1,3-Dipolar Cycloadditions: Investigation of Cycloadditions of *C*-Aryl-*N*-(4-Chlorophenyl) Nitrones to *N*-Cinnamoyl Piperidines

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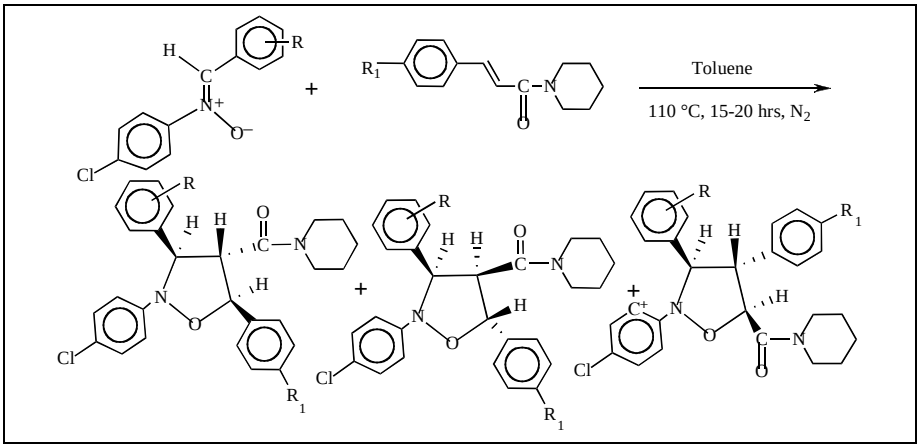
Received April 13, 2006



Investigation of cycloadditions of *C*-aryl-*N*-(4-chlorophenyl)nitrones to *N*-cinnamoyl piperidines was carried out. Two diastereoisomeric and one regioisomeric cycloadducts, and in some cases ring-opened compounds were characterized by spectroscopic and X-ray data. Molecular modelling was carried out for conformational studies.

J. Heterocyclic Chem., **44**, 137 (2007).

INTRODUCTION

The 1,3-dipolar cycloaddition of nitrones to electron-deficient olefins constitutes the best procedure for the synthesis of isoxazolidines [1-4]. Exploiting this strategy as the key step, several classes of biologically active compounds as well as natural products have been synthesized [2-5]. As a part of our investigations in this particular field [6-9], we have recently carried out the $\pi^4s + \pi^2s$ cycloaddition of *C*-aryl-*N*-(4-chlorophenyl) nitrones to *N*-cinnamoyl piperidines. The main objective of this investigation was to study the regio- and stereochemical course of nitrone cycloaddition reaction to 1,2-disubstituted olefins as well as the substitution effect on the aryl rings of the substrate. This communication gives a report of this investigation.

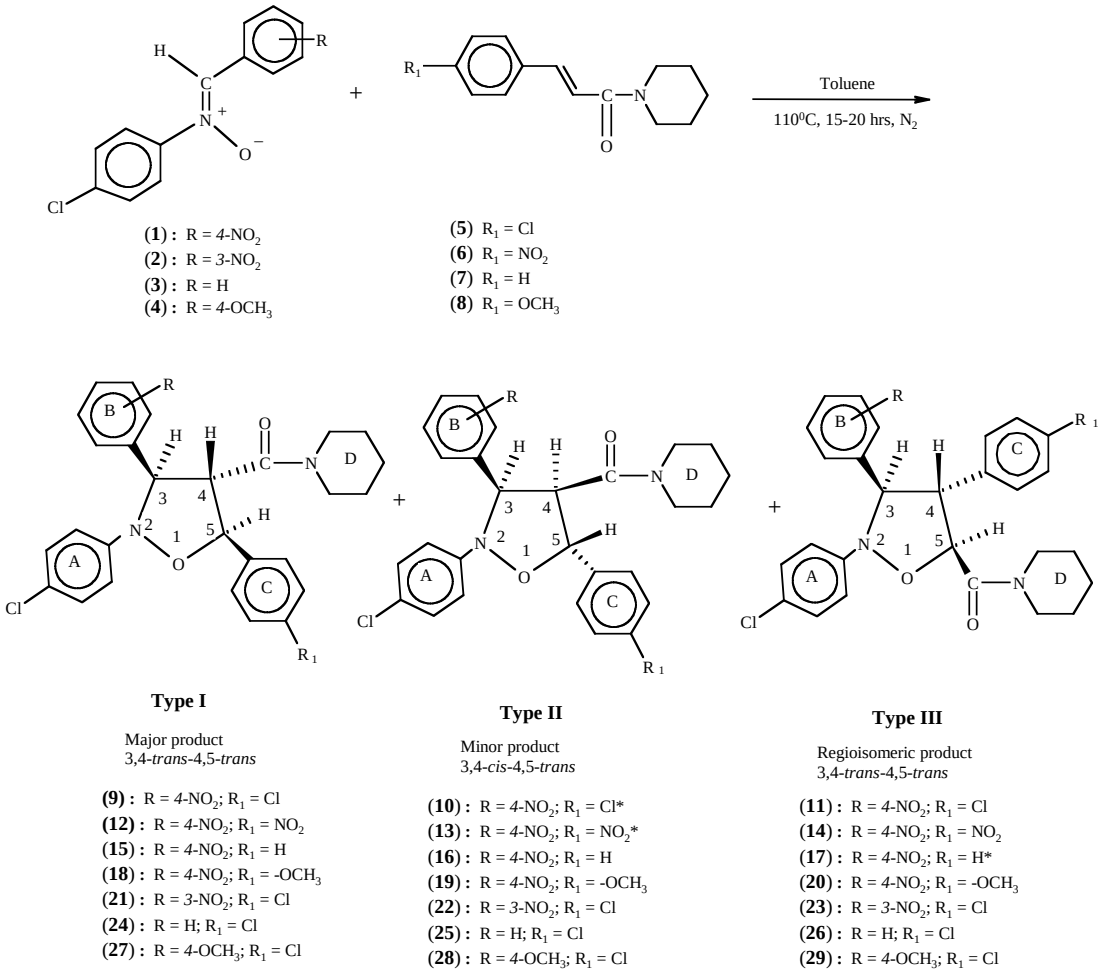
RESULTS AND DISCUSSION

A new series of nitrones, *viz*. *C*-aryl-*N*-(4-chlorophenyl) nitrones, were chosen for the present cycloaddition studies. A total of seven reactions were carried out varying the substituents on the aryl rings from electron-donating to electron-withdrawing groups (Scheme I). These nitrones were initially synthesized by the conventional procedure of heating *N*-(4-chlorophenyl)-hydroxylamine with the appropriate aldehydes in ethanol.

Subsequently, an improved microwave assisted procedure similar to that developed by the authors for the *C*-aryl-*N*-methyl nitrones [9] was used.

1,3-Dipolar cycloadditions of *C*-aryl-*N*-(4-chlorophenyl) nitrones (**1**-**4**) to *N*-cinnamoyl piperidines (**5**-**8**) afforded mixture of diastereoisomeric products (types **I**, **II**) and small amounts of regioisomeric products (type **III**); in some cases ring-opened compounds (**9a**, **10a**, **13a**, **17a**), were also obtained (Scheme 1).

The reactions were carried out using three-fold molar excess of the dipolarophile, to enhance reaction rates and hence yields, in refluxing toluene under nitrogen atmosphere for about 15-20 hrs. At the end of this period, only small amounts of the nitrones survived. Removal of the solvent under reduced pressure and chromatography over neutral alumina furnished the products. The all-*trans* isomers (type **I**) were the major products isolated from all the reactions in this series. The diastereoisomeric 3,4-*cis*-4,5-*trans* (type **II**) 5-aryl-4-piperidinyloxoisoxazolidine cycloadducts were isolated in some cases, the others were characterized from the ^{1}H NMR spectra of the crude reaction mixture. The regioisomeric (type **III**) 4-aryl-5-piperidinyloxoisoxazolidines were identified from the ^{1}H NMR spectra of the crude reaction mixture. Product ratios of the cycloadducts were determined by ^{1}H NMR analysis



Scheme 1

of crude reaction mixture. The product ratios for the different series of cycloadducts were found to be as follows: 100:14:11:7 (**9**:**10**:**11**:**9a**), 100:49:17 (**12**:**13a**:**14**), 100:24:21 (**15**:**16**:**17**), 100:10:7 (**18**:**19**:**20**), 100:14:8 (**21**:**22**:**23**), 100:8:6 (**24**:**25**:**26**), 100:14:8 (**27**:**28**:**29**), respectively.

All the isolated products showed amide bands at 1600-1650 cm^{-1} in their respective IR spectra. The three types of cycloadducts (*viz*. type **I**, type **II** and type **III**) could be differentiated from their ^{1}H and ^{13}C NMR characteristics. The C(3)H doublet (in the series **9**, **10**, **11**) appeared at δ 5.37 ppm in (**9**) and δ 4.52 ppm in (**10**), C(5)H was found as a doublet at δ 5.20 ppm (**9**) and δ 4.88 ppm (**10**). C(4)H resonated comparatively upfield for both (**9**) and (**10**) at δ 3.65 ppm. In the regioisomeric compound (**11**) [type **III** series], H-3 and H-5 were shielded by ~0.7 and 1.0 ppm, respectively, compared to (**9**); the benzylic H-4 (double doublet) was deshielded by ~1.0 ppm. These relationships were typical of all the compounds belonging to the different series. Two-dimensional ^{1}H-^{1}H-COSY and HMBC experiments established 2-aryl-3,4,5-trisubstituted isoxazolidine derived structures for all cycloadducts; the sequence -O-C(5)H-C(4)H-C(3)H-N(2)Ar was found to be present in all cases. Two-dimensional long-range COSY experiments revealed correlations between the benzylic proton and C(3)H for all three types of cycloadducts. Such long-range correlations exists between C(5)H and benzylic protons in types **I** and **II**; in type **III** cycloadducts the correlation is between C(4)H and the benzylic protons. Thus types **I** and **II** cycloadducts are 2-(4-chlorophenyl)-3,5-diaryl-4-piperidinyloxoisoxazolidine derivatives stereoisomeric at C(3); the relative *trans*-C(4)H-C(5)H stereochemistry follows from the substrate amide. The type **III** cycloadducts, on the other hand are regioisomers, with 2-(4-chlorophenyl)-3,4-diaryl-5-piperidinyloxoisoxazolidine structures.

The ring-opened compounds of isoxazolidine ring system were identified from the presence of two hydroxyl protons *viz*. >N-OH and 5-OH. These two hydroxyl protons, *viz*. >N-OH and 5-OH, showed long-range

coupling with H-3, H-4, and H-5 protons (as well as to each other) respectively in TOCSY spectra.

The X-Ray crystallographic analysis of a representative compound of type **I**, *viz* (**9**) (R= 4-NO_2; R_1= Cl) showed that the compound had all-*trans* stereochemistry, including the lone pair of ring nitrogen [N2, *trans* to C(3)H] (Figure 1). The relative configuration of the minor cycloadducts followed as 3,4-*cis* (type **II**). The regio-isomers of type **III** were given the relative configuration shown, on the basis of NMR comparisons with the other cycloadducts, and similar cycloadducts derived from *C*-aryl-*N*-phenyl nitrones [8,9], for which the X-Ray crystallographic analysis were performed.

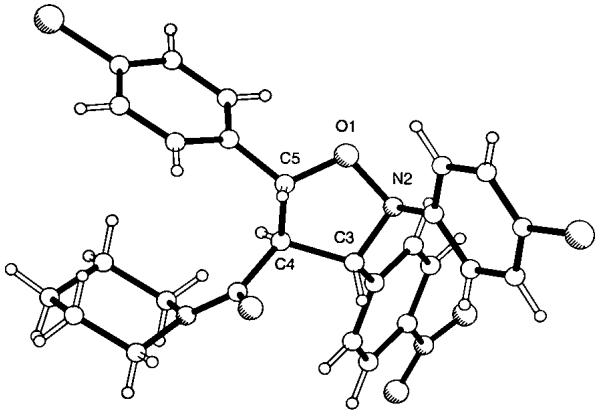


Figure 1. PLUTO projection of **9** (all-*trans* isomer).

Interest was then focused on the conformational analysis and computer-assisted energy minimisation of the stereoisomeric (**9**) and (**10**). Energy minimisation of the all-*trans* isomer (**9**), and the corresponding diastereoisomeric (**10**) was carried out considering the corresponding non-chlorinated analogues by conjugate gradient method [10,11] using DISCOVER Molecular Simulation Program (version 2.98) running on a Silicon Graphics O_2 workstation. In these cases normal completion of conjugate gradient was achieved in 1000 steps of energy evaluations. The derived structures are given in Figure 2 for (**9**) and Figure 3 for (**10**). From the relative values of potential energy it was found that the energy content of 3,4-*cis*-4,5-*trans* isomer was about 3.6 kcal/mol greater than all-*trans* isomer (Table 1). This value of potential energy reflects the overall stability of the 3,4-*trans*-4,5-*trans* (all-*trans*) isomer, which was found as a major product in this series of reactions.

Table 1

Relative values of potential energy of isomer (**9**) and (**10**).

Isomer	Relative P.E. (kcal/mol)
all-*trans*	0.0
3,4-*cis*-4,5-*trans*	3.6

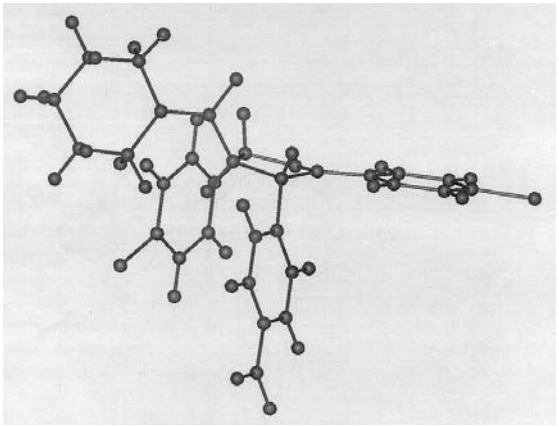


Figure 2. Molecular modelling of **9** (all-*trans* isomer).

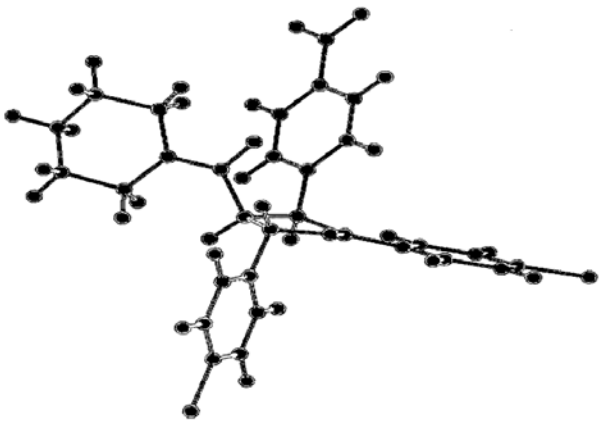


Figure 3. Molecular modelling of **10** (3,4-*cis*-4,*5-trans* isomer).

The all-*trans* isomer is obtained by the *endo*-mode of approach of the dipolarphile with respect to the carbonyl group. Several publications have analysed the regio-selectivity and diastereoselectivity of the 1,3-dipolar cycloadditions of nitrones on the basis of FMO interactions [2,12,13]. Most authors have explained the favoured *endo*-mode of approach with respect to the carbonyl group, to be due to favourable 'Secondary orbital interactions', on the other hand, others have proposed that other factors are responsible. Our experimental results seem to indicate steric and dipolar factors that favour the all-*trans*-cycloadduct, should also play a significant role in the transition state leading to it.

In conclusion, detailed study of 1,3-dipolar cyclo-addition of C-aryl-*N*-(4-chlorophenyl) nitrones to *N*-cinnamoyl piperidines has been carried out including energy calculations of cycloadducts. The major products in all the cases are formed by *endo*- addition. Only small but perceptible changes of product ratios on changing the aryl ring substituents were observed usually. However, when the dipolarophile was a 4-nitro derivative; the relative proportion of the diasteroisomeric cycloadduct (Type II) became comparatively much higher.

EXPERIMENTAL

General. Melting points were recorded on a Köfler block apparatus and are uncorrected. Neutral alumina was used for column chromatography, and silica gel (60-120 mesh) for TLC. Petrol refers to the petroleum ether AR (b.p. 60-80°). Analytical samples were routinely dried over $CaCl_2$ *in vacuo* at room temperature. IR spectra were recorded in KBr pellets with a Perkin-Elmer RX-1 FT-IR, and UV spectra in spectroscopic grade ethanol (Merck) with a Hitachi U-3501 instrument. Mass spectra were recorded with a JEOL JMS600 mass spectrometer. Elemental analysis (C, H, N) were conducted using the Perkin-Elmer 2400 Series II elemental analyser, their results were found to be in good agreement (± 0.2%) with the calculated values for C, H, N. 300 MHz ^{1}H NMR, 75.5 MHz ^{13}C NMR and two-dimensional spectra (COSY, XHCORR) were recorded in $CDCl_3$ and d_6-DMSO solution with a Bruker AM-300L spectrometer (chemical shifts in δ ppm and *J* in Hz). 500 MHz ^{1}H NMR, 125 MHz ^{13}C NMR and corresponding two-dimensional correlation experiments (DQF, TOCSY, HMQC and HMBC) were recorded with a Bruker DRX 500 NMR spectrometer (11.7 Tesla). (A-C) refers to the respective rings (Scheme I).

The compound *N*-(4-chlorophenyl)hydroxylamine, m.p. 89-90 °C was prepared from 4-chloronitrobenzene by adopting the method used for obtaining *N*-phenylhydroxylamine from nitrobenzene [14]. Initially the nitrones were prepared as described in our early communications [7,8,9]. The *C*-aryl-*N*-(4´-chlorophenyl) nitrones were also synthesised by a more convenient method using microwave irradiation techniques from the appropriate aromatic aldehyde and *N*-(4-chlorophenyl) hydroxylamine. This improved procedure was similar to that developed by the authors for *C*-aryl-*N*-methyl nitrones [9]. In this procedure the aromatic aldehyde was taken with a small excess of *N*-(4-chlorophenyl) hydroxylamine (1:1.2 molar ratio) in dry dichloromethane in an Erlenmeyer flask. The reaction mixture was subjected to microwave irradiation for periods varying from 1-4 min. For *C*-phenyl-*N*-(4-chlorophenyl) nitrone the yield, after 4 min was 91.5%. Similar reaction times and yields were found for the other nitrones. At the end of the reaction period the post-reaction mixture was worked up, and the residue was analysed by ^{1}H NMR. The nitrones were crystallised from ethanol, methanol or petrol-benzene mixture and characterised from their FT-IR, 300 MHz ^{1}H NMR and 75.5 MHz ^{13}C NMR spectra.

General Method. A hot solution of nitrones **1-4** (0.0066 mol) in anhydrous toluene (20 ml) was added to a solution of piperidides **5-8** (3 x 0.0066 mol) in anhydrous toluene (20 ml). The reaction mixture was refluxed under a nitrogen atmosphere for 15-20 hrs. The reaction was monitored by TLC and by 300 MHz ^{1}H NMR analyses. The solvent was removed from the crude reaction mixture, and the mixture was chromatographed over neutral alumina to separate the products.

Reaction of *C*-(4-Nitrophenyl)-*N*-(4´-chlorophenyl) nitrone (1) with Piperidide of 4-Chlorocinnamic acid (5). 3*RS*-(3*R, 4*S**,5*R**)-2-(4´-Chlorophenyl)-3-(4´´-nitrophenyl)-5-(4-chlorophenyl)-4-piperidinyl-oxoisoxazolidine (9); $C_{27}H_{25}N_3O_4Cl_2$).** White crystals; m.p.: 164°C; yield: 1.73 g (70%); IR: ν = 2937, 2860 (m, -CH_2-), 1636 (s, amide >C=O), 827 (m, 1, 4-disubstituted benzene ring); cm^{-1}; UV:λ_{max} (log ε) = 249 (4.01) nm; ^{1}H NMR (d_6-DMSO, δ, 500 MHz): 5.18 (1H, d, J=7.0, H-3), 3.83 (1H, dd, J=7.0, 9.3, H-4), 5.03 (1H, d, J= 9.3, H-5), 3.29 (1H, m, H_A-2′), 3.15 (1H, m, H_B-2′), 2.65 (2H, m, H-6′), 1.04 (2H, m, H-3′), 1.16 (2H, m, H-4′), 0.73 (1H, m, H_A-5′), 0.47 (1H, m, H_B-5′), 6.78 (2H, d, J=8.7, A,H-2,6), 7.12 (2H, d, J=8.7, A,H-3,5), 7.61 (2H, d, J=8.7, B,H-2,6), 8.09 (2H, d, J=8.7, B,H-3,5), 7.29 (2H, d, J=8.4, C,H-2,6), 7.36 (2H, d, J=8.4, C,H-3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 74.9 (C-3), 63.9 (C-4), 84.5 (C-5), 43.0 (C-2′), 25.7 (C-3′), 24.1 (C-4′), 26.4 (C-5′), 46.9 (C-6′), 165.8 (>C=O), 150.0 (A,C-1), 115.7 (A,C-2,6), 127.9 (A,C-3,5), 135.2 (A,C-4), 147.0 (B,C-1), 127.1 (B,C-2,6), 124.1 (B,C-3,5), 148.4 (B,C-4), 127.6 (C,C-1), 129.2 (C,C-2,6), 129.1 (C,C-3,5), 134.4 (C,C-4) ppm: MS(FAB): m/z = 527 (M^++2), 385 (M^+ - C_7H_5OCl), 301 (385 – $C_5H_{10}NO$; 18%), 283 (M^+ – $C_{12}H_{17}NO_2Cl$; 100% base peak), 259 (M^+ – $C_{14}H_{17}NO_2Cl$; 11%), 154 (266 – $C_6H_{10}NO$; 100% base peak), 136 (249 – C_6H_4Cl – 2H$^\bullet$; 68%). *Anal*. Calcd. for $C_{27}H_{25}N_3O_4Cl_2$: C, 61.76; H, 4.80; N, 8.01. Found: C, 61.69 ; H, 4.72; N, 7.90.

1*RS*-(1*R,2*R**,3*S**)-1´-[*N*-Hydroxy-*N*-(4-chlorophenyl)-amino]-1´-(4-nitrophenyl)-3-[hydroxy-3-(4-chlorophenyl)]-propanoyl piperidines, (10a; $C_{27}H_{27}N_3O_5Cl_2$).** Light brown solid; m.p.: 236°C; yield: 0.25 g (10%) ; IR: ν = 3377, 3285 (m, -OH), 2934 -2850 (m, -CH_2-), 1607 (s, amide >C=O), 830 (m, 1, 4-disubstituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 254 (3.71) nm; ^{1}H NMR (d_6-DMSO, δ, 500 MHz): 4.52 (1H, t, J=8.2, H-3), 3.49 (1H, br.t, H-4), 4.88 (1H, dd, J=7.3, 3.5, H-5), 6.63 (1H, d, J=7.3, >N-OH), 5.85 (1H, d, J=3.5, 5-OH), 2.76 (4H, m, H-2′,6′), 0.73 (2H, m, H-3′), 1.02 (2H, m, H-4′), 0.59 (2H, m, H-5′), 6.33 (2H, d, J=8.8, A,H-2,6), 6.84 (2H, d, J=8.8, A,H-3,5), 7.42 (2H, d, J=8.7, B,H-2,6), 7.90 (2H, d, J=8.7, B,H-3,5), 7.06 (2H, d, J=8.5, C,H-2,6), 7.10 (2H, d, J=8.5, C,H-3.5) ppm; ^{13}C NMR (d_6-DMSO, δ, 125.5 MHz) 59.6 (C-3), 53.7 (C-4), 74.4 (C-5), 42.4 (C-2′), 25.9 (C-3′), 24.4 (C-4′), 26.3 (C-5′), 47.1 (C-6′), 167.9 (>C=O), 146.7 (A,C-1), 115.6 (A,C-2,6), 129.5 (A,C-3,5), 121.2 (A,C-4),147.3 (B,C-1),129.9 (B,C-2,6), 123.7 (B,C-3,5), 150.8 (B,C-4), 132.4 (C,C-1), 129.7 (C,C-2,6), 128.2 (C,C-3,5), 142.8 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{27}N_3O_5Cl_2$: C, 61.80; H, 4.82; N, 9.02. Found: C, 61.65; H, 4.76; N, 7.94.

3*RS*-(3*R,4*S**,5*R**)-2-(4´-chlorophenyl)-3-(4´´-nitrophenyl)-4-(4-chlorophenyl)-5-piperidinyl-oxoisoxazolidine (11;** $C_{27}H_{25}N_3O_4Cl_2$). The regioisomeric cycloadduct (**11**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.38 (1H, d, J=7.9, H-3), 5.00 (1H, dd, J=7.9, 6.7, H-4), 5.17 (1H, d, J=6.7, H-5).

1*RS*-(1*R,2*R**,3*S**)-1′-[*N*-hydroxy-*N*-(4-chlorophenyl)-amino]-1′-(4-nitrophenyl) 3-[hydroxy-3-(4-chlorophenyl)] propanoyl piperidines, (9a; $C_{27}H_{27}N_3O_5Cl_2$).** White crystalline solid; m.p.: 170°C; yield; 0.25 g (10%); IR: ν = 3421, 3346 (m, -OH), 2934, 2861 (m, -CH_2-), 1626 (s, amide >C=O), 819 (m, 1, 4-disubstituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 254 (4.24) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 4.80 (1H, d, J=7.4, H-3), 3.20 (1H, dd, J=7.4, 4.5, H-4), 4.65 (1H, d, J=4.5, H-5), 5.39 (1H, s, >N-OH), 3.96 (1H, s, 5-OH), 3.56 (1H, m, H_A-2′), 3.28 (1H, m, H_B-2′), 2.99 (2H, m, H-6′), 1.50 (4H, m, H-3′,4′), 1.18 (2H, m, H-5′), 6.13 (2H, d, J=8.7 A,H-2,6), 6.92 (2H, d, J=8.7, A,H-3,5), 7.17 (2H, d, J=8.5, B,H-2,6), 7.93 (2H, d, J=8.5, B,H-3,5), 6.92 (2H, d, J=8.4, C,H-2,6), 7.11 (2H, d, J=8.4, C,H-3,5) ppm. ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 60.4 (C-3), 54.6 (C-4), 71.2 (C-5), 41.9 (C-2′), 26.2 (C-3′), 24.2 (C-4′), 27.9 (C-5′), 44.3 (C-6′), 172.0 (>C=O), 150.0 (A,C-1), 115.3 (A,C-2,6), 129.0 (A,C-3,5), 136.0 (A,C-4), 147.0 (B,C-1), 128.5 (B,C-2,6), 123.5 (B,C-3,5), 148.0 (B,C-4), 127.0 (C,C-1), 130.0 (C,C-2,6), 129.1 (C,C-3,5), 145.0 (C,C-4) ppm. *Anal*. Calcd. for

$C_{27}H_{27}N_3O_5Cl_2$: C, 61.80; H, 4.82; N, 8.02. Found: C, 61.62; H, 4.74; N, 7.97.

Reaction of *C*-(4-Nitrophenyl)-*N*-(4′-chlorophenyl) nitrone (1) with Piperidide of 4-Nitrocinnamic acid (6). 3*RS*-(3*R,4*S**,5*R**)-2-(4′-chlorphenyl)-3-(4′′-nitrophenyl)-5-(4-nitrophenyl)-4-piperidinyl-oxoisoxazolidine (12, $C_{27}H_{25}N_4O_6Cl$).** Yellowish crystals; m.p.: 184°C; yield: 1.44 g (57%); IR: ν = 2940, 2860 (m, -CH_2-), 1638 (s, amide >C=O), 838 (m, 1,4-disubstituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 255 (4.14) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.49 (1H,d, J=9.3, H-3), 3.73 (1H, t, J=8.6, H-4), 5.33 (1H, d, J=9.1, H-5), 3.56 (2H, m, H-2′), 2.72 (2H, m, H-6′), 1.46 (4H, m, H-3′,4′), 0.93 (1H, m, H_A-5′), 0.81 (1H, m, H_B-5′), 6.91 (2H, d, J=8.8, A,H-2,6), 7.23 (2H, d, J=8.8, A,H-3,5), 7.71 (2H, d, J=8.6, B,H-2,6), 8.29 (2H, d, J=8.6, B,H-3,5), 7.64 (2H, d, J=8.6, C,H-2,6), 8.26 (2H, d, J=8.6, C,H-3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 74.9 (C-3), 63.3 (C-4), 83.3 (C-5), 43.7 (C-2′), 25.5 (C-3′), 23.8 (C-4′), 26.2 (C-5′), 46.7 (C-6′), 165.2 (>C=O), 149.2 (A,C-1), 115.7 (A,C-2,6), 128.9 (A,C-3,5), 147.1 (A,C-4), 147.8 (B,C-1), 124.2 (B,C-2,6), 123.8 (B,C-3,5), 148.1 (B,C-4), 127.9 (C,C-1), 126.9 (C,C-2,6), 126.6 (C,C-3,5), 143.2 (C,C-4) ppm. MS (EI): m/z = 536(M^+), 409 (M^+ - C_6H_4NCl-2H$^\bullet$), 276 [M^+ – $C_{14}H_{16}N_2O_3$], 260 [M^+ - $C_{13}H_9N_2O_3Cl$; 100% base peak], 385 [M^+ - $C_7H_5NO_3$], 150 [M^+ – $C_{20}H_{20}N_3O_3Cl$ - H$^\bullet$], 176 (260 – $C_5N_{10}NO$; 63%), 138 (259 – $C_6H_4NO_2$ + H$^\bullet$), 125 ($C_6H_6NCl^+$; 100% base peaks), 111 ($C_6H_4Cl^+$), 84 ($C_5H_{10}N^+$), 102 (150-NO_2-2H$^\bullet$). *Anal*. Calcd. for $C_{27}H_{25}N_4O_6Cl$: C, 60.45; H, 4.70; N, 10.45. Found: C, 60.38; H, 4.65; N, 10.40.

1*RS*-(1*R,2*R**,3*S**)-1′-[*N*-hydroxy-*N*-(4-chlorophenyl)-amino]-1′-(4-nitrophenyl)-3-hydroxy-3-(4-nitrophenyl)-propanoyl piperidine (13a, $C_{27}H_{27}N_4O_7Cl$).** White needle shaped crystals; m.p.: 230°C; yield: 0.59 g (29%); IR: ν = 3349, 3271 (m, -OH), 2934, 2858 (m, -CH_2-), 1607 (s, amide >C=O), 856, 819 (m, 1,4-disubstituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 255 (4.29) nm; ^{1}H NMR (d_6-DMSO, δ, 300 MHz): 4.64 (1H, t, J=7.4, H-3), 3.79 (1H, br. t, H-4), 5.24 (1H, dd, J=6.4, 3.6, H-5), 6.83 (1H, d, J=7.9, >N-OH), 6.19 (1H, d, J=3.6), 3.04 (2H, m, H-2′), 2.86 (2H, m, H-6′), 1.20 (4H, m, H-3′,4′), 0.98 (1H, m, H_A-5′), 0.71 (1H, m, H_B-5′), 6.52 (2H, d, J=8.5, A, H-2,6), 7.02 (2H, d, J=8.5, A,H-3,5), 7.58 (2H, d, J=8.5, B,H-2,6), 8.09 (2H, d, J=8.5, B,H-3,5), 7.47 (2H, d, J=8.5, C,H-2,6), 8.06 (2H, d, J=8.5, C,H-3,5) ppm; ^{13}C NMR (d_6-DMSO, δ, 75.5 MHz): 57.4 (C-3), 51.4 (C-4), 72.1 (C-5), 40.8 (C-2′), 24.3 (C-3′), 22.7 (C-4′), 24.7 (C-5′), 45.5 (C-6′), 166.2 (>C=O), 150.0 (A,C-1), 113.9 (A,C-2,6), 128.3 (A,C-3,5), 145.7 (B,C-1), 127.4 (B,C-2,6), 121.7 (B,C-3,5), 148.9 (B,C-4), 119.6 (C,C-1), 127.6 (C,C-2,6), 122.0 (C,C-3,5), 144.9 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{27}N_4O_7Cl$: C, 60.47; H, 4.72; N, 10.50. Found: C, 60.33; H, 4.62; N, 10.43.

3RS-(3R*,4S*,5R*)-2-(4′-chlorophenyl)-3-(4′′-nitrophenyl)-4-(4-nitrophenyl)-5-piperidinyl-oxoisoxazolidine (14, $C_{27}H_{25}N_4O_6Cl$). The regioisomeric cycloadduct **(14)** was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.55 (1H, d, J=8.8, H-3), 4.95 (1H, br. t), 5.06 (1H, d, J=9.5).

Reaction of *C*-(4-Nitrophenyl)-*N*-(4′-chlorophenyl) nitrone (1) with Piperidide of Cinnamic acid (7). 3*RS*-(3*R,4*S**,5*R**)–2-(4-chlorophenyl)-3-(4′-nitrophenyl)-5-phenyl-4-piperidinyloxo-isoxazolidine, (15, $C_{27}H_{26}N_3O_4Cl$).** White crystals; m.p.: 150°C; yield: 0.6 g (56%); IR: ν = 2936, 2857 (m, -CH_2-), 1626 (s, amide >C=O), 834 (m, 1,4-disubstituted benzene ring), 758, 699 (m, mono-substituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 250 (4.35) nm; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 5.51 (1H, d, J=7.5, H-3), 3.77 (1H, dd, J=7.5, 9.5, H-4), 5.23 (1H, d, J=9.5, H-5), 3.64 (1H, m, H_A-2′), 3.40 (1H, m, H_B-2′), 2.74 (2H, m, H-6′), 1.40 (4H, m, H-3′,4′), 0.95 (1H, m, H_A-5′), 0.64 (1H, m, H_B-5′), 6.93 (2H, d, J=8.9, A,H-2,6), 7.22 (2H, d, J=8.9, A,H-3,5), 7.73 (2H, d, J=8.7, B,H-2,6), 8.26 (2H, d, J=8.7, B,H-3,5), 7.38-7.44 (5H, m, C,H-2,3,4,5,6) ppm; ^{13}C NMR ($CDCl_3$, δ, 125.5 MHz): 75.2 (C-3), 64.5 (C-4), 85.7 (C-5), 44.3 (C-2′), 26.1 (C-3′), 24.5 (C-4′), 26.6 (C-5′), 47.3 (C-6′), 166.2 (>C=O), 150.5 (A,C-1), 115.9 (A,C-2,6), 129.4 (A,C-3,5), 127.5 (A,C-4), 149.3 (B,C-1), 127.4 (B,C-2,6), 124.8 (B,C-3,5), 148.1 (B,C-4), 135.6 (C,C-1), 127.1 (C,C-2,6), 129.5 (C,C-3,5), 129.8 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{26}N_3O_4Cl$: C, 66.11; H, 5.34; N, 8.54. Found: C, 65.90; H, 5.27; N, 8.47.

3*RS*-(3*R,4*R**,5*S**)-2-(4-chlorophenyl)-3-(4′-nitrophenyl)-5-phenyl-4-piperidinyloxo-isoxazolidine (16**, $C_{27}H_{26}N_3O_4Cl$). White shiny crystals; m.p.: 240°C; yield: 0.25 g (24%); IR: ν = 2939, 2859 (m, -CH_2-), 1609 (s, amide >C=O), 858 (m, 1,4-disubstituted benzene ring), 770, 702 (m, mono-substituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 252 (4.32) nm; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 5.08 (1H, d, J=9.5, H-3), 3.41 (1H, dd, J=9.5, 7.1, H-4), 5.27 (1H, d, J=7.1, H-5), 3.07 (1H, m, H_A-2), 2.94 (1H, m, H_B-2′), 2.73 (1H, m, H_A-6′), 2.56 (1H, m, H_B-6′), 1.01 (2H, m, H-3′), 1.23 (2H, m, H-4′), 0.82 (1H, m, H_A-5′), 0.62 (1H, m, H_B-5′), 6.30 (2H, d, J=8.8, A,H-2,6), 7.00 (2H, d, J=8.8, A,H-3,5), 7.61 (2H, d, J=8.7, B,H-2,6), 8.12 (2H, d, J=8.7, B,H-3,5), 7.39 (2H, d, J=7.2, C,H-2,6), 7.32 (2H, t, J=7.3, C,H-3,5), 7.29 (1H, d, J=7.2, C,H-4) ppm; ^{13}C NMR ($CDCl_3$, δ, 125.5 MHz): 61.2 (C-3), 54.7 (C-4), 76.7 (C-5), 42.5 (C-2′), 25.4 (C-3′), 24.1 (C-4′), 26.0 (C-5′), 46.9 (C-6′), 177.0 (>C=O), 145.5 (A,C-1), 115.8 (A,C-2,6), 128.6 (A,C-3,5), 128.4 (A,C-4), 148.0 (B,C-1), 126.9 (B,C-2,6), 124.0 (B,C-3,5), 152.0 (B,C-4), 142.5 (C,C-1), 128.9 (C,C-2,6), 128.8 (C,C-3,5), 129.3 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{26}N_3O_4Cl$: C, 66.11; H, 5.34; N, 8.54. Found: C, 65.94; H, 5.29; N, 8.45.

1*RS*-(1*R,2*S**,3*R**)-1′-*N*-hydroxy-*N*-(4′-chlorophenyl)-amino]-1′-(4′-nitrophenyl)-2-phenyl-3-hydroxy-3-propanoylpiperidine (17a, $C_{27}H_{28}N_3O_5Cl$).** White flakes; m.p.: 156°C; yield: 0.12 g (12%); IR: ν = 3422, 3300 (m, -OH), 2940, 2900 (m, -CH_2-), 1626 (s, amide >C=O), 821 (m, 1,4-disubstituted benzene ring), 703 (m, mono-substituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 254 (4.19) nm; ^{1}H NMR ($CDCl_3$, δ, 500 MHz): 4.95 (1H, br.t, J ~7, H-3), 3.25 (1H, dd, J=8, 3, H-4), 4.80 (1H, dd, J= 9, H-5), 5.46 (1H, d, J=6, >N-OH), 4.00 (1H, d, J=9, 5-OH), 3.58 (1H, m, H_A-2′), 3.36 (1H, m, H_B-2′), 3.26 (1H, m, H_A-6′), 3.00 (1H, m, H_B-6′), 1.43 (2H, m, H-3′), 1.53 (2H, m, H-4′), 1.25 (1H, m, H-5′), 6.40 (2H, d, J=9, A,H-2,6), 7.00 (2H, d, J=9, A,H-3,5), 7.26 (2H, d, J=8.5, B,H-2,6), 7.99 (2H, d, J=8.5, B,H-3,5), 7.04 (2H, dd, J=7, 2.3, C,H-2,6), 7.21-7.23 (3H, m, C,H-3,4,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 125.5 MHz): 60.7 (C-3), 55.9 (C-4), 71.3 (C-5), 44.2 (C-2′), 25.8 (C-3′), 24.4 (C-4′), 26.4 (C-5′), 47.0 (C-6′), 172.4 (>C=O), 145.2 (A,C-1), 115.4 (A,C-2,6), 129.4 (A,C-3,5), 123.3 (A,C-4), 147.3 (B,C-1), 128.8 (B,C-2,6), 123.7 (B,C-3,5), 149.9 (B,C-4), 139.5 (C,C-1), 128.2 (C,C-2,6), 129.2 (C,C-3,4,5) ppm. *Anal*. Calcd. for $C_{27}H_{28}N_3O_5Cl$: C, 63.15; H, 5.36; N, 8.56. Found: C, 65.95; H, 5.39; N, 8.48.

Reaction of *C*-(4-Nitrophenyl)-*N*-(4′-chlorophenyl) nitrone (1) with Piperidide of 4-Methoxycinnamic acid (8). 3*RS*-(3*R,4*S**,5*R**)-2-(4-chlorophenyl)-3-(4-nitrophenyl)-5-(4-methoxyphenyl)-4-piperidinyloxoisoxazolidine, (18, $C_{28}H_{28}N_3O_5Cl$).** White crystals; m.p.: 150°C; yield: 0.48 g (83 %); IR: ν = 2934, 2854 (m, -CH_2-), 1634 (s, amide >C=O), 829

(s, 1,4-disubstituted benzene ring), cm^{-1}; UV: λ_{max} (log ε) = 250 (4.35) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.53 (1H, d, J=7.5, H-3), 3.76 (1H, t, J=8.5, H-4), 5.16 (1H, d, J= 9.5, H-5), 3.60 (1H, m, H_A-2′), 3.44 (1H, m, H_B-2′), 2.75 (2H, m, H-6′), 1.36 (4H, m, H-3′,4′), 0.95 (1H, m, H_A-5′), 0.70 (1H, m, H_B-5′), 3.81 (3H, s, -OC<u>H</u>$_3$), 6.91 (2H, d, J=8.5, A,H-2,6), 7.35 (2H, d, J=8.5, A,H-3,5), 7.72 (2H, d, J=8.5, B,H-2,6), 8.27 (2H, d, J=8.5, B,H-3,5), 7.21 (1H, d, J=8.5, C,H-2,6), 6.91 (1H, d, J=8.5, C,H-3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 74.8 (C-3), 64.0 (C-4), 85.2 (C-5), 43.9 (C-2′), 25.7 (C-3′), 24.2 (C-4′), 26.3 (C-5′), 46.9 (C-6′), 166.1 (>C=O), 55.4 (-O<u>C</u>H$_3$), 150.2 (A,C-1), 115.5 (A,C-2,6), 128.2 (A,C-3,5), 147.0 (A,C-4), 147.8 (B,C-1), 127.0 (B,C-2,6), 124.3 (B,C-3,5), 149.0 (B,C-4), 126.8 (C,C-1), 129.0 (C,C-2,6), 114.5 (C,C-3,5), 160.5 (C,C-4) ppm.

Anal. Calcd. for $C_{28}H_{28}N_3O_5Cl$: C, 64.36; H, 5.41; N, 8.04. Found: C, 64.42; H, 5.37; N, 8.00.

3*RS*-(3*R,4*R**,5*S**)-2-(4-chlorophenyl)-3-(4-nitrophenyl)-5-(4-methoxyphenyl)-4-piperidinyloxoisoxazolidine, (19, $C_{28}H_{28}N_3O_5Cl$).** The diastereomeric cycloadduct (**19**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 4.86 (1H, d, J=9, H-3), 4.09 (1H, br, t, H-4), 5.88 (1H, d, J=8.5, H-5).

3*RS*-(3*R,4*S**,5*R**)-2-(4-Chlorophenyl)-3-(4-nitrophenyl)-4-(4-methoxyphenyl)-5-piperidinyl-oxoisoxazolidine (20, $C_{28}H_{28}N_3O_5Cl$).** The regioisomeric cycloadduct (**20**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 4.89 (1H, d, J=6, H-3), 4.38 (1H, br. t, H-4), 4.51 (1H, d, J=7.5, H-5)

Reaction of *C*-(3-Nitrophenyl)-*N*-(4′-chlorophenyl) nitrone (2) with Piperidide of 4-Chlorocinnamic acid (5). 3*RS*-(3*R,4*S**,5*R**)-2-(4-Chlorophenyl)-3-(3-nitrophenyl)-5-(4-chlorophenyl)-4-piperidinyloxo-isoxazolidine (21; $C_{27}H_{25}N_3O_4Cl_2$).** White crystals; m.p.: 164°C; yield: 0.43 g (82%); IR: ν = 2930, 2860 (m, -CH_2-), 1624 (s, amide >C=O), 823.7 (s, 1,4-disubstituted benzene ring), 688 (m, meta-substituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 247.5 (3.68) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.43 (1H, d, J=7.7, H-3), 3.74 (1H, dd, J=7.7, 9.4, H-4), 5.26 (1H, d, J= 9.4, H-5), 3.56 (1H, m, H-2′), 2.78 (2H, m, H-6′), 1.40 (4H, m, H-3′,4′), 0.95 (1H, m, H_A-5′), 0.80 (1H, m, H_B-5′), 6.90 (2H, d, J=8.8, A,H-2,6), 7.20 (2H, d, J=8.8, A,H-3,5), 8.40 (1H, s, B,H-2), 8.20 (1H, d, J=8.2, B,H-4), 7.60 (1H, t, J=8.0, B,H-5), 7.90 (1H, d, J=7.7, B,H-6) 7.28-7.37 (4H, m, C,H-2,6,3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 75.3 (C-3), 64.2 (C-4), 84.8 (C-5), 44.3 (C-2′), 26.1 (C-3′), 24.5 (C-4′), 26.8 (C-5′), 47.4 (C-6′), 166.1 (>C=O), 149.3 (A,C-1), 115.9 (A,C-2,6), 128.3 (A,C-3,5), 135.5 (A,C-4), 143.8 (B,C-1), 132.5 (B,C-2), 151.9 (B,C-3), 130.6 (B,C-4), 121.5 (B,C-5), 123.4 (B,C-6), 134.3 (C,C-1), 129.6 (C,C-2,6), 129.5 (C,C-3,5), 127.7 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{25}N_3O_4Cl_2$: C, 61.73; H, 4.78; N, 8.00. Found: C, 61.60; H, 4.73; N, 7.92.

3*RS*-(3*R,4*R**,5*S**)-2-(4-Chlorophenyl)-3-(3-nitrophenyl)-5-(4-chlorophenyl)-4-piperidinyloxo-isoxazolidine (22; $C_{27}H_{25}N_3O_4Cl_2$).** The diastereomeric cycloadduct (**22**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 4.89 (1H, d, J=10, H-3), 3.80 (1H, br. t, H-4), 5.92 (1H, d, J=9, H-5)

3*RS*-(3*R,4*S**,5*R**)-2-(4-Chlorophenyl)-3-(*3*-nitrophenyl)-4-(4-chlorophenyl)-5-piperidinyloxo-isoxazolidine (23; $C_{27}H_{25}N_3O_4Cl_2$).** The regioisomeric cycloadduct (**23**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 4.88 (1H, d, J=7, H-3), 4.51 (1H, br. t, J~7-7.5, H-4), 4.68 (1H, d, J=7.5, H-5)

Reaction of *C*-Phenyl-*N*-(4-chlorophenyl) nitrone (3) with Piperidide of 4-Chlorocinnamic acid (29). 3*RS*-(3*R,4*S**,5*R**)-2-(4-chlorophenyl)-3-phenyl-5-(4-chlorophenyl)-4-piperidinyl-oxo-isoxazolidine (24, $C_{27}H_{26}N_2O_2Cl_2$).** Pale yellow crystals; m.p.: 120°C; yield: 0.40 g (80%); IR: ν = 2937, 2859 (m, -CH_2-), 1637 (s, amide >C=O), 825 (s, 1,4-disubstituted benzene ring), 757, 700 (m, mono-substituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 249.5 and 225 (3.15 and 3.34) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.14 (1H, d, J=8.2, H-3), 3.76 (1H, t, J=8.8, H-4), 5.38 (1H, d, J= 9.3, H-5), 3.50 (2H, m, H-2′), 2.75 (2H, m, H-6′), 1.60 (2H, m, H-3′), 1.42 (1H, m, H-4′), 0.87 (1H, m, H_A-5′), 0.80 (1H, m, H_B-5′), 6.90 (2H, d, J=7, A,H-2,6), 7.17 (2H, d, J=7, A,H-3,5), 7.50 (2H, d, J=7.1, B,H-2,6), 7.30-7.40 (3H, m, B,H-3,4,5), 7.30-7.42 (4H, m, C,H-2,6,3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 76.1 (C-3), 63.8 (C-4), 83.9 (C-5), 43.7 (C-2′), 25.7 (C-3′), 24.2 (C-4′), 26.0 (C-5′), 46.9 (C-6′), 167.3 (>C=O), 150.6 (A,C-1), 115.9 (A,C-2,6), 128.9 (A,C-3,5), 135.3 (A,C-4), 140.6 (B,C-1), 127.8 (B,C-2,6), 126.3 (B,C-3,5), 128.2 (B,C-4), 127.0 (C,C-1), 129.2 (C,C-2,6), 129.0 (C,C-3,5), 134.6 (C,C-4) ppm. *Anal*. Calcd. for $C_{27}H_{26}N_2O_2Cl_2$: C, 67.42; H, 5.44; N, 5.86. Found: C, 67.36; H, 5.55; N, 5.80.

3*RS*-(3*R,4*R**,5*S**)-2-(4-chlorophenyl)-3-phenyl-5-(4-chlorophenyl)-4-piperidinyloxo-isoxazolidine(25; $C_{27}H_{26}N_2O_2Cl_2$).** The diastereomeric cycloadduct (**25**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 6.02 (1H, d, J=9, H-3), 3.70 (1H, br. t, H-4), 4.67 (1H, d, J=10.5, H-5).

3*RS*-(3*R,4*S**,5*R**)-2-(4-chlorophenyl)-3-phenyl-4-(4-chlorophenyl)-5-piperidinyloxo-isoxazolidine (26; $C_{27}H_{26}N_2O_2Cl_2$).** The regioisomeric cycloadduct (**26**) was detected from the ^{1}H-NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.03 (1H, d, J=7, H-3), 4.86 (1H, t, J=4, H-4), 4.49 (1H, d, J=4, H-5).

Reaction of *C*-(4-Methoxyphenyl)-*N*-(4′-chlorophenyl) nitrone (4) with Piperidide of 4-Chlorocinnamic acid (5). 3*RS*-(3*R,4*S**,5*R**)-2-(4-chlorophenyl)-3-(4-methoxyphenyl)-5-(4-chlorophenyl)-4-piperidinyloxoisoxazolidine (27, $C_{28}H_{28}N_2O_3Cl_2$).** White crystalline solid; m.p.: 255°C; yield: 0.38 g (74%); IR: ν = 2934, 2856 (m, -CH_2-), 1611 (s, amide >C=O), 827 (s, 1,4-disubstituted benzene ring) cm^{-1}; UV: λ_{max} (log ε) = 252.5 and 229 (3.74 and 3.88) nm; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.25 (1H, d, J=7, H-3), 3.30 (1H, dd, J=7.5, 10, H-4), 4.94 (1H, d, J= 10, H-5), 3.02 (1H, m, H-2′), 2.69 (2H, m, H-6′), 1.25 (4H, m, H-3′,4′), 1.00 (1H, m, H_A-5′), 0.80 (1H, m, H_B-5′), 3.73 (3H, s, -OC<u>H</u>$_3$), 6.77 (2H, d, J=8.5, A,H-2,6), 7.00 (2H, d, J=8.5, A,H-3,5), 7.20 (2H, d, J=8.5, B,H-2,6), 6.47 (2H, d, J=8.5, B,H-3,5), 7.20 (2H, d, J=8.5, C,H-2,6), 7.34 (2H, d, J=8.6, C,H-3,5) ppm; ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 70.1 (C-3), 62.1 (C-4), 76.1 (C-5), 42.2 (C-2′), 25.1 (C-3′), 23.9 (C-4′), 25.6 (C-5′), 46.5 (C-6′), 55.3 (C-O<u>C</u>H$_3$), 182.1 (>C=O), 159.3 (A,C-1), 114.1 (A,C-2,6), 128.1 (A,C-3,5), 147.0 (A,C-4), 147.8 (B,C-1), 127.0 (B,C-2,6), 117.1 (B,C-3,5), 166.0 (B,C-4), 146.0 (C,C-1), 129.1 (C,C-2,6), 128.3 (C,C-3,5), 147.7 (C,C-4) ppm. *Anal*. Calcd. for $C_{28}H_{28}N_2O_3Cl_2$: C, 65.75; H, 5.56; N, 5.49. Found: C, 65.88; H, 5.50; N, 5.40.

3*RS*-(3*R,4*R**,5*S**)-2-(4-Chlorophenyl)-3-(4-methoxyphenyl)-5-(4-chlorophenyl)-4-piperidinyloxoisoxazolidine (28, $C_{28}H_{28}N_2O_3Cl_2$).** The diastereomeric cycloadduct (**28**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.97 (1H, d, J=11, H-3), 3.99 (1H, br. t, H-4), 5.00 (1H, d, J=10, H-5)

3*RS*-(3*R,4*S**,5*R**)-2-(4-Chlorophenyl)-3-(4-methoxyphenyl)-4-(4-chlorophenyl)-5-piperidinyloxoisoxazolidine (29,** $C_{28}H_{28}N_2O_3Cl_2$). The regioisomeric cycloadduct (**29**) was detected from the ^{1}H NMR spectrum of the crude reaction mixture. ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.34 (1H, d, J=9.5, H-3), 4.78 (1H, br. t, H-4), 4.60 (1H, d, J=10, H-5).

Acknowledgments. The authors thank the Indian Council for Cultural Relation (ICCR) for financial assistance to P. K. Biswas.

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[15] The LURE DCI Synchrotron facility in Orsay, France, was used to record the Crystal structure data for compound **9**. An Image Plate system (MAR345) was used as the detector. Recording was done under cryotemperature condition, at –50°C. The crystals were triclinic, space group P-1, with 1 molecule/asymmetric unit. Crystallographic Data for compound **9** have been deposited with the Cambridge Crystallographic Data Centre as CCDC 235163. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).