Pergamon

Tetrahedron, Vol. 53, No. 34, pp. 11869-11880, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00760-6

Cyclic Nitrone-Ethene Cycloaddition Reactions

Herman P. Perzanowski, Said S. Al-Jaroudi, Mohamed I. M. Wazeer, and Sk. Asrof Ali*

Chemistry Department, King Fahd University of Petroleum and Minerals, Dhahran 31261, Saudi Arabia

Abstract: Addition reactions of ethene onto several cyclic nitrones afforded [n,3,0]heterobicyclicalkanes devoid of any substituents in the ring skeleton. These fused ring systems with a bridgehead nitrogen, capable of undergoing nitrogen inversion, allowed us to determine the stereochemistry of the ring fusion and the thermodynamic stability of the *cis*, *trans* isomers. Some of the cycloadducts on peracid induced ring opening gave a new series of nitrones capable undergoing further cycloaddition reactions. © 1997 Published by Elsevier Science Ltd.

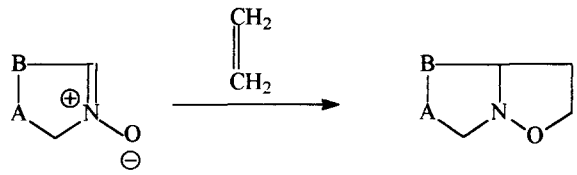
Introduction

Nitrone cycloaddition reaction, by virtue of its regio-, stereo-, face-, and chemo-selectivity, has etched an important place in organic synthesis.[1] Nitrone functionality embedded in the cyclic systems has been extensively utilised to incorporate and elaborate pyrrolidine and piperidine moieties so widespread in nature.[1] The inter- and intra-molecular[2] addition reactions of both cyclic and acyclic nitrones have been prudently used as a key step in the synthesis of natural products of biological interest.[3] Even though a multitude of various classes of dipolarophiles has been widely used in the nitrone cycloadditions, the reaction of cyclic nitrones with the simplest of alkenes, ethene, to the best of our knowledge, has not been reported.

Herein we present the cycloaddition of the cyclic nitrones **(1)-(5)** with ethene and also report the effect of ring size on the stereochemistry of the ring juncture of the bicyclic cycloadducts **(6)-(10)**, which are devoid of any substituents (scheme 1). To make the addition reaction more versatile, the regiochemistry of the peracid induced ring opening of the isoxazolidines **6**, **7** and **10** to generate new nitrones, is also investigated.

Results and Discussion

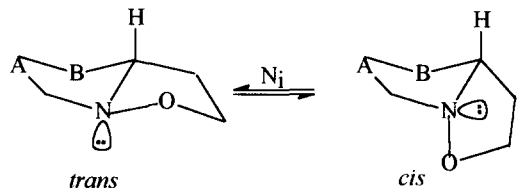
The addition reaction of the cyclic nitrones **(1)-(5)** with ethene (3 to 4 atm, 100-130°C, 7-14 h) gave the bicyclic adducts **(6)-(10)** in good yields (scheme 1).



	A—B	
1	$(CH_2)_2$	**6**
2	$(CH_2)_3$	**7**
3	$(CH_2)_4$	**8**
4	$(CH_2)_5$	**9**
5	$CH_2\,O\,CH_2$	**10**

Scheme 1.

The cycloadducts **(6-10)** can, in principle, exist as *trans* and *cis* isomers (scheme 2). The *cis*,and *trans* isomers can be interconverted by the relatively slow nitrogen inversion process. The presence of the adjacent heteroatom oxygen slows the lone pair inversion in the nitrogen[4] to such an extent that at ambient or lower temperatures, the presence of two interconverting isomers could be identified by NMR spectroscopy which offers a convenient way to measure the nitrogen inversion barrier as well as the relative stability of the *cis* and *trans* isomers.



trans *cis*

(6-10)

Scheme 2.

The proton spectra in many cases were complex with coupling to neighbouring protons and most often proton signals show a certain amount of overlap. Therefore the ^{13}C NMR spectra were used in the calculations of energy barriers in all compounds. The coalescence method could not be used because the populations for the exchange sites are not equal. Hence a complete band shape analysis, corresponding to a non-coupled two-site exchange with unequal populations was employed to obtain accurate exchange rate constants by fitting NMR band shapes. This method is well known[5] to be fraught with difficulties, and considerable errors result in thermodynamic parameters $\Delta H^{\#}$ and $\Delta S^{\#}$ if Eyring plots are used. In fact, many of the errors are systematic in nature, and those for $\Delta H^{\#}$ and $\Delta S^{\#}$ often result in mutually compensatory errors so

that $\Delta G^{\#}$ is better defined. The $\Delta G^{\#}$ values calculated for -25°C (near the coalesence temperature) are reported in the Table 1. (In making use of Eyring Plots it was assumed that the transmission coefficient was unity.) The calculated constant K for the major <=> minor equilibrium are also given in the Table 1. The ^{13}C integrations were found to be satisfactory when compared to the ^{1}H integrations, in cases where the proton spectra gave non overlapping signals for the two isomers.

Table 1: Free Energy of Activation ($\Delta G^{\#}$) for nitrogen inversion, Equilibrium Constant (K), and Free Energy change (ΔG^{o}) for major <=> minor isomerization of the cycloadducts in $CDCl_3$

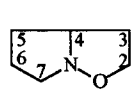
Adduct	$\Delta G^{\#}$ (kJ/mol^{-1})[a]	K	ΔG^{o} (kJ/mol^{-1})[b]
6	-	0	
7	70.4	0.32	+2.8
8	54.9	0.18	+3.2
9	54.7	0.16	+4.5
10	72.2	0.16	+4.5

[a] at -25°C [b] at -50°C

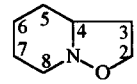
Absence of minor isomer in the 5/5 system (**6**) precludes the determination of the $\Delta G^{\#}$ value for this compound. The 6/5 systems as represented by **7** and **10** have higher $\Delta G^{\#}$ values than the 7/5 (compound **8**) and 8/5 (compound **9**) by a magnitude of over 15 kJ/mol. Transition state for nitrogen inversion process requires the flattening of the nitrogen due to change in hybridization from pyramidal (sp^3) to planar (sp^2) state. Since all compounds have the isoxazolidine moiety (5 membered ring) in common, one has to consider how well the other part of the fused system can better tolerate the extended CNC angle of 120° in the transition state. Needless to say a larger ring can tolerate this angular constraint than a smaller one. Compound **10** with an additional heteroatom decreases the size of the of the six-membered ring, hence has a higher $\Delta G^{\#}$ than that for **7**.

Next we determined the stereochemistry of the ring junctures of the major and minor isomers in the bicyclic systems by ^{13}C NMR spectroscopy. The ^{13}C NMR chemical shifts are assigned on the basis of the published data on indolizidine,[6] isoxazolidines,[7] general chemical shift arguments, DEPT ^{13}C NMR spectra and are reported in Table 2. The ^{13}C NMR spectra of compound **6** showed sharp signals over the temperature range of -50° to +50°C indicating the presence of a single isomer with *cis* geometry at the ring juncture. For [3,3,0]bicyclooctane, the carbocylic counterpart of the compound **6**, the free energy difference of approximately 25 kJ/mol favours[8] the *cis* over the *trans* isomer. Geometric constraints thus prevent *cis* <=> *trans* interconversion by nitrogen inversion in isoxazolidine **6**. For [4,3,0]bicyclononane,

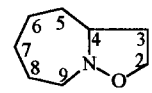
Table 2 . ^{13}C NMR Chemical Shifts[a] of Adducts in $CDCl_3$



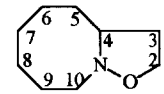
6



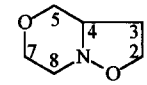
7



8



9



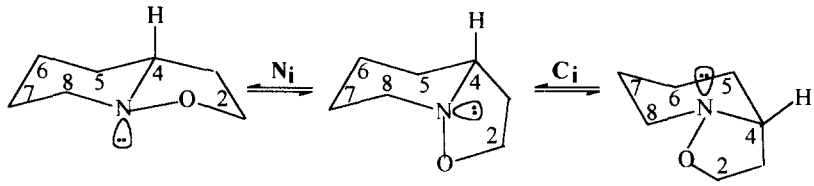
10

Adduct		C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
6	*cis*	65.6	31.9	64.6	24.1	37.3	56.7	-	-	-
7	*cis*	65.4	30.5	59.5	25.4	23.5	19.2	49.4	-	-
	trans	64.5	34.3	66.3	29.3	24.8	23.9	55.1	-	-
8	*cis*	63.6	35.5	65.8	30.0	25.0	24.4	26.9	52.0	-
	trans	64.9	37.7	66.2	30.3	24.0	25.0	25.4	57.4	-
9	*cis*	64.4	34.5	64.8	30.6	26.1	24.2	24.2	27.2	52.4
	trans	64.4	39.4	63.8	35.7	25.8	23.1	23.4	26.0	58.5
10	*cis*	65.6	28.9	59.1	65.3	-	64.9	49.1	-	-
	trans	64.5	30.4	64.4	70.3	-	65.5	55.7	-	-

[a] in ppm relative to internal TMS at -50 °C

hydrindane, the carbocyclic counterpart of the isoxazolidine **7**, however, the ΔG° value of around 1.6 kJ mol^{-1} at 25°C favours[8] the *trans* isomer. The isoxazolidine[7] can, in principle, exist in three different forms, the *trans* isomer and the *cis* pair **A** and **B** (Scheme 3). Whereas the *cis* pair is in rapid equilibrium by the chair inversion (C_i), one of the *cis* conformers is converted into the *trans* isomer by a relatively slow nitrogen inversion process (N_i). The ^{13}C NMR spectra of isoxazolidine **7** at 0°C showed signals due to the two distinct isomers, and our study indicates that the major form is the *trans* isomer. The C-7 is assigned to a higher field than C-6 on the basis of the former experiencing a γ-anti effect[6] due to the oxygen at position 1, which causes shielding. All carbons, except C-2, in the minor isomer of **7** are more shielded than the corresponding carbons of the major isomer. The axial oxygen in the *cis* form **A** and the axial CH_2 in **B** (scheme 3) by virtue of having γ-gauche interaction with C-5, C-7 and C-6, C-8, respectively, causes shielding[6] and thus provides evidence that the minor isomer is indeed the *cis* pair. It is also noted that in comparison to the corresponding carbon of the *trans* isomer the shielding is larger for the C-7 (4.7 ppm) than the C-6 (1.3 ppm). This points to the fact that the *cis* pair **A** and **B** are not equally populated, but the equilibrium is shifted in favour of conformer **A**;

this is in accordance with the fact that an oxygen substituent is better tolerated than an alkyl substituent in the axial position.



7, *trans* 7, *cis*–**A** 7, *cis*–**B**

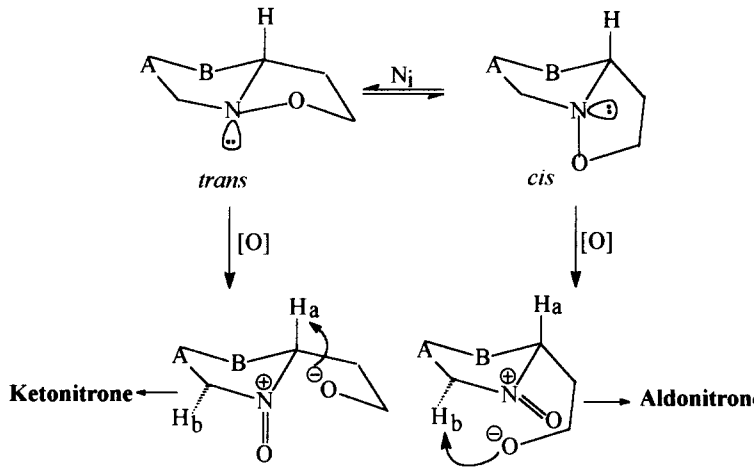
Scheme 3.

For perhydroazulene, [5,3,0]bicyclodecane, the carbocyclic counterpart of compound **8**, the difference in the free energy between the *cis* and *trans* isomers was reported to be small.[8] For cycloheptane skew or twist chair form is expected to be more stable than the boat form. Strictly speaking the substituents in the seven or eight membered rings do not occupy the well defined axial or equatorial positions as in cyclohexane. The trends in the chemical shifts of seven- or eight- membered ring carbons between the two isomers are expected to be different from that of the six-membered ring carbons as the conformations of the higher membered ring systems are quite different. The trends in the chemical shifts of the C-3, C-5 and N-CH_2 carbon between the major and minor isomers are similar in compounds **7**,**8**, and **9**. So we may assume the stereochemistry of the ring junction in the 6/5, 7/5, and 8/5 ring systems are similar for the major isomers and as such the major and minor isomers have *trans* and *cis* ring junctures, respectively. Interestingly the compound **10** with a 6/5 fused ring system with an additional heteroatom in the ring skeleton, however, is found to have the major isomer with a *cis* ring fusion. The ^{13}C chemical shifts of C-2, C-3, C-4 and C-8 of the major isomer of **10** are found to be similar to those of the minor isomer of **7**. Like the compound **7**, the carbons of the major *cis* isomer in **10** are more shielded than the corresponding carbons of the *trans* isomer except for C-2.

In order to obtain further support for the assignment of the stereochemistry of the ring juncture in these bicyclic systems, we carried out the peracid-induced ring opening of the isoxazodines **6**, **7** and **10** to generate nitrones (scheme 4). The regiochemical detail of this reaction along with the composition of the *cis* , *trans* isomers of the parent isoxazolidines are included in Table 3.

Recently it was demonstrated[9] that the peracid oxidation (in aprotic solvent) of isoxazolidines with *cis* and *trans* ring junction would give aldo- and keto-nitrone, respectively (scheme 4). Orientation of the nitrogen lone pair dictates the regiochemical outcome of the oxidation. Transfer of oxygen followed by ring opening gives the nitrosonium inner salts. As shown in scheme 4, kinetic-controlled intramolecular

abstraction of the hydrogen by the alkoxide ion in its immediate vicinity (H_a in case of *trans* and H_b in case of *cis* isomer) generates the nitrones. As is evident from the Table 3, the isoxazolidine **6** with *cis* ring juncture afforded the aldonitrone **11** exclusively (scheme 5). The peracid oxidation of the isoxazolidine **6** in protic solvent, however, becomes thermodynamic-controlled due to the protonation of the alkoxide ion and as such gave the more stable ketonitrone **12** as the major product.



Scheme 4.

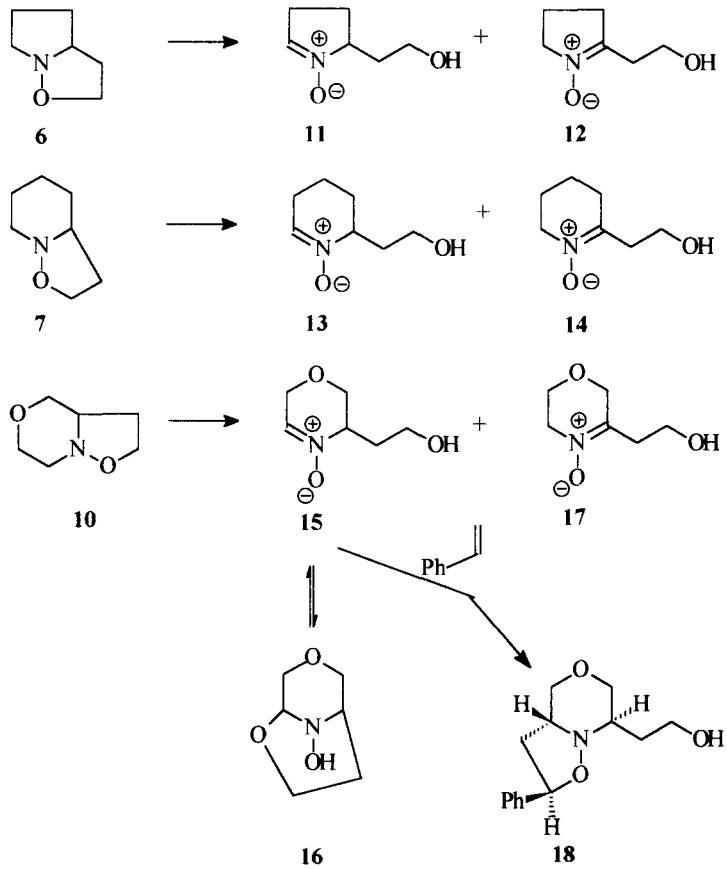
Table 3: Composition of invertomers and regiochemistry of MCPBA induced ring opening of isoxazolidines **6, 7** and **10**

Compound	Solvent	% composition of invertomers		% composition[a] of nitrones	
		cis	*trans*	Aldonitrone	Ketonitrone
6	CH_2Cl_2			**(11)** (100)	**(12)** (~0)
	CH_3OH	100	~0	(35)	(65)
	CH_3CO_2H			(12)	(88)
7	CH_2Cl_2	24	76	**(13)** (23)	**(14)** (77)
10	CH_2Cl_2	86	14	**(15)** (82)	**(17)** (18)

[a] composition of nitrones are shown in parenthesis

While the compound **7** with a *cis/trans* ratio of 24:76 afforded the aldo- (**13**) and the keto-(**14**)-nitrone, in the respective ratio of 23:77, the adduct **10** with a *cis/trans* ratio of 86:14 gave aldo-(**15**<=>**16**) and keto (**17**)-nitrone in a ratio of 82:18, respectively (scheme 5). The population ratio of the adducts and the ratio of the regioisomeric nitrones are very much the same, thus giving further credence to the assignment based on the NMR analysis.

It is quite interesting to note that among aldonitrones **11**, **13** and **15** only the latter exists in equilibrium with its bicyclic tautomer **16**. The equilibrium mixture underwent addition reaction with styrene smoothly at 50 °C to give the adduct **18**. The stereochemistry as depicted in **18** is based on the sterically favourable approach of styrene from the least hindered face of the nitrone **15** with *exo*-orientation of the phenyl substituent.



Scheme 5

The present study elaborates the stereochemistry of several parent heterobicyclic systems for the first time and provides a reference point for the study of substituent effects on the population of isomeric ring

junctures. Results of the peracid induced ring opening of several isoxazolidines to give new nitrones would indeed be helpful in proper utilization of these high yielding reactions.

Experimental

All melting points are uncorrected. IR spectra were recorded on a Nicolet 5 DBX FT IR and are reported in wave numbers (cm^{-1}). The ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-200 and a JEOL GX 270 NMR spectrometers operating at a proton frequency of 200.0 and 270.0 MHz, respectively using deutereochloroform as solvent and TMS as internal standard. Variable temperature NMR spectra were recorded using XL-200 variable temperature accessory and the temperatures were calibrated using standard chemical shifts of methanol at low temperatures. Mass spectra at 70 ev E.I. were recorded on a Ribermag GC-MS system, R-10-10 with quadrupole mass filter and Riber 400 acquisition system. Elemental analyses were performed on a Carlo-Erba 1106 Elemental Analyser. Cycloaddition reactions were carried out under a positive atmosphere of nitrogen. Silica gel chromatographic separations were performed with flash silica (Baker Chemical Co.). All solvents were reagent grade.

Hexahydropyrrolo[1,2-b]isoxazole (6).- A solution of the nitrone **(1)** (prepared from its corresponding hydroxylamine (3.80 g, 43.7 mmol) by HgO oxidation) in xylene (200 cm^3) in a pressure bottle was reacted with ethene at a pressure of 3.0 atm at 125°C for 7 h with shaking. The reaction mixture was extracted with 10% aqueous HCl solution (2 x 20 cm^3), the acid layer was washed with ether (2 x 25 cm^3) and then basified and saturated with K_2CO_3. The aqueous layer was extracted with ether (2 x 10 cm^3) and the resulting organic layer was dried (Na_2SO_4) and fractionated under vacuum using a vigreux column to obtain the cycloadduct **(6)** as a colorless liquid, $b.p._{30\ mm\ Hg}$ 74°C, (3.74g, 76%), **(6)**.HCl, colourless crystals (methanol-ether), m.p. 136-137 °C (Found: C, 47.9; H, 8.2; N, 9.25. $C_6H_{11}NO.HCl$ requires C, 48.16; H, 8.09; N, 9.36%); $\nu_{max.}$(neat) 2968, 2869, 1451, 1290, 1212, 1170, 1054, 1035, 1010, 918, 900, and 764 cm^{-1}; δ_H (+50°C) 1.58 (1 H, m),1.70 (1 H, m), 1.83-2.06 (3 H, m), 2.46 (1 H, dq, *J* 6.8, 12.5 Hz), 3.06 (1 H, dt, *J* 6.8, 14.2 Hz), 3.19 (1H, dt, *J* 6.8, 14.2 Hz), 3.71(1 H, m), 3.85 (2 H, m); δ_C ($CDCl_3$, +20°C) 65.6, 64.6, 56.7, 37.3, 31.9, 24.1. At -50°C both the ^{1}H and ^{13}C NMR spectrum remained virtually identical. Mass spectrum: *m/z* 113 (M^+ 100%)

Hexahydro-2H-isoxazolo[2,3-a]pyridine (7).- A solution of the nitrone **(2)** (prepared from its corresponding hydroxylamine (3.20 g, 31.7 mmol) by HgO oxidation) in ethanol (200 cm^3) was reacted with ethylene at a pressure of 3.0 atm at 125°C for 10 h with shaking. Concentrated HCl (10 cm^3) was added to the cooled reaction mixture and ethanol was removed by a gentle stream of N_2. The residue was saturated with K_2CO_3, and the aqueous layer was then extracted with ether (3 x 10 cm^3). The organic layer was dried (Na_2SO_4) and fractionated under vacuum using a vigreux column to obtain the cycloadduct **(7)** as a colorless

liquid, b.p. $_{27\ mm\ Hg}$ 75°C, (3.53 g, 88%). **(7).**HCl, colourless crystals (methanol-ether), m.p. 114-116 °C (Found: C, 51.2; H, 8.7; N, 8.5. $C_7H_{13}NO.HCl$ requires C, 51.37; H, 8.62; N, 8.56%). $\nu_{max.}$(neat) 2935, 2877, 2820, 1451, 1441, 1316, 1309, 1263, 1145, 1120, 1074, 1055, 1002, 984, 933, 846, and 765 cm^{-1}; δ_H (-50°C), major invertomer, 1.11-2.40 (9 H, m), 2.50 (1 H, m), 3.48 (1 H, m), 3.96 (2 H, m); minor invertomer has the following non overlapping peaks at δ 2.65 (1 H, m), 3.04 (1 H, m), 3.60 (1 H, m), 4.22 (1 H, m). Integration of several proton signals indicated the presence of major and minor isomers in a ratio of 78: 22. The ^{1}H NMR spectrum at +50°C showed broadened signals. Mass spectrum: *m/z* 127 (M^+ 30.8%.).

(3aαH)Perhydro[1,2]oxazolo[2, 3-a]azepine (8).- A solution of the nitrone (**3**) (prepared from its corresponding hydroxylamine (2.70 g, 23.5 mmol) by HgO oxidation) in ethanol (150 cm^3) was reacted with ethene at a pressure of 3.0 atm at 120°C for 14 h. Similar work up as in the case of the compound **7** afforded the cycloadduct (**8**) as a colorless liquid, b.p.$_{7\ mm\ Hg}$ 74°C, (1.38 g, 42%). **(8).**HCl, white crystals (methanol-ether), m.p. 175-177 °C (Found: C, 53.9; H, 9.2; N, 7.8. $C_8H_{15}NO.HCl$ requires C, 54.08; H, 9.08; N, 7.89%). $\nu_{max.}$(neat) 2927, 2861, 1452, 1350, 1324, 1282, 1183, 1158, 1044, 1019, 946, 908, and 803 cm^{-1}; δ_H ($CDCl_3$, +50°C) 1.43-2.05 (9 H, m, including 1 H , dq, J 7.5, 12.5 Hz at δ 1.90), 2.41 (1 H, dq, J 6.8, 12.5 Hz), 2.68 (1 H, m), 2.83 (1 H, m), 3.45 (1 H, m), 3.85 (2 H, t, J 6.8 Hz). There were changes the in ^{1}H NMR spectrum at -50°C especially a minor isomer signal at δ 2.90-3.15 (2 H, m) integrated to 14%, and the signal for the C(2)H at δ(3.80-4.11) became very complex. δ_C ($CDCl_3$, +55°C) 26.1, 26.3 (2C), 31.3, 38.6, 57.2, 65.6, 66.8. Mass spectrum: *m/z* 141 (M+ 100%)

Perhydroazocino[1,2-b][1,2]oxazolidine (9).- A solution of the nitrone (**4**)[10] (550 mg, 4.26 mmol) was dissolved in ethanol (50 cm^3) and reacted with ethene at a pressure of 4.0 atm at 130°C for 12 h. Similar workup as in the case of the compound **7** followed by chromatographic purification using dichloromethane/ether (97 : 03) mixture as an eluant gave the cycloadduct (**9**) as a colorless liquid (390 mg, 59%). **(9).**HCl, colourless liquid. (Found: C, 56.2; H, 9.5; N, 7.2. $C_9H_{17}NO.HCl$ requires C, 56.39; H, 9.46; N, 7.31%); $\nu_{max.}$(neat) 2918, 2853, 1455, 1357, 1323, 1261, 1215, 1166, 1125, 1040, 1002, 969, 915, 891, 873, and 730 cm^{-1}; δ_H (+50°C) 1.33-1.98 (11 H, m), 2.38 (1 H, m), 2.76 (1 H, m), 2.95 (1 H, m), 3.29 (1 H, m), 3.80 (2 H, m). At -50 °C the ^{1}H NMR spectrum failed to separate the major and minor conformer signals. Mass spectrum: m/z 155 (M^+ 100%)

Perhydro[1,2]oxazolo[3,2-c][1,4]oxazine (10).- A solution of the nitrone (**5**) (prepared from its corresponding hydroxylamine (2.50 g, 24.3 mmol) by HgO oxidation) in ethanol (150 cm^3) was reacted with ethene at a pressure of 3.0 atm and 100°C for 10 h. The reaction mixture was then extracted with 10% aqueous HCl solution (2 x 15 cm^3); the acid layer was washed with ether (2 x 25 cm^3), saturated with K_2CO_3, and then extracted with ether (3 x 10 cm^3). The organic layer was dried (Na_2SO_4) and fractionated under

vacuum to obtain the cycloadduct **(10)** as a colorless liquid, b.p. $_{14\ mm\ Hg}$ 77°C, (1.73 g, 55%). **(10)**.HCl, colourless liquid. (Found: C, 43.3; H, 7.4; N, 8.4. $C_6H_{11}NO_2$.HCl requires C, 43.51; H, 7.31; N, 8.46%); $\nu_{max.}$(neat) 2967, 2864, 1463, 1455, 1388, 1361, 1315, 1309, 1272, 1255, 1122, 1089, 1037, 978, 939, 915, 858, 783, 728, and 679 cm^{-1}; δ_H (-50°C) 2.21 (1 H, m), 2.35 (1 H, m), 2.90 (2 H, m), 3.30 (1 H, m), 3.53 (1 H, m), 3.73-4.06 (4 H, m), 4.16 (1 H, m). The major and minor conformer proton signals of the adduct **(10)** are overlapping at -50°C except for a minor signal at δ 1.88 (1 H, dq, J 6.8, 11.5 Hz) for the minor conformer. Integration of the signal gave a ratio of major and minor isomers as 86:14. Mass spectrum: *m/z* 129 (M^+ 71%).

General Procedure for the Metachloroperbenzoic Acid (MCPBA) Oxidation of the Cycloadducts (6,7,10).-

(A) *In dichloromethane*:- To a stirred solution of the cycloadduct (2.00 mmole) in dry dichloromethane (30 cm^3) at -10C° was added MCPBA (2.40 mmole) in one portion. After completion of the reaction (30 min, -10°) as indicated by TLC in ether, a saturated solution of K_2CO_3 (15 cm^3) was added to the stirred solution. The emulsified mixture was filtered to remove the precipitated salt of potassium *m*-chlorobenzoate and the precipitate was washed with a liberal excess of chloroform. The aqueous layer was extracted with $CHCl_3$ (4x20 cm^3). The combined organic layers were dried (Na_2SO_4), and concentrated to give the products in 90-100% yield.

(B) *In methanol*:- The procedure is the same as described under **(A)** except methanol (30 cm^3) at -10C° was used . After completion of the reaction the methanol was removed under a slow stream of nitrogen. To the residual mixture was added $CHCl_3$. The rest of the procedure was as in **(A)** (yield: 92%).

(C) *In acetic acid*:- The procedure is the same as described under **(B)** except acetic acid (10 cm^3, 20°C) was used. After completion of the reaction acetic acid was removed under a slow stream of nitrogen. (yield: 95%). The resulting nitrones are very soluble in water and saturated solutions of K_2CO_3 must be used to insure the extraction of the nitrone into the organic layer

MCPBA Oxidation of the Adduct 6:- The peracid induced ring opening of the adduct in dichloromethane afforded the aldonitrone **11** as the sole isomer as a pale yellow liquid. The cyclic nitrone **11** on silica gel chromatography using 1:1 methanol-ether mixture as eluant did not give pure sample. The CHN analysis was not carried out because of the presence of minor contaminants, presumably arising out of decomposition of the nitrone. $\nu_{max.}$(neat) 3390, 2976, 2939, 2894, 1650, 1601, 1461, 1440, 1352, 1233, 1195, 1064 and 676 cm^{-1}; δ_H 1.80-2.12 (2 H, m), 2.24 (1 H, m), 2.54 (1 H, m), 2.74 (2 H, m), 3.80 (2 H, m), 4.20 (1 H, m), 5.50 (1 H, br OH), 7.07 (1 H, m). Mass spectrum: *m/z* 130 (M^++1, 100%), 129 (M^+, 10%). Similar oxidation in protic solvents methanol and acetic acid gave a mixture of nitrones **11** and **12** with the latter as the major isomer in each case. The ketonitrone **(12)** has the following ir and proton NMR signals $\nu_{max.}$(neat) 3375, 2967, 2929, 2883, 1626, 1454, 1438, 1380, 1366, 1256, 1207, 1165, 1069, 1045 and 635 cm^{-1}; δ_H 2.17 (2H,

quint, *J* 8.0 Hz), 2.73 (2 H, t, *J* 6.5 Hz),2.88 (2 H, t, *J* 7.0 Hz), 3.85 (2 H, t, *J* 6.5 Hz), 4.06 (2 H, t, *J* 8.0 Hz). The ratio of the nitrones was determined by the integration of several proton signals.

MCPBA Oxidation of the Adduct (7):- The peracid induced ring opening of the adduct **(7)** in dichloromethane afforded a non separable mixture of the aldo-**(13)** and ketonitrone **(14)** in a ratio of 23:77, respectively; pale yellow liquid, $\nu_{max.}$(neat) 3385, 2957, 2933, 2864, 1629, 1447, 1427, 1378, 1196, 1141, 1052, 1026 and 670 cm^{-1}; the major ketonitrone **14** has the following proton signals ; δ_H 1.62-2.12 (4 H, m), 2.54 (2 H, m), 2.80 (2 H, t, *J* 7.0 Hz), 3.80 (2 H, m), 3.89 (2 H, t, *J* 7.0 Hz), 5.80 (1 H, br OH). Mass spectrum (**14**); *m/z* 144 (M^++1, 100%), 143 (M^+, 51.5%). The olefinic proton of the minor aldonitrone **13** appeared at 7.29 (1 H, t, *J* 4.0 Hz).

MCPBA Oxidation of the Adduct 10 and Cycloaddition Reaction of the Ring Opened Products with Styrene: The peracid oxidation of the adduct **(10)** in dichloromethane afforded a mixture of products **(15), (16)** and **(17)** in an approximate ratio of 25:55:20 respectively. The ratio was estimated by the integration of the olefinic protons at δ 7.10 ppm (t, J 2.5 Hz) of **(15)**, the bridgehead proton of **(16)** at δ 4.78 ppm (1 H, m), and the allylic proton of **(17)** at δ 2.74 ppm (2 H, t). The mixture of the ring opened products (from 2.00 mmol of the adduct **10** was taken in chloroform (5 cm^3) and reacted with styrene (1 cm^3) at 20 °C for 24 h and 50 °C for 6 h. After removal of the solvent and excess styrene the residual liquid was taken in water (5 cm^3) and extracted with ether (6x5 cm^3). The aqueous layer contained the ketonitrone **(17)** which did not undergo addition reaction under the reaction conditions. After removal of water by a gentle stream of N_2 the residue was purified by chromatography using 2:1 ether-methanol as an eluant to give the ketonitrone **(17)** as colorless crystals (30 mg, 10.3% overall from the original adduct **10**), m.p. 93-94 °C (ether-dichloromethane) (Found: C, 49.5; H, 7.7; N, 9.5. $C_6H_{11}NO_3$ requires C, 49.64; H, 7.64; N, 9.65%); $\nu_{max.}$(KBr) 3290, 2952, 2896, 1639, 1441, 1195, 1158, 1133, 1112, 1088, 1053, 1022, 880 and 742 cm^{-1}; δ_H 2.74 (2 H, t, J 5.5 Hz), 3.89 (2 H, m), 3.96 (2 H, t, J 5.5 Hz), 4.05 (2 H, t, J 5.0 Hz), 4.43 (2 H, s), 5.18 (1 H, br OH). Mass spectrum; *m/z* 146 (M^++1, 100%), 145 (M^+, 19.5%).

The ether layer was dried (Na_2SO_4), concentrated and the residual liquid chromatographed using ether as an eluent to give a mixture of cycloaddition products **18** and its minor isomer (60 mg) followed by the adduct **18** (270 mg) (66.3% overall from the adduct **10**) as a colorless liquid. (Found: C, 67.3; H, 7.65; N, 5.6. $C_{14}H_{19}NO_3$ requires C, 67.44; H, 7.68; N, 5.62%); $\nu_{max.}$(neat) 3390, 3032, 2967, 2910, 2873, 1495, 1460, 1454, 1362, 1266, 1152, 1117, 1077, 1062, 1017, 993, 968, 923, 761, 723, 701 and 657 cm^{-1}; δ_H 1.81 (2 H, m), 2.13 (1 H, m), 2.81-4.24 (10 H, m), 5.41 (1 H, dd, J 4.1, 10.2 Hz), 7.40 (5 H, m). Mass spectrum: *m/z* 249 (M^+ 14.8%). Careful analysis of the nmr spectrum of the crude cycloaddition reaction mixture indicated a ratio of 82:18 for the adduct **(18)** and the unreacted nitrone **(17)**, respectively. Signals at δ 5.41, 2.74 and 4.43 were used for the determination of the ratio.

Acknowledgements: Facilities provided by King Fahd University of Petroleum and Minerals, Dhahran are gratefully acknowledged.

References

1. (a) Confalone, P. N. and Huie, E. M. *Organic Reactions*, **1988**, *36*, 1-173. (b) Tufariello, J. J. in "*1,3 - Dipolar Cycloaddition Chemistry*", ed. Padwa, A. Wiley-Interscience, New York, **1984**, *2*, 83-168.
2. (a) Ida, H. and Kibyashi, *Yuki. Gosei. Kagaku. Kyokaishi*, **1983**, *41*, 241. (b) Balasubramanian, N. *Org. Prep. Proceed. Int.*, **1985**, vol. 2, ch. 9.
3. (a)Tufariello, J. J.; Mullen, G. B.; Tegeler, J. J.; Trybulski, E. J.; Ali, Sk. A. *J. Am. Chem. Soc.*, **1978**, *101*, 2435. (b) Oppolzer, W. *Angew. Chem. Intl. Ed.*, **1977**, *16*, 10.
4. (a) Riddel, F. G. *Tetrahedron*, **1981**, *37*, 849. (b) Perrin, C. L.;Thorburn, J. D.; and Elsheimer, S. *J. Org. Chem.*, **1991**, *56*, 7034.
5. Sandstrom, J., *Dynamic NMR Spectroscopy*, **1982**, Academic Press, London.
6. Kalinowski, H.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*, **1988**, Wiley, Chichester, U. K.
7. (a) Wazeer, M.I. M. and Ali, Sk. A. *Magn. Reson. Chem.*, **1993**, *31*, 12-16. (b) Wazeer, M. I. M.; Almuallem, H. A.; and Ali, Sk. A. *J. Phys. Org. Chem.*, **1993**, *6*, 326 - 332. (c) Wazeer, M. I. M. and Ali, Sk. A. *Canad. J. Appl. Spectry.*, **1993**, *38*, 22-25.
8. Eliel, E L. and Wilen, S. H. "*Stereochemistry of Organic Compounds*", John-Wiley & Sons Inc., New York, **1994**.
9. (a) Ali, Sk. A.;and Wazeer, M. I. M. *Tetrahedron Lett.*, **1992**, *33*, 3219. (b) Ali, Sk. A. and Wazeer, M. I. M. *Tetrahedron Lett.* **1993**, *34*, 137
10. Al Jaroudi, S. S.; Perzanowski, H. P.; Wazeer, M. I. M.; and Ali, Sk. A. *Tetrahedron*, **1997**, *53*, 5581.

(*Received in UK* 15 *May* 1997; *revised* 27 *June* 1997; *accepted* 3 *July* 1997)