J. Indian Inst. Sci., May–June 2001, **81**, 313–323

Recent studies on 1,3-dipolar cycloadditions of nitrones†

AVIJIT BANERJI* AND PIYALI SENGUPTA
Centre for Advanced Studies on Natural Products, Department of Chemistry, University of Calcutta, University College of Science, 92, Acharya Prafulla Chandra Road, Kolkata, West Bengal 700 009, India.
email:ab@cucc.ernet.in; Phone:91-33-3506387; Fax: 91-33-2410322.

Received on November 11, 2000.

Abstract

Some recent developments on 1,3-dipolar cycloadditions of nitrones are reviewed with particular reference to the work carried out in our research group. We investigated the cycloadditions of *C*-aryl-*N*-phenylnitrones and *C*-aryl-*N*-methylnitrones to substituted cinnamic acid piperidides with reference to regioselectivity and stereoselectivity of the processes. Similar studies were made with the cyclic nitrones 1-pyrroline-1-oxide and 3,4,5,6-tetrahydropyridine-1-oxide. The selectivity of nitrone cycloadditions to 5-phenyl-1,3-pentadienamide was also probed. Detailed NMR, X-ray crystallographic studies and molecular mechanics calculations were carried out for structural and conformational studies. The related work of other research groups has also been included.

Keywords: 1,3-Dipolar cycloadditions, nitrones, isoxazolidines.

1. Introduction

1,3-Dipolar species are 4π-electron systems, where the π-electrons are delocalised over three atomic centres.[1] In valence bond terms the electronic structures of the 1,3-dipolar species are represented as resonance hybrids of canonical forms that involve charge separation. Several groups have employed theoretical methods of various complexities to calculate the orbital energies and electron distributions in 1,3-dipolar species.[2, 3] A number of reviews have appeared on the chemistry of 1,3-dipolar species, with special emphasis on their cycloaddition reactions with multiple bonds.[1]

Nitrones, an important category of 1,3–dipolar species,[1] undergo facile concerted $[_{\pi}4_{s}+_{\pi}2_{s}]$-cycloadditions to olefins and acetylenes to yield isoxazolidines and isoxazolines, respectively. These reduced isoxazole derivatives have been used as templates to generate several types of 1, 3-difunctionalised compounds, which serve as key synthetic intermediates.[1f] Considerable regio- and stereochemical control can be exerted in these cycloadditions by choosing appropriate substituents on the dipole and the dipolarophiles (Table I).[1–4] Detailed studies on the regioselectivity of nitrone cycloadditions to mono-substituted olefins and acetylenes revealed that the 5-substituted heterocycles were preferentially formed from most substrates. However, strongly electron-withdrawing substituents in the dipolarophile changed the selectivity to favour the formation of the 4-substituted heterocyclic systems. Stereoselectivity seems to be influenced by both electronic and steric factors, and is often very delicately balanced. Some earlier results are presented in Table I.[4] Recent studies have revealed that the use of transition metal-complexed nitrones dramatically affect stereoselectivites.[4g] The aryl-$Cr(CO)_3$-complexed *C*-phenyl-*N*-methylnitrone reacted with olefins CH_2=CHX (X = Ph, OMe, OAc) to regioselectively yield the 5-substituted

† Dedicated to Prof. S. C. Bhattacharyya.
*Author for correspondence.

Table I
Regioselectivity in nitrone cycloaddition reactions

Sl no.	Olefins	Nitrones	Ratio of **5**:**4** substitution	Stereoselectivity	Ref.
	Monosubstituted				
1	Ph–CH=CH_2	*C*, *N*-Diphenyl	~ 100 : 0	C^3-Ph:C^5-Ph/*cis:trans* (*exo:endo*) 90:10	4a
2	Ph–CH=CH_2	*C*-Phenyl-*N*-methyl	~ 100 : 0	C^3-Ph:C^5-Ph/*cis:trans* (*exo:endo*) 67:33	4a
3	MeO_2C–CH=CH_2	*C*, *N*-Diphenyl	~ 100 : 0	Two regioisomers ~57:43	4a
4	AcO–CH=CH_2	*C*, *N*-Diphenyl	~ 100 : 0	Only *cis*	4b
5	PhO_2S–CH=CH_2	*C*-Phenyl-*N*-Methyl	32 : 68		4c
6	MeO_2C–C≡CH	*C*-Phenyl-*N*-Methyl	42 : 58		4d
7	CH_2=CH–NO_2	*C*-Phenyl-*N*-Methyl	~ 0 : 100	*cis:trans* 67:33	4c
	Disubstituted				
8*	*E*-Me–CH=CH–CO_2Me	*C*, *N*-Diphenyl	~ 100 : 0	Two stereoisomers; 15:85, major H^3, H^4, H^5; *trans, trans*	4a, 4f
9**	*E*-Ph–CH=CH–NO_2	*C*-Benzoyl-*N*-Phenyl	~ 100 : 0	Only H^3, H^4, H^5; *trans, trans*	4a

*:5-Methyl-4-methoxylcarbonyl; **:5-Methyl-4-nitro.

heterocyclics with >98% stereoselectivity in favour of the 3,5-*cis* isomer. The uncomplexed nitrone (**17**) underwent cycloadditions with the same substrates with much lower stereoselectivity (X = Ph, OMe, OAc with *cis:trans* ratios of 69:31; 46:54; 67:33, respectively).

Less work had been done earlier with 1,2-disubstituted olefins. Since the regio- and stereoselectivities should be affected by both substituents, it was of interest to us to find out the overall outcome. These investigations would be of synthetic value, as the resultant cycloadducts would have three contiguous chiral centres. Our investigations were, therefore, directed towards the study of some typical nitrone cycloadditions with 1,2-disubstituted olefins.[5–13] We have investigated the reactions of *C*,*N*-diarylnitrones (**1**–**4**) and *C*-aryl-*N*-methylnitrones (**17**–**20**) with 1,2-disubstituted olefins where the dipolarophiles had the reacting double bond conjugated with an aryl group and a carbonyl group. Similar reactions[10–13] were carried out with cyclic nitrones, viz. 1-pyrroline-1-oxide (**28**) and 3,4,5,6-tetrahydropyridine-1-oxide (**29**). The results of some of these studies are briefly presented here along with related work of other research groups.

2. Cycloadditions of *C*-aryl-*N*-phenylnitrones and *C*-aryl-*N*-methylnitrones

We have generated the *C*-aryl-*N*-phenyl and *C*-aryl-*N*-methylnitrones by the usual literature method:[14] (i) by warming aryl aldehydes with *N*-phenylhydroxylamine in ethanolic solution, and then allowing the reaction mixtures to stand overnight; (ii) by refluxing aryl aldehydes and *N*-methylhydroxylamine hydrochloride for several hours in methylene chloride in the presence of sodium bicarbonate. We have found recently that the time of reaction can be reduced to the order of minutes by using microwave irradiation techniques.[15]

Our initial studies involved cycloadditions of the four *C*-aryl-*N*-phenylnitrones (**1**–**4**) to the conjugated lactone butenolide (**5**) (Chart I).[5] Previous to our investigations, there was only one report of nitrone cycloaddition to a conjugated lactone.[16] Refluxing the reactants in toluene (or

heating in toluene solution in a sealed tube at 110ºC–115ºC) for 12 h yielded two regioisomeric bicyclic cycloadducts in each of the reactions. The 3*RS*-(3*R**,3a*R**,6a*S**)-2,3,6,6a-tetrahydrofuro[3,4-d]isoxazole cycloadducts (3,3a-*cis* isomer) (**6**) were the major products with of the 3*RS*-(3*R**,3a*S**,6a*R**)-isomer (3,3a-*trans* isomer) (**7**) being obtained in smaller amounts as minor products. Small amounts of a ring-opened butanolide (**8**), derived from the major cycloadduct (**6**) were also obtained.

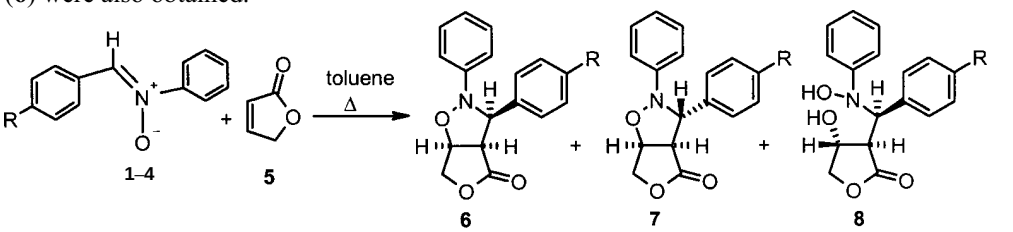


CHART I. Cycloaddition of *C*-aryl-*N*-phenylnitrones to butenolide.

Much of our subsequent efforts have been devoted to the detailed studies of the cycloaddition of *C*,*N*-diarylnitrones (**1–4**) to the cinnamic acid piperidides (**9–12**)[5b,6–8,10] (Chart II). The *para*-substituents on both the dipole and dipolarophile varied from the strongly electron-withdrawing nitro to the strongly electron-donating methoxyl. Literature shows that propylene, styrene and methyl acrylate react with *C*,*N*-diphenylnitrone (**1**) to regioselectively yield 5-substituted isoxazolidines as major cycloadducts (Table I). Substitution at both the ends of a double bond is expected to yield product(s) whose regiochemistry will be directed by both the substituents. Earlier reports show that both methyl crotonate and β-nitrostyrene give isooxazolidine cycloadducts where the electron-withdrawing group is situated at the 4-position (Table I). We are interested in finding out how sensitive the cycloaddition regioselectivities are to changes in aryl substitution on the dipole and dipolarophile. It is satisfying to observe that in several instances in the course of our investigations the small perturbations caused by changes in *para*-substituents led to some perceptible changes in regioselectivities.

The reactions of nitrones (**1–4**) with dipolarophiles (**9–12**) were performed in refluxing toluene under nitrogen atmosphere for 30–40 h (Chart II). Two series of cycloadducts, viz., the 3,4-*trans*-4,5–*trans*-5-aryl-4-piperidinyloxoisoxazolidines (**14**) as major products and the diastereoisomeric 3,4-*cis*-4,5–*trans* 5-aryl-4-piperidinyloxoisoxazolidines (**15**) as minor products could be isolated from all the reactions.[5b,6–8,10] The proportion of the cycloadducts in the crude product mixture was determined by ^{1}H NMR analysis (see Table II for representative examples), the de (diastereoisomeric excess) was estimated to be 75–85% in favor of the major cycloadduct (**14**).

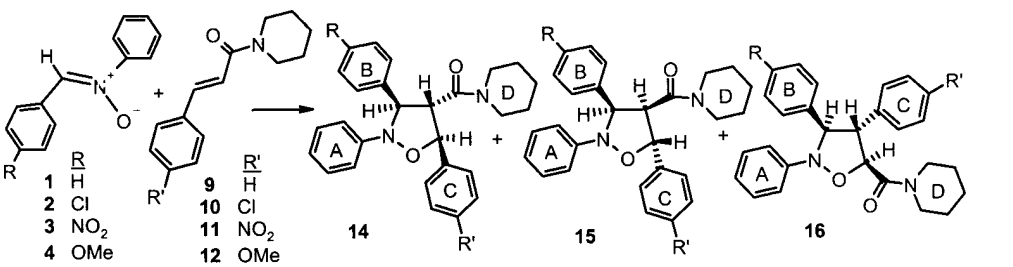
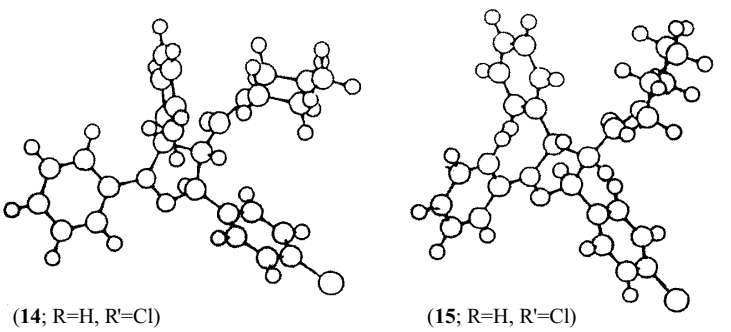


CHART II. Cycloaddition of *C*-aryl-*N*-phenylnitrones to cinnamic acid piperidides.

Table II
Relative proportions of products obtained on cycloaddition of *C*-aryl-*N*-phenyl-nitrones(1, 2, 4) to Cinnamic acid piperidides (9,10)

Substituents	3,4-trans-4,5-trans isomer (major product) **14**	3,4-trans-4,5-trans isomer (major product) **15**	3,4-trans-4,5-trans regioisomer **16**
R=NO_2; R'=Cl	84	7.5	8.5
R=H; R'= H	92.5	7.5	0
R=H; R'=Cl	87	8.5	4.5
R=Cl; R'= H	90	10	0
R=NO_2; R'=Cl	82	7	11

Monitoring of the reactions by 300 MHz ^{1}H NMR spectroscopy showed that the relative ratios of the regio- and stereoisomeric cycloadducts remained similar as the reaction proceeded. The observed relative yields at the end of the reaction seem to be those of kinetic control. In the reactions, where electron-withdrawing groups were present on the aryl rings of the dipolarophile or the nitrone, the regioisomeric 3,4-*trans*-4,5-*trans*-4-aryl-5-piperidinyloxoisoxazolidine cycloadducts (**16**) were also formed. The regiosiomeric cycloadducts could be distinguished from their COSY-LR spectra and MS fragmentation patterns. H-3 and H-5 in **14** and **15** showed long range coupling in their COSY-LR spectra with the *ortho* protons of the attached aryl rings; in contrast, the COSY-LR spectrum of **16** showed LR-correlations of H-3 and H-4 with *ortho*-aromatic protons. Structural and stereochemical assignments were confirmed by X-ray crystallographic analyses. Calculations on energy minimisation of the stereo- and regioisomeric cycloadducts were done by the conjugate gradient method using the DISCOVER module of Insight-II Molecular Model package (MSI Inc.).[17] Representative calculated minimum energy conformations of the diastereoisomeric cycloadducts are shown in Fig. 1. The potential energy of the most stable conformer of the all-*trans* cycloadduct (**14**; R=H, R'=Cl) was calculated to be 3.9 kcal/mole less than that of the corresponding 3,4-*cis*-4,5-*trans* isomer (**15**; R=H, R'=Cl).



(**14**; R=H, R'=Cl) (**15**; R=H, R'=Cl)

FIG. 1. Conformations of (**14** and **15**; R=H, R'=Cl) calculated by DISCOVER module of Insight-II molecular model package.

The observed regio- and stereochemical courses of cycloadditions could be explained on the basis of FMO theory.[1–4] It has been established that the formation of the regioisomer for which the HOMO–LUMO coefficient pairings are (large–large + small–small) in the transition state would be favored. It is also apparent that greater the differentiation in magnitude of the FMO coeffi-

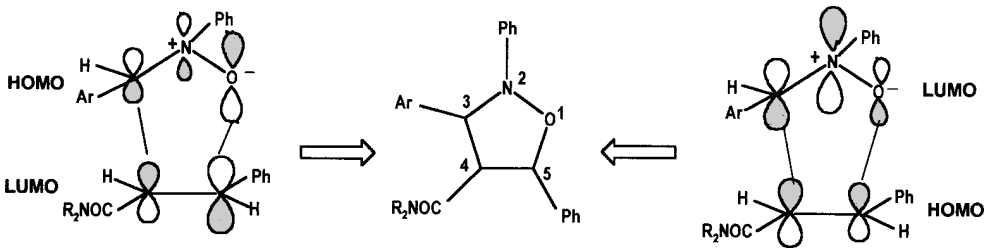


FIG. 2. Regiocontrol of cycloaddition of *C*-aryl-*N*-phenylnitrones to cinnamic acid piperidides.

cients in each of the reactants the greater would be the regioselectivity. The *C*,*N*-diarylnitrones (**1**-**4**) have $C_{O\text{-}3} > C_{C\text{-}1}$ in the HOMO and $C_{O\text{-}3} < C_{C\text{-}1}$ in the LUMO (see, for example, Jouçla's work[2e]). For these nitrones, both pairs of HOMO–LUMO interactions would favor the formation of the same regioisomeric transition state that would lead to 2,3,5-triaryl-4-piperidinyloxoisoxazolidine cycloadducts (**14** and **15**) (Fig. 2). The introduction of a *p*-nitro group on the *C*-aryl ring of the nitrone as in (**3**) reduces the LUMO energy, making the cycloaddition of the Sustmann Type III (dipole–LUMO controlled). Further, the differentiation in the magnitude of the coefficients $C_{O\text{-}3}$ and $C_{C\text{-}1}$ is reduced in the LUMO compared to *C*-phenylnitrone.[2e] Overall, this would lead to a loss of regioselectivity. Similarly, the presence of an electron-withdrawing group such as *p*-nitro in the dipolarophile would lower both LUMO and HOMO energies, and reduces the difference in magnitude between the orbital coefficients on C-2 and C-3. Hence, cycloadditions involving **11** as the dipolarophile would be expected to be less regioselective than those of **9**. Similar effects on the loss of regioselectivity with *p*-chloro substituents, both on the nitrone and the dipolarophile, would be expected, albeit to a lesser degree. A high degree of *endo*-stereoselectivity was observed in these cycloadditions. *C*,*N*-diarylnitrones exist preferentially with the aryl rings *trans* to each other.[1-3] We could reconfirm by ^{1}H NMR studies that the configuration of the *C*,*N*-diarylnitrones did not change under the reaction conditions, viz., prolonged refluxing in toluene did not give any of the *cis*-diarylnitrone (**13**). *Endo* approach of the dipolarophile leading to 3,4-*trans* cycloadducts (**14**) is expected to predominate due to the presence of favorable secondary orbital interactions in the transition state (Fig. 3).

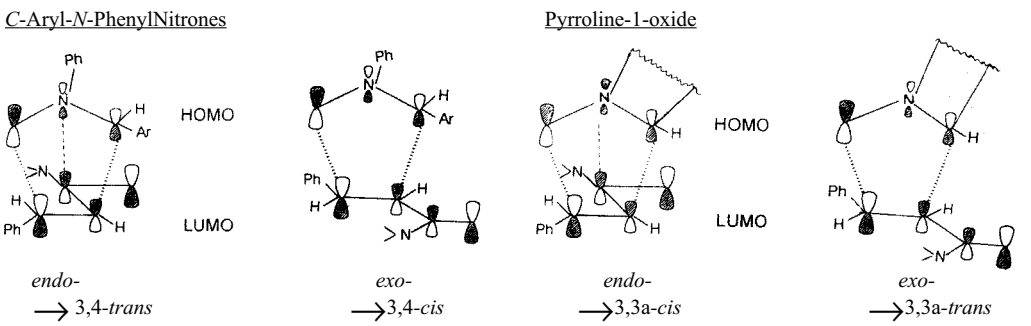
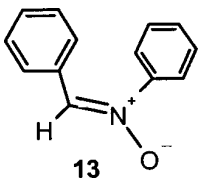


FIG. 3. Stereocontrol of cycloaddition of *C*-aryl-*N*-phenylnitrone and 1-pyrroline-1-oxide to cinnamic acid piperidides.

A similar series of cycloaddition reactions was carried out with *C*-aryl-*N*-methylnitrones (**17**–**20**) with the cinnamic acid piperidides (**1**-**4**) (Chart III).[7b, 8b, 10] The results obtained were broadly similar, the 3,4-*trans*-4,5-*trans*-2-methyl-3,5-diaryl-4-piperidinyloxoisoxazolidine cycloadducts



(**21**) were the major products, with the diastereoisomeric 3,4-*cis*-4,5-*trans*-2-methyl-3,5-diaryl-4-piperidinyloxoisoxazolidine cycloadducts (**22**) being the minor products.

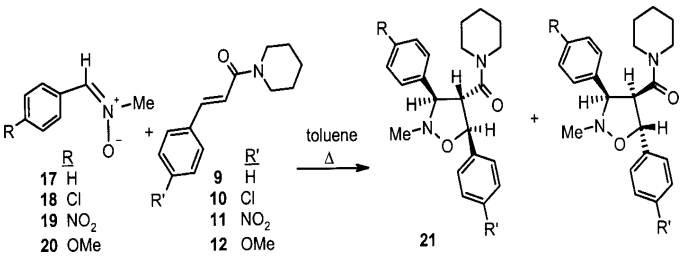


Chart III. Cycloaddition of *C*-aryl-*N*- methylnitrones to cinnamic acid piperidides.

In another series of investigations, the reactions between equimolar proportions of the 5-phenyl-2*E*,4*E*-dienamide (**23**) and the *C*-aryl-*N*-phenylnitrones (**1**–**4**) were studied.[9,10] To suppress the formation of *bis* adducts, the nitrone in toluene solution was added over a period of a few hours to a refluxing toluene solution of the dipolarophile in order to maintain an excess of the dipolarophile at all times. The reaction occurred preferentially at the α,β-conjugated double bond to give cycloadducts (**24**) as major products, and the regiosiomeric adducts (**25**) as minor products (Chart IV). However, the observed regioselectivity was much less than for the cinnamic acid piperidides.

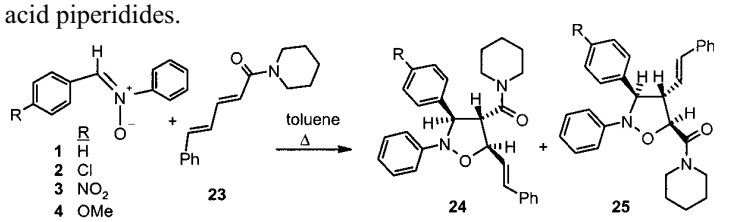


Chart IV. Cycloaddition of *C*-aryl-*N*- phenylnitrones to 5-phenyl-2*E*,4*E*-pentadienamide.

Other groups have reported the cycloaddition of *C*-aryl-*N*-phenylnitrones to 1,2- and tetra-substituted double bonds. An interesting communication has recently reported the cycloaddition of *C*-aryl-*N*-phenylnitrones (aryl = Ph, *p*-tolyl, *p*-anisyl) to the furan-2,3-diones (**26a**) and pyrrole-2,3-diones (**26b**) to regio- and stereoselectively (Chart V) yield adducts (**27**).[4e,h,i] A Japanese

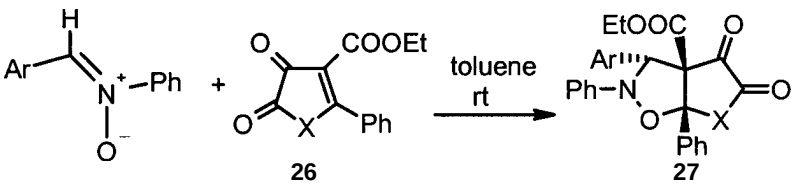
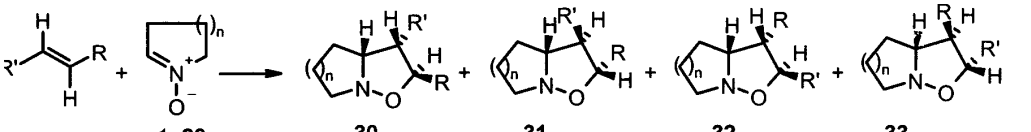


Chart V. Cycloaddition of *C*-aryl-*N*- phenylnitrones to various dipolarophiles.



	R	R'	(30)	(31)	(32)	(33)
n=1	OEt	H	92	8	—	—
	Ph	H	91	9	—	—
	CO_2Me	H	43	37	9	11
n= 2	Ph	H	95	5	—	—
	CO_2Me	H	69	15	6	10
n= 1	Me	CO_2Me	93	7	—	—
n= 2	Ph	CO_2Me	87	13	—	—
	Ph	CHO	100	0	—	—
	Me	CO_2Me	90	10	—	—
	Me	CHO	100	0		

Chart VI. Cycloadditions of 1-pyrroline-1-oxide and 3,4,5,6-tetrahydropyridine-1-oxide to various dipolarophiles.

group[18] has reported that cycloadditions of homoadamantane-incorporated nitrones, viz., 4-azahomoadamantane-4-ene-*N*-oxide and 5-methyl-4-azahomoadamantane-4-ene-*N*-oxide with various alkenes proceeded with low regio- and stereoselectivities.

3. Cycloadditions of cyclic nitrones

Ali and coworkers[19] have carried out fairly extensive studies on the cycloadditions of several mono- and disubstituted dipolarophiles with 1-pyrroline-1-oxide (**28**) and 3,4,5,6 tetrahydropyridine-1-oxide (**29**) (Chart VI). All four types of cycloadducts (**30**–**33**) were obtained in certain cases. Ali reportedly obtained the ratios from NMR analysis.

We reacted 1-pyrroline-1-oxide (**28**) with the dipolarophiles (**9**–**11**) in refluxing toluene solution.[10–12] Two regioisomeric cycloadducts based on 2-aryl-3-piperidinyloxo-2,3,3a,4,5,6-hexahydropyrrolo[1,2-b]isoxazole (**34**) and 3-aryl-2-piperidinyloxo-2,3,3a,4,5,6-hexahydropyrrolo-[1,2-b]isoxazole (**35**) (Chart VII) were obtained in each case. The structures and relative configurations (3,3a-*cis*) of the product were established on the basis of spectroscopic data and X-ray crystallographic analysis. Both regioisomeric products were obtained by the *endo* approach of the nitrone (Fig. 3), in which favorable secondary MO interactions were present.

We then investigated the series of cycloadditions of the 6-membered cyclic nitrone 3,4,5,6-tetrahydropyridine-1-oxide (**29**)[10,11,13] with the same four dipolarophiles (**9**–**12**). Earlier reports

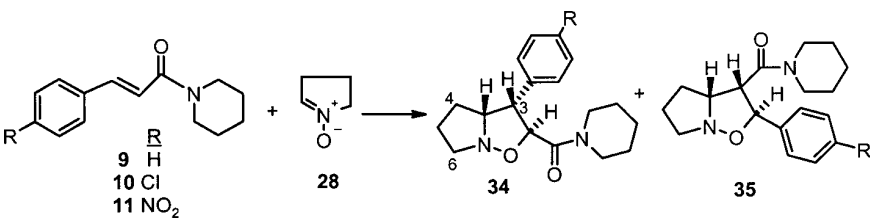


Chart VII. Cycloaddition of 1-pyrroline-1-oxide to cinnamic acid piperidides.

on the cycloaddition of this nitrone had reported opposite regioselectivities to the addition to styrene and methyl acrylate (Chart VII). We observed that the overall selectivity of the cycloadditions was less than for the acyclic nitrones; all the four possible types of regio- and stereoisomeric cycloadducts (**36–39**) could be isolated (Chart VIII). The 6,5-ring system allows more conformational mobility than the corresponding 5–5 ring system as in **34** and **35**. It was not surprising, therefore, to note that two series of cycloadducts, viz., **38** and **39**, had two rapidly interconverting conformers each of almost similar stability present in solution at ambient temperatures. The presence of two conformers could be established by ^{1}H NMR studies. Eventually, X-ray crystallographic studies were used to establish the structure and stereochemistry of the four different types of cycloadducts.

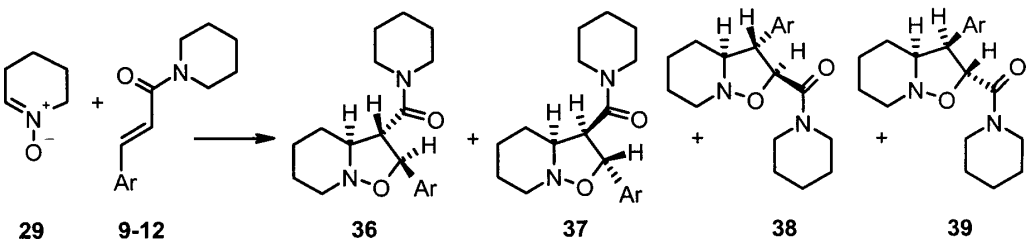


CHART VIII. Cycloaddition of 3,4,5,6-tetrahydropyridine-1-oxide to cinnamic acid piperidides.

Cycloadditions of **28** and **29** to benzoquinone monoketals (**40** and **41**) have been reported[20] (Chart IX). The cycloadditions of **28** were reported to proceed with poor stereo-and chemo selectivity to give mixtures of both *endo* (**42**) and *exo* (**43**) adducts, as well as *bis* adducts. With the 6-membered nitrone (**29**) high *exo* selectivity was reported, though quantitites of *bis* cycloadduct were formed. These studies were extended to the thio derivatives of these monoketals.

A number of papers have appeared on the cycloaddition of cyclic nitrones.[21] Studies were carried out by an Italian group[21a] on the cycloaddition of the cyclic nitrone 3, 4-dihydroisoquinoline-*N*-oxide to symmetrically disubstituted acyclic (*Z*)- and (*E*)-olefins and cyclic olefins. The formation of both possible stereoisomers was noted. Van Eijk has reported the cycloaddition of 4-membered cyclic nitrones with mono- and disubstituted conjugated dipolarophiles.[21b] The cycloaddition of substituted 5-membered cyclic nitrones to methylenecyclopropanes with high diastereofacial selectivity has been reported.[21c] The cycloaddition of mono-substituted alkenes to 2-alkyltetrahydropyridine-1-oxide proceeds via *exo* transition state and provides a stereoselective route for the preparation of *trans*-2,6-dialkylpiperidines by the reductive cleavage of the resulting perhydroisooxazolopyridine.[21d] This route has been used to synthesize the fire-ant venom alkaloid solenopsin A[21d] and andrachamine.[21e]

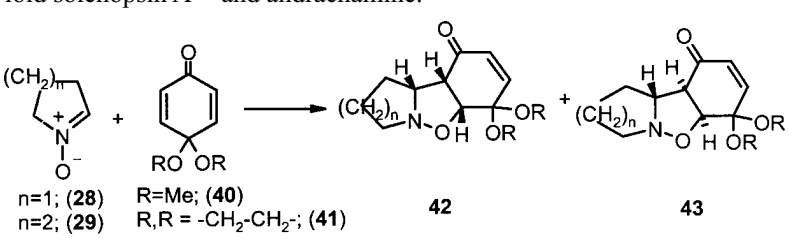


CHART IX. Cycloaddition of 1-pyrroline-1-oxide and 3,4,5,6-tetrahydropyridine-1-oxide to benzoquinone monoketal.

Acknowledgements

Research scholars and associates involved in the cycloaddition work undertaken by us are Sebanti Basu (neé Sinha), Sunanda Dutta (neé Haldar), Piyali Sengupta (Mrs Saha), Kaustabh Kumar Maiti, Hari Pada Seal (from Bangladesh) and Debasis Banerjee. Professor (Mrs) Julie Banerji of our Department, and Professor Thierry Prangé and Dr Alain Neuman of the Laboratoire de Chimie Structurale Biomoleculaire, Université Paris Nord, Bobigny, France, were also associated with different aspects of the work. Financial assistance from the University Grants Commission (UGC), India, Council of Scientific and Industrial Research (CSIR), India, and the Indian Council of Cultural Relations (ICCR) is gratefully acknowledged.

References

1. a. Gilchrist, T. L. and Storr, R. C. — *Organic reactions and orbital symmetry*, 2nd edn, Cambridge University Press, 1979.
   b. Huisgen, R. — *Angew. Chemie.*, 1963, **75**, 604.
   c. Padwa, A. (ed.) — *1,3-Dipolar cycloaddition chemistry*, Vols 1 and 2, Wiley-Interscience, 1984.
   d. Black, D. St. C., Crozier, R. F. and Davies, V. C. — *Synthesis*, 1975, 205.
   e. Banerji, A. and Sahu, A. — *J. Sci. Ind. Res.,* 1986, **45**, 355.
   f. Torssell, K. B. G. — *Nitrile oxides, nitrones and nitronates in organic synthesis*, VCH Weinheim, 1988.
   g. Trost, B. M. and Fleming, I. — *Comprehensive organic synthesis*, Vols 4 and 5, Pergamon Press, 1991.
2. a. Sustmann, R. — *Tetrahedron Lett.*, 1971, 2717.
   b. Sustmann, R. — *Pure Appl. Chem.*, 1974, **40**, 569.
   c. Houk, K. N., Sims, J., Duke, R. R. Jr, Strozner, R. W. and George, J. K. — *J. Am. Chem. Soc.*, 1973, **95**, 7287 and 7301.
   d. Fleming, I. — *Frontier orbitals and organic chemical reactions*, Academic Press, 1976.
   e. Jouçla, M., Tonnard, F., Gree, D. and Hamelin, J. — *J. Chem. Res.,* 1978, *(S)* 240, (M) 2901.
   f. Rastelli, A., Gandolfi, R. and Amade, M. S. — *J. Org. Chem.,* 1998, **63**, 7425.
3. a. Brandi, A., Cannavo, P., Pietrusiewicz, K. M., Zablocka, M. and Wieczorek, M. — *J. Org. Chem*., 1989, **54**, 3073.
   b. Houk, K. N. *et al.* — *J. Am. Chem. Soc*., 1984, **106**, 3880.
   c. Koizumi, T., Arai, Y. and Takayama, H. — *Tetrahedron Lett.*, 1987, **28**, 3689.
4 a. Huisgen, R., Grashey, R., Hauck, H. and Seidl, H. — *Chem. Ber*., 1968, **101**, 2043, 2548, 2559, 2568; 1969, **102**, 736.
   b. Deshong, P., Dicken, C. M., Staib, R. R., Freyer, A. J. and Weinreb, S. M. — *J. Org. Chem.,* 1982, **47**, 4397.

	c. Sims, J. and Houk, K. N.	*J. Am. Chem. Soc.,* 1973, **95**, 5798.
	d. Seidl, H., Huisgen, R. and Knorr, R.	*Chem. Ber.*, 1969, **102**, 904.
	e. Sano, T., Horiguchi, Y., Toda, J., Imafuka, K. and Tsuda, Y.	*Chem. Pharm. Bull*., 1984, **32**, 497.
	f. Joucla, M., Grée, D. and Hamelin, J.	*Tetrahedron*, 1973, **29**, 2315.
	g. Mukai, C., Kim, In. J., Cho, W. J., Kido, M. and Hanaoka, M.	*J. Chem. Soc., Perkin Trans. 1,* 1993, 2495.
	h. Hisham, A. and Abd El-Nabi	*J. Chem. Res. (S)*, 1996, 466.
	i. Saalfrank, R. W. *et al.*	*Chem. Ber*., 1991, **124**, 2289.
5	a. Banerji, A. and Basu, S.	*Tetrahedron*, 1992, **42**, 3335.
	b. Sebanti Sinha (Mrs Basu)	*Studies on natural products,* Ph. D. Thesis, Calcutta University, 1990.
6.	Banerji, A. *et al*.	*Indian J. Chem. B,* 1998, **37**, 105.
7.	a. Banerji, A. *et al.*	*Monatsh. Chem.*, 2000, **131**, 901.
	b. Banerji, A., Haldar (née Dutta), S., Maiti, K. K., Prangé, T. and Neumann, A.	Communicated to *Monatsh. Chem.*
8.	a. Haldar, S.	*Studies on cycloaddition reactions and marine natural products,* Ph. D. Thesis, Calcutta University, 1995.
	b. Maiti, K. K.	*Studies on cycloaddition reactions and organometallic compounds,* Ph. D. thesis, Calcutta University, 1999.
9.	a. Seal, H. P.	*Studies on organometallic compounds and cycloaddition reactions,* Ph. D. Thesis, Calcutta University, 1994.
	b. Banerji, A. *et al.*	Communicated to *Indian J. Chem.*
10.	a. Banerji, A., Banerji, J., Basu (née Sinha), S., Haldar (née Dutta) , S. and Sengupta, P.	*5th Asian Chemical Congress,* Kuala Lumpur, Malaysia, November 8–12, 1993.
	b. Banerji, A., Banerji, J., Haldar (née Dutta), S., Basu (née Sinha), S. and Banerji, D.	*10th Int. Conf. on Organic Synthesis (IUPAC),* Bangalore, India, December 11–16, 1994.
	c. Banerji, A.	*15th Professor Mukarram Hussain Khundakar Memorial Lecture,* Dhaka University, Bangladesh, Dec. 1998.
11.	Sengupta, P.	*Studies on heterocycles and NMR studies on acetylenic compounds*, Ph. D. Thesis, Calcutta University, 1994.
12.	Banerji, A., Sengupta, P., Neumann, A. and Prangé, T.	*Indian J. Chem. B,* 1998, **37**, 15.
13.	Banerji, A., Sengupta, P., Banerji, D., Prangé, T. and Neumann, A.	Communicated to *J. Chem. Res.*
14.	Sandler, S. R. and Karo, W.	*Organic functional group preparations*, Part III, Ch. 9, Academic Press, 1972.
15.	Banerji, A. *et al*.	Communicated to *Synth. Commun.*
16.	Panfil, I. and Chmielenski, M.	*Tetrahedron*, 1985, **41**, 4713.

17. a. Brooks, C. L. III, Karplus, M. and Pettit, B. M. — *Proteins: A theoretical perspective of dynamics, structure and thermodynamics*, Wiley, 1987, pp. 23–31.

    b. Grant, G. H. and Richard, W. G. — *Computational chemistry*, Oxford Chemistry Primers, Oxford University Press, 1995.

18. Yu, Y., Ohno, M., Eguchi, S., Kawal, T. and Terada, Y. — *Tetrahedron*, 1997, **53**, 5413**.**

19. a. Tufariello, J. J. and Ali, Sk. A. — *Tetrahedron Lett.*, 1978, 4647.

    b. Ali, Sk. A. and Wazeer, M. I. M. — *Tetrahedron,* 1988, **44**, 5911.

    c. Ali, Sk. A. and Wazeer, M. I. M. — *Tetrahedron,* 1988, **44**, 187.

    d. Ali, Sk. A. and Wazeer, M. I. M. — *J. Chem. Soc., Perkin Trans. 1*, 1988, 597.

    e. Ali, Sk. A., Khan, J. H., Wazeer, M. I. M. and Perzawski, H. P. — *Tetrahedron,* 1989, **45**, 5979.

20. de March, P., Escoda, M., Figuerdo, M. and Font, J. — *Tetrahedron Lett*., 1995, **36**, 8665.

21 a. Burdisso, M., Gamba, A. and Gandolfi, R. — *Tetrahedron*, 1988, **44**, 3735.

    b. Van Eijk, P. J. S. S., Verboom, W., van Veggel, F. C. J. M., Reinherdt, D. N. and Harkema, S. — *Recl. Trav. Chim. Pays-Bas*, 1988, **107**, 142.

    c. Cordero, F. M. *et al.* — *J. Org. Chem*., 1990, **55**, 1762.

    d. Adams, D. R., Carruthers, W. and Williams, M. J. — *J. Chem. Soc., Perkin Trans. 1*, 1989, 1507.

    e. Carruthers, W., Coggins, P. and Weston, J. B. — *J. Chem. Soc., Perkin Trans. 1*, 1990, 2323.