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POLYFUNCTIONALIZED HEXAHYDRO-1(2H)-PENTALENONES BY REARRANGEMENT OF BICYCLIC 1,2-OXAZINE N-OXIDE DERIVATIVES

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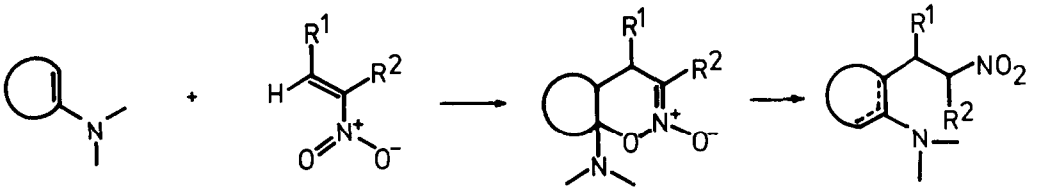
Abstract - The title heterocycles rearrange into a mixture of diastereoisomeric hexahydro-1(2H)-pentalenone derivatives, which undergo nucleophilic eliminative ring fission by methanol to give 1-amino-2-nitroalkylated cyclopentancarboxylic esters. The X-ray structure determination of hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-piperidinyl)-1(2H)-pentalenone |2S-(2α,3α,3aα,6aα)| is also reported.

Cyclic enamines have been shown[1,2] to react with nitroolefins to give 1,2-oxazine N-oxide derivatives, whose stabilities are related to the nature of the substituents R^1 and R^2 on the heterocyclic ring. Usually they open into the corresponding nitroalkylated enamines.



R^1= Ph, R^2= Me; R^1= H, R^2= Ph.

Recently we have found that 1,2-oxazine N-oxide derivatives with a carbonyl group in the fused carbocyclic ring undergo a different fate.[3] The heterocyclic systems 2, derived from the cross-conjugated enamines 1[†] and (E)-(2-nitro-1-propenyl)-benzene (R^1= Ph, R^2= Me), undergo a rearrangement reaction, instead of giving the expected ring opening products 3 (Scheme 1).

We would like to report here the results of a study of the rearrangement reaction, which proceeds on 2 in aprotic solvents, such as acetonitrile or toluene, and is favoured by heating. In the case of pyrrolidine, the rearrangement occurs also spontaneously at r.t. in the solid state. The resulting products 4 and 5, separated by flash chromatography, show the carbonyl absorption band at 1750 cm^{-1},

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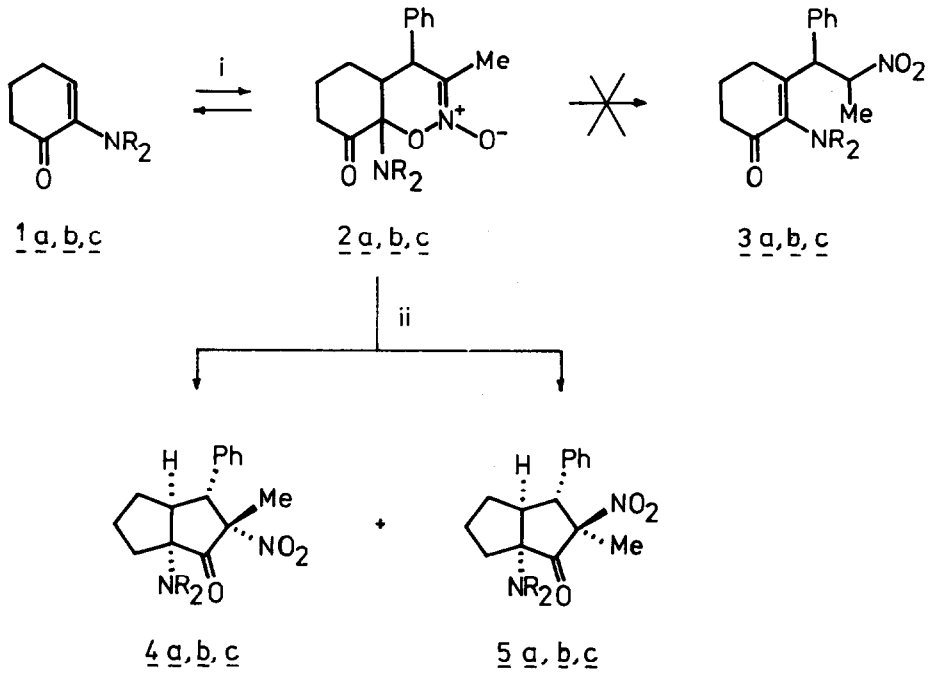
[†]In contrast, the fully conjugated enamines, i.e. the 3-amino-2-cyclohexen-1-one systems, do not react under the same mild conditions. More forcing conditions lead to complicated mixtures of compounds, not further studied.[4,5] It is interesting to note that the simple 2-cyclohexen-1-one does not react either with the above mentioned nitroolefin under any conditions.



(i) $PhCH=C(Me)NO_2$, r.t.; (ii) CH_3CN, Δ
a: NR_2 = 4-morpholinyl; b: NR_2 = 1-piperidinyl; c: NR_2 = 1-pyrrolidinyl

Scheme 1

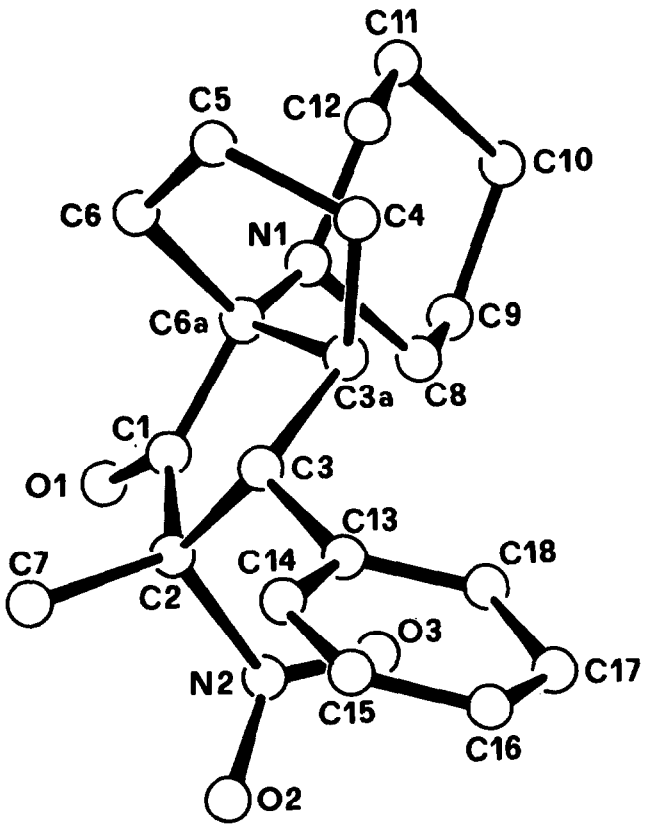
which is indicative of its insertion in a five-membered ring, and the asymmetric stretching band of the nitro group at 1545 cm^{-1}. However, neither the ^1H NMR nor the ^{13}C NMR data were diagnostic. Therefore the less polar isomer of the piperidino derivatives, that is 4b, was examined by X-ray crystallography and was shown to be hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-piperidinyl)-1(2H)-pentalenone |2S-(2α,3α,3aα,6aα)|† (Fig.1).

An experiment of spin-spin decoupling was carried out on 4b, as the chemical shifts of H-3 and H-3a were rather unusual, the benzylic proton resonating upfield (2.8-3.0 ppm) compared with the bridge proton (3.4-3.7 ppm) (Fig.2).

Irradiation at 3.64 ppm caused the doublet at 2.55 ppm to collapse to a singlet and simplified the multiplet centered at 1.69 ppm. Decoupling the proton doublet at 2.55 ppm reduced the multiplicity of the signal at 3.64 ppm to a doublet and no other changes were observed in the spectrum. Finally, irradiation at 1.69 ppm collapsed the signal at 3.64 ppm to a broad doublet. Therefore H-3a was assigned the lower field signal and its unusual shift is to be ascribed to the effect of the nitro group.

In compounds 5, the range of the benzylic proton resonances was 3.95-4.10 ppm. However, the vicinal coupling constant J_{33a} had the same value for both diastereoisomers, thus proving the antiperiplanar relationship of the proton in question. As a consequence, the configurations around C-3 and C-3a are also the same in both isomers 4 and 5. It then follows that they only differ in the configuration around C-2 (the cis fusion follows from the mechanism of formation of the two pentalenone systems)[3] and the |2R-(2α,3β,3aβ,6aβ)| configuration is assigned to compounds 5.

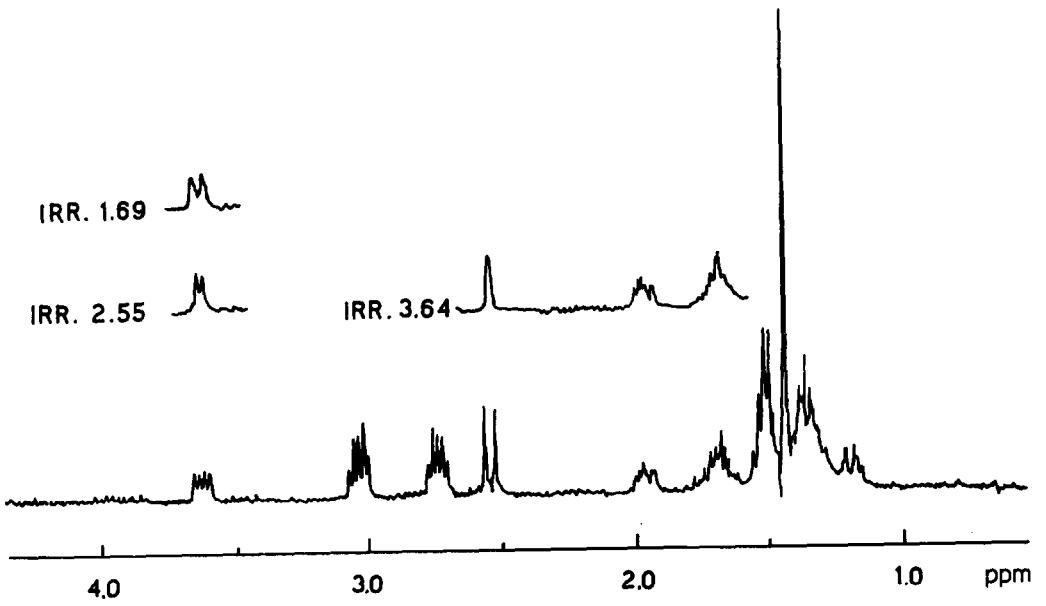
†We are dealing with racemic modifications.



View of molecule A of 4b along a

Fig. 1†

†For reasons of consistency the pentalenone numbering is used also in the structure

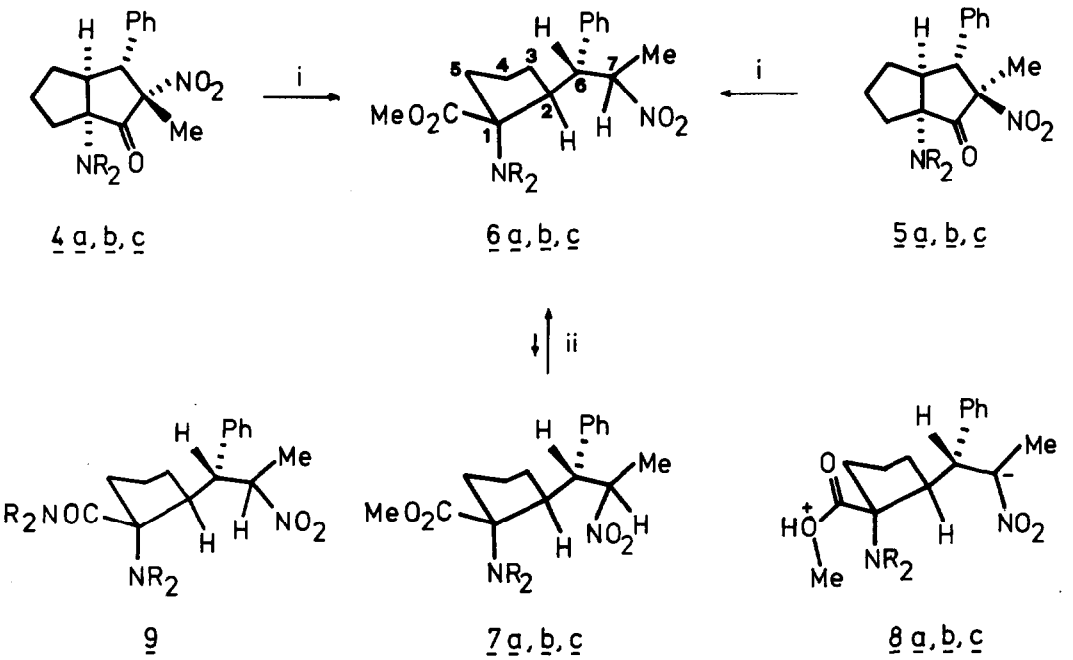


Partial 300 MHz ^{1}H NMR spectrum of 4b

Fig. 2

On the other hand, the cis relationship of the methyl group and the phenyl one in compounds 5 is confirmed by the upfield shift (-6 ppm) of the methyl carbon atom compared with that of the corresponding isomers 4, resulting from the steric compression of a gauche interaction.

Furthermore, that compounds 5 differed from the corresponding diastereoisomers 4 only in the configuration around C-2 was also proved chemically by means of a ring cleavage reaction. When compounds 4 and 5 were dissolved in methanol at r.t., the underwent nucleophilic eliminative ring fission of the type exo:O=C:C:5[6] to give the same 1-amino-2-nitroalkylated cyclopentacarboxylic esters 6, as products of kinetic control (Scheme 2).



(i) MeOH, r.t.; (ii) MeOH, Δ

a: NR_2 = 4-morpholinyl; b: NR_2 = 1-piperidinyl; c: NR_2 = 1-pyrrolidinyl

Scheme 2

By moderate heating in methanol, the amino esters 6 equilibrated into a mixture of 6 and 7, owing to the presence of the easily isomerizable center C-7. The ratios 6:7 varied from 7:3 to 6:4, depending on the amine moiety. It is evident that formation of the same adducts 6 from both ketones 4 and 5 presume a common intermediate of type 8, whose protonation is influenced by steric hindrance. The question of the configuration assignments to C-7 in 6 and 7 is left open.

The pentalenone derivatives 4 could be converted into the corresponding diastereoisomers 5, by the use of an excess of secondary amine such as piperidine or pyrrolidine in refluxing toluene. Simple heating was ineffective even at temperatures higher than 100°.

The mechanism we propose for this isomerization involves the initial attack of the secondary amine to the carbonyl group, followed by cleavage of the C_1-C_2 bond. The resulting carbanion would then collapse onto the carbonyl group with displacement of the base. During this ring closure, the nitro group would preferably assume the anti position with respect to the adjacent phenyl group, to avoid

electronic interactions, thus originating the diastereoisomers 5. However, the intermediacy of the tertiary amides 9, although not separated, cannot be excluded, as the corresponding primary amides, which were formed from the pentalenone systems 4 and ammonia by a lethargic reaction at r.t., actually cyclized to give the corresponding pentalenones 5. All the attempts to synthesize the tertiary amides 9 from the corresponding amino esters 6 resulted in the direct formation of the systems 5. In contrast, by heating the amino esters 6 in toluene the corresponding pentalenones 4 were formed. This type of formation of α-nitroketones is reported as rare.[7]

Cleavage of the pentalenone derivatives 4 and 5 with formation of the corresponding amino esters was also accomplished by means of other alcohols, provided they were primary and not hindered. For instance ethanol worked well, as did benzylic alcohol and ethylene glycol, whereas propanols and t-butyl alcohol did not react at all.

EXPERIMENTAL

The ^{1}H NMR spectra were run on either a JNM-60-HL Jeol or on a Varian XL-100 or on a Bruker CXP-300 spectrometer, with tetramethylsilane as internal standard. The ^{13}C NMR spectra were run on a Bruker WP-80 spectrometer at 20.1 MHz. The solvent for ^{13}C NMR spectra was $CDCl_3$ with tetramethylsilane as internal reference. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. Flash chromatography was performed on Merck Kieselgel (40-63 μm). M.ps were measured on a Büchi 510 apparatus.

General Procedure for the reaction of 2-amino-cyclohex-2-en-1-ones (1) with (E)-(2-nitro-1-propenyl)-benzene. (E)-(2-nitro-1-propenyl)-benzene (11 mmoles) was added to 1 (11 mmoles) at room temp. and the two reactants mixed thoroughly until the mixture became liquid. Then the mixture was allowed to stand at room temp. until it solidified. The solid 2 (100% yield) was filtered with the aid of a small amount of dry ether.

4a,5,6,7,8,8a-Hexahydro-3-methyl-8a-(4-morpholinyl)-8-oxo-4-phenyl-4H-1,2-benzoxazine N-oxide (2a). M.p. 116-7° (Found: C,66.12; H,6.94; N,8.08. Calc for $C_{19}H_{24}N_2O_4$: C,66.26; H,7.02; N,8.13%); IR (nujol): 1730 (C=O), 1620 (C=N$^+$), 1120 cm^{-1} (C-O-C); ^{1}H NMR ($CDCl_3$): δ 7.2 (m,5H,Ph), 3.72 (m,4H,CH_2OCH_2), 3.4 (dq J_1 1.5 Hz, J_2 10.5 Hz, CHPh), 1.7 (d J 1.5 Hz,Me).

4a,5,6,7,8,8a-Hexahydro-3-methyl-8-oxo-8a-(1-piperidinyl)-4-phenyl-4H-1,2-benzoxazine N-oxide (2b). M.p. 90-1° (Found: C,70.24; H,7.60; N,8.14. Calc for $C_{20}H_{26}N_2O_3$: C,70.15; H,7.65; N,8.18%); IR (nujol): 1730 (C=O), 1620 cm^{-1} (C=N$^+$); ^{1}H NMR ($CDCl_3$): δ 7.4 (m,5H,Ph), 3.45 (dq J_1 1.5 Hz, J_2 10.5 Hz, 1H, CHPh), 1.75 (d J 1.5 Hz,Me).

4a,5,6,7,8,8a-Hexahydro-3-methyl-8-oxo-4-phenyl-8a-(1-pyrrolidinyl)-4H-1,2-benzoxazine N-oxide (2c). M.p. 48-51° (Found: C,69.56; H,7.23; N,8.48. Calc for $C_{19}H_{24}N_2O_3$: C,69.49; H,7.37; N,8.53%); IR (nujol): 1730 (C=O), 1615 cm^{-1} (C=N$^+$); ^{1}H NMR ($CDCl_3$): δ 7.5 (m,5H,Ph), 3.7 (dq,1H,CHPh), 3.3 (m,4H,CH_2NCH_2), 2.0 (d J 1.5 Hz,Me).

General Procedure for the formation of 6-amino-hexahydro-2-methyl-3-phenyl-2-nitro-1(2H)-pentalenone (4) and (5). Compound 2 was heated in dry acetonitrile, under nitrogen, for 4-8 h. The solvent was eliminated and isopropanol was added. By scratching, the isomer 4 precipitated. The mother liquors, which contained a mixture of 4 and 5, were separated by flash chromatography using light petroleum-EtOAc (4:1) as eluent.

Hexahydro-2-methyl-6a-(4-morpholinyl)-2-nitro-3-phenyl-1(2H)-pentalenone [2S-(2α,3α,3aα,6aα)] (4a). M.p. 160.5°, from isopropanol (Found: C,66.9; H,6.87; N,8.02. Calc for $C_{19}H_{24}N_2O_4$: C,66.26; H,7.02; N,8.13%); IR (nujol): 1745 (C=O), 1545 (NO_2), 1600, 1495, 750, 700 (Ph), 1110 cm^{-1} (C-O-C); ^{1}H NMR ($CDCl_3$): δ 7.4 (m,5H,Ph), 4.0-3.55 (t+m,5H,CH_2OCH_2,H-3a), 3.55-2.60 (m+d J_{33a} 12.0 Hz,5H,H-3, CH_2NCH_2), 1.75 (s,Me); ^{1}H NMR (C_6D_6): δ 7.35 (m,5H,Ph), 3.75 (t,4H,CH_2OCH_2), 3.60 (dd,1H,H-3a), 3.0 (m,CH_2NCH_2), 2.7 (d J_{33a} 12.0 Hz,H-3), 1.5 (s,Me); ^{13}C NMR (multiplicity): 207.4(s), 133.7(s), 128.9(d), 95.4(s), 81.8(s), 67.8(t), 55.8(d), 48.0(t), 46.7(d), 32.4(t), 28.9(t), 23.0(t), 21.2 ppm (q).

Hexahydro-2-methyl-6a-(4-morpholinyl)-2-nitro-3-phenyl-1(2H)-pentalenone 2R-(2α,3β,3aβ,6aβ) (5a). M.p. 124-5°, from isopropanol (Found: C,66.1; H,6.93; N,7.96. Calc for $C_{19}H_{24}N_2O_4$: C,66.26; H,7.02; N,8.13%); IR (nujol): 1745 (C=O), 1535 (NO_2), 1595, 1575, 1490, 710, 700 (Ph), 1110 cm^{-1} (C-O-C); ^{1}H NMR ($CDCl_3$): δ 7.4 (m,5H,Ph), 4.05 (d J_{33a} 12.0 Hz, 1H,H-3), 3.8 (t,4H,CH_2OCH_2), 3.1 (bdd, J_{33a} 12.0 Hz,1H,H-3a), 2.75 (m,4H,CH_2NCH_2), 1.45 (s,3H,Me); ^{13}C NMR (multiplicity): 135.2(s), 129.2(d), 129.1(d), 128.6(d), 97.9(s), 79.6(s), 67.6(t), 51.6(d),

47.8(t), 45.3(d), 30.4(t), 28.6(t), 24.0(t), 16.3 ppm (q).

Hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-piperidinyl)-1(2H)-pentalenone |2S-(2α,3α,3aα,6aα)| (4b). M.p. 133-4°, from isopropanol (Found: C,70.28; H,7.58; N,8.08. Calc for $C_{20}H_{26}N_2O_3$: C,70.15; H,7.65; N,8.18%); IR (nujol): 1750 (C=O), 1545 (NO_2), 1595, 1495, 750, 700 cm^{-1} (Ph); 300 MHz ^1H NMR (C_6D_6): δ 3.64 (dd J_{33a} 11.0 Hz, J_{3a4} 6.0 Hz,1H,H-3a), 3.06 (m,2H,CH_2N), 2.75 (m,2H,CH_2N), 2.55 (d J_{33a} 11.0 Hz, H-3), 1.45 (s,3H,Me); ^{13}C NMR (multiplicity): 207.2 (s), 133.9 (s), 128.9 (d), 128.5(d), 95.4(s), 82.6(s), 55.8(d), 48.9(t), 46.7(d), 33.3(t), 29.4 (t), 27.2(t), 24.9(t), 23.2(t), 21.7 ppm (q).

Hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-piperidinyl)-1(2H)-pentalenone |2R-(2α,3β,3aβ,6aβ)| (5b). M.p. 85-6°, from isopropanol (Found: C,70.06; H,7.44; N,8.12. Calc for $C_{20}H_{26}N_2O_3$: C,70.15; H,7.65; N,8.18%); IR (nujol): 1750 (C=O), 1600, 1585, 705 (Ph), 1545 cm^{-1} (NO_2); 100 MHz ^1H NMR (C_6D_6): δ 7.1 (m,5H,Ph), 4.05 (d J_{33a} 11.2 Hz,H-3), 2.8 (dd J_{33a} 11.2 Hz, J_{3a4} 5.2 Hz,1H,H-3a), 1.37 (s, Me); ^{13}C NMR (multiplicity): 206.2(s), 133.3(s), 127.8(d), 127.2(d), 97.7(s), 79.3(s), 50.5(d), 47.6(t), 44.0(d), 29.5(t), 28.3(t), 25.6(t), 23.7(t), 22.9(t), 15.3 ppm (q).

Hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-pirrolidinyl)-1(2H)-pentalenone |2S-(2α,3α,3aα,6aα)| (4c). M.p. 128-9°, from isopropanol (Found: C,69.23; H,7.28; N,8.45. Calc for $C_{19}H_{24}N_2O_3$: C,69.49; H,7.37; N,8.53%); IR (nujol): 1740 (C=O), 1600, 1595, 705 (Ph), 1545 cm^{-1} (NO_2); ^1H NMR (C_6D_6): δ 7.1 (m,5H,Ph), 3.75 (bdd, J_{33a} 11.2 Hz,H-3a), 3.2 (m,4H,$NCH_2CH_2CH_2$), 2.75 (d J_{33a} 11.2 Hz,H-3), 1.5 (s,Me); ^{13}C NMR (multiplicity): 209.6(s), 134.0(s), 129.1(d), 129.0(d), 128.8(d), 95.8(s), 80.4(s), 55.8(d), 48.9(d), 47.6(t), 34.1(t), 28.5(t), 4.4(t), 23.3(t), 21.5 ppm (q).

Hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-pirrolidinyl)-1(2H)-pentalenone |2R-(2α,3β,3aβ,6aβ)| (5c). M.p. 113-4°, from acetonitrile (Found: C,69.32; H,7.25; N,8.45. Calc for $C_{19}H_{24}N_2O_3$: C,69.49; H,7.37; N,8.53%); IR (nujol): 1740 (C=O), 1600, 1580, 700 (Ph), 1530 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$): δ 7.4 (m,5H,Ph), 4.1 (d J_{33a} 11.6 Hz,1H,H-3), 3.35-2.50 (m,5H,H-3a,CH_2NCH_2), 2.5-1.5 (m,10H,$CH_2CH_2CH_2$, $CH_2CH_2CH_2N$), 1.45 (s,3H,Me); ^1H NMR (CD_3COCD_3): δ 7.4 (m,5H,Ph), 4.1 (d J_{33a} 11.6 Hz,1H,H-3), 3.4 (dd J_{33a} 11.6 Hz,1H,H-3a), 1.45 (s,3H,Me); ^{13}C NMR (multiplicity): 209.0(s), 134.9(s), 128.9(d), 128.8(d), 128.2(d), 97.9(s), 78.4(s), 52.2(d), 47.6 (t), 46.6(d), 30.9(t), 29.6(t), 24.1(t), 23.8(t), 16.2 ppm (q).

Reactions of 4 and 5 with methanol. Compounds 4 and 5 were dissolved in methanol at room temp. Elimination of the solvent furnished compounds 6.

Methyl ester of 1-(4-morpholinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxylic acid (6a). M.p. 119-20°, from methanol (Found: C,62.32; H,7.58; N,7.74. Calc for $C_{19}H_{28}N_2O_5$: C,62.62; H,7.74; N,7.69%); IR (nujol): 1720 (C=O), 1600, 1580, 730, 705 (Ph), 1530 (NO_2), 1120 cm^{-1} (C-O-C); ^1H NMR ($CDCl_3$): δ 7.3 (m,5H,Ph), 5.9 (dq J_{67} 5.0 Hz, J_{78} 6.5 Hz,1H,H-7), 3.78 (s,3H,OMe), 3.75 (m,4H,CH_2OCH_2), 3.50 (dd J_{26} 9.0 Hz, J_{67} 5.0 Hz,H-6), 2.55 (m,5H,CH_2NCH_2,H-2), 1.3 (d J 6.5 Hz,3H,Me). ^{13}H NMR (multiplicity): 173.8(s), 137.2(s), 129.8(d), 128.6(d), 127.9(d), 83.8(d), 78.6(s), 67.6(t), 52.0(d), 51.4(q), 48.9(t), 43.3(d), 28.8(t), 26.5(t), 20.9(t), 15.3 ppm (q).

By heating in methanol 6a equilibrated into a 6:4 mixture of 6a and 7a. The mixture had m.p. 124-5°. ^1H NMR ($CDCl_3$): δ 7.3, 7.0 (2m,5H,Ph), 6.3 (dq J_{67} 2.0 Hz, J_{78} 7.0 Hz, 0.4H,H-7), 5.9 (dq J_{67} 5.0 Hz, J_{78} 6.5 Hz,0.6H,H-7), 3.80, 3.78 (2s,OMe), 1.45 (d J_{78} 7.0 Hz,1.2H,Me), 1.30 (d J_{78} 6.5 Hz,1.8H,Me).

Methyl ester of 1-(1-piperidinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentacarboxylic acid (6b). M.p. 124-4°, from methanol (Found: C,67.5; H,7.92; N,7.46. Calc for $C_{21}H_{30}N_2O_4$: C,67.4; H,8.07; N,7.48%); IR (nujol): 1720 (C=O), 1600, 1580, 730, 700 (Ph), 1535 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$): δ 7.20 (m,5H,Ph), 6.25 (dq J_{67} 2.5 Hz, J_{78} 6.5 Hz,1H,H-7), 3.82 (s,3H,OMe), 3.55 (dd J_{26} 11.0 Hz, J_{67} 2.5 Hz,1H,H-6), 1.35 (d J_{78} 6.5 Hz,3H,Me); ^{13}C NMR (multiplicity): 174.6(s), 137.3(s), 129.3(d), 128.0(d), 127.2(d), 82.6(d), 79.3(s), 53.7(d), 51.3(q), 49.5(t), 43.2(d), 29.1(t), 26.8(t), 26.3(t), 25.0(t), 20.1(t), 14.0 ppm (q).

By heating in methanol, 6b gave a mixture of 6b and 7b in ratio 6:4, m.p. 114-5°. ^1H NMR ($CDCl_3$): δ 7.20 (m,5H,Ph), 6.30 (dq J_{67} 1.5 Hz, J_{78} 6.5 Hz,H-7), 6.25 (dq J_{67} 2.5 Hz, J_{78} 6.5 Hz,H-7), 3.83 (s,1.8H,OMe), 3.75 (s,1.2H,OMe), 1.45, 1.35 (2d J_{78} 6.5 Hz,Me).

Methyl ester of 1-(1-pyrrolidinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxylic acid (6c). M.p. 96-8°, from methanol (Found: C,67.1; H,7.72; N,7.75. Calc for $C_{20}H_{28}N_2O_4$: C,66.6; H,7.83; N,7.77%); IR (nujol): 1720 (C=O), 1600, 1580, 720, 700 (Ph), 1530 cm^{-1} (NO_2); ^1H NMR (C_6D_6): δ 7.2 (m,5H,Ph), 5.8 (dq J_{67} 5.25 Hz, J_{78} 6.75 Hz,1H,H-7), 3.75 (s,3H,OMe), 3.55 (dd J_{26} 9.9 Hz, J_{67} 5.2 Hz,1H,H-6), 2.65 (bm,5H,CH_2NCH_2,H-2), 2.15-1.30 (bm,10H,5CH_2), 1.3 (d J_{78} 6.75 Hz,Me); ^{13}C NMR (multiplicity): 174.8(s), 137.3(s), 130.0(d), 128.5(d), 127.7(d), 84.1(d), 77.3(s), 51.5(d), 51.1(q), 47.9(t), 47.5(d), 29.6(t), 28.4(t), 24.2(t), 22.0(t),15.3 ppm (q).

In chloroform 6c gave a 3:7 mixture of its diastereoisomer 7c and itself, m.p. 102°, from light petroleum. ^1H NMR ($CDCl_3$): δ 7.2 (m,5H,Ph), 6.0 (dq J_{67} 2.5 Hz, J_{78} 6.75 Hz,H-7), 5.8 (dq J_{67} 5.25 Hz, J_{78} 6.75 Hz,H-7), 3.74 (s,2.1H,OMe), 3.71 (s,0.9H,OMe), 1.45 (d J_{78} 6.75 Hz,0.9H,Me), 1.30 (d J_{78} 6.75 Hz,2.1H,Me).

Reactions of isomerization of 4 into 5. Compounds 4 (1.5 mmoles) were added to a solution of piperidine or pyrrolidine (3.0 ml, 30 mmoles) in toluene (30 ml) and the mixture refluxed overnight. Elimination of the solvent left the corresponding isomers 5.

Reaction of 4 with aqueous ammonia. Compounds 4 (1.5 mmoles) in acetonitrile were added to aqueous ammonia (4:1) (8 ml). After one week the solid formed was filtered and identified as a pair of diastereoisomeric 1-amino-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxamides.

1-(4-Morpholinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxamide. M.p. 208-210°, from methanol (Found: C,63.4; H,7.44; N,11.46. Calc for $C_{19}H_{27}N_3O_4$: C,63.14; H,7.53; N,11.63%); IR ($CHCl_3$): 3450, 3300 (HN), 1680, 1650 (C=O), 1570, 1540 (NO_2), 1490, 700 (Ph), 1110 cm^{-1} (C-O-C); ^1H NMR ($CDCl_3$): δ 7.3 (m,7H,Ph,NH_2), 5.85 (m, 1H,H-7), 3.8 (m,4H,CH_2OCH_2), 3.5 (m,1H,H-6), 3.1 (m,1H,H-2), 2.6 (m,4H,CH_2NCH_2), 1.36, 1.35 (2d J_{78} 6.75 Hz,3H,Me).

1-(1-Piperidinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxamide. M.p. 182-184°, from methanol (Found: C,66.7; H,7.97; N,11.50. Calc for $C_{20}H_{29}N_3O_3$: C,66.83; H,8.13; N,11.69%); IR ($CHCl_3$): 3495, 3330 (NH), 1670 (C=O), 1540 (NO_2), 1490, 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$): δ 7.4 (m,6H,Ph,NH), 6.7 (bd,1H,NH), 5.75 (m,1H,H-7), 3.8 (dd J_{26} 10.5 Hz, J_{67} 3.0 Hz,1H,H-6), 3.45-2.35 (m,5H,CH_2NCH_2,H-2), 1.5, 1.4 (2d J_{78} 6.75 Hz,Me).

1-(1-Pyrrolidinyl)-2-(1-phenyl-2-nitropropyl)-cyclopentancarboxamide. M.p. 174-175°, from methanol (Found: C,66.2; H,7.72; N,12.25. Calc for $C_{19}H_{27}N_3O_3$: C,66.06; H,7.88; N,12.16%); IR ($CDCl_3$): 3500, 3340 (NH), 1670 (C=O), 1540 (NO_2), 1490, 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$):δ7.4 (m,6H,Ph,NH), 6.3 (bd,1H,NH), 5.7 (m,1H,H-7), 3.8 (dd J_{26} 9.75 Hz, J_{67} 3.75 Hz,1H,H-6), 3.6-2.6 (m,5H,CH_2NCH_2,H-2), 1.8 (m,10H, $CH_2CH_2CH_2$,$NCH_2CH_2CH_2$), 1.5, 1.4 (2d J_{78} 6.75 Hz,Me).

X-Ray structure determination of hexahydro-2-methyl-2-nitro-3-phenyl-6a-(1-piperidinyl)-1(2H)-pentalenone [2S-(2α,3α,3aα,6aα)] (4b).

Crystal data. Formula $C_{20}H_{21}N_2O_3$; M = 337.4. The crystals are monoclinic, they belong to the space group $P2_1/c$, Z = 8 (two crystallographically independent molecules A and B in the asymmetric unit), with a = 9.024(2), b = 16.754(3), c = 24.036(4) Å, β = 91.46(4)°, V = 3632.8(9) Å^3.

Intensity measurements. Mo-K_α radiation, λ = 0.71069 Å, μ(Mo-K_α) = 0.40 cm^{-1}. 5654 reflections were collected in the range $3° < \theta < 24°$ with θ/2θ scan using a scan width of 1.1° and a speed of 0.05°s^{-1}, Lorentz and polarization effects were taken into account, while neither absorption or extinction corrections were applied. During data collection, the intensities of two reference reflections, monitored every two hours, indicated no significant decay of the sample.

Structure determination and refinement. The structure was solved with Multan 80[8] giving the sign to 400 reflections with the aid of 4247 phase relationships. Both molecules A and B appeared quite clearly on the E-map. Refinement was carried out with SHELX 76[9]. The last cycles were carried out assigning anisotropic thermal parameters to all non hydrogen atoms, while hydrogens were located at calculated positions. The final R factor was 0.054 and it was obtained with a weighting function of the form $1/w = \sigma^2(F_o) + 0.0266\ F_o^2$. Positional parameters, bond lengths, bond angles and some torsion angles are set out in the Tables 1-4.

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Table 1. Positional parameters ($x10^4$) and equivalent isotropic temperature factors ($Å^2$) for 4b with E.S.D.S. in brackets.

Molecule A

	x	y	z	B
O(1)	4092(3)	1988(2)	6006(1)	5.1(2)
O(2)	6390(4)	204(2)	6466(1)	6.8(3)
O(3)	5433(3)	1000(2)	7048(1)	5.3(2)
N(1)	4221(3)	3204(1)	6852(1)	3.3(2)
N(2)	6093(3)	867(1)	6622(1)	3.8(2)
C(1)	5212(3)	2149(2)	6268(1)	3.3(2)
C(2)	6575(3)	1581(2)	6288(1)	3.1(2)
C(3)	7760(3)	2054(2)	6625(1)	2.9(2)
C(3a)	6925(3)	2680(2)	6967(1)	2.9(2)
C(4)	7812(4)	3453(2)	7029(2)	4.0(3)
C(5)	7550(4)	3911(2)	6477(2)	4.7(3)
C(6)	6225(4)	3510(2)	6181(1)	3.7(2)
C(6a)	5558(3)	2900(2)	6593(1)	3.0(2)
C(7)	7027(4)	1306(2)	5714(1)	4.5(3)
C(8)	3593(3)	2657(2)	7261(2)	4.5(3)
C(9)	2033(4)	2919(2)	7399(2)	5.3(3)
C(10)	2035(4)	3767(2)	7628(3)	5.0(3)
C(11)	2773(4)	4307(2)	7220(2)	4.8(3)
C(12)	4322(4)	4008(2)	7090(1)	4.3(3)
C(13)	8913(3)	1560(2)	6946(1)	3.2(2)
C(14)	10186(4)	1319(2)	6688(1)	4.6(3)
C(15)	11280(4)	882(2)	6956(2)	5.7(3)
C(16)	11111(5)	679(2)	7506(2)	5.9(4)
C(17)	9866(4)	914(2)	7778(2)	5.4(3)
C(18)	8764(3)	1356(2)	7499(1)	4.1(3)

Molecule B

	x	y	z	B
O(1)	8992(2)	1997(1)	229(1)	4.9(2)
O(2)	11426(3)	232(1)	-322(1)	6.3(3)
O(3)	10426(3)	1057(1)	-815(1)	5.7(2)
N(1)	9093(3)	3269(1)	-574(1)	3.5(2)
N(2)	10971(3)	896(1)	-416(1)	3.9(2)
C(1)	10093(3)	2155(2)	-21(1)	3.3(2)
C(2)	11439(3)	1580(2)	-41(1)	3.4(2)
C(3)	12629(3)	2084(2)	-345(1)	3.1(2)
C(3a)	11773(3)	2727(2)	-684(1)	3.2(2)
C(4)	12653(3)	3501(2)	-730(1)	4.1(2)
C(5)	12441(4)	3933(2)	-174(1)	4.7(3)
C(6)	11178(3)	3503(2)	120(1)	3.7(2)
C(6a)	10446(3)	2931(2)	-315(1)	3.1(2)
C(7)	11916(4)	1258(2)	524(1)	4.5(3)
C(8)	8498(4)	2796(2)	-1043(2)	4.7(3)
C(9)	6930(4)	3051(2)	-1191(2)	5.8(3)
C(10)	6824(4)	3929(2)	-1326(2)	5.2(3)
C(11)	7532(4)	4401(2)	-850(1)	5.2(3)
C(12)	9103(4)	4119(2)	-729(1)	4.5(3)
C(13)	13796(3)	1617(2)	-652(1)	3.3(2)
C(14)	15066(3)	1380(2)	-365(2)	4.6(3)
C(15)	16195(4)	969(2)	-623(2)	5.4(3)
C(16)	16053(4)	803(2)	-1181(2)	5.3(3)
C(17)	14799(4)	1035(2)	-1478(2)	4.9(3)
C(18)	13672(4)	1436(2)	-1214(1)	4.1(2)

Table 2. Bond lengths (Å) with E.S.D.S. in brackets.

	molecule A	molecule B
O(1)-C(1)	1.208(4)	1.204(4)
O(2)-N(2)	1.206(4)	1.206(3)
O(3)-N(2)	1.217(4)	1.220(4)
N(1)-C(6a)	1.463(4)	1.469(3)
N(1)-C(8)	1.468(4)	1.468(4)
N(1)-C(12)	1.464(4)	1.473(4)
C(1)-C(2)	1.555(4)	1.552(4)
C(1)-C(6a)	1.510(4)	1.518(4)
C(2)-N(2)	1.511(4)	1.510(4)
C(2)-C(3)	1.545(4)	1.561(4)
C(2)-C(7)	1.518(4)	1.515(4)
C(3)-C(3a)	1.541(4)	1.546(4)
C(3)-C(13)	1.525(4)	1.518(4)
C(3a)-C(4)	1.527(4)	1.526(4)
C(3a)-C(6a)	1.551(4)	1.547(4)
C(4)-C(5)	1.547(5)	1.535(5)
C(5)-C(6)	1.531(5)	1.537(5)
C(6)-C(6a)	1.556(4)	1.553(4)
C(8)-C(9)	1.519(5)	1.512(5)
C(9)-C(10)	1.523(5)	1.509(5)
C(10)-C(11)	1.504(5)	1.519(5)
C(11)-C(12)	1.525(5)	1.516(5)
C(13)-C(14)	1.388(4)	1.380(4)
C(13)-C(18)	1.381(4)	1.388(4)
C(14)-C(15)	1.384(5)	1.388(5)
C(15)-C(16)	1.377(6)	1.373(6)
C(16)-C(17)	1.372(6)	1.379(5)
C(17)-C(18)	1.397(5)	1.386(5)

Table 3. Bond angles (°) with E.S.D.S in brackets.

	molecule A	molecule B
C(6a)-N(1)-C(8)	113.8(2)	113.6(2)
C(6a)-N(1)-C(12)	116.3(2)	118.0(2)
C(8)-N(1)-C(12)	109.5(2)	109.4(2)
O(2)-N(2)-O(3)	123.2(3)	122.9(3)
O(2)-N(2)-C(2)	119.6(3)	120.0(2)
O(3)-N(2)-C(2)	117.1(2)	117.0(2)
O(1)-C(1)-C(2)	122.0(3)	122.4(3)
O(1)-C(1)-C(6a)	128.0(3)	127.4(3)
C(2)-C(1)-C(6a)	110.0(2)	110.1(2)
N(2)-C(2)-C(3)	109.3(2)	108.5(2)
N(2)-C(2)-C(7)	109.3(2)	109.5(2)
C(1)-C(2)-N(2)	105.2(2)	106.4(2)
C(1)-C(2)-C(3)	103.8(2)	103.2(2)
C(1)-C(2)-C(7)	112.9(3)	113.4(2)
C(3)-C(2)-C(7)	115.7(3)	115.4(2)
C(2)-C(3)-C(3a)	106.7(2)	106.4(2)
C(2)-C(3)-C(13)	116.2(2)	116.3(2)
C(3a)-C(3)-C(4)	111.5(2)	112.1(2)
C(3)-C(3a)-C(6a)	104.2(2)	103.6(2)
C(3)-C(3a)-C(13)	115.9(2)	116.4(2)
C(4)-C(3a)-C(6a)	105.3(2)	105.3(2)
C(3a)-C(4)-C(5)	105.5(3)	105.2(2)
C(4)-C(5)-C(6)	106.4(3)	106.8(3)
C(5)-C(6)-C(6a)	107.6(3)	106.6(2)
N(1)-C(6a)-C(1)	110.4(2)	110.2(2)
C(1)-C(6a)-C(6)	107.1(2)	107.7(2)
C(3a)-C(6a)-C(6)	102.1(2)	101.6(2)
N(1)-C(8)-C(9)	110.0(3)	110.5(3)
C(8)-C(9)-C(10)	110.8(3)	112.3(3)
C(9)-C(10)-C(11)	108.8(3)	108.8(3)
C(10)-C(11)-C(12)	110.0(3)	110.9(3)
N(1)-C(12)-C(11)	109.5(3)	109.7(3)
C(3)-C(13)-C(14)	119.1(3)	118.9(3)
C(3)-C(13)-C(18)	122.7(3)	123.2(2)
C(14)-C(13)-C(18)	118.2(3)	117.9(3)
C(13)-C(14)-C(15)	121.5(3)	122.0(3)
C(14)-C(15)-C(16)	119.6(4)	119.0(3)
C(15)-C(16)-C(17)	119.9(4)	120.2(3)
C(16)-C(17)-C(18)	120.3(4)	120.1(3)
C(13)-C(18)-C(17)	120.5(3)	120.7(3)

Table 4. Anisotropic thermal parameters with E.S.D.S. in brackets.

Molecule A

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O(1)	4.6(2)	4.7(1)	5.7(1)	1.5(1)	-4.5(1)	-3.1(1)
O(2)	9.8(3)	3.0(1)	7.6(2)	-0.5(2)	2.6(2)	-1.1(2)
O(3)	5.6(2)	4.6(1)	5.7(1)	0.6(1)	3.6(2)	1.9(1)
N(1)	3.4(2)	2.8(1)	3.6(1)	0.6(1)	0.1(1)	-0.1(1)
N(2)	3.8(2)	2.9(1)	4.6(1)	-0.2(1)	-0.1(1)	-0.9(1)
C(1)	3.6(2)	3.4(1)	2.8(1)	0.1(2)	-1.1(2)	-0.3(1)
C(2)	3.6(2)	2.8(1)	3.0(1)	0.3(1)	0.1(1)	-0.4(1)
C(3)	3.2(2)	2.7(1)	2.9(1)	0.1(1)	0.0(1)	0.1(1)
C(3a)	3.2(2)	2.7(1)	2.7(1)	0.0(1)	-0.3(1)	-0.4(1)
C(4)	3.9(3)	3.6(1)	4.5(2)	-0.3(2)	-1.2(2)	-1.8(2)
C(5)	5.1(3)	3.8(2)	5.2(2)	-2.0(2)	1.4(2)	-0.7(2)
C(6)	4.6(2)	3.4(1)	3.2(1)	0.8(2)	0.5(2)	0.7(2)
C(6a)	3.2(2)	2.9(1)	2.7(1)	0.1(1)	-0.6(1)	-0.4(1)
C(7)	5.4(3)	4.8(2)	3.4(1)	0.4(2)	0.4(2)	-3.2(2)
C(8)	3.8(3)	3.6(1)	6.1(2)	0.3(2)	2.7(2)	1.9(2)
C(9)	4.4(3)	4.4(2)	7.3(2)	0.1(2)	2.9(2)	-0.3(2)
C(10)	4.4(3)	5.6(2)	5.0(2)	1.5(2)	1.8(2)	-1.8(2)
C(11)	5.2(3)	3.9(2)	5.3(2)	1.7(2)	1.7(2)	-1.8(2)
C(12)	4.6(3)	3.3(1)	4.9(2)	0.5(2)	1.2(2)	-2.0(2)
C(13)	3.2(2)	2.8(1)	3.4(1)	-0.2(1)	-0.8(1)	-0.3(1)
C(14)	4.5(3)	4.8(2)	4.3(2)	2.5(2)	-0.2(2)	-2.1(2)
C(15)	4.8(3)	5.2(2)	6.8(2)	4.1(2)	-2.5(2)	-3.1(2)
C(16)	6.1(4)	3.6(2)	7.7(3)	1.8(2)	-4.9(3)	0.8(2)
C(17)	5.9(3)	4.8(2)	5.3(2)	-1.6(2)	-2.8(2)	3.7(2)
C(18)	3.6(3)	4.4(2)	4.2(2)	-0.7(2)	-0.8(2)	1.8(2)

Molecule B

O(1)	4.6(2)	4.5(1)	5.8(1)	0.8(1)	3.9(1)	2.3(1)
O(2)	7.9(2)	3.1(1)	7.8(2)	0.7(1)	-1.5(2)	-0.1(1)
O(3)	6.8(2)	5.1(1)	5.2(1)	0.7(1)	-3.5(1)	-1.9(1)
N(1)	3.8(2)	3.2(1)	3.4(1)	0.6(1)	0.1(1)	0.2(1)
N(2)	4.0(2)	3.3(1)	4.5(1)	-0.1(1)	0.9(1)	0.1(1)
C(1)	3.7(2)	3.6(1)	2.7(1)	-0.3(1)	1.3(1)	-0.2(1)
C(2)	3.9(2)	3.2(1)	3.1(1)	-0.2(1)	0.7(1)	0.1(1)
C(3)	3.2(2)	3.2(1)	3.1(1)	-0.4(1)	0.3(1)	-0.1(1)
C(3a)	3.4(2)	3.3(1)	2.9(1)	0.0(1)	0.8(1)	0.4(1)
C(4)	4.3(2)	3.6(1)	4.3(1)	-1.1(2)	2.2(2)	0.6(2)
C(5)	5.3(3)	3.7(1)	4.9(2)	-1.3(2)	0.1(2)	-0.1(2)
C(6)	4.4(2)	3.5(1)	3.1(1)	0.6(2)	0.0(1)	-0.7(1)
C(6a)	3.2(2)	3.4(1)	2.6(1)	0.5(1)	0.5(1)	-0.1(1)
C(7)	5.2(3)	4.6(2)	3.8(1)	1.2(2)	0.6(2)	2.5(2)
C(8)	4.5(3)	4.1(2)	5.3(2)	1.0(2)	-2.3(2)	-1.7(2)
C(9)	4.3(3)	5.7(2)	7.4(2)	1.2(2)	-3.6(2)	-0.3(2)
C(10)	5.2(3)	5.6(2)	4.7(2)	2.5(2)	-1.5(2)	0.8(2)
C(11)	6.5(3)	4.6(2)	4.4(2)	3.7(2)	-1.0(2)	0.5(2)
C(12)	5.7(3)	3.4(1)	4.3(2)	0.7(2)	-1.6(2)	0.6(2)
C(13)	3.5(2)	3.0(1)	3.6(1)	-0.2(1)	0.8(1)	-0.5(1)
C(14)	4.0(3)	5.0(2)	4.8(2)	2.0(2)	-0.9(2)	-0.5(2)
C(15)	4.3(3)	4.8(2)	7.1(2)	2.2(2)	0.1(2)	-0.6(2)
C(16)	4.3(3)	4.7(2)	6.9(2)	0.9(2)	3.2(2)	-1.7(2)
C(17)	5.7(3)	4.6(2)	4.5(2)	0.7(2)	2.6(2)	-2.0(2)
C(18)	4.4(2)	4.2(1)	3.6(1)	0.4(2)	0.9(2)	-1.2(2)