1,3-Dipolar Cycloadditions. Part XII - Selective Cycloaddition Route to 4-Nitroisoxazolidine Ring Systems [1]

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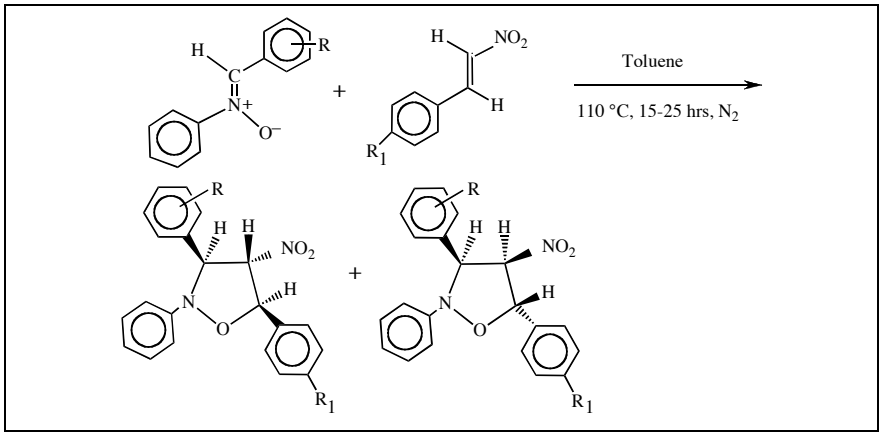

Cycloadditions of *C,N*-diarylnitrones to *β*-nitrostyrenes occurred to yield two diastereoisomeric cycloadducts, the 3,4-*trans*-4,5-*trans* substituted isoxazolidine derivatives being formed selectively as the major products. These were characterised by spectroscopic and X-ray data. Conformational studies were carried out by X-ray crystallography and Molecular Modelling.

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INTRODUCTION

Isoxazolidines can be regarded as templates for 1,3-difunctionalised compounds which can be used in the synthesis of several types of biologically active molecules [2-12]. These isoxazolidines become even more attractive as intermediates if a nitro group, which can be transformed into several functionalities, is present in the ring. With the objective of synthesising substituted 4-nitroisoxazolidines, we have carried out a series of 1,3-dipolar cycloadditions of nitrones with *trans*-*β*-nitrostyrene and its *p*-nitro derivative. Due to the presence of the conjugated nitro group, the *β*–nitrostyrenes have low-lying LUMOs, and these cycloadditions would be essentially of Sustmann Type I ($Dipole_{HOMO}$-$Dipolarophile_{LUMO}$) [13]. In view of the highly polarised nature of the dipolarophile frontier orbitals, a high degree of regioselectivity is expected to yield the desired 4-nitroisoxazolidines.

We report here the synthesis of a number of 3,4-*trans*-4,5-*trans*-3,5-diaryl-2-phenyl-4-nitroisoxazolidine cycloadducts with high regio- and stereo-selectivity. The structures and stereochemistry of these cycloadducts as well as the minor cycloadducts, with 3,4-*cis*-4,5-*trans* stereochemistry were settled by detailed spectroscopic, and for selected products, - X-ray crystallographic, analysis. We were also interested in the conformational aspects of these compounds, and carried out computer-assisted energy minimisations.

RESULTS AND DISCUSSION

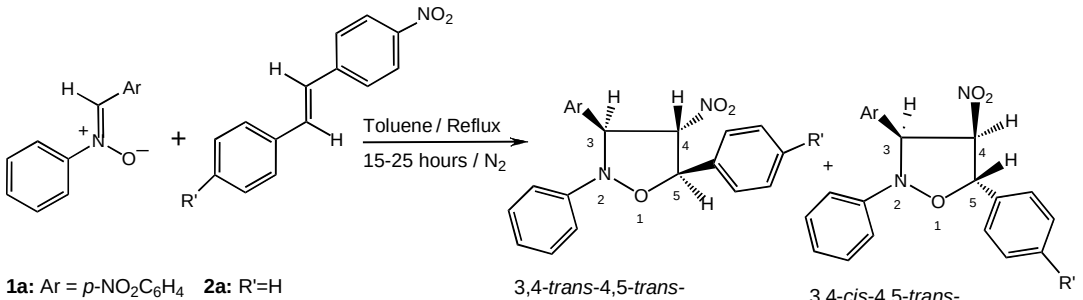
Cycloadditions of six *C*-aryl-*N*-phenyl aldonitrones (**1a**-**f**) with *β*-nitrostyrene **2a** and 4-nitro-*β*-nitrostyrene **2b** were investigated. Five of these nitrones (**1a**-**e**) had *C*-aryl rings with substituents varying from the electron withdrawing nitro-group to the electron-donating methoxy group, whereas the *C*-furyl-*N*-phenyl nitrone was new.

The cycloadditions were performed by refluxing the nitrones with equimolar amounts or with slight molar excess of the dipolarophiles under nitrogen atmosphere for 15-25 hrs. Conversions to products were usually above 80%. The 3,4-*trans*-4,5-*trans*-3,5-diaryl-2-phenyl-4-nitroisoxazolidine cycloadducts (Type A) were the major cycloadducts in all the reactions. The corresponding diastereoisomeric 3,4-*cis*-4,5-*trans*-3,5-diaryl-2-phenyl-4-nitroisoxazolidine cycloadducts (Type B) were obtained as the minor products in almost all the reactions. The product ratios of the cycloadducts were determined by ^{1}H NMR analysis of the crude reaction mixtures. The IR

spectra of all the isolated pure compounds in all series of cycloadducts showed the expected bands for the nitro group (*ca.* 1500-1550, 1350 cm^{-1}) and for the aromatic moieties. The UV spectra of the cycloadducts lacked the strong absorptions characteristic of the conjugated nitro groups, thus indicating that cycloadditions had occurred.

The EI-MS analysis of a typical example **3aa**, showed the molecular ion-peak at *m/z* 391 (87%). Other important peaks appeared at *m/z* 344 (8%; M^+-HNO_2), 285 (25%; M^+-PhCHO) and the fragments obtained from electron-impact induced cycloreversion at *m/z* 242 (10%), and 149 (7.5%). The loss of the elements of PhCHO, and a peak at *m/z* 238 from concomitant cleavage at N-2/C-3 and C-4/C-5, confirmed the presence of a phenyl group at C-5. The 300 MHz ^{1}H NMR spectra of the products belonging to both types A and B showed that H-3 and H-5 protons appeared as doublets and there was no coupling between them. Further, the H-3, H-5 protons showed long-range coupling with aromatic protons in COSY-LR spectrum, thereby showing their benzylic nature. The H-4 proton coupled to both H-3 and H-5 and appeared as double doublet. H-4 correlations to aromatic protons were not observed in the COSY-LR. This established the structure of the major isomers to be 2-phenyl-3,5-diaryl-4-nitro-isoxazolidine derivatives. A typical representative of the major cycloadducts, *viz*. **3aa**, showed the presence of the H-3 doublet at δ5.77 in its ^{1}H NMR spectrum. This was coupled to a double- doublet H-4 at δ5.27, which in turn was coupled with the downfield H-5 doublet at δ5.84; $J_{3,4}$ and $J_{4,5}$ were respectively 3.7 and 5.8 Hz. The magnitude of $J_{3,4}$ seemed to indicate a 3,4-*trans* orientation for **3aa**. The relative stereochemistry and conformation of **3aa** was confirmed by its X-ray crystallographic analysis [14]. The ORTEP projection of this molecule is shown in Figure 1. Compound **3aa** crystallised in the triclinic system with the space group P-1. The heterocyclic ring is in the distorted envelope conformation, with 3,4- and 4,5-substituents *trans*, as well as the nitrogen phenyl substituent with respect to the 3-aryl group. The oxygen forms the tip of the envelope. Cycloadducts **3 (ba**, **ca, da, ea, fa, cb** and **ab)**, which were the major cycloadducts in the reactions of **1(a-f)** respectively, showed ^{1}H and ^{13}C NMR characteristics very similar to those of **3aa**. Thus, all these belonged to the 3,4-*trans*-4,5-*trans*-series (Type A cycloadducts). Cycloadducts **3cb** and **3ab,** also belonging to Type A, were obtained from 4-nitro-*trans*-β-nitrostyrene **2b** and nitrones **1c** and **1a** respectively. The 300 MHz ^{1}H NMR spectrum of **3cb** in d_6-DMSO showed that H-3 and H-5 protons appeared at δ5.75 and δ6.16 as doublets and the H-4 proton as δ5.93 as a double doublet; $J_{3,4}$ and $J_{4,5}$ were respectively 3.2 and 4.2 Hz. The relative stereochemistry of **3cb** as 3,4-*trans*-4,5-*trans* was confirmed by X-ray crystallographic analyses [14]. This compound crystallised in the monoclinic form in the space group $P2_{1/}n$. The ORTEP diagram for **3cb** is shown in Figure 2. The five-membered heterocyclic ring exists as a twist envelope, in between the two idealised envelope conformations with the tips being at N2 and O1. Owing to significant ring puckering all substituents come in quasi-axial or quasi-equatorial positions. The nitrogen atom of

Scheme-1



1a: Ar = *p*-$NO_2C_6H_4$ **2a:** R'=H
b: Ar = *p*-ClC_6H_4 **b:** R'=NO_2
c: Ar = C_6H_5
d: Ar = *p*-$OCH_3C_6H_4$
e: Ar = *m*-$NO_2C_6H_4$
f: Ar= 2-furyl

3,4-*trans*-4,5-*trans*-(3RS)-2-phenyl-3,5-diaryl-4-nitroisoxazolidines

3,4-*cis*-4,5-*trans*-(3RS)-2-phenyl-3,5-diaryl-4-nitroisoxazolidines

3aa: Ar=*p*-$NO_2C_6H_4$;	R'=H		**4aa:** Ar=*p*-$NO_2C_6H_4$;	R'=H
ba: Ar=*p*-ClC_6H_4;	R'=H		**ba:** Ar=*p*-ClC_6H_4;	R'=H
ca: Ar=C_6H_5;	R'=H		**ca:** Ar=C_6H_5;	R'=H
da: Ar=*p*-$OCH_3C_6H_4$;	R'=H		**da:** Ar=*p*-$OCH_3C_6H_4$;	R'=H
ea: Ar=*m*-$NO_2C_6H_4$;	R'=H		**ea:** Ar=*m*-$NO_2C_6H_4$;	R'=H
fa: Ar=2-furyl;	R'=H		**fa:** Ar=2-furyl;	R'=H
cb: Ar=C_6H_5;	R'=NO_2		**cb:** Ar=C_6H_5;	R'=NO_2
ab: Ar=p-$NO_2C_6H_4$;	R'=NO_2		**ab:** Ar=p-$NO_2C_6H_4$;	R'=NO_2

the isoxazolidine ring is pure pyramidal. In the relative configurations shown, the lone pair on N(2) is set above the plane by convention. A statistical disorder of the orientation of the nitro group at C(4) was observed in the crystal lattice at room temperature. This is a dynamic process but X-ray diffraction gives only an "average" static view of the phenomenon. During refinements, this group was modelised as a three static-component group (three positions with the sum of occupancies equal to one, for the two rotating oxygens, i.e. 0.4:0.35:0.25). Cycloadduct **3ab** showed similar spectroscopic properties and hence also belonged to Type A.

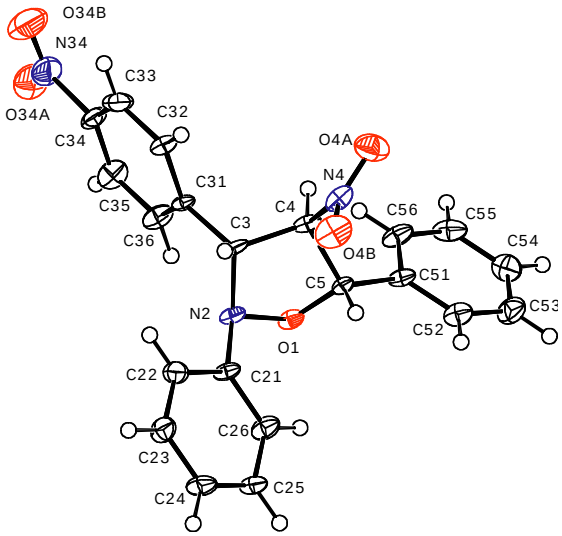


Figure 1. Structure of **3aa** as determined by X-Ray crystallographic analysis (ORTEP Projection).

The minor cycloadducts Type B were established to have 3,4-*cis*-4,5-*trans*-configuration. COSY-LR spectra of this type of cycloadducts showed long range correlations of H-3 and H-5 with aromatic protons. This established the overall structure as 3,4-*cis*-4,5-*trans*-3,5-diaryl-2-phenyl-4-nitroisoxazolidine. The signals of H-3, H-4, H-5 are situated close together. Cycloadducts **4(aa, ba, ca, da, ea, fa, cb** and **ab)** belong to this type of cycloadduct.

Conformational analysis and energy minimisation of the all-*trans* isomer along with its minor stereoisomer 3,4-*cis*, 3,4-*trans* have been carried out by taking advantage of the X-ray crystallographic data of the Type A isomers.

Energy minimisation of the 3,4-*trans*-4,5-*trans* isomer **3aa** (Type A), 3,4-*cis*-4,5-*trans* **4aa** (Type B) was carried out by conjugate gradient method using DISCOVER Molecular Simulation Program (Version 2.98) [15]. In all cases normal completion of conjugate gradient was achieved in less than 2000 steps of energy evaluations; the energy minimisation was stopped when the RMS derivative of energy reached a value of 0.001 kcal/mol.

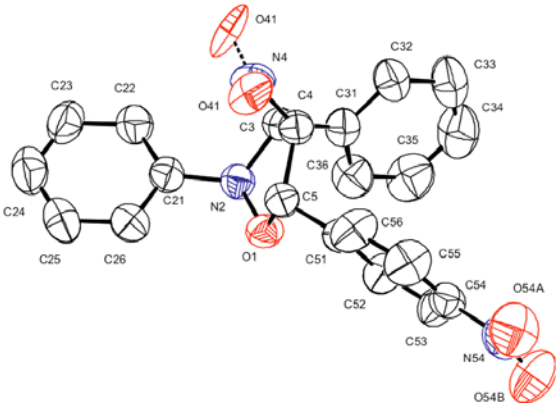


Figure 2. Structure of **3cb** as determined by X-Ray crystallographic analysis (ORTEP Projection. Only one rotamer of the nitro group at C4 is shown for clarity).

The relative potential energy of **4aa** compared to **3aa** was calculated to be 2.15 kcal/mol. The X-ray structure of all-*trans* isomer (compound **3aa**) has close similarity with the model structure of minimum energy.

The reaction of the new nitrone *C*-furfuryl-*N*-phenyl nitrone (**1f**) with *trans* β-nitrostyrene was carried out by refluxing for 16 hrs. in dry toluene under nitrogen atmosphere. The major product was confirmed as **3fa**, *i.e.* 3,4-*trans*-4,5-*trans* isomer from its NMR characteristics. Thus the selectivity of the cycloaddition process of this C-2-furfuryl nitrone was similar to the *C*-phenyl nitrone. This nitrones was prepared by reacting furfural with *N*-phenylhydroxylamine.

EXPERIMENTAL

General. Melting points were recorded on an electrically heated Kofler Block and are uncorrected. UV spectra were recorded on a Hitachi U-3501 spectrophotometer in 95% aldehyde free spectroscopic ethanol. IR spectra were recorded on KBr disc or as a thin film on a Perkin-Elmer FT-IR model. Mass spectra were recorded on a JEOL JMS-600 Mass spectrometer. Column chromatography (CC) was carried out using neutral alumina and silica gel. TLC was performed using silica gel G. Petrol refers to the fraction, b.p. 60-80°. Anhydrous sodium sulphate was used for drying extracts. Analytical samples were routinely dried over anhydrous calcium chloride *in vacuo* at room temperature. The starting materials prepared were identified by comparison of their melting points with those reported in the literature; as well as from elemental analyses and from IR spectra. NMR spectra were recorded in $CDCl_3$ or in d_6-DMSO solution on a Bruker AM-300L equipped with an ASPECT-3000 computer and an Array Processor using a switchable dual ^1H-^{13}C 5 mm dual probe (normal and inverse) at ambient temperature. X-Ray crystallographic data were recorded at room temperature at the LURE synchrotron facility, Orsay, France (MoKα λ= 0.953 Å) for **3aa**, and on a PHILIPS PW 1100 diffractometer (operating the CuKα radiation, λ= 1.5418 Å) for **3cb.** The two structures were solved using the SHELXS program [16] and anisotropically refined using SHELXL [17].

General procedure for the Cycloaddition Reactions. A solution of the nitrone (3.5-5.4 mM) in anhydrous toluene (10-15 ml) was added at a time to a solution of the dipolarophile (usually 1 to 1.5 molar proportions) in anhydrous toluene (10-15 ml). The reaction mixture was refluxed for several hours under nitrogen atmosphere. The progress of the reaction was monitored by TLC and 300 MHz ^{1}H NMR. After the reaction period solvent was removed from the reaction mixture by distillation under reduced pressure in a Büchi rotary evaporator. The residue was analysed by 300 MHz ^{1}H NMR and then subjected to Column Chromatography over silica gel, and sometimes over neutral alumina.

Reaction of C-(4-nitrophenyl)-*N*-phenyl nitrone with β-nitrostyrene).

3RS(3R*,4S*,5R*)-2,5-Diphenyl-3-(4-nitro-phenyl)-4-nitro isoxazolidine (3aa). Light yellowish crystals, m.p. 126 ºC (yield 84%) from 30% benzene in petrol; IR (KBr): 1556, 1347, 834, 750, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.26 (1H, dd, *J*=3.8, 5.9, H-4), 5.77 (1H, d, *J*=3.8, H-3), 5.84 (1H, d, *J=5.9,* H-5), ~7.02 (1H, obscured by H-2, H-6, H_{A-4}), 7.09 (2H, d, J=7.9 $H_{A-2,6}$), 7.34 (2H, dis. dd, $H_{A-3,5}$), 7.37-7.42 (5H, br. s, $H_{C-2,6,3,5,4}$), 7.77 (2H, d, *J*=8.8, $H_{B-2,6}$), 8.28 (2H, d, *J*=8.8, $H_{B-3,5}$); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 73.5 (C-3), 83.6 (C-5), 101.4 (C-4), 115.3 ($C_{A-2,6}$), 124.0 (C_{A-4}), 124.9 ($C_{B-3,5}$), 127.0 ($C_{C-2,6}$), 128.2 ($C_{B-2,6}$), 129.6 ($C_{C-3,5}$), 129.9 ($C_{A-3,5}$), 130.0 (C_{C-4}), 135.0 (C_{C-1}), 145.7 (C_{B-1}), 148.5 (C_{A-1}), 148.8 (C_{B-4}), EI-MS: m/z 391 (M^+), 285, 238, 226, 192, 165, 105, and 77. Anal. Calcd for $C_{21}H_{17}N_3O_5$: C, 64.44; H, 4.34; N, 10.73 %. Found: C, 64.29; H, 4.43; N, 10.92%.

X-ray data. Triclinic, P-1 (Z=2) with a=7.242(2); b=8.371(2); c=16.587(2) Å; α=84.32(4); β=78.72(4) and γ=70.01(4)°. Final *R* (1639 observed *F*) = 0.079 and *R* (all 1652 *F* data) = 0.085. Energy minimisations done by DISCOVER Molecular Simulation Program (Version 2.98) [15] for **3aa** and **4aa** were accurate to the extent of ± 0.2 kcal/mole.

3RS(3R*,4R*,5S*)-2,5-Diphenyl-3-(4-nitrophenyl)-4-nitro isoxazolidine (4aa). Canary yellow crystals, m.p.192 ºC (yield 16%) from 75% benzene in petrol. IR (KBr): 1552, 1347, 837, 749, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.41 (2H, m, H-3,4), 5.75 (1H, d, *J*=3.3, H-5), 7.09 (2H, d, *J*=8.0, $H_{A-2,6}$), 7.13 (1H, t, 7.4, H_{A-4}), 7.30 (2H, br.t, *J*= ~7.8, $H_{A-3,5}$), 7.40 (5H, br. s, $H_{C-2,6,3,5,4}$), 7.76 (2H, d, *J*=8.6, $H_{B-2,6}$), 8.32 (2H, d, *J*=8.6, $H_{B-3,5}$); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 73.7 (C-3), 81.8 (C-5), 99.6 (C-4), 118.4 ($C_{A-2,6}$), 125.1 ($C_{B-3,5}$), 125.4 (C_{A-4}), 126.9 ($C_{C-2,6}$), 128.8 ($C_{B-2,6}$), 129.2 ($C_{A-3,5}$), 129.4 ($C_{C-3,5}$), 130.2 (C_{C-1}), 130.2 (C_{C-4}), 148.2 (C_{A-1}), 148.2 (C_{B-4}), not found (C_{B-1}). *Anal.* Calcd. for $C_{21}H_{17}N_3O_5$: C, 64.44; H, 4.34; N, 10.73%. Found: C, 64.46; H, 4.48; N, 10.80%.

Reaction of C-(4-chlorophenyl)-*N*-phenyl nitrone with β-nitrostyrene.

3RS(3R*,4S*,5R*)-2,5-Diphenyl-3-(4-chlorophenyl)-4-nitro isoxazolidine (3ba). Yellow microcrystalline solid (yield 82%) was obtained from 20% benzene in petrol. IR (KBr): 1555, 1361, 834, 785, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.26 (1H, dd, *J*=4.0, 5.7, H-4), 5.57 (1H, d, *J*=4.0, H-3), 5.78 (1H, d, *J*=5.7, H-5), 7.08 (2H, d, *J*=7.9, $H_{A-2,6}$), 7.29-7.49 (3H, m, $H_{A-3,4,5}$), 7.35 (2H, d, *J*=8.2, $H_{B-2,6}$), 7.37-7.42(br. s, $H_{c-2,3,4,5,6}$), 7.47 (2H, d, *J*=8.2, $H_{B-3,5}$); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 73.4 (C-3), 83.1(C-5), 101.5 (C-4), 115.3 ($C_{A-2,6}$), 123.4 (C_{A-4}), 126.6 ($C_{C-2,6}$), 128.3 ('$C_{B-2,6}$), 129.0 ($C_{B-3,5}$), 129.3 ($C_{C-3,5}$), 129.3 (C_{C-4}), 129.5 ($C_{A-3,5}$), 134.6 (C_{C-1}), 135.3 (C_{B-4}), 136.7 (C_{B-1}), 148.9 (C_{A-1}). *Anal.* Calcd. for $C_{21}H_{17}N_2O_3Cl$: C, 66.23; H, 4.50; N, 7.36%. Found: C, 66.10; H, 4.66; N, 7.45%.

Reaction of C-phenyl-*N*-phenyl nitrone with β-nitrostyrene.

3RS(3R*,4S*,5R*)-2,3,5-Triphenyl-4-nitroisoxazolidine (3ca). Yellow amorphous solid (yield 86%) was obtained from 30% benzene in petrol. IR (KBr): 1554, 1360, 756, 697; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.32 (1H, dd, *J*=4.2, 5.9, H-4), 5.60 (1H, d, *J*=4.2, H-3), 5.78 (1H, d, *J*=5.9 H-5), 7.04 (H, t, J=7.5), 7.10 (2H, d, *J*=8.4, $H_{A-2,6}$), 7.30 (2H, t, *J*=8.0, $H_{A-3,5}$), 7.36-7.44 (other Aromatic-H), 7.53 (2H, d, *J*=6.5, $H_{B-2,6}$); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 74.2 (C-3), 83.2 (C-5), 101.7 (C-4), 115.3 ($C_{A-2,6}$), 129.3 ($C_{A-3,5}$), 123.1 (C_{A-4}), 126.6 ($C_{C-2,6}$), 126.7 ($C_{B-2,6}$), 128.6 (C_{B-4}), 129.0 ($C_{C-3,5}$), 129.2 ($C_{B-3,5}$), 129.2 (C_{C-4}), 135.5 (C_{C-1}), 138.2 (C_{B-1}), 149.2 (C_{A-1}). *Anal* Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.81; H, 5.24; N, 8.09%. Found: C, 72.93; H, 5.10; N, 8.01%.

Reaction of C-(4-methoxyphenyl)-*N*-phenyl nitrone with β-nitrostyrene

3RS(3R*,4S*,5R*)-2,5-Diphenyl-3-(4-methoxyphenyl)-4-nitro isoxazolidine (3da). Orange red amorphous solid (yield 72%) was obtained from 30% benzene in petrol; IR (KBr): 1554, 1362, 836, 759, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.30 (1H, dd, *J*=4.4, 5.8, H-4), 5.49 (1H, d, *J*=4.4, H-3), 5.77 (1H, d, *J=5.8,* H-5), 6.90 (2H, d, *J*=8.7, $H_{B-3,5}$), 7.06 (1H, dis. t, H_{A-4}), 7.09 (2H, d, J=8.0, $H_{A-2,6}$), 7.30 (2H, d, *J*=8.0, $H_{A-3,5}$), obscured (2H, $H_{B-2,6}$), 7.38-7.45 (5H, br. s, $H_{C-2,6,3,5,4}$); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 74.1 (C-3), 83.0 (C-5), 101.8 (C-4), 114.8 ($C_{B-3,5}$), 115.6 ($C_{A-2,6}$), 123.2 (C_{A-4}), 126.6 ($C_{C-2,6}$), 128.1($C_{B-2,6}$), 129.0 (C_{C-4}), 129.1 ($C_{A-3,5}$), 129.1 ($C_{C-3,5}$), 130.0 (C_{B-1}), 135.9 (C_{C-1}), 149.3 (C_{A-1}), 159.8 (C_{B-4}). Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44%. Found: C, 70.08; H, 5.43; N, 7.58%.

Reaction of *C*-(3-Nitrophenyl)-*N*-phenyl nitrone with β-nitrostyrene.

3RS(3R*,4S*,5R*)-2,5-Diphenyl-3-(3-nitrophenyl)-4-nitro isoxazolidine (3ea). Yellow amorphous solid (yield 68%) was obtained from 30% benzene in petrol; IR (KBr): 1541, 1352, 812, 756, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.28 (1H, dd, *J*=3.65, 5.9, H-4), 5.76 (1H, d, *J*=3.65, H-3), 5.83 (1H, d, *J=5.9,* H-5), 7.07 (1H, t, 7.4, H_{A-4}), 7.10 (2H, d, J=7.8, $H_{A-2,6}$), 7.33 (2H, dd, 7.8, 7.4 $H_{A-3,5}$), 7.38-7.40 (5H, brd. s, $H_{C-2,6,3,5,4}$), 7.60 (1H, t, ~8.0, H_{B-5}), 7.89 (1H, d, 7.7, H_{B-6}), 8.21 (1H, dd, *J*=1.1, 8.2, H_{B-4}), 8.45 (1H, s, H_{B-2}); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 73.4 (C-3), 83.7 (C-5), 101.4 (C-4), 115.4 ($C_{A-2,6}$), 122.4 (C_{B-2}), 124.0 (C_{A-4}), 124.1 (C_{B-4}), 127.0 ($C_{C-2,6}$), 129.6 ($C_{C-3,5}$), 129.9 ($C_{A-3,5}$), 130.0 (C_{C-4}), 130.8(C_{B-5}), 133.2 (C_{B-6}), 135.0 (C_{C-1}), 141.0 (C_{B-1}), 148.9 (C_{A-1}), 149.3(C_{B-3}). *Anal.* Calcd. for $C_{21}H_{17}N_3O_5$: C, 64.44; H, 4.34; N, 10.73%. Found: C, 64.55; H, 4.45; N, 10.64%.

3RS(3R*,4R*,5S*)-2,5-Diphenyl-3-(3-nitrophenyl)-4-nitro isoxazolidine (4ea). Yellow amorphous solid (yield 18%) from 75% benzene in petrol. IR (KBr): 1538, 1347, 812, 748, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.42 (2H, m, H-3,4), 5.78 (1H, d, 5.5, H-5), 7.11 (2H, d, J=7.0, $H_{A-2,6}$), 7.14 (1H, t, 7.0, H_{A-4}), 7.30 (2H, t, *J*= 7.5, $H_{A-3,5}$), 7.39-7.44 (5H, brd. s, $H_{C-2,6,3,5,4}$), 7.65 (H, t, ~8.0, H_{B-5}), 7.87 (H, d, 7.5, H_{B-6}), 8.28 (H, dd, *J*=1.5,7.5, H_{B-4}), 8.47 (H, br. t, 1.5 H_{B-2}); ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 73.7 (C-3), 81.8 (C-5), 99.7 (C-4), 118.6 ($C_{A-2,6}$), 122.8 (C_{B-2}), 124.6 (C_{B-4}),125.4 (C_{A-4}), 126.9 ($C_{C-2,6}$), 129.2

($C_{A-3,5}$), 129.5 ($C_{C-3,5}$), 130.1 (C_{C-4}), 131.1 (C_{B-5}), 131.4 (C_{C-1}), 133.8 (C_{B-6}), 140.1 (C_{B-1}), 148.3 (C_{A-1}), 149.5 (C_{B-3}). *Anal.* Calcd. for $C_{21}H_{17}N_3O_5$: C, 64.44; H, 4.34; N, 10.73%. Found: C, 64.46; H, 4.48; N, 10.80%.

Ratio of **3ea**:**4ea** in crude reaction mixture by ^{1}H NMR - 77:23

Reaction of *C*-(2-Furyl)-*N*-phenyl nitrone with β-nitrostyrene.

3RS(3R*,4S*,5R*)-2,5-Diphenyl-3-furyl-4-nitroisoxazolidine (3fa). Yellow amorphous solid (yield 68.5%) was obtained from 10% benzene in petrol. IR (KBr): 1556, 1361, 754, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.54 (1H, dd, *J*=3.3, 6.0, H-4), 5.71 (1H, d, *J=6.0,* H-5), 5.77 (1H, d, *J*=3.3, H-3), 6.39 (1H, dd, *J*=3.1, 1.8, H_{B-4}), 6.45 (1H, d, 3.1, H_{B-3}), 7.07 (1H, t, 7.4, H_{A-4}), 7.15 (2H, d, J=7.8, $H_{A-2,6}$), 7.34 (2H, dd, 7.8, 7.4, $H_{A-3,5}$), 7.40-7.45 (3H, m, $H_{C-3,5,4}$), 7.46 (1H, dis. d, H_{B-5}), 7.50 (2H, dd, *J*=7.6, 1.8, $H_{B-2,6}$): ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 68.6 (C-3), 84.0 (C-5), 98.1 (C-4), 109.7 (C_{B-3}), 111.2 (C_{B-4}), 115.7 ($C_{A-2,6}$), 123.8 (C_{A-4}), 127.4 ($C_{C-2,6}$), 129.4 ($C_{A-3,5}$), 129.8 (C_{C-4}), 129.6 ($C_{C-3,5}$), 135.5 (C_{C-1}), 143.8 (C_{B-5}), 148.8 (C_{A-1}), 150.0 (C_{B-2}). *Anal* Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.84; H, 4.79; N, 8.33%. Found: C, 67.65; H, 4.66; N, 8.00%.

3RS(3R*,4R*,5S*)-2,5-Diphenyl-3-furyl-4-nitroisoxazolidine (4fa). Canary yellowish amorphous solid (yield 25%) was obtained from 30% benzene in petrol. IR (KBr): 1555, 1370, 745, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.15 (1H, d, 8.9, H-5), 5.44 (1H, dd, *J*=7.1, 8.9, H-4), 6.09 (1H, d, *J*=7.1, H-3), 6.37 (1H, dd, *J*=3.2, 1.9, H_{B-4}), 6.51 (1H, d, 3.3, H_{B-3}), 7.07 (1H, dd, 8.2, 1.0, H_{A-4}), 7.09 (2H, d, J=7.4, $H_{A-2,6}$), 7.28 (2H, t, *J* = ~7.5, $H_{A-3,5}$), 7.40-7.51 (5H, m, $H_{C-2,6,3,5,4}$), 7.48 (H, d, 3.3, H_{B-5}). ^{13}C NMR ($CDCl_3$, δ, 75.5 MHz): 67.6 (C-3), 81.2 (C-5), 95.1 (C-4), 111.5 (C_{B-3}), 111.9 (C_{B-4}), 118.5 ($C_{A-2,6}$), 125.0 ($C_{A-3,5}$), not found (C_{A-4}), not found (C_{B-2}), not found (C_{C-1}), 127.1 ($C_{C-2,6}$), 129.5 ($C_{C-3,5}$), 129.8 (C_{C-4}), 144.2 (C_{B-5}), 149.2 (C_{A-1}). *Anal* Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.84; H, 4.79; N, 8.33%. Found: C, 67.65; H, 4.76; N, 8.20%.

Reaction of *C*,*N*-Diphenyl nitrone with 4-nitro β-nitrostyrene.

3RS(3R*,4S*,5R*)-2,3-Diphenyl-5-(4-nitrophenyl)-4-nitro isoxazolidine (3cb). Yellow crystals, m.p.170° (yield 40%) was obtained from 50% benzene in petrol. IR (KBr): 1550, 1344, 849, 754, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 5.75 (1H, d, *J*=3.2, H-3), 5.93 (1H, dd, *J*=3.2, 4.2, H-4), 6.16 (1H, d, *J=4.2,* H-5), 7.01 (2H, t, 7.3, $H_{A-3,5}$), 7.11 (2H, d, *J*=8.5, $H_{B-3,5}$), 7.27 (2H, d, *J*=8.0, $H_{B-2,6}$), 7.29-7.32 (1H, m, H_{B-4}), 7.37 (1H, d, J=7.6, H_{A-4}), 7.45 (2H, d, J=7.7, $H_{A-2,6}$), 7.75 (2H, d, *J*=8.7, $H_{C-2,6}$), 8.24 (2H, d, *J*=8.7, $H_{B-3,5}$); ^{13}C-NMR (d_6-DMSO, δ, 75.5 MHz): 72.7 (C-3), 80.8 (C-5), 99.6 (C-4), 116.1 ($C_{A-2,6}$), 123.4 (C_{A-4}), 123.8 ($C_{C-3,5}$), 127.2 ($C_{B-3,5}$), 128.2 ($C_{C-2,6}$), 128.4 (C_{B-4}), 129.0 ($C_{B-2,6}$), 129.2 ($C_{A-3,5}$), 137.5 (C_{B-1}), 143.8 (C_{C-1}), 147.7 (C_{A-1}), 148.3 (C_{C-4}). *Anal.* Calcd. for $C_{21}H_{17}N_3O_5$: C, 64.44; H, 4.34; N, 10.73%. Found: C, 64.24; H, 4.43; N, 10.67%.

X-ray data. Monoclinic, space group $P2_1/n$ (Z=4) with a=11.140(3); b=18.123(3); c=10.113(3) Å and β=110.99(5)°. Final *R* (2743 observed *F*) = 0.064 and *R* (all 3149 *F* data) = 0.081

Reaction of C-(4-Nitrophenyl)-*N*-(4'-chlorphenyl) nitrone) with 4-nitro -β-nitrostyrene).

3RS(3R*,4S*,5R*)-2-(Chlorophenyl)-3-(4-nitrophenyl)-4-nitro-5-phenyl isoxazolidine (3ab). Canary yellow crystals, m.p. 212° (yield 87%) was obtained from 50% benzene in petrol. IR (KBr) 1519, 1346, 841, 687 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ, 300 MHz): 6.07 (1H, dd, *J*=4.7, 2.2, H-4), 6.16 (1H, d, *J*=4.7, H-3), 6.21 (1H, d, *J=2.2,* H-5), 7.23 (2H, d, J=8.9, $H_{A-2,6}$), 7.35 (2H, d, 8.9, $H_{A-3,5}$), 7.65 (1H, d, J=8.7, $H_{B-2,6}$), 7.77 (2H, d, *J*=8.7, $H_{B-3,5}$), 8.21 (2H, d, *J*=8.5, $H_{C-2,6}$), 8.24 (2H, d, *J*=8.4, $H_{B-3,5}$); ^{13}C-NMR (d_6-DMSO, δ, 75.5 MHz): 71.5 (C-3), 81.6 (C-5), 98.6 (C-4), 117.4 ($C_{A-2,6}$), 123.9 ($C_{C-3,5}$), 124.0 ($C_{B-3,5}$), 127.3 (C_{A-4}), 128.5 ($C_{C-2,6}$), 128.7 ($C_{B-2,6}$), 129.1 ($C_{A-3,5}$), 142.6 (C_{C-1}), 144.8 (C_{B-1}), 147.0 (C_{A-1}), 147.5 (C_{C-4}), 147.9 (C_{B-4}). *Anal.* Calcd for $C_{21}H_{15}N_4O_7Cl$: Calc. for C, 53.57; H, 3.21; N, 11.9%. Found: C, 53.72; H, 3.53; N, 9.89%.

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