone (22).-By heating in acetonitrile for 5 h, the heterocycle 11 partially converted into its isomer 22 (25% yield, after crystallization with isopropanol), m.p. 154-6°C. (Found: C, 66.8; H, 7.02; N, 8.8. $C_{19}H_{24}N_2O_4$ requires: C, 66.26; H, 7.02; N, 8.13%). MS (70 eV): 316 (M^+), 153 (100%), 117 (30%). IR: 1745 (C=O), 1540 (NO_2), 1590, 740, 700 (Ph), 1125 cm^{-1} (C-O-C); ^1H NMR, δ: 7.5 (m, 5H, Ph), 3.8 (t, 4H, CH_2OCH_2), 3.25-2.25 (m, 6H, CH_2NCH_2, H-4, H-4a), 1.35 (d, J=6.4 Hz, 3H, Me); ^{13}C NMR (multiplicity): 209.5 (s), 136.3 (s), 130.0 (d), 129.0 (d), 127.8 (d), 85.7 (s), 81.6 (s), 68.0 (2t), 49.3 (d), 47.7 (2t), 42.2 (d), 30.6 (t), 29.0 (t), 23.1 (t), 13.5 (q).

|2R*-(2α,3α,3aα,6aα)|-hexahydro-3-methyl-6a-(4-morpholinyl)-2-nitro-2-phenyl-1(2H)-pentalenone (23).-By heating in toluene with an excess of piperidine for 8 h, the compound 22 was transformed into its isomer 23. IR ($CDCl_3$): 1740 (C=O), 1550 cm^{-1} (NO_2); ^1H NMR, δ: 7.5 (m, 5H, Ph), 3.7 (m, 4H, CH_2OCH_2), 1.1 (d, J=6.5 Hz, 3H, Me); ^{13}C NMR (multiplicity): 208.9 (s), 133.1 (s), 129.1 (d), 129.0 (d), 128.9 (d), 82.3 (s), 80.5 (s), 67.5 (2t), 48.4 (2t), 47.4 (d), 44.2 (d), 40.8 (t), 30.2 (t), 24.7 (t), 18.5 (q).

|2-(1-methyl-2-nitroethyl-2-phenyl)-1-(4-morpholinyl)-cyclopentancarboxylic ester (24 a, b).-By heating in refluxing methanol for 5h, compound 22 opened into a 3:1 mixture of diastereoisomers 24 a and b. IR ($CHCl_3$): 1720 (C=O), 1550 (NO_2), 1120 cm^{-1} (C-O-C); ^1H NMR, δ: 7.6 (m, 5H, Ph), 5.7 (d, J=10.5 Hz, 0.65 H, $CHNO_2$), 5.4 (d, J=10.5 Hz, 0.35 H, $CHNO_2$), 3.75, 3.70 (2s, 3H, OMe), 3.5 (t, 4H, CH_2OCH_2), 0.95 (d, J=6.75 Hz, 2H, Me), 0.5 (d, J=6.75 Hz, 1H, Me).

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