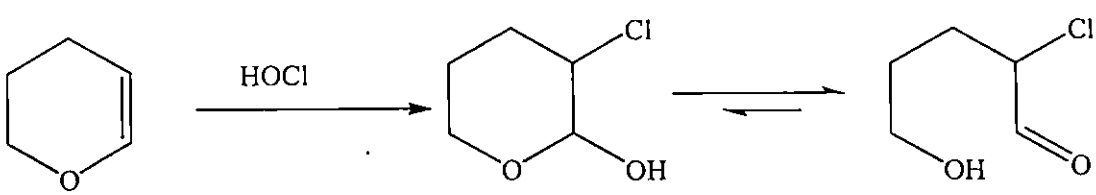
CHAPTER II

Experimental Section

All the melting points were determined in open capillary tube and were uncorrected. ^{1}H NMR spectra were recorded with a Bruker – Avans DPX 400 spectrometer (400MHz, FT NMR) using tetramethyl silane as internal standard. ^{13}C NMR spectra were recorded on the same instrument at 100 MHz. The coupling constants (*J*) are given in hertz (Hz). Chemical shift values are given in δ ppm with tetramethyl silane as internal standard. IR spectra were obtained with a Perkin – Elmer RX 1881 machine as film for all the products. MS and HRMS spectra were recorded with a Jeol – SX 102 (FAB) instrument. Elemental analysis (C,H,N) were performed with a Perkin – Elmer 2400 series CHN analyzer. Analytical thin layer chromatography (TLC) was performed on both Fluka silica gel and Merk precoated silica gel plates (60 F_{254}). Visualization was done by exposing to iodine vapour. All the chemicals and reagents along with common solvents were purified after receiving from commercial suppliers using established procedures. *N*-cyclohexyl hydroxylamine was prepared following the methodology as already reported. *N*-phenyl hydroxylamine was prepared following the standard methods available in the literature.

Reaction type I

Preparation of Chlorohydrin



a **b**

2-Chloro-5-hydroxy pentanal

Scheme 1

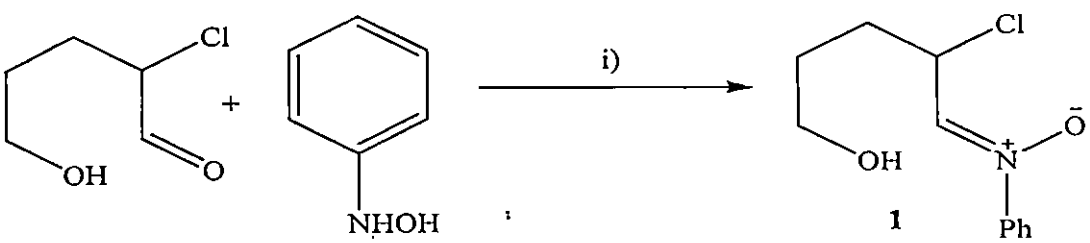
Hypochlorous acid was prepared following the standard methodology available in inorganic text books[1,2,3]. To a saturated solution of sodium bicarbonate, chlorine gas was passed till saturation. After the completion of reaction, the product was isolated by shaking with ether vigorously in a separatory funnel and finally collected by reduced pressure vacuum pump. Pure hypochlorous acid was obtained as greenish white liquid.

In a 100 mL conical flask, dihydropyran and hypochlorous acid (1 equivalent each) was taken in a required amount of DMSO as solvent and was stirred with a magnetic stirrer for 5 – 6 hour. The reaction was monitored by TLC (R_f = 0.76). After completion of the reaction the product (chlorohydrine) was isolated with ether and finally obtained under reduced pressure as a greenish gummy liquid[3].

Spectral data of 2-Chloro-5-hydroxy pentanal

Greenish gummy liquid, 74.6%; IR ($CHCl_3$): 3600 – 3200 (br), 2920 (s), 1720 (s), 1440 (m), 1380 (s), 1340 (m), 1284 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.75 (1H, CHO), 5.06 (d, 1H, J = 6 Hz, -OCH), 5.23 – 4.96 (br, 1H, -OH, exchanged in D_2O), 4.10 – 3.93 (dt~m, 1H, CHCl), 3.80 – 3.4 (m, 4H, CH_2); MS (*m/z*): 136 (M^+), 118, 108, 102, 78, 69.

Preparation of *N*-phenyl-α-chloronitrone (1)



i) anhydrous $MgSO_4$, RT, 12 hr, N_2 environment

Scheme 2

N-phenylhydroxylamine[4] (250 mg, 2.11 mmole) was added to chlorohydrin solution (1 equivalent) taken in diethyl ether (50 mL) and anhydrous $MgSO_4$. The solution was kept at room temperature for 12 hour with constant stirring with a magnetic stirrer under nitrogenous atmosphere. The formation of nitrone was monitored by TLC (R_f = 0.32). After completion of the reaction, the nitrone was isolated under reduced pressure as white needle shaped crystals, m.p, 58°C (uncorrected). The nitrone was unstable and decomposes at room temperature when kept for longer period.

Spectral data of (*Z*)-*N*-(2-chloro-5-hydroxypentylidene)aniline oxide:

White needle shape crystals, 93%, IR ($CHCl_3$): 3660 – 3520 (br), 1610 (s), 1440 (m), 1150 (s), 784 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.73 – 7.28 (m, 5H, C_6H_5), 6.45 (d, 1H, J = 6.06 Hz, $CH{=}N^+$), 5.12 (br, 1H, OH, exchanged in D_2O), 3.66 (dt~m, 1H, J = 6.06, 6.08 Hz, CHCl), 2.04 – 1.25 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 142.04 ($CH{=}N^+$), 134.80, 133.00, 131.60, 130.00 (aromatic carbons), 95.30 (CHCl), 31.45, 28.60, 25.40 (3 CH_2 carbons); HRMS – EI: Calcd. for $C_{11}H_{14}O_2NCl$, (M), 225.0864, Found M^+, 225.0852.

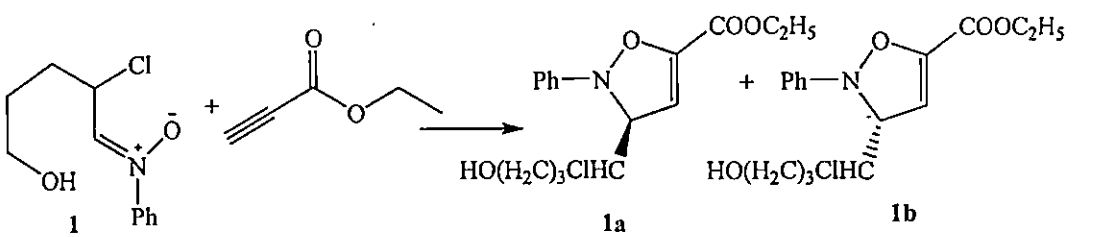
General Procedure for 1,3-dipolar cycloaddition reaction with alkynes at RT

Since *N*-phenyl-α-chloro nitrone may decompose at RT therefore the nitrone was used immediately after isolation for the cycloaddition reactions with dipolarophiles (alkynes) in a 1:1 ratio. In a 100 mL conical flask nitrone 1 (2.20 mmol), alkyne (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 10 - 12 hour. The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was evaporated off and the products (all the cycloadducts were obtained as diastereomers) were purified and separated by column chromatography using ethyl acetate-hexane combinations to furnish pure cycloadducts. This procedure was followed for all the substrates listed in Table I.

Table 1

- Ethyl propiolate
- Dimethyl acetylene dicarboxylate
- Phenyl methyl propiolate
- Acetylene dicarboxylic acid

1. Ethyl propiolate cycloadducts



Scheme 3

In a 100 mL conical flask *N*-phenyl-α-chloro nitrone (2.20 mmol) and ethyl propiolate (1 equivalent) was added to a 50 mL dry ether and stirred at RT with a magnetic stirrer under nitrogenous atmosphere for 12 hour. The progress of the reaction was monitored by TLC (R_f = 0.42, 0.44). After completion of the reaction, the solvent was

evaporated under rotary evaporator and the mixture of diastereoisomers were purified and separated by column chromatography using ethyl acetate-hexane to furnish white viscous liquids. **1a**: 73 mg, 70 %; **1b**: 36 mg, 22 %.

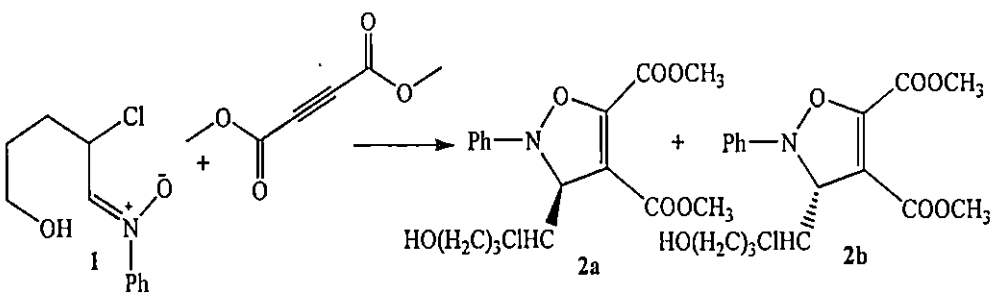
1a. Spectral data of (3*S*)-ethyl 3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-5-carboxylate

White viscous liquid, 70%; IR ($CHCl_3$): 3560 – 3490 (br), 2945 (s), 1770 (m), 1680 (s), 1430 (m), 1260 (m), 780 (s) cm^{-1} .^{1}H NMR ($CDCl_3$): δ 7.02 – 6.92 (m, 5H, C_6H_5), 5.10 - 5.02 (br, 1H, OH, exchanged in D_2O), 4.80 – 4.64 (t, 1H, J = 9.26 Hz, C_3H), 4.26 - 4.12 (dd, 2H, J = 6.24, 6.36 Hz, $COOCH_2CH_3$), 3.82 - 3.50 (dd, 1H, J = 6, 9.28 Hz, CHCl), 3.35 – 3.26 (d, 1H, J = 7.5 Hz, C_4H), 3.00 – 2.62 (m, 6H, CH_2 protons), 1.40 – 1.24 (t, 3H, J = 4.36 Hz, $COOCH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 168.40 (carbonyl carbon), 133 – 126 (6 aromatic carbons), 93 (CHCl), 86 (C_5), 78 (C_3), 55 (C_4), 32, 30 ($COOCH_2CH_3$), 26, 25, 23 (3 CH_2 carbons); MS (*m/z*): 326 (M^+), 295, 253, 249, 219, 108, 77, 73; HRMS – EI: Calcd. for $C_{16}H_{20}O_4NCl$ (M) 325.5944, Found M^+, 325.5932.

1b. Spectral data of (3*R*)-ethyl 3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-5-carboxylate

White viscous liquid, 22 %; IR ($CHCl_3$): 3520 - 3440 (br), 2925 (s), 1755 (s), 1675 (m), 1440 (m), 1345 (m), 770 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.52 – 7.35 (m, 2 x 5H, C_6H_5 protons), 5.15 - 5.05 (br, 1H, -OH, exchangeable in D_2O), 4.54 - 4.43 (dd, 1H, J = 2.52, 4.18 Hz, CHCl), 4.08 - 3.92 (d, 1H, J = 2.54 Hz, C_3H), 3.62 (s, 3H, -$COOCH_3$), 1.95 - 1.50 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 168 (carbonyl carbon), 138 – 126 (6 x 2 aromatic carbons), 90 (CHCl), 87 (C_5), 76 (C_3), 54 (C_4), 45 (-$COOCH_3$), 39, 35, 33 (3 CH_2 carbons); MS (*m/z*): 326 (M^+), 295, 253, 219, 108, 77, 73; HRMS – EI: Calcd. for $C_{16}H_{20}O_4NCl$ (M) 325.5944, Found M^+, 325.5926.

2. Dimethyl acetylene dicarboxylate cycloadducts



Scheme 4

In a 100 mL conical flask, *N*-phenyl-α-chloro nitrone (2.20 mmol) and dimethyl acetylene dicarboxylate (1 equivalent) was added to a 50 mL dry ether and stirred at RT with a magnetic stirrer under nitrogenous atmosphere for 10 hr. The progress of the reaction was monitored by TLC (R_f = 0.46, 0.40). After completion of the reaction, the solvent was evaporated under rotary evaporator and the mixture of diastereoisomers were purified and separated by column chromatography using ethyl acetate-hexane to furnish white viscous liquids.

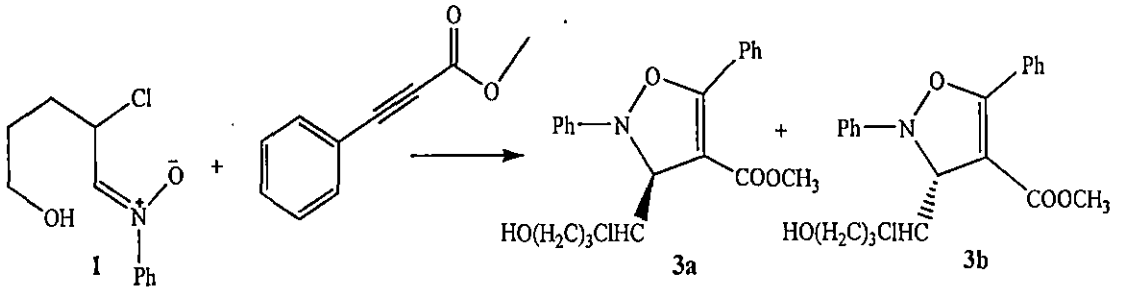
2a. Spectral data of (3*S*)-dimethyl 3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylate

White viscous liquid, 69 %; IR ($CHCl_3$): 3545 – 3480 (br), 2820 (s), 1745 (s), 1700 (m), 1670 (m), 1420 (s), 1260 (m), 775 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.75 - 7.54 (m, 5H, C_6H_5 protons), 5.22 - 5.05 (br, 1H, OH; exchanged in D_2O), 4.86 - 4.75 (d, 1H, J = 9.25 Hz, C_3H), 4.26 – 4.10 (dd, J = 6, 9.26 Hz, CHCl), 3.68 (s, 3H,- $COOCH_3$),3.56 (s, 3H,- $COOCH_3$), 2.20 - 2.05 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 169, 168.4 (carbonyl carbons), 133 - 126 (6 aromatic carbons), 94 (CHCl), 87.50 (C_5), 76 (C_3), 59.45 (C_4), 44, 43 (OCH_3), 36, 34, 30 (3 CH_2 carbons); MS (*m/z*): 370 (M^+), 339, 311, 293, 283, 262, 252, 234, 204, 108, 77, 59, 31; HRMS – EI: Calcd. for $C_{17}H_{20}O_6NCl$, (M) 369.64240, Found M^+, 369.64128.

2b. Spectral data of (3*R*)-dimethyl 3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylate

White viscous liquid, 27%; IR ($CHCl_3$): 3555 – 3485 (br), 2825 (s),1740 (s),1710 (m), 1660 (m), 1425 (s), 1260 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.70 - 7.56 (m, 5H, C_6H_5 protons), 5.20 - 5.08 (br 1H, OH, exchanged in D_2O), 4.88 - 4.74 (d, 1H, J = 2.58 Hz, C_3H), 4.36 – 4.26 (dd, J = 4, 2.26 Hz, CHCl), 3.66 (s, 3H, - $COOCH_3$), 3.54 (s, 3H,- $COOCH_3$), 2.12 - 1.95 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 169, 168 (carbonyl carbons), 134 - 126 (6 aromatic carbons), 95 (CHCl), 88.5 (C_5), 74 (C_3), 56 (C_4), 44, 42 (OCH_3), 36, 35, 30 (3 CH_2 carbons); MS (*m/z*): 370 (M^+), 311, 293, 262, 252, 234, 204, 108, 77, 59, 31; HRMS – EI: Calcd. for $C_{17}H_{20}O_6NCl$, (M), 369.6420, Found M^+, 369.6405.

3. Phenyl methyl propiolate cycloadducts



Scheme 5

In a 100 mL conical flask, *N*-phenyl-α-chloro nitrone (2.20 mmol) and phenyl methyl propiolate (1 equivalent) was added to a 50 mL dry ether and stirred at RT with a magnetic stirrer under nitrogenous atmosphere for 13 hour. The progress of the reaction was monitored by TLC (R_f = 0.46, 0.40). After completion of the reaction, the solvent was evaporated under reduced pressure and the mixture of diastereoisomers were purified and separated by column chromatography using ethyl acetate-hexane to furnish white viscous liquid.

3a. Spectral data of (3*S*)-methyl 3-(1-chloro-4-hydroxybutyl)-2,5-diphenyl-2,3-dihydroisoxazole-4-carboxylate

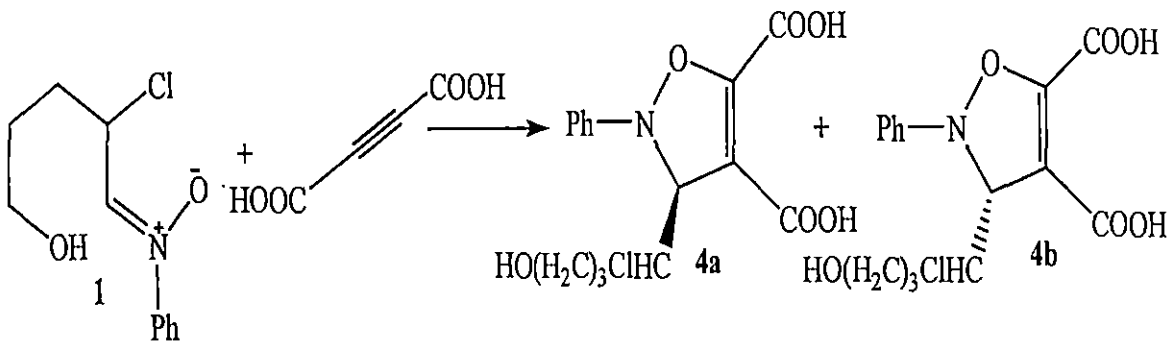
White viscous liquid, 75%; IR ($CHCl_3$): 3570 – 3420 (br), 2933 (s), 2246 (m), 1813 (m), 1662 (s), 1480 (s), 1324 (s), 1225 (s), 1105 (s), 993 (m), 779 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 - 7.38 (m, 2x5H; C_6H_5 protons), 5.10 - 4.95 (br, 1H, -OH, exchangeable in D_2O), 4.55 - 4.40 (dd, 1H, J = 9.22, 6.18 Hz, CHCl), 4.05 - 3.90 (d, 1H, J = 9.2 Hz, C_3H), 3.60 (s, 3H, - $COOCH_3$), 1.95 - 1.72 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 168 (carbonyl carbon), 137 – 126 (6x2 aromatic carbons), 92 (CHCl), 88 (C_5), 73 (C_3), 58 (C_4), 45 (-$COOCH_3$), 36, 34, 33 (3 CH_2 carbons); MS (*m/z*): 388 (M^+), 357, 329, 311, 283, 280, 203, 105, 77; HRMS – EI: Calcd. for $C_{21}H_{22}O_4NCl$ (M), 387.7000, Found M^+, 387.6990.

3b. Spectral data of (3*R*)-methyl 3-(1-chloro-4-hydroxybutyl)-2,5-diphenyl-2,3-dihydroisoxazole-4-carboxylate

White viscous liquid, 24 %; IR ($CHCl_3$): 3520 - 3440 (br), 2925 (s), 1755 (s), 1675 (m), 1440 (m), 1345 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.52 – 7.35 (m, 2x5H, C_6H_5 protons), 5.15 - 5.05 (br, 1H, - OH, exchangeable in D_2O), 4.54 - 4.43 (dd, 1H, J = 2.52, 4.18 Hz, CHCl), 4.08 - 3.92 (d, 1H, J = 2.54 Hz, C_3H), 3.62 (s, 3H, -

$COOCH_3$), 1.95 - 1.50 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 168 (carbonyl carbon), 138 - 126 (6x2 aromatic carbons), 90 (CHCl), 87 (C_5), 76(C_3), 54 (C_4), 45 (-$COOCH_3$), 39, 35, 33 (3 CH_2 carbons); MS (*m/z*): 388 (M^+), 357, 329, 311, 283, 280, 203, 105, 77; HRMS - EI: Calcd. for $C_{21}H_{22}O_4NCl$ (M) 387.7000, Found M^+ 387.6982.

4. Acetylene dicarboxylic acid cycloadducts



Scheme 6

In a 100 mL conical flask nitrone 1 (2.20 mmol), acetylene dicarboxylic acid (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 14 hour. The progress of the reaction was monitored by TLC (R_f = 0.38, 0.40). After completion of the reaction the crude products were concentrated on a rotary evaporator and finally the products were purified and separated by column chromatography using ethyl acetate-hexane to furnish colourless viscous liquids.

4a. Spectral data of (3*S*)-3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylic acid

Coluorless viscous liquid, 73%; IR ($CHCl_3$): 3545 – 3480 (br), 1760 (s), 1685 (m), 1420 (s), 1260 (m), 780 (s) cm^{-1}, ^1H NMR ($CDCl_3$): δ 10.12 (s, 1H, COOH), 10.04 (s, 1H, COOH), 7.75 - 7.54 (m, 5H, C_6H_5 protons), 5.22 - 5.05 (br, 1H, OH, exchanged in D_2O), 4.75 (d, 1H, J = 9.25 Hz, C_3H), 4.26 (q, 1H, J = 6, 9.26 Hz, CHCl), 2.20 - 1.75 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 180.60, 178.40 (carbonyl carbons of COOH), 133.90, 132.00, 130.50, 128.65 (aromatic carbons), 94.00 (CHCl), 87.50 (C_5), 76.00 (C_3), 59.40 (C_4), 36.00, 34.00, 32.00 (3 CH_2 carbons); MS (*m/z*): 341 (M^+), 310, 296, 268, 251, 236 ; HRMS – EI: Calcd. for $C_{15}H_{16}O_6NCl$, (M), 341.6080, Found M^+ , 341.6070.

4b. Spectral data of (3*R*)-3-(1-chloro-4-hydroxybutyl)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylic acid

White viscous liquid, 24 %; IR ($CHCl_3$): 3560 – 3465 (br), 1765 (s), 1680 (m), 1430 (s), 1260 (m), 782 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.16 (s, 1H, COOH), 10.00 (s, 1H, COOH), 7.40 - 7.24 (m, 5H, C_6H_5 protons), 5.20 - 5.08 (br, 1H, OH, exchanged in D_2O), 4.60 (d, 1H, J = 2.50 Hz, C_3H), 4.20 (q, 1H, J = 2.20, 3.55 Hz, CHCl), 2.10 - 1.64 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 182.40, 177.60 (carbonyl carbons of COOH), 134.00, 132.70, 131.50, 129.60 (aromatic carbons), 92.40 (CHCl), 88.50 (C_5), 76.77 (C_3), 58.46 (C_4), 37.00, 36.00, 34.00 (3 CH_2 carbons); MS (*m/z*): 341 (M^+), 310, 296, 268, 251, 236; HRMS – EI: Calcd. for $C_{15}H_{16}O_6NCl$, (M), 341.6080, Found M^+ 341.6064.

General Procedure for 1,3-dipolar cycloaddition reaction of nitrone 1 in aqueous phase

To run a chemical reaction under an environment friendly condition is a challenge now-a-days. In touch with the recent developments we have also successfully carried out aqueous phase cycloaddition reaction of *N*-phenyl-α-chloronitrone[5,6]. Surprisingly aqueous phase condition gave high yield, greater selectivity in a much lesser time. Details are discussed in **results and discussion** chapter.

General procedure for cycloaddition (for diastereomers)

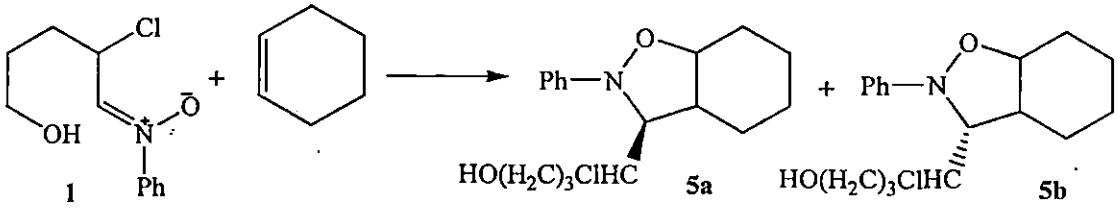
In a 50 mL conical flask, nitrone **1** (1 mmol), dipolarophile (1 mmol) and water (15 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 4-5 hr. The progress of the reaction was monitored by TLC. After completion of the reaction, the products were extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The mixture of diastereomers were purified and separated by column chromatography using ethyl acetate-hexane to afford cycloadducts. This procedure was followed for the substrates listed in **Table 2.**

Table 2. List of dipolarophiles used for cycloaddition reaction in aqueous phase

- Cyclohexene
- *N*-methyl maleimide
- *N*-phenyl maleimide

- *N*-cyclohexyl maleimide
- *p*-OMe-*N*-phenyl maleimide
- Acenapthylene
- Ethyl acrylate
- Methyl vinyl ketone

5. Synthesis of Cyclohexene cycloadducts



Scheme 7

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added cyclohexene (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 14 hr. The progress of the reaction was monitored by TLC (R_f = 0.36, 0.46). The products were extracted with ether (2 x 25 mL), the organic layers were washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The mixture of diastereomers were purified and separated by column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as reddish gummy liquid.

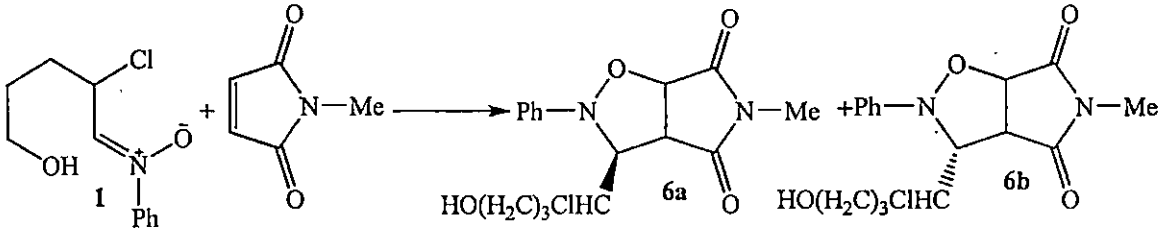
5a. Spectral data of 4-chloro-4-{(3*S*)-2-phenyl octahydrobenzo[*d*]isoxazol-3-yl}butan 1-ol

Reddish gummy liquid, Yield: 60%; IR($CHCl_3$): 3490 - 3370 (br), 2924 (s), 2850 (m), 2766 (m), 1542 (s), 1443 (m), 1250 (s), 774 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.28 - 7.14 (m, 5H, C_6H_5), 5.37 (d, 1H, J = 8.20 Hz, C_5H), 5.22 - 5.14 (br, 1H,exchanged in D_2O), 4.50 (dd, 1H, J = 9.2, 7.34 Hz, C_3H), 4.12 (dd, 1H, J = 9.40, 7.10 Hz, C_4H), 3.58 (q, 1H, J = 4.26, 6.20 Hz, CHCl), 1.80 - 1.14 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 130.00, 129.00, 128.40, 127.30 (aromatic carbons), 88.50 (C_5), 78.00 (C_3), 66.20 (CH_2OH), 54.60 (C_4), 52.60 (CHCl), 33.00, 31.00, 29.00, 27.00, 25.00, 24.40 (6 CH_2 carbons); MS (*m/z*): 309 (M^+), 227, 226, 211, 148, 147, 107, 77, 59, 31; HRMS-EI: Calcd. for $C_{17}H_{24}O_2NCl$ (M) 309.6330, Found (M^+) 309.6318.

5b. Spectral data of 4-chloro-4-{(3*R*)-2-phenyl octahydrobenzo[*d*]isoxazol-3-yl}butan 1-ol

Reddish gummy liquid, Yield: 28%; IR ($CHCl_3$): 3512 – 3454 (br), 2920 (s), 2854 (m), 2766 (m), 1550 (s), 1440 (m), 1256 (s), 802 (m), 778 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.26 - 7.14 (m, 5H, C_6H_5), 5.30 (d, 1H, J = 8.20 Hz, C_5H), 5.13 -5.04 (br, 1H,exchanged in D_2O), 4.36 (dd, 1H, J = 3.36, 2.23 Hz, C_3H), 4.20 (q, 1H, J = 2.54, 3.16 Hz, C_4H), 3.27 (q,1H, J = 3.26, 5.20 Hz, CHCl), 1.74 - 1.28 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 132.00, 131.00, 129.50, 128.20 (aromatic carbons), 87.00 (C_5), 76.00 (C_3), 63.60 (CH_2OH), 55.40 (C_4), 51.20 (CHCl), 30.00, 29.15, 28.00, 25.40, 24.00, 21.30 (6 CH_2 carbons); MS (*m/z*): 309 (M^+), 278, 250, 211, 227, 202, 148, 124, 107, 82, 77, 59, 31; HRMS-EI: Calcd. for $C_{17}H_{24}O_2NCl$ (M) 309.6330, Found M^+ 309.6314.

6. Synthesis of *N*-methyl maleimide cycloadducts



Scheme 8

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added *N*-methyl maleimide (1 mmol) at RT under nitrogen atmosphere and the reaction mixture was stirred for 4 hr. The progress of the reaction was monitored by TLC (R_f = 0.38, 0.40). The products were extracted with ether (2 x 25 mL), the organic layers were washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The mixture of diastereomers were purified and separated by column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as white solids.

6a. Spectral data of (3*S*)-3-(1-chloro-4 hydroxy butyl)-5 methyl-2-phenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione:

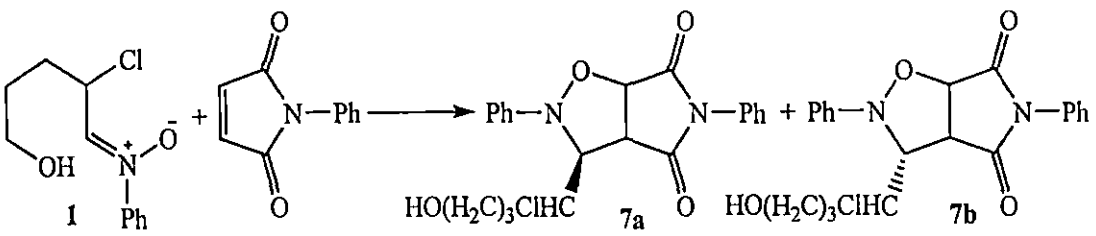
White solid, 75.6%; IR ($CHCl_3$): 3590 - 3460 (br), 2924 (m), 2840 (m), 1755 (s), 1660 (s), 1485 (m), 1340 (m), 803 (s), 774 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.15 – 6.98 (m, 5H, C_6H_5), 5.22 (d, 1H, J = 6.8 Hz, C_5H), 5.08 – 5.00 (br, 1H, OH, exchanged in D_2O), 4.55 (dd, 1H, J = 6.84, 9.2 Hz, C_3H), 3.76 (dd, 1H, J = 8.06, 9.20 Hz, C_4H),

3.40 (s, 3H, CH_3), 3.14 – 2.96 (dt~m, 1H, CHCl), 1.95 - 1.52 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 174.60, 173.40 (carbonyl carbons), 134.50, 133.20, 132.00, 130.60 (aromatic carbons), 88.00 (C_5), 73.00 (C_3), 62.20 (CH_2OH), 58.00 (C_4), 52.40 (CHCl), 39.42 (CH_3), 26.00, 23.00 (2 CH_2 carbons); MS (*m/z*): 340 (M^+ +2), 338 (M^+), 323, 307, 261, 247, 231, 107, 77, 59; HRMS – EI: Calcd. for $C_{16}H_{19}O_4N_2Cl$ (M) 338.1338, Found M^+, 338.1324; Found: C, 56.57, H, 5.49, N, 8.19 %; $C_{16}H_{19}O_4N_2Cl$ requires C, 56.63, H, 5.60, N, 8.25 %

6b. Spectral data of (3*R*)-3-(1-chloro-4 hydroxy butyl)- 5 methyl-2-phenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione:

White solid, 20.4%; IR ($CHCl_3$): 3580 – 3465 (br), 2895 (m), 1764 (s), 1660 (s), 1482 (m), 1355 (m), 805 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.20 – 7.08 (m, 5H, C_6H_5), 5.26 (d, 1H, J = 6.0 Hz, C_5H), 5.10 – 4.94 (br, 1H, OH, exchanged in D_2O), 4.10 (dd, 1H, J = 2.50, 4.06 Hz, C_3H), 3.60 (dd, 1H, J = 2.52, 4.26 Hz, C_4H), 3.44 (s, 3H, CH_3), 3.22 – 3.05 (dt~m, 1H, CHCl), 1.88 - 1.44 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 172.5, 171 (carbonyl carbons), 133, 132, 130.3, 128.6 (aromatic carbons), 88.6 (C_5), 74 (C_3), 61.4 (CH_2OH), 58.2 (C_4), 54 (CHCl), 37 (CH_3), 24, 21 (2 CH_2 carbons); MS (*m/z*): 338 (M^+), 307, 261, 246, 231, 139, 111, 107, 77, 31; HRMS – EI: Calcd. for $C_{16}H_{19}O_4N_2Cl$ (M) 338.1338, Found M^+, 338.1320; Found: C, 56.50; H, 5.52; N, 8.16 % ; $C_{16}H_{19}O_4N_2Cl$ requires C, 56.63; H, 5.60; N, 8.25 %.

7. Synthesis of *N*-phenyl maleimide cycloadducts



Scheme 9

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added *N*-phenyl maleimide (1 mmol) at RT under nitrogen atmosphere and the reaction mixture was stirred for 4 hr. The progress of the reaction was monitored by TLC (R_f = 0.34, 0.42).The products were extracted with ether (2 x 25 mL), the organic layers were washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The mixture of diastereomers were purified and separated by

column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as yellow and yellowish white solids.

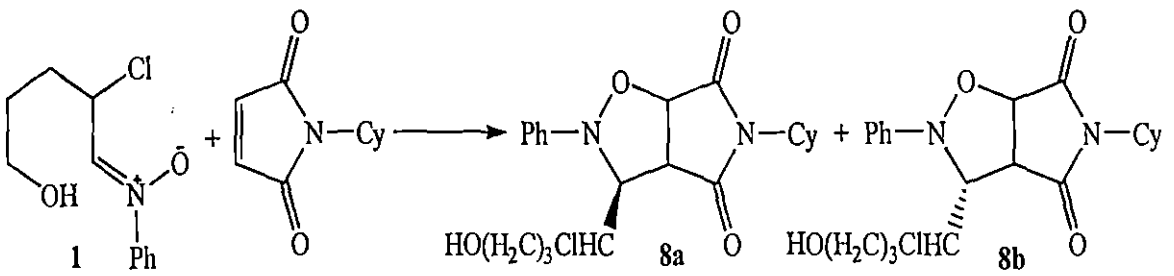
7a. Spectral data of (3*S*)-3-(1-chloro-4 hydroxy butyl)-2,5-diphenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione:

White solid, 70.8%; IR ($CHCl_3$): 3660 – 3408 (br), 3016 (s), 2937 (s), 2362 (m), 1720 (s), 1482 (s), 1217 (s), 1078 (s), 758 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 - 7.40 (m, 2 x5H, C_6H_5 protons), 5.42 (d, 1H, J = 8.24 Hz, C_5H), 5.05 - 4.95 (br, 1H, OH, exchanged in D_2O), 4.46 (dd, 1H, J = 9.25, 7.28 Hz, C_3H), 3.76 (dd, 1H, J = 9.22, 6.08 Hz, C_4H), 3.22 – 3.07 (dt~m, 1H, CHCl), 1.82 - 1.35 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 175.50, 173.60 (carbonyl carbons), 138.00, 137.00, 135.60, 134.35, 133.70, 132.00, 131.40, 130.00 (aromatic carbons), 87.50 (C_5), 76.00 (C_3), 64.00 (CH_2OH), 59.40 (C_4), 52.00 (CHCl), 28.00, 26.00 (2 CH_2 carbons); MS (*m/z*): 400 (M^+), 341, 323, 287, 246, 216, 173, 107, 77, 59, 31; HRMS – EI: Calcd. for $C_{21}H_{21}O_4N_2Cl$, (M) 400.1494, Found M^+, 400.1478, Found C, 66.70; H, 5.20; N, 6.82 %; $C_{21}H_{21}O_4N_2Cl$, requires C, 66.84; H, 5.23; N, 6.98%.

7b. Spectral data of (3*R*)-3- (1-chloro-4 hydroxy butyl)- 2,5 diphenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5H,6a*H*)-dione:

Yellowish white solid, 23.2%; IR ($CHCl_3$): 3560 – 3470 (br), 2865 (m), 1760 (s), 1684 (s), 1465 (m), 1370 (m), 810 (m), 772 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.35 - 7.14 (m, 2 x 5H, C_6H_5 protons), 5.24 (d, 1H, J = 7.20 Hz, C_5H), 5.00 - 4.92 (br, 1H, OH, exchanged in D_2O), 4.38 (dd, 1H, J = 3.25, 2.24 Hz, C_3H), 3.52 (dd, 1H, J = 4.42, 2.08 Hz, C_4H) , 3.37 – 3.20 (m, 1H, CHCl), 1.74 - 1.46 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 174.40, 171.80 (carbonyl carbons), 137.20, 136.40, 135.00, 134.50, 133.00, 132.80, 130.60, 129.00 (aromatic carbons), 85.00 (C_5), 72.60 (C_3), 64.50 (CH_2OH), 57.40 (C_4), 53.60 (CHCl), 28.00, 27.00 (2 CH_2 carbons); MS (*m/z*): 402 (M^+ +2), 400 (M^+), 295, 246, 216, 211, 189, 154, 107, 77, 31; HRMS – EI: Calcd. for $C_{21}H_{21}O_4N_2Cl$, (M), 400.1494, Found M^+ 400.1483, Found C, 66.54; H, 5.14; N, 6.75 %; $C_{21}H_{21}O_4N_2Cl$, requires C, 66.84; H, 5.23; N, 6.98%.

8. Synthesis of *N*-cyclohexyl maleimide cycloadducts



Scheme 10

To a stirred solution of nitrone 1 (1 mmol) in 15 mL water was added *N*-cyclohexyl maleimide (1 mmol) at RT under nitrogen atmosphere and the reaction mixture was stirred for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.39, 0.44). The products were extracted with ether (2 x 25 mL), the organic layers were washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The mixture of diastereomers were purified and separated by column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as dark yellow and yellow crystals.

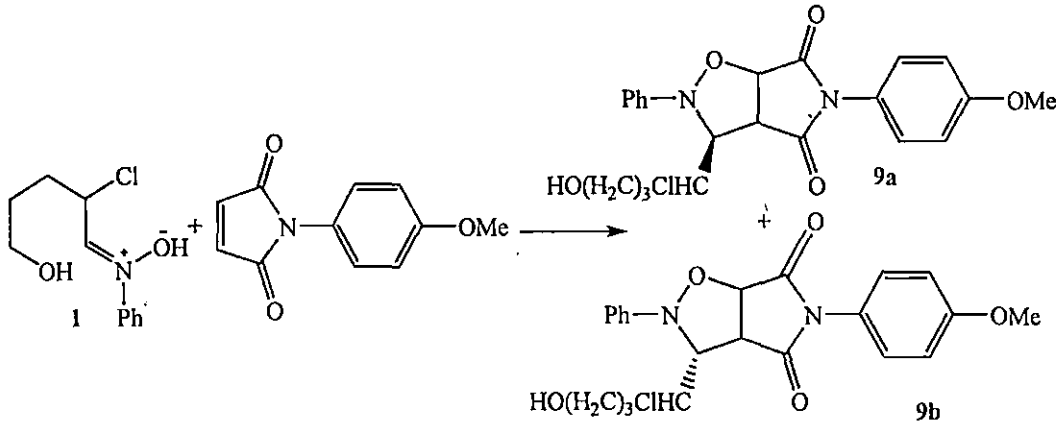
8a. Spectral data of (3*S*)-3- (1-chloro-4 hydroxy butyl)-5-cyclohexyl – 2- phenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6a*H*)-dione:

Dark yellow crystals, 68%; IR ($CHCl_3$): 3510 – 3370 (br), 2930 (s), 2350 (s), 1710 (s), 1598 (m), 1502 (s), 1457 (m), 1394 (s), 1145 (s), 1073 (s), 1029 (s), 831 (s), 756 (s), 696 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.02 – 6.92 (m, 5H, C_6H_5), 5.32 (d, 1H, J = 6.12 Hz, C_5H), 5.10 - 5.02 (br, 1H, OH, exchanged in D_2O), 4.52 (dd, 1H, J = 9.26, 6.08 Hz, C_3H), 4.26 (dd, 1H, J = 9.24, 7.06 Hz, C_4H), 3.20 – 2.94 (dt~m, 1H, CHCl), 1.64 – 1.24 (m, 17H, cyclohexyl and CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 172.30, 170.20 (carbonyl carbons), 131.30, 130.50 128.60, 127.40 (aromatic carbons), 86.00 (C_5), 78.00 (C_3), 62.50 (CH_2OH), 55.52 (C_4), 50.66 (CHCl), 30.00, 28.40, 26.70, 25.40, 24.35, 23.50, 22.20, 19.00 (cyclohexyl and CH_2 carbons); MS (*m/z*): 406 (M^+), 375, 347, 329, 324, 222,107,77,59,31; HRMS – EI: Calcd. for $C_{21}H_{27}O_4N_2Cl$ (M) 406.1962, Found M^+ 406.1949.

8b. Spectral data of (3*R*)-3- (1-chloro-4 hydroxy butyl)-5-cyclohexyl – 2- phenyl dihydro-2*H* pyrrolo[3,4-*d*]isoxazole-4,6(5*H*, 6 a*H*)-dione:

Yellow crystals, 27%; IR ($CHCl_3$): 3630 – 3535 (br), 2865 (s), 1760 (s), 1680 (s), 1440 (m), 1375 (m), 1265 (m), 810 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.22 – 7.04 (m, 5H, C_6H_5), 5.26 (d, 1H, J = 7.22 Hz, C_5H), 5.18 - 5.06 (br, 1H, OH, exchanged in D_2O), 4.43 (dd, 1H, J = 4.32, 3.26 Hz, C_3H), 4.14 (dd, 1H, J = 3.22, 2.08 Hz, C_4H), 3.38 – 3.20 (m, 1H, CHCl), 1.72 – 1.38 (m, 17H, cyclohexyl and CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 170.70, 169.80 (carbonyl carbons), 135.30, 134.50, 133.80, 132.50 (aromatic carbons), 84.30 (C_5), 75.00 (C_3), 61.60 (CH_2OH), 53.50 (C_4), 53.00 (CHCl), 27.00, 26.50, 25.40, 24.00, 23.00, 21.50, 20.00, 19.00 (cyclohexyl and CH_2 carbons); MS (*m/z*): 408 (M^+ +2), 406 (M^+), 323, 216, 179, 139, 107, 83, 77, 59; HRMS – EI: Calcd. for $C_{21}H_{27}O_4N_2Cl$ (M) 406.1962, Found M^+, 406.1943..

9. Synthesis of *p*-OMe-*N*-phenyl maleimide cycloadducts



Scheme 11

To a well stirred solution of nitrone 1(1 mmol) in 15 mL water, *p*-OMe-*N*-phenyl maleimide (1 mmol) was added at RT under N_2 atmosphere and the reaction mixture was stirred further for 5 hour. The progress of the reaction was monitored by TLC (R_f = 0.38, 0.40). After completion of the reaction the products were extracted with a ether (2 x 25 mL). The organic layer was washed with brine water (2 x 15 mL), dried over sodium sulphate and concentrated. The mixture of diastereomers were purified and separated by column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as white solids.

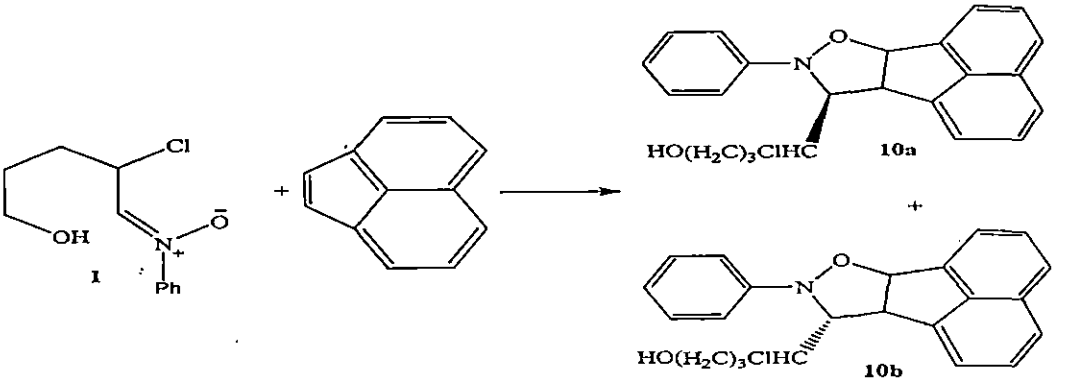
9a. Spectral data of (3*S*)-3-(1-chloro-4-hydroxybutyl)-5-(4-methoxyphenyl)-2-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione:

White solid, 70.8%; IR ($CHCl_3$): 3520 – 3465 (br), 2874 (m), 1765 (s), 1670 (s), 1445 (m), 1370 (m), 1175 (m), 805 (m), 772 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50-7.34 (m, 9H, C_6H_5 protons), 5.28 (d, 1H, J = 6.88 Hz, C_5H), 5.08 - 4.93 (br, 1H, OH, exchanged in D_2O), 4.84 (dd, 1H, J = 9.20, 8.02 Hz, C_3H), 3.86 (dd, 1H, J = 9.24, 7.08 Hz, C_4H), 3.34 (s, 3H, OCH_3), 3.26 - 3.14 (dt~m, 1H, CHCl), 1.85-1.42 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 175.20, 174.00 (carbonyl carbons), 159.80, 135.00, 134.60, 133.20, 131.40, 130.60, 129.50, 128.00 (aromatic carbons), 86.00 (C_5), 72.00 (C_3), 62.00 (CH_2OH), 56.00 (C_4), 54.00 (OMe), 50.00 (CHCl), 18.00, 17.00 (2 CH_2 carbons); MS (*m/z*): 432 (M^+ +2), 430 (M^+), 399, 371, 353, 323, 322, 219, 211, 108, 107, 59, 31; HRMS – EI: Calcd. for $C_{22}H_{23}O_5N_2Cl$, (M) 430.1599, Found M^+, 430.1586.

9b. Spectral data of (3*S*)-3-(1-chloro-4-hydroxybutyl)-5-(4-methoxyphenyl)-2-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione:

White solid, 21.2%; IR ($CHCl_3$): 3510 – 3420 (br), 2880 (m), 1760 (s), 1680 (s), 1455 (m), 1360 (m), 1160 (m), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.45 - 7.30 (m, 9H, C_6H_5 protons), 5.23 (d, 1H, J = 7.40 Hz, C_5H), 5.14 - 4.90 (br, 1H, OH, exchanged in D_2O), 4.72 (dd, 1H, J = 4.20, 2.32 Hz, C_3H), 3.54 (q, 1H, J = 2.84, 3.25 Hz, C_4H), 3.30 (s, 3H, OCH_3), 3.38 – 3.22 (dt~m, 1H, CHCl), 1.68 - 1.32 (m, 6H, CH_2 protons); ^{13}C NMR ($CDCl_3$): δ 174.40, 172.50 (carbonyl carbons), 158.40, 135.60, 134.30, 133.00, 132.00, 130.50, 129.30, 128.80 (aromatic carbons), 82.50 (C_5), 74.00 (C_3), 63.00 (CH_2OH), 55.50 (C_4), 53.80 (-OMe), 51.40 (-CHCl), 16.00, 15.00 (2 CH_2 carbons); MS (*m/z*): 430 (M^+), 399, 270, 246, 155, 139, 108, 107, 77, 59; HRMS – EI: Calcd. for $C_{22}H_{23}O_5N_2Cl$, (M) 430.1599, Found, M^+, 430.1566.

10. Synthesis of Acenaphthylene cycloadducts



Scheme 12

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added acenapthylene (1equivalent) *in-situ* at the time of formation of nitrone (monitored by TLC) at RT under nitrogen atmosphere and the reaction mixture was stirred for further 7 hr. The progress of the reaction was monitored by TLC (R_f = 0.40, 0.38). The products were extracted with ether (2 x 25 mL), the organic layers were washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and were concentrated under a rotary evaporator and finally the cycloadducts were purified and separated by silica gel column chromatography using ethyl acetate-hexane and were obtained as bright yellow crystals.

10a. Spectral data of 4-chloro-4-((9*S*) 8-phenyl-6b,8,9,9a-tetrahydroacenaphtho[1,2-*d*]isoxazol-9-yl)butan-1-ol:

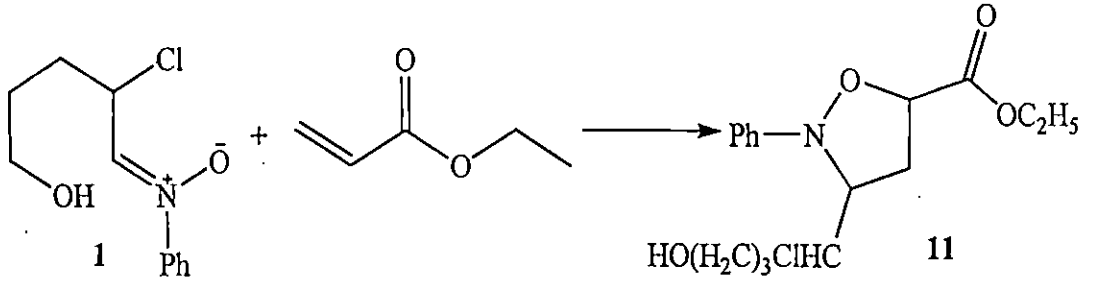
Bright yellow crystals, 73 %; IR ($CHCl_3$): 3455 - 3370 (br), 2960 (m), 2720 (m), 1710 (s), 1480 (m), 1280 (s), 778 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.28 – 7.20 (m, 5H, C_6H_5), 6.96 – 6.93 (m, 6H, napthylene ring protons), 5.26 (d, 1H, J = 6.50 Hz, C_5H), 4.88 (br, 1H exchanged in D_2O), 4.79 (dd, 1H, J = 9.2, 7.34 Hz, C_3H), 4.12 (dd, 1H, J = 9.40, 7.10 Hz, C_4H), 3.51 (dt~m, 1H, J = 4.26, 6.20 Hz, CHCl), 1.64 – 1.21 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 138.00, 137.70, 136.96, 135.40, 134.30, 133.00, 132.45, 131.76, 130.68, 128.64, 127.40, 126.30 (aromatic carbons), 86.90 (C_5), 78.10 (C_3), 66.20 (CH_2OH), 54.35 (C_4), 52.60 (CHCl), 31.00, 29.70, 27.65 (3 CH_2 carbons); MS (*m/z*): 379 (M^+), 320, 302, 272, 227, 152, 107, 77, 59; HRMS – EI: Calcd. for $C_{23}H_{22}O_2NCl$ (M) 379.8980, Found M^+ 379.8963.

10b. Spectral data of 4-chloro-4-((9*R*)8-phenyl-6b,8,9,9a-tetrahydroacenaphtho[1,2-*d*]isoxazol-9-yl)butan-1-ol:

Bright yellow crystals, 23 %; IR ($CHCl_3$): 3456 - 3375 (br), 2967 (m), 2726 (m), 1720 (s), 1474 (m), 1280 (s), 786 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.36 – 7.27 (m, 5H, C_6H_5), 7.05 – 6.90 (m, 6H, napthylene ring protons), 5.30 (d, 1H, J = 7.16 Hz, C_5H), 4.82 – 4.73 (br, 1H exchanged in D_2O), 4.60 (dd, 1H, J = 2.34, 2.53 Hz, C_3H), 4.28 (dd, 1H, J = 4.12, 3.10 Hz, C_4H), 3.46 (q, 1H, J = 6.08, 7.42 Hz, CHCl), 1.76 – 1.60 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 137.34, 136.10, 135.00, 134.63, 133.24, 132.00, 131.00, 130.16, 128.60, 127.45, 126.00, 124.70 (aromatic carbons), 87.00 (C_5), 76.30 (C_3), 68.50 (CH_2OH), 53.30 (C_4), 50.74 (CHCl), 30.00, 29.00, 28.35 (3 CH_2 carbons); MS (*m/z*):

381 (M^++2), 379 (M^+), 320, 302, 272, 227, 152, 107, 77, 59; HRMS – EI: Calcd. for $C_{23}H_{22}O_2NCl$ (M) 379.8980, Found M^+, 379.8967.

11. Synthesis of ethyl-3-(1-chloro-4 hydroxy butyl)-2-phenyl isoxazolidine-5-carboxylate (Ethyl acrylate cycloadduct)



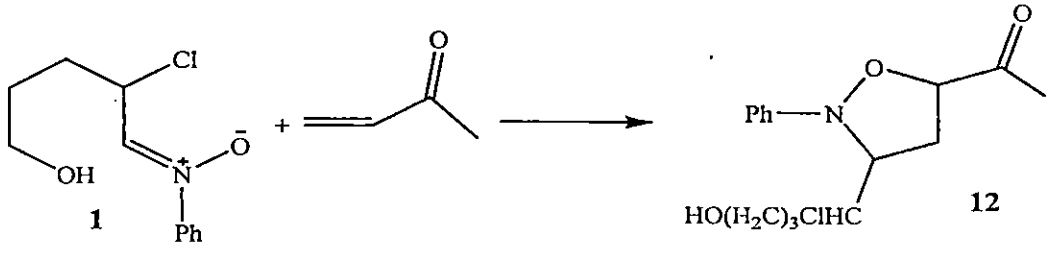
Scheme 13

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added ethyl acrylate (1 mmol) at RT under nitrogen atmosphere and the reaction mixture was stirred for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.48).The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified and separated by column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as white gummy liquid.

Spectral data:

White gummy liquid, 93%; IR ($CHCl_3$): 3580 – 3480 (br), 3095 (m), 2250 (m), 1898 (m), 1711 (s), 1636 (s), 1503 (m), 1392 (s), 1144 (s), 1029 (s), 908 (m), 831 (s), 756 (s) cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 7.28 (m, 5H, C_6H_5), 4.88 (br, 1H, -OH, exchanged in D_2O), 4.11 (t, 1H, J = 8.2 Hz, C_5H), 3.86 (q, 1H, J = 7.22 Hz, C_3H), 3.51 (dd, 2H, J = 9.24, 8.18 Hz, C_4 2H), 2.29 (dt~m, 1H, CHCl), 1.64 (t, 3H, J = 7.22 Hz, CH_3CH_2CO), 1.23 (q, 2H, J = 7.52 Hz, -OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 167.40 (carbonyl carbon), 136.40, 134.50, 133.20, 132.60 (aromatic carbons), 88.00 (C_5), 76.00 (C_3), 63.00 (CH_2OH), 60.00 (CH_2 carbon of -OCH_2CH_3), 58.00 (C_4), 55.00 (CHCl), 32.00, 24.50 (2 CH_2 carbons), 16.00 (CH_3 carbon of -OCH_2CH_3); MS (*m/z*): 329 (M^+ +2), 327 (M^+), 296, 282, 254, 221, 219, 207, 177, 147, 142, 108, 107, 77, 73, 31; HRMS - EI: Calcd. for $C_{16}H_{22}O_4NCl$ (M) 327.8190, Found M^+, 327.8179.

12. Synthesis of 1-(3-(1-chloro-4-hydroxy butyl)-2-phenyl isoxazolidin-5yl) ethanone (Methyl vinyl ketone cycloadduct)



Scheme 14

To a stirred solution of nitrone **1** (1 mmol) in 15 mL water was added methyl vinyl ketone (1 mmol) at RT under nitrogen atmosphere and the reaction mixture was stirred for 8 hr. The progress of the reaction was monitored by TLC (R_f = 0.44).The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified and separated by column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as pale yellow oil.

Spectral data:

Pale yellow oil, 91%; IR ($CHCl_3$): 3570 - 3440 (br), 3042 (s), 2924 (m), 2166 (m), 1930 (s), 1628 (s), 1422 (s), 1199 (m), 1147 (s), 1080 (s), 826 (s), 773 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.16 - 7.04 (m, 5H, C_6H_5), 5.32 (t, 1H, J = 7.82 Hz, C_5H), 5.10 – 5.00 (br, 1H, exchanged in D_2O), 4.54 – 4.43 (dt, 1H, J = 8.30 Hz, C_3H), 4.28 (dd, 2H, J = 9.48, 7.10 Hz, C_4 2H), 3.78 – 3.62 (m, 1H, CHCl), 2.12 (s, 3H, $COCH_3$), 1.86 - 1.54 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 195.22 (carbonyl carbon), 132.00, 131.55, 130.00, 128.40 (aromatic carbons), 88.00 (C_5), 78.00 (C_3), 66.00 (CH_2OH), 58.00 (C_4), 53.50 (CHCl), 24.60 ($COCH_3$), 19.00, 17.00 (2 CH_2 carbons); MS (*m/z*): 297 (M^+), 282, 267, 265, 254, 221, 211, 191, 177, 147, 107, 86, 77, 43, 31; HRMS-EI: Calcd. for $C_{15}H_{20}O_3NCl$ (M) 297.1437, Found M^+, 297.1426.

Synthesis of α-amino nitrones[7,8]

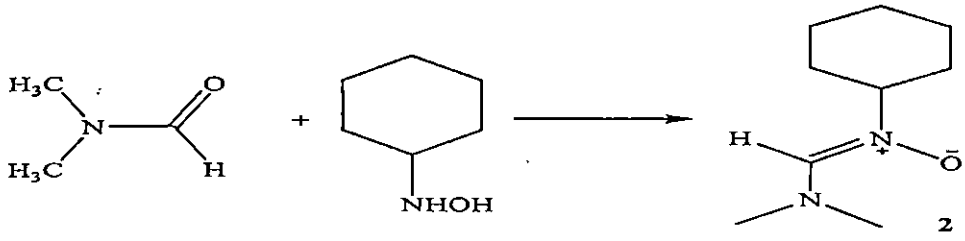
Reaction type II

General procedure for the preparation of nitrone 2 at elevated temperature

Initially, the preparation of *N*-cyclohexyl-α-amino nitrone was carried out at elevated temperature following the general methodology of synthesis of α-amino nitrones as

suggested by Eschenmoser et al[9]. To a well stirred solution of *N*-cyclohexyl hydroxylamine[10] (8.7 mmol) and *N,N*-dimethyl formamide (9 mL, 1 equivalent) was added about 2 gms of anhydrous $MgSO_4$ and the reaction mixture was refluxed for 8-10 hour but no definite conclusion for the formation of nitrone **2** was observed. The isolated product under constant observation did not show specific bands for α-amino nitrone in the ^1H NMR, ^{13}C NMR and IR spectrum. Therefore it was concluded that the gummy liquid obtained was a decomposed product. And hence this methodology was not followed.

General procedure for the preparation of *N*-cyclohexyl-α-aminonitrone (2) at room temperature



Scheme 15

N-cyclohexyl hydroxylamine (8.7 mmol) was added to dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent) in presence of anhydrous $MgSO_4$. The reaction mixture was kept at RT with constant stirring with a magnetic stirrer under N_2 atmosphere for 8 hour. The formation of nitrone **2** was monitored by TLC (R_f = 0.34, silica gel; ethyl acetate : benzene = 1: 10). The nitrone **2** was isolated by extraction with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over sodium sulphate and concentrated on a rotary evaporator and finally obtained as white crystalline solid (m.p 48^0c, uncorrected). The nitrone decomposes when kept at room temperature for a longer period and hence it was either used right after its synthesis (for aqueous phase cycloaddition reactions) or as *in-situ* for general cycloaddition reactions.

Spectral data of (*Z*)-*N*-((dimethylamino)methylene)cyclohexanamine oxide

White crystalline solid, 88%; IR ($CHCl_3$): 3440 (m), 1600 (s), 1360 (m), 1310 (m), 1120 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.81 (br, 6H, NMe_2), 3.30 (s,1H,$HC=N^+-O^-$), 2.50 - 2.16 (m, 1H, N-CH proton), 1.66 – 1.59 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 144.62 ($CH=N^+$), 43.00, 40.72 (*N* - methyl carbons), 32.00, 30.64, 27.32, 26.08, 25.15, 24.74

(cyclohexyl carbons); HRMS – EI: Calcd. for $C_9H_{18}N_2O$, (M) 170.2560, Found, M^+, 170.2555.

General Procedure for 1,3-dipolar cycloaddition reaction at elevated temperature

Initially, the freshly prepared nitrone **2** (prepared at RT) was used for cycloaddition reactions with dipolarophiles at elevated temperature following the conventional general methodology of cycloaddition reactions. Nitrone **2** (2.20 mmol) and *N*-phenyl maleimide (1 equivalent) was added in THF (20 mL) under N_2 atmosphere and the reaction mixture was refluxed for 12 hour. The progress of the reaction was monitored by TLC. The solvent was concentrated on a rotary evaporator and the products were purified by silica gel column chromatography using ethyl acetate – hexane combinations. But this methodology was not followed due to poor yield (nearly 40%) of cycloadducts.

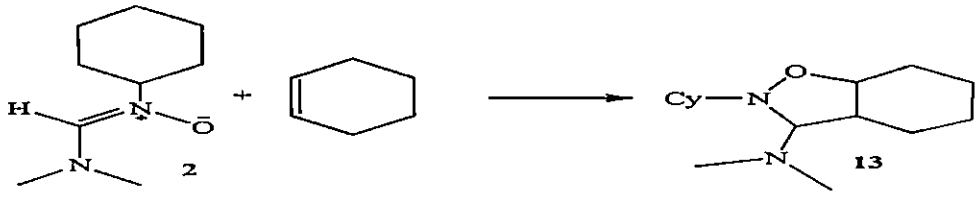
General Procedure for 1,3-dipolar cycloaddition reaction with nitrone 2 (*in-situ* synthesis)

As nitrone **2** decomposes slowly at room temperature, therefore in majority of the reactions *in-situ* reactions were performed for the synthesis of isoxazolidines directly. Dipolarophiles (1 equivalent) were added at the time of formation of nitrone **2** and the reaction mixture was stirred at RT with a magnetic stirrer under N_2 atmosphere for further 8 - 10 hour. The progress of the reaction was monitored by TLC. The reaction mixture was concentrated on a rotary evaporator and the crude cycloadducts were purified and separated by silica gel column chromatography using ethyl acetate – hexane combinations. This procedure was followed for all the substrates (alkenes and alkynes) listed in **Table 5**.

Table 5.

Alkenes	*Alkynes*
➢ Cyclohexene	➢ Phenyl methyl propiolate
➢ *N*-Phenyl maleimide	➢ Dimethyl acetylene dicarboxylate
➢ *N*-Methyl maleimide	➢ Ethyl propiolate
➢ *N*-Cyclohexyl maleimide	➢ Propiolic acid
➢ *P*-OMe-*N*-phenyl maleimide	
➢ Ethyl acrylate	
➢ Methyl vinyl ketone	
➢ Styrene	
➢ Acenaphthylene	
➢ *p*-benzoquinone	

13. Synthesis of 2-cyclohexyl-*N,N*-dimethyloctahydrobenzo[*d*]isoxazol-3-amine (cyclohexene cycloadduct)



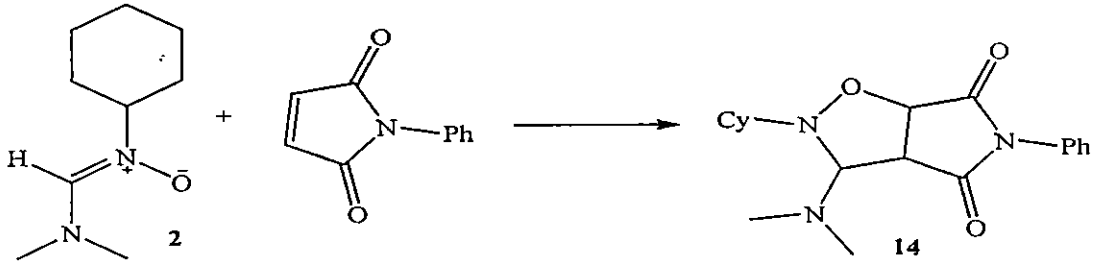
Scheme 16

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), cyclohexene (1 equivalent) was added at the time of formation of nitrone **2** (monitored by TLC) at RT under nitrogen atmosphere and the reaction mixture was stirred for further 10 hr. The progress of the reaction was monitored by TLC (R_f = 0.54). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as reddish gummy liquid.

Spectral Data:

Reddish gummy liquid, 76 %; IR ($CHCl_3$): 3190 - 3065 (br), 2924 (s), 2850 (m), 1555 (s), 1443 (m), 1250 (s), 970 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.37 (d, 1H, J = 8.20 Hz, C_5H), 4.50 (d, 1H, J = 9.20 Hz, C_3H), 4.12 (dd, 1H, J = 9.40, 7.10 Hz, C_4H), 2.64 – 2.52 (br, 6H, $N - CH_3$ protons), 1.80 - 1.14 (m, 19H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 88.55 (C_5), 78.75 (C_3), 54.42 (C_4), 39.56, 38.00 ($N - CH_3$ carbons), 33.70, 31.82, 29.43, 27.00, 25.40, 24.14, 22.80, 20.60, 18.90, 17.42 (cyclohexyl carbons); MS (*m/z*): 252 (M^+), 208, 170, 169, 154, 153, 141, 125, 113, 111, 98, 84, 83, 82; HRMS-EI: Calcd. for $C_{15}H_{28}N_2O$ (M) 252.4020, Found M^+, 252.4006.

14. Synthesis of 2-cyclohexyl-3-(dimethylamino)-5-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-phenyl maleimide cycloadduct):



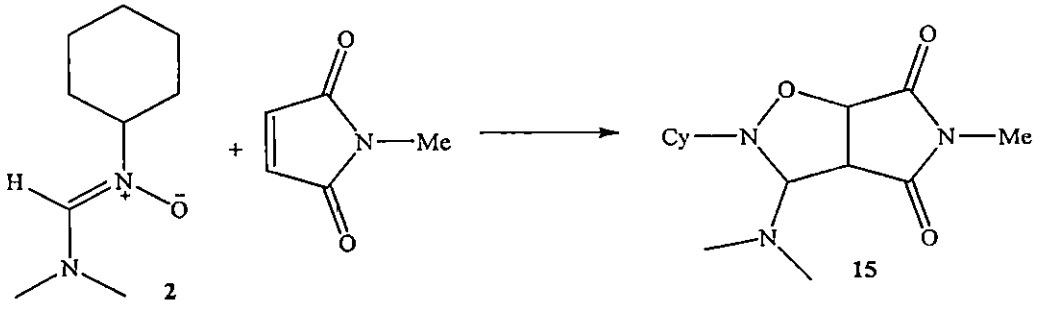
Scheme 17

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), *N*-phenyl maleimide (1 equivalent) was added *in-situ* at the time of formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 8 hour. The progress of the reaction was monitored by TLC (R_f = 0.52). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as white solid.

Spectral data:

White solid, 93 %; IR ($CHCl_3$): 3345-3130 (br), 3013 (s), 2933 (m), 2362 (m), 1662 (s), 1508 (m), 1387 (s), 1219 (m), 1098 (s), 927 (m), 829 (w), 759 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 - 7.44 (m, 5H, C_6H_5), 4.82 (d, 1H, *J* = 6.06 Hz, C_5H), 4.46 (d, 1H, *J* = 9.22 Hz, C_3H), 3.90 (dd, 1H, *J* = 6.06, 9.08 Hz, C_4H), 2.68 – 2.57 (br, 6H, N – CH_3 protons), 2.20 - 1.70 (m, 11H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 178.90, 169.50 (carbonyl carbons), 136.00, 134.70, 132.65, 130.45 (aromatic carbons), 87.50 (C_5), 76.00 (C_3), 59.40 (C_4), 37.65, 36.80 (*N* - methyl carbons), 30.00, 27.80, 26.00, 24.80, 23.20, 21.65 (cyclohexyl carbons); MS (*m/z*): 343 (M^+), 328, 313, 299, 266, 260, 230, 189, 183, 154, 113, 83, 77, 44, 30; HRMS - EI: Calcd. for $C_{19}H_{25}O_3N_3$ (M), 343.2370, Found M^+, 343.2355; Found C, 66.40; H, 7.22; N, 12.20 %; $C_{19}H_{25}O_3N_3$ requires C, 66.47; H, 7.28; N, 12.24 %.

15. Synthesis of 2-cyclohexyl-3-(dimethylamino)-5-methyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-methyl maleimide cycloadduct):



Scheme 18

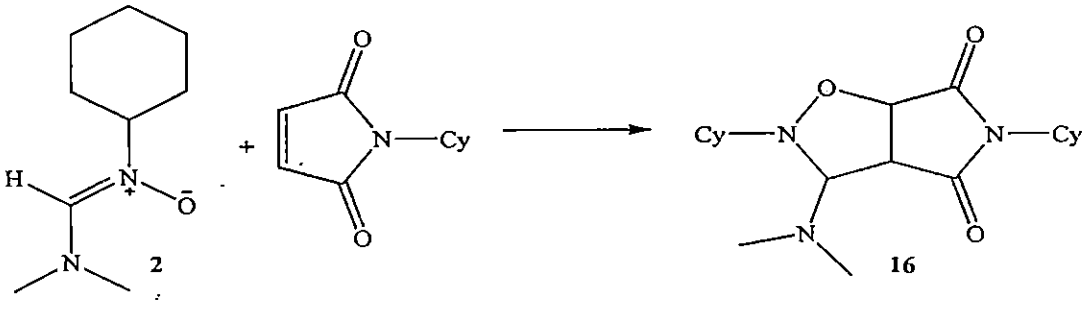
To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), *N*-methyl maleimide (1 equivalent) was

added *in-situ* at the time of formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 10 hour. The progress of the reaction was monitored by TLC (R_f = 0.48). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as white solid.

Spectral data:

White solid, 82 %; IR ($CHCl_3$): 3445-3230 (br), 2932 (s), 2361 (s), 1660 (s), 1498 (m), 1390 (s), 1255 (s), 1102 (m), 663 (s) (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.22 (d, 1H, J = 6.0 Hz, C_5H), 4.05 (d, 1H, J = 9.0 Hz, C_3H), 3.76 (dd, 1H, J = 6.14, 9.00 Hz, C_4H), 3.40 (s, 3H, CH_3), 2.85 - 2.76 (br, 6H, *N*-CH_3 protons), 1.95 - 1.62 (m, 11H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 169.64, 167.20 (carbonyl carbons), 88.00 (C_5), 73.00 (C_3), 58.00 (C_4), 39.00, 38.00 (*N*-CH_3 carbons), 36.50 (methyl carbon), 28.80, 26.95, 25.00, 24.30, 22.84, 20.55 (cyclohexyl carbons); MS (*m/z*): 281 (M^+), 266, 251, 237, 198, 168, 142, 113, 83, 44, 30; HRMS – EI: Calcd. for $C_{14}H_{23}O_3N_3$ (M) 281.2160, Found M^+, 281.2148; Found C, 59.97; H, 7.69; N, 15.01 %; $C_{14}H_{23}O_3N_3$ requires C, 60.04; H, 7.85; N, 15.08 %.

16. Synthesis of 2,5-dicyclohexyl-3-(dimethylamino)dihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-cyclohexyl maleimide cycloadduct):



Scheme 19

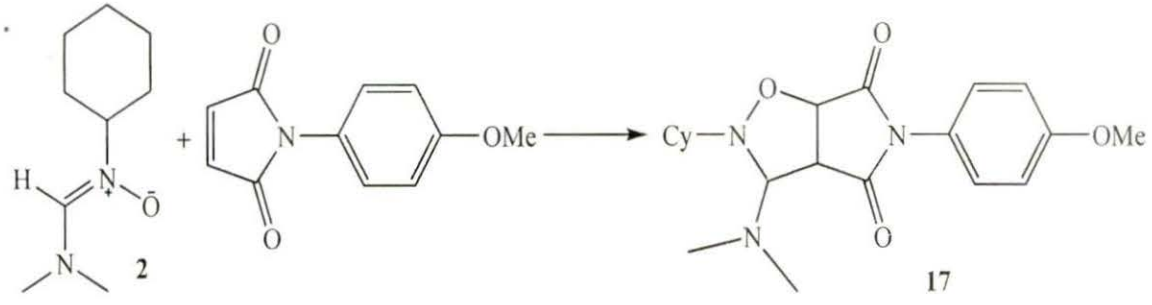
To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N*,*N*-dimethyl formamide (9 mL, 1 equivalent), *N*-cyclohexyl maleimide (1 equivalent) was added *in-situ* at the time of formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 11 hour. The progress of the reaction was monitored by TLC (R_f = 0.42). The product was

extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as pale yellow solid.

Spectral data:

Pale yellow solid, 90 %; IR ($CHCl_3$): 3150 (br), 2920 (s), 1770 (s), 1680 (s), 1440 (m), 1260 (m), 1130 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.31 (d, 1H, J = 6.10 Hz, C_5H), 2.99 (br, 6H, $N - CH_3$ protons), 2.85 (d, 1H, J = 9.30 Hz, C_3H), 2.50 – 2.46 (m, 10 H, maleimide substituted cyclohexyl protons), 2.19 (dd, 1H, J = 8.00, 9.32 Hz, C_4H), 1.66 - 1.57 (m, 10H, 2-substituted cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 173.80, 171.14 (carbonyl carbons), 86.80 (C_5), 78.65 (C_3), 55.30 (C_4), 39.00, 38.00 (2 methyl carbons), 33.00, 31.00, 28.90, 27.00, 25.86, 24.30, 23.00, 22.75, 21.00, 20.20, 18.70, 16.30 (12 signals, cyclohexyl carbons); MS (*m/z*): 349 (M^+), 319, 305, 266, 251, 226, 195, 183, 154, 113, 83, 44, 30; HRMS – EI: Calcd. for $C_{19}H_{31}O_3N_3$ (M) 349.4750, Found M^+ 349.4745; Found C, 65.26; H, 8.74; N, 12.06 %; $C_{19}H_{31}O_3N_3$ requires C, 65.32; H, 8.88; N, 12.03 %.

17. Synthesis of 2-cyclohexyl-3-(dimethylamino)-5-(4-methoxyphenyl)dihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*p*-OMe-*N*-phenyl maleimide cycloadduct):



Scheme 20

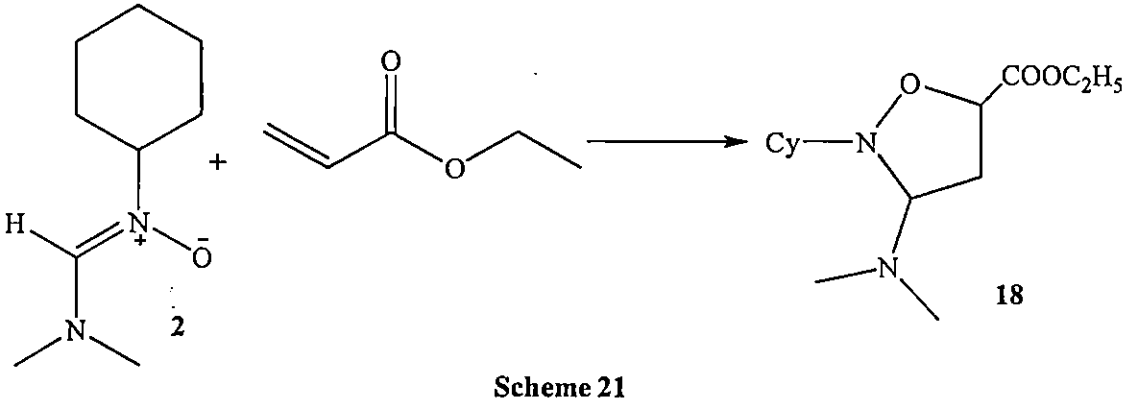
To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), *p*-methoxy-*N*-phenyl maleimide (1 equivalent) was added *in-situ* at the time of formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 9 hour. The progress of the reaction was monitored by TLC (R_f = 0.46). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water

(2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as white crystalline solid.

Spectral data:

White crystalline solid; 89 %; IR ($CHCl_3$): 3223 (br), 2932 (s), 2361 (s), 1660 (s), 1498 (m), 1390 (m), 1255 (m), 1102 (m), 773 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.83 - 7.77 (m, 4H, C_6H_5 proton), 5.10 (d, 1H, J = 6.24 Hz, C_5H), 4.43 (d, 1H, J = 8.40 Hz, C_3H), 3.72 (dd, 1H, J = 9.23, 7.10 Hz, C_4H), 3.40 (s, 3H, -OCH_3 protons), 2.58 - 2.50 (br, NMe_2), 1.94 – 1.62 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 174.54, 172.90 (carbonyl carbons), 88.60 (C_5), 75.74 (C_3), 52.30 (C_4), 41.50, 40.00 (*N*-Me carbons), 33.80 (methoxy carbon), 33.44, 30.76, 28.55, 26.80, 24,32, 22.40 (cyclohexyl carbons); MS (*m/z*): 373(M^+), 342, 290, 260, 246, 203, 170, 166, 113, 107, 83; HRMS – EI: Calcd. for $C_{20}H_{27}O_4N_3$ (M) 373.2530, Found M^+, 373.2514; Found C, 65.26; H, 8.74; N, 12.06 %; $C_{19}H_{31}O_3N_3$ requires C, 65.32; H, 8.88; N, 12.03 %.

18. Synthesis of ethyl 2-cyclohexyl-3-(dimethylamino)isoxazolidine-5-carboxylate (Ethyl acrylate cycloadduct)



Scheme 21

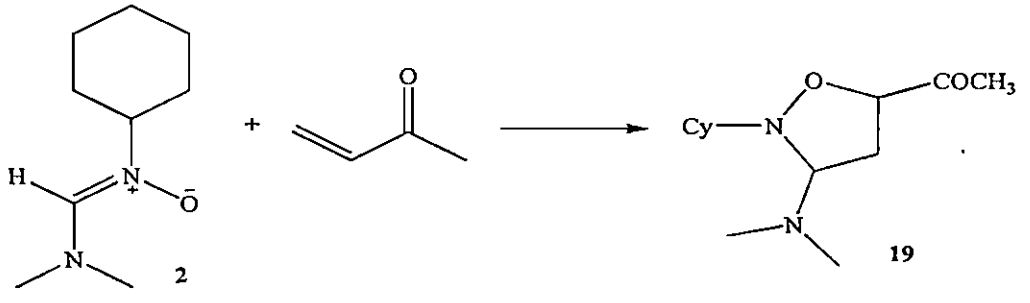
To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), ethyl acrylate (1 equivalent) was added *in-situ* at the time of formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 12 hour. The progress of the reaction was monitored by TLC (R_f = 0.60). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was

purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as white gummy liquid.

Spectral data:

White gummy liquid, 87 %; IR ($CHCl_3$): 3340-3230 (br), 2936 (s), 2121 (m), 1661 (s), 1495 (s), 1440 (s), 1390 (m), 1254 (m), 1105 (s), 1063 (m), 665 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.24 (t, 1H, J = 6.80 Hz, C_5H), 4.82 (t, 1H, J = 9.25 Hz, C_3H), 4.54 (q, 2H, J = 4.50, 6.60 Hz, -O$\underline{CH_2}CH_3$), 3.80 (dd, 2H, J = 9.24, 8.60 Hz, C_4 2H), 2.54 – 2.46 (br, 6H, N – CH_3 proton), 1.46 (t, 3H, J = 6.00 Hz, $OCH_2\underline{CH_3}$), 1.30 – 0.94 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 204.30 (ester carbonyl carbon), 88.70 (C_5), 76.43 (C_3), 58.22 (C_4), 42.56 ($COO\underline{CH_2}CH_3$), 38.60, 36.86 (NMe_2), 33.60, 32.00, 30.20, 28.40, 25.32, 23.00 (cyclohexyl carbons),18 ($COOCH_2\underline{CH_3}$); MS (*m/z*): 270 (M^+), 226, 225, 197, 157, 154, 116, 113, 83, 73, 44; HRMS-EI: Calcd. for $C_{14}H_{26}O_3N_2$ (M) 270.1935, Found M^+, 270.1926.

19. Synthesis of 1-(2-cyclohexyl-3-(dimethylamino)isoxazolidin-5-yl)ethanone (Methyl vinyl ketone cycloadduct):



Scheme 22

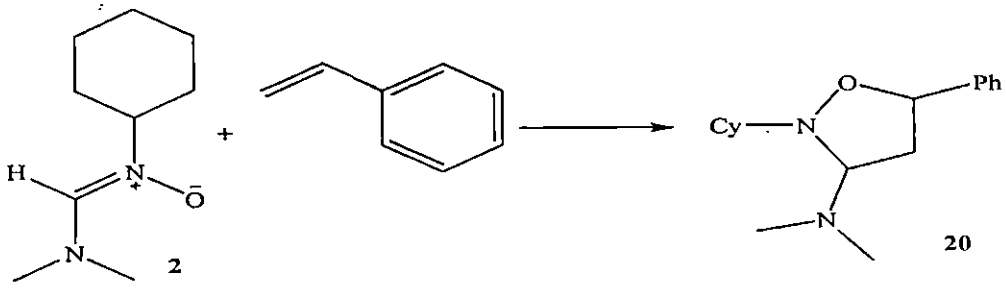
To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1equivalent), methyl vinyl ketone (1 equivalent) was added *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 14 hour. The progress of the reaction was monitored by TLC (R_f = 0.52). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel column chromatography using ethyl acetate-hexane and was obtained as yellow oil.

Spectral data:

Yellow oil, 90 %; IR ($CHCl_3$): 3205 (br), 2925 (s), 2780 (m), 1740(s), 1660 (s), 1480 (m), 1280 (s), 970 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.90 (t, 1H, J = 7.82 Hz, C_5H), 4.54 (t,

1H, J = 9.24 Hz, C_3H), 4.14 (dd, 2H, J = 9.48, 7.10 Hz, C_4 2H), 3.64 (s, 3H, $COCH_3$), 2.64 - 1.92 (br, 6H, NMe_2), 1.36 - 0.94 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 190.50 (carbonyl carbon), 86.00 (C_5), 76.00 (C_3), 55.80 (C_4), 43.00, 40.20 (NMe_2), 30.52 ($CO\underline{CH_3}$), 28.40, 27.00, 25.70, 23.65, 22.00, 20.40 (6 CH_2carbons); MS (*m/z*): 240 (M^+), 197, 196, 186, 154, 127, 113, 83, 44, 43; HRMS-EI: Calcd. for $C_{13}H_{24}O_2N_2$ (M) 240.1830, Found M^+, 240.1814.

20. Synthesis of 2-cyclohexyl-*N*,*N*-dimethyl-5-phenylisoxazolidin-3-amine (styrene cycloadduct):



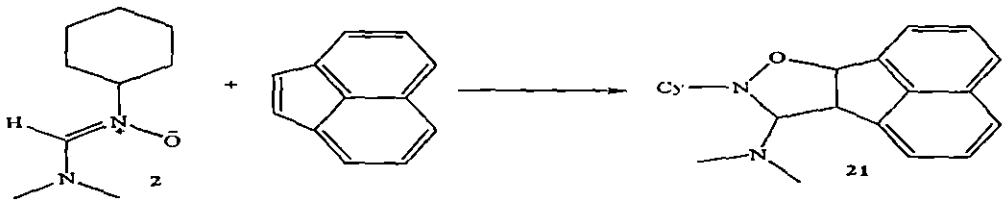
Scheme 23

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N*,*N*-dimethyl formamide (9 mL, 1 equivalent), styrene (1 equivalent) was added *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 14 hour. The progress of the reaction was monitored by TLC (R_f = 0.52). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel column chromatography ethyl acetate - hexane and was obtained as colourless liquid.

Spectral data:

Colourless liquid, 88%; IR ($CHCl_3$): 3210 (m), 1735 (s), 1660 (s), 1420 (m), 1300 (m), 1225 (s), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.60 - 7.44 (m, 5H, C_6H_5 protons), 5.10 (t, 1H, J = 6.16 Hz, C_5H), 4.35 (t, 1H, J = 6.24 Hz, C_3H), 3.55 (dd, 2H, J = 7.12, 8.10 Hz, C_4 2H), 2.45 - 2.30 (br, 6 *N*-methyl protons), 1.76 – 1.24 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 134.00, 133.00, 131.50, 130.40 (aromatic carbons), 85.00 (C_5), 74.00 (C_3), 56.00 (C_4), 36.00, 35.00 (2 x CH_3 carbons), 26.00, 24.70, 23.00, 22.00, 20.60, 18.00 (cyclohexyl carbons); MS (*m/z*): 274 (M^+), 230, 197, 191, 153,111, 83, 77, 51,44; HRMS – EI: Calcd. for $C_{17}H_{26}N_2O$ (M) 274.4054, Found M^+, 274.4039.

21. Synthesis of 8-cyclohexyl-*N*,*N*-dimethyl-6b,8,9,9a-tetrahydroacenaphtho[1,2-*d*]isoxazol-9-amine (acenaphthylene cycloadduct):



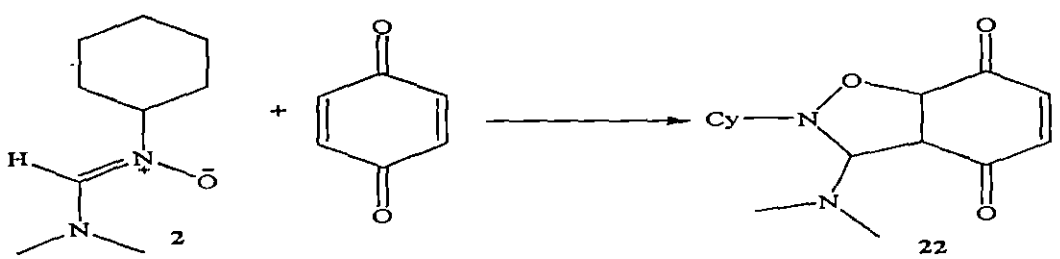
Scheme 24

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), acenaphthylene (1 equivalent each) was added *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 48 hour. The progress of the reaction was monitored by TLC (R_f = 0.52). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel column chromatography using ethyl acetate-hexane and was obtained as bright yellow crystalline solid.

Spectral data:

Bright yellow crystalline solid, 95%; IR ($CHCl_3$): 3425 (m), 1710 (s), 1680 (s), 1390 (m), 1260 (s), 760 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.46 - 7.26 (m, 6H, naphthalene ring protons), 4.37 (d, 1H, J = 6.08 Hz, C_5H), 3.18 (d, 1H, J = 6 Hz, C_3H), 2.89 (dd, 1H, J = 6.08, 6.28 Hz, C_4H), 2.45 (br, 6 *N*-Me protons), 1.90 – 1.11 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 138.00, 136.40, 135.00, 133.75, 132.80, 130.70, 128.55, 127.00 (aromatic carbons), 84.90 (C_5), 73.88 (C_3), 58.50 (C_4), 46.00, 44.22 (2 x CH_3 carbons), 26.32, 25.00, 24.10, 22.65, 20.43, 19.54 (cyclohexyl carbons); MS (*m/z*): 322 (M^+), 239, 209, 195, 170, 152, 113, 83, 44; HRMS – EI: Calcd. for $C_{21}H_{26}N_2O$ (M) 322.2420, Found M^+ 322.2408.

22. Synthesis of 2-cyclohexyl-3-(dimethylamino)-3,3a-dihydrobenzo[*d*]isoxazole-4,7(2*H*,7a*H*)-dione (*p*-benzoquinone cycloadduct):



Scheme 25

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), *p*-benzoquinone (1 equivalent each) was added *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 45 hour. The progress of the reaction was monitored by TLC (R_f = 0.49). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel-column chromatography using ethyl acetate-hexane and was obtained as dark brown crystals.

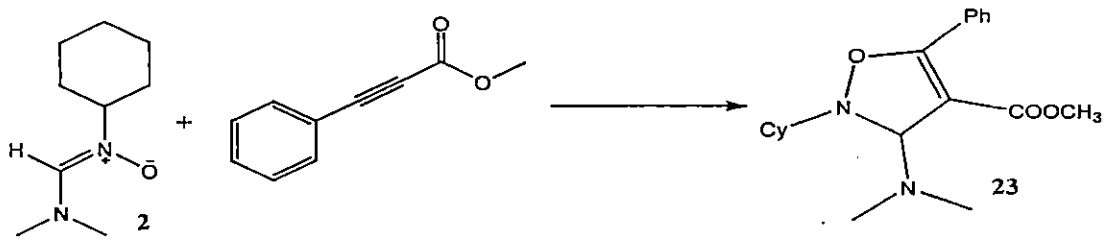
Spectral data:

Dark brown crystals, 94%; IR ($CHCl_3$): 3230 (br), 2950 (s), 2845 (m), 2766 (m), 1750 (s), 1610 (s), 1445 (m), 1230 (s), 810 (m), 790 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.46 – 7.26 (m, 2H, aromatic protons), 5.24 (d, 1H, J = 6.02 Hz, C_5 H), 3.68 (d, 1H, J = 7.42 Hz, C_3H), 3.34 (dd, 1H, J = 6.80, 6.88 Hzs, C_4H), 2.45 (br, 6 H, NMe_2), 1.80 – 1.25 (m, 11H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 192.50, 190.00 (carbonyl carbons), 87.00 (C_5), 74.00 (C_3), 57.40 (C_4), 41.00, 39.50 (NMe_2), 34.40, 32.58 ($CO\underline{CH_2CH_2}CO$), 28.40, 27.00, 25.70, 23.65, 22.00, 20.40 (6 CH_2 carbons); MS (*m/z*): 278 (M^+), 250, 222, 206, 195, 167, 139, 124, 83; HRMS – EI: Calcd. for $C_{15}H_{22}N_2O_3$ (M) 278.2020, Found M^+ 278.2008.

General Procedure for 1,3-dipolar cycloaddition reaction of nitrone 2 with alkynes[7a]

N-cyclohexyl-α-amino nitrone is highly unstable and decomposes at RT and hence the nitrone was used immediately after its isolation for the cycloaddition reaction with dipolarophiles (alkynes) in a 1:1 ratio. In a 100 mL conical flask nitrone **1** (2.20 mmol), ethyl propiolate (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 12 hour. The progress of the reaction was monitored by TLC (R_f = 0.72). The crude product was concentrated under a rotary evaporator and finally the product was purified by silica gel column chromatography using ethyl acetate-hexane combinations and was obtained as colourless gummy liquid. This procedure was followed for all the substrates listed in Table **5**.

23. Synthesis of methyl 3-(dimethylamino)-2,5-diphenyl-2,3-dihydroisoxazole-4-carboxylate (phenyl methyl propiolate cycloadduct):



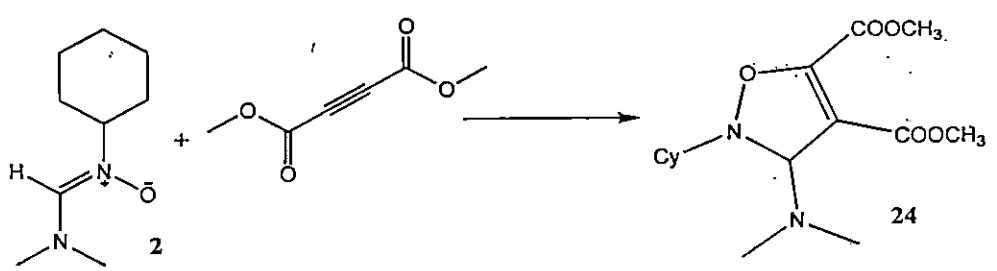
Scheme 26

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N*,*N*-dimethyl formamide (9 mL, 1 equivalent), phenyl methyl propiolate was added (1 equivalent) *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 14 hour. The progress of the reaction was monitored by TLC (R_f = 0.62). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel column chromatography using ethyl acetate-hexane combinations and was obtained as colourless gummy liquid.

Spectral data:

Colourless gummy liquid, 96 %; IR ($CHCl_3$): 3379-3125 (br), 2936 (s), 1900 (m), 1780 (s), 1445 (m), 1295 (m), 1106 (s), 900 (s), 758 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.64 – 7.53 (m, 5H, C_6H_5 protons), 4.05 (s, 1H, C_3H), 3.63 (s, 3H, – $COOCH_3$), 2.76 (br, 6H, NMe_2), 1.95 - 1.66 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 172.50 (carbonyl carbon), 137.00, 135.40, 134.00, 132.60 (aromatic carbons), 88.42 (C_5), 73.76 (C_3), 57.40 (C_4), 45.00 (-$COOCH_3$), 33.13, 29.50 (*N* - CH_3 carbons), 26.00, 24.80, 23.40, 21.80, 20.00, 18.70 (CH_2 carbons); MS (*m/z*): 330 (M^+), 286, 247, 246, 225, 194, 148, 105 (B.P), 83, 77, 31; HRMS – EI: Calcd. for $C_{19}H_{26}O_3N_2$ (M) 330.1935, Found M^+, 330.1919.

24. Synthesis of dimethyl 3-(dimethylamino)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylate (dimethyl acetylene dicarboxylate cycloadduct):



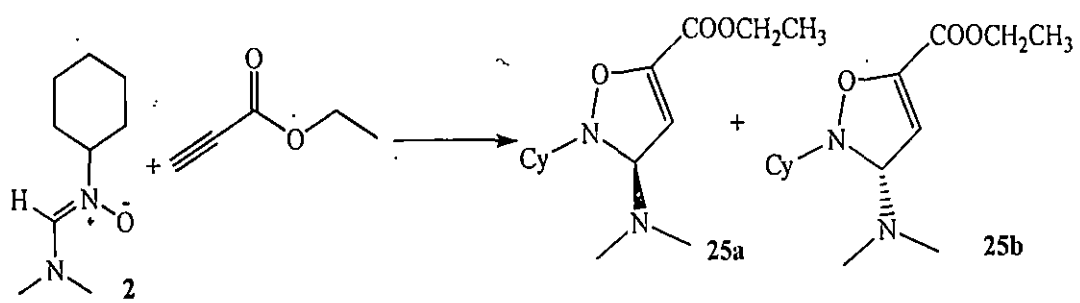
Scheme 27

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), dimethyl acetylene dicarboxylate was added (1 equivalent) *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 18 hour. The progress of the reaction was monitored by TLC (R_f = 0.58). The crude product was concentrated under a rotary evaporator and finally the cycloadduct was purified by silica gel column chromatography using ethyl acetate-hexane combinations and was obtained as red liquid.

Spectral data:

Red liquid, 92 %; IR ($CHCl_3$): 3145 (m), 2820 (m), 1745 (s),1700 (m), 1670 (m), 1420 (s), 1260 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.75 (s, 1H, C_3H), 3.66 (s, 3H,-$COOCH_3$), 3.60 (s, 3H, -$COOCH_3$), 2.68 (br, 6H, NMe_2), 2.05 - 1.64 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 186.70, 184.67 (carbonyl carbons), 87.50 (C_5), 76.42 (C_3), 59.48 (C_4), 44.42, 43.54 ($COO\underline{C}H_3$), 31.65, 29.48 (N - CH_3 carbons), 25.80, 24.30, 23.90, 22.70, 20.60, 18.50 (CH_2 carbons); MS (*m/z*): 312 (M^+), 281, 268, 229, 228, 225 (B.P), 194, 185, 87, 83, 59, 44, 31; HRMS – EI: Calcd. for $C_{15}H_{24}O_5N_2$ (M) 312.1677, Found M^+, 312.1668.

25. Synthesis of ethyl propiolate cycloadducts (diastereomers)



Scheme 28

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), ethyl propiolate was added (1 equivalent) *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 6 hour. The progress of the reaction was monitored by TLC (R_f = 0.44, 0.50). The crude products were concentrated under a rotary evaporator and finally the cycloadducts were purified and

separated by silica gel column chromatography using ethyl acetate-hexane and were obtained as white viscous liquids.

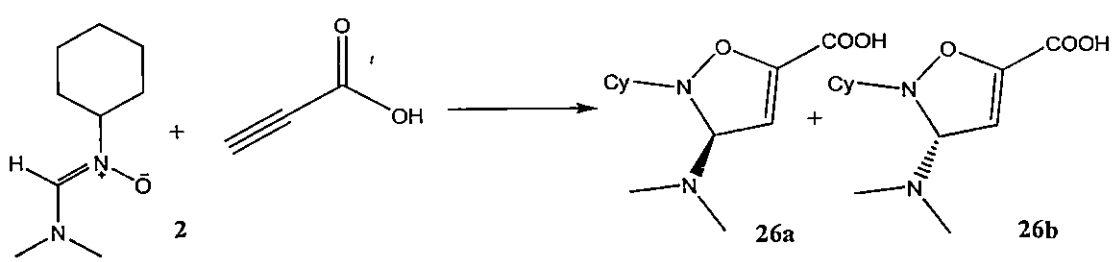
25a. Spectral data of (*S*)-methyl 3-(dimethylamino)-2-phenyl-2,3-dihydroisoxazole-5-carboxylate:

Red gummy liquids, 70 %; IR ($CHCl_3$): 3165 (m), 2945 (s), 1770 (m), 1680 (s), 1656 (s), 1430 (m), 1260 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.64 (d, 1H, J = 9.30 Hz, C_3H), 4.26 (dd, 2H, J = 6.24, 6.36 Hz, $COOCH_2CH_3$), 3.35 (d, 1H, J = 9.20 Hz, C_4H), 2.76 (br, 6H, NMe_2), 2.04 – 1.67 (m, 11H), 1.40 (t, 3H, J = 4.36 Hz, $-COOCH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 173.40 (carbonyl carbon), 86.00 (C_5), 78.00 (C_3), 55.00 (C_4), 32.00 ($COOCH_2CH_3$), 30.00 ($COOCH_2CH_3$), 28.80, 27.30 (*N* - CH_3 carbons), 25.00, 23.70, 22.20, 20.80, 19.00, 18.40 (CH_2 carbons); MS (*m/z*): 268 (M^+), 224, 195 (B.P), 185, 184, 141, 83, 73; HRMS – EI: Calcd. for $C_{14}H_{24}O_3N_2$ (M) 268.1779, Found M^+, 268.1763.

25b. Spectral data of (*R*)-methyl 3-(dimethylamino)-2-phenyl-2,3-dihydroisoxazole-5-carboxylate:

Red gummy liquids, 22%; IR ($CHCl_3$): 3160 (m), 2955 (s), 1770 (m), 1684 (s), 1658 (s), 1435 (m), 1255 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.58 (d, 1H, J = 2.53 Hz, C_3H), 4.32 (dd, 2H, J = 7.14, 6.16 Hz, $COOCH_2CH_3$), 3.26 (d, 1H, J = 2. 58 Hz, C_4H), 2.66 (br, 6H, NMe_2), 2.24 – 2.12 (m, 1H, *N*-CH proton), 1.94 – 1.53 (m, 10H), 1.24 (t, 3H, J = 4.08 Hz, $COOCH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 172.70 (carbonyl carbon), 88.10 (C_5), 76.60 (C_3), 57.20 (C_4), 33.40 ($COOCH_2CH_3$), 31.70 ($COOCH_2CH_3$), 29.00, 27.80 (*N* - CH_3 carbons), 26.10, 24.00, 23.00, 21.40, 20.20, 18.30 (6 CH_2 carbons); MS (*m/z*): 268 (M^+), 224, 223, 195 (B.P), 185, 184, 141, 83, 73, 45; HRMS-EI: Calcd. for $C_{14}H_{24}O_3N_2$ (M) 268.1779, Found; M^+, 268.1756.

26. Synthesis of Propiolic acid cycloadducts (diastereomers):



Scheme 29

To a stirred solution of *N*-cyclohexylhydroxylamine (8.7 mmol) and dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent), propiolic acid was added (1 equivalent) *in-situ* at the time formation of nitrone **2** (monitored by TLC) at RT under N_2 atmosphere and the reaction mixture was stirred for further 11 hour. The progress of the reaction was monitored by TLC (R_f = 0.38, 0.54). The crude products were concentrated under a rotary evaporator and finally the cycloadducts were purified and separated by silica gel column chromatography using ethyl acetate-hexane and were obtained as colourless liquids.

26a. Spectral data of (*S*)-2-cyclohexyl-3-(dimethylamino)-2,3-dihydroisoxazole-5-carboxylic acid

Colourless liquids, 68%; IR ($CHCl_3$): 3144 (m), 2942 (s), 1765 (m), 1684 (s), 1660 (s), 1440 (m), 1310 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 10.8 (s, 1H, - COOH), 4.52 (d, 1H, *J* = 9.46 Hz, C_3H), 3.82 (d, 1H, *J* = 9.44 Hz, C_4H), 2.58 (br, 6H, NMe_2), 2.12 – 1.70 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 181.30 (carbonyl carbon), 87.00 (C_5), 78.50 (C_3), 56.50 (C_4), 32.20, 30.70 (N - CH_3 carbons), 27.00, 25.30, 24.20, 23.00, 21.00, 18.00 (CH_2 carbons); MS (*m/z*): 240 (M^+), 196, 195 (B.P), 167, 157, 83, 73, 45; HRMS – EI: Calcd. for $C_{12}H_{20}O_3N_2$ (M) 240.1467, Found; M^+, 240.1452.

26b. Spectral data (*R*)-2-cyclohexyl-3-(dimethylamino)-2,3-dihydroisoxazole-5-carboxylic acid

Colourless liquids, 21%; IR ($CHCl_3$): 3155 (m), 2950 (s), 1770 (m), 1680 (s), 1655 (s), 1444 (m), 1250 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 11.4 (s, 1H, - COOH), 4.63 (d, 1H, *J* = 2.56 Hz, C_3H), 3.75 (d, 1H, *J* = 2. 64 Hz, C_4H), 2.53 (br, 6H, NMe_2), 2.40 – 2.28 (m, 1H, N-CH proton), 1.90 – 1.53 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 180.00 (carbonyl carbon), 88.40 (C_5), 76.70 (C_3), 57.50 (C_4), 34.00, 32.80 (*N* - CH_3 carbons), 28.00, 27.40, 25.10, 23.14, 22.20, 19.00 (6 CH_2 carbons); MS (*m/z*): 240 (M^+), 196, 195(B.P), 167, 157, 156, 83, 73, 45, 44; HRMS – EI: Calcd. for $C_{12}H_{20}O_3N_2$ (M) 240.1467, Found M^+ 240.1449.

General Procedure for 1,3-dipolar cycloaddition reaction of nitrone 2 in aqueous media

Since *N*-cyclohexyl-α-amino nitrone[7] (**2**) decomposes at room temperature therefore all the cycloaddition reactions were performed with freshly prepared nitrone **2** in

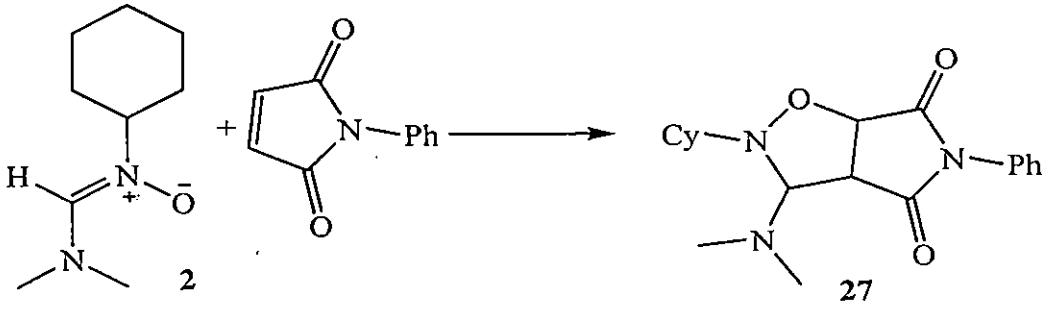
aqueous media. In a 50 mL conical flask nitrone **2** (1 mmol), dipolarophile (alkene / alkynes, 1 equivalent) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5-10 hour. The progress of the reaction was monitored by TLC. After completion of the reaction the products were extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The products were purified by column chromatography using ethyl acetate-hexane to afford pure cycloadducts. This procedure was followed for all the substrates listed in **Table 6.**

Table 6.

Alkenes

- *N*-Phenyl maleimide
- *N*-Methyl maleimide
- *N*-Cyclohexyl maleimide
- Styrene
- Ethyl acrylate
- Acenaphthylene
- Tetrachloro ethylene

27. Synthesis of 2-cyclohexyl-3-(dimethylamino)-5-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-phenyl maleimide cycloadduct)



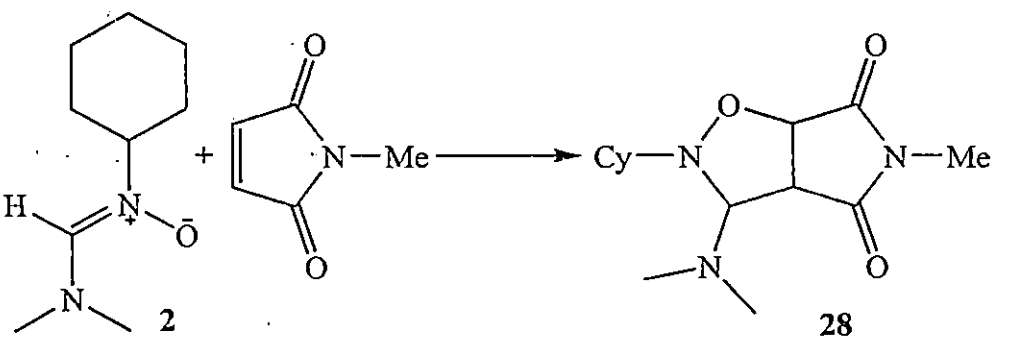
Scheme 30

In a 50 mL conical flask, nitrone **2** (1 mmol), *N*-phenyl maleimide (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.48). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate-hexane and was obtained as white crystals.

Spectral data:

White crystals, 95%; IR ($CHCl_3$): 3350 (br), 3040 (s), 2900 (m), 2800 (m), 2375 (s), 1660 (s), 1470 (m), 1320 (m), 1090 (s), 938 (m), 815 (w), 775 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 - 7.44 (m, 5H, C_6H_5), 4.90 (d, 1H, J = 6.06 Hz, C_5H), 4.46 (d, 1H, J = 6.08 Hz, C_3H), 3.90 (dd, 1H, J = 6.06, 6.08 Hz, C_4H), 3.22-3.10 (m,1H,N-CH), 2.90 – 2.78 (br, 6H, *N*-Me protons), 2.20 - 1.82 (m, 10H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 168.00, 166.00 (carbonyl carbons), 136-126.5 (6 signals, 6 aromatic carbons), 87.50 (C_5), 76.00 (C_3), 59.40 (C_4), 37.00, 36.00 (2 methyl carbons), 30.00, 28.54, 27.00, 25.20, 24.00, 22.00 (6 cyclohexyl carbons); MS (*m/z*): 343 (M^+), 328, 313, 299, 266, 260, 230, 189, 183, 154, 113, 83, 77; HRMS - EI: Calcd. for $C_{19}H_{25}O_3N_3$ (M) 343.4270, Found M^+ 343.4261; Found: C, 66.40; H, 7.22; N, 12.20 %; $C_{19}H_{25}O_3N_3$ requires C, 66.47; H, 7.28; N, 12.24 %.

28. Synthesis of 2-cyclohexyl-3-(dimethylamino)-5-methyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-methyl maleimide cycloadduct):



Scheme 31

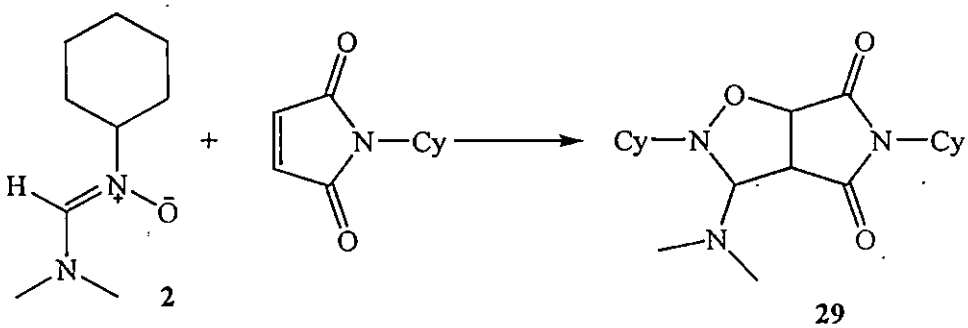
In a 50 mL conical flask, nitrone **2** (1 mmol), *N*-methyl maleimide (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.54). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate- hexane and was obtained as white crystals.

Spectral data:

White crystals, 94%; IR ($CHCl_3$): 3370 (br), 2860 (s), 2310 (s), 1680 (s), 1465 (m), 1325 (m), 1280 (s), 1100 (m), 702 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.34 (d, 1H, J = 6.02

Hz, C_5H), 4.15 (d, 1H, J = 6.0 Hz, C_3H), 3.60 (dd, 1H, J = 6.14, 6.26 Hz, C_4H), 3.40 (s, 3H, CH_3), 2.85 – 2.71 (br, 6H, N-CH_3 protons); 1.95 - 1.42 (m, 11H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 170.00, 168.50 (carbonyl carbons), 88.00 (C_5), 73.00 (C_3), 54.42 (C_4), 39.02, 37.00, 36.34 (3 methyl carbons), 28.00, 26.80, 25.00, 23.75, 22.80, 21.00 (cyclohexyl carbons); MS (*m/z*): 281 (M^+), 266, 251, 237, 198, 153, 128, 111, 83; HRMS – EI: Calcd. for $C_{14}H_{23}O_3N_3$ (M) 281.2160, Found; M^+, 281.2143; Found: C, 59.97; H, 7.69; N, 15.01 %; $C_{14}H_{23}O_3N_3$ requires C, 60.04; H, 7.85; N, 15.08 %.

29. Synthesis of 2,5-dicyclohexyl-3-(dimethylamino)dihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*N*-cyclohexyl maleimide cycloadduct):



Scheme 32

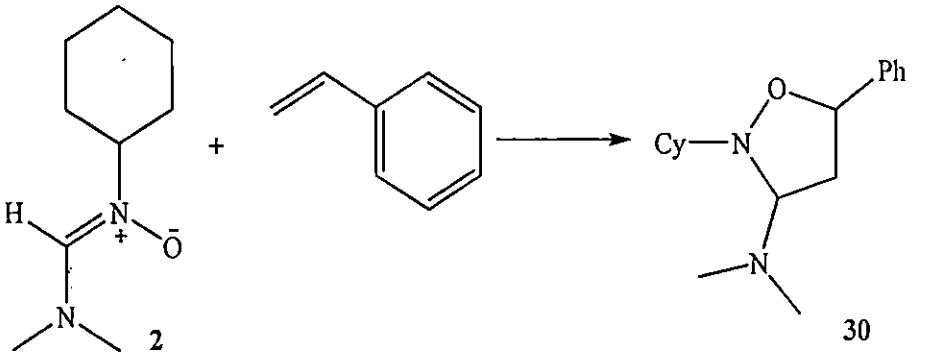
In a 50 mL conical flask, nitrone **1** (1 mmol), *N*-cyclohexyl maleimide (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.58). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified and crystallized from ethyl acetate- hexane and was obtained as white crystals.

Spectral data:

White crystals, 95%; IR ($CHCl_3$): 3150 (br), 2920 (s), 1770 (s), 1680 (s), 1440 (m), 1260 (m), 1130 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.10 (d, 1H, J = 6.10 Hz, C_5H), 4.80 (d, 1H, J = 6.08 Hz, C_3H), 4.26 (dd, 1H, J = 6.00, 6.06 Hz, C_4 2H), 3.82-3.20 (m, 2x1H, N-CH), 2.84 – 2.73 (br, 6H, N – CH_3), 2.20 – 1.05 (m, 20H, cyclohexyl protons); ^{13}C NMR ($CDCl_3$): δ 168.40, 166.30 (carbonyl carbons), 86.00 (C_5), 78.00 (C_3), 55.00 (C_4), 39.40, 38.00 (2 methyl carbons), 33.00, 31.86, 30.12, 28.65, 27.00,

25.86, 24.80, 23.60, 22.75, 21.00, 20.10, 18.00 (cyclohexyl carbons); MS (*m/z*): 349 (M^+), 319, 305, 266, 251, 196, 183; 153, 111, 83; HRMS – EI: Calcd. for $C_{19}H_{31}O_3N_3$ (M) 349.4750, Found; M^+, 349.4745; Found: C, 65.26; H, 8.74; N, 12.06 %; $C_{19}H_{31}O_3N_3$ requires C, 65.32; H, 8.88; N, 12.03 %.

30. Synthesis of 2-cyclohexyl-*N*,*N*-dimethyl-5-phenylisoxazolidin-3-amine (Styrene cycloadduct):



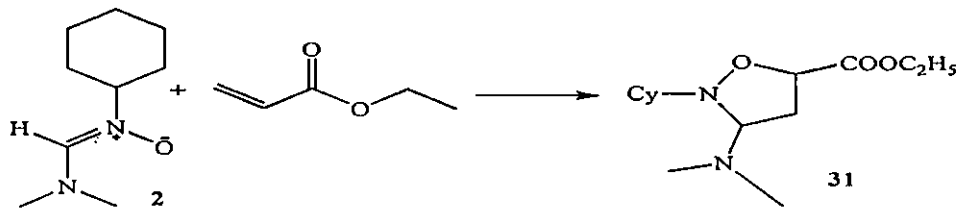
Scheme 33

In a 50 mL conical flask, nitrone **2** (1 mmol), styrene (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.50). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate- hexane and was obtained as colourless liquid.

Spectral data:

Colourless liquid, 94%; IR ($CHCl_3$): 3210 (m), 1735 (s), 1660 (s), 1420 (m), 1300 (m), 1225(s), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.60 - 7.44 (m, 5H, C_6H_5 protons), 5.10 (t, 1H, *J* = 6.08 Hz, C_5H), 4.35 (t, 1H, *J* = 6.16 C_3H), 3.70 (dd, 2H, *J* = 6.12, 6.10 Hz, $C_4$2H), 2.45 - 2.30 (br, m, 6 *N*-methyl protons), 1.76 - 1.24 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 134.30, 132.80, 130.64, 128.70 (aromatic carbons), 85.80 (C_5), 74.50 (C_3), 56.40 (C_4), 36.70, 35.00 (2 CH_3 carbons), 26.00, 24.20, 23.00, 22.42, 20.00, 18.90 (6 cyclohexyl carbons); MS (*m/z*): 274 (M^+), 230, 197, 191, 153,111, 83, 77; HRMS – EI: Calcd. for $C_{17}H_{26}N_2O$ (M) 274.4054, Found M^+, 274.4038.

31. Synthesis of ethyl 2-cyclohexyl-3-(dimethylamino)isoxazolidine-5-carboxylate (ethyl acrylate cycloadduct):



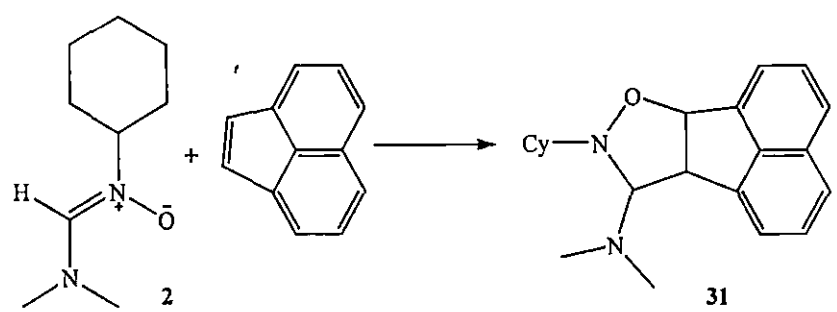
Scheme 34

In a 50 mL conical flask, nitrone **2** (1 mmol), ethyl acrylate (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.62). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate-hexane and was obtained as colourless liquid.

Spectral data:

Colourless liquid, 92%; IR ($CHCl_3$): 3330 (br), 2930 (s), 2150 (m), 1781 (s), 1675 (s), 1450 (s), 1365 (m), 1254 (m), 1110 (s), 1250 (m), 670 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.20 (t, 1H, *J* = 6.76 Hz, C_5H), 4.86 (t, 1H, *J* = 9.40 Hz, C_3H), 4.56 (q, 2H, -$O\underline{CH_2}CH_3$), 3.84 (dd, 2H, *J* = 7.65, 6.62 Hz, C_4 2H), 3.44 (t, 3H, $OCH_2\underline{CH_3}$), 2.42 - 1.84 (br, m, 6H, NMe_2), 1.56 - 1.24 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 202.80 (ester carbonyl carbon); 87.80 (C_5), 76.40 (C_3), 58.85 (C_4), 44.00, 43.00 ($COOCH_2CH_3$), 37.20, 35.42 (NMe_2), 31.00, 30.00, 28.00, 27.20, 26.10, 25.00 (6 CH_2 carbons); MS (*m/z*): 270 (M^+), 226, 197, 157, 154, 116, 113, 83, 73, 44; HRMS-EI: Calcd. for $C_{14}H_{26}O_3N_2$ (M) 270.1935, Found M^+, 270.1922.

32. Synthesis of 8-cyclohexyl-*N*,*N*-dimethyl-6b,8,9,9a-tetrahydroacenaphtho[1,2-*d*]isoxazol-9-amine (acenaphthylene cycloadduct):



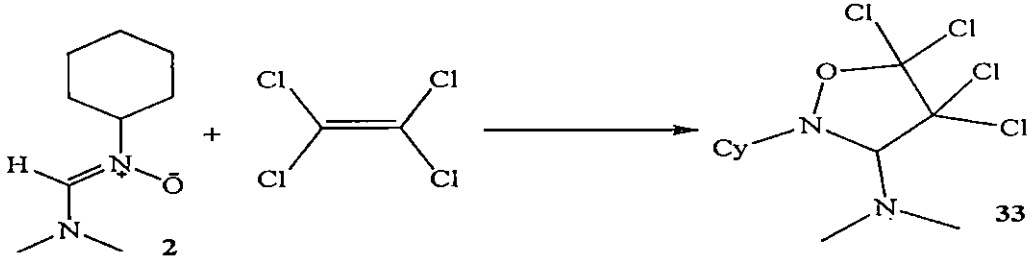
Scheme 35

In a 50 mL conical flask, nitrone **2** (1 mmol), acenaphthylene (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.54). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate-hexane and was obtained as bright yellow crystalline solid.

Spectral data:

Bright yellow crystalline solid, 94%; IR ($CHCl_3$): 3425 (m), 1710 (s), 1680 (s), 1390 (m), 1260 (s), 760 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.46 - 7.30 (m, 6H, naphthalene ring protons); 5.00 (d, 1H, J = 6.08 Hz, C_5H), 4.50 (d, 1H, J = 6 Hz, C_3H), 3.56 (dd, 1H, J = 6.08, 6.28 Hz, C_4H), 2.40 - 2.30 (br, m, 6 *N*-Me protons), 1.66 – 1.28 (m, 11H); ^{13}C NMR ($CDCl_3$): δ 138.00, 136.50, 134.20, 133.70, 132.24, 131.60, 130.00, 128.50, 127.00 (aromatic carbons), 83.00 (C_5), 73.20 (C_3), 58.00 (C_4), 46.00, 44.00 (2 CH_3 carbons), 32.00, 30.50, 28.50, 27.00, 25.00, 24.10 (6 cyclohexyl carbons); MS (*m/z*): 322 (M^+), 239, 209, 195, 170, 152, 113, 113, 83, 44. HRMS – EI: Calcd. for $C_{21}H_{26}N_2O$ (M) 322.2420, Found; M^+, 322.2432.

33. Synthesis 4,4,5,5-tetrachloro-2-cyclohexyl-*N*,*N*-dimethylisoxazolidin-3-amine (tetrachloro ethelene cycloadduct):



Scheme 36

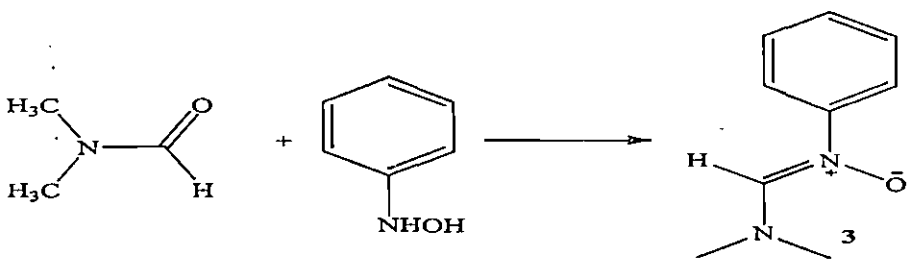
In a 50 mL conical flask, nitrone **2** (1 mmol), acenaphthylene (1 mmol) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.34). After completion of the reaction, the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated. The product was purified by column chromatography using ethyl acetate-hexane and was obtained as pale yellow oily liquid.

Spectral data:

Pale yellow oily liquid, 96%; IR ($CHCl_3$): 3310 (br), 3020 (m), 2170 (s), 1860 (s), 1460 (m), 1330 (m), 1150 (s), 875 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.24 - 4.16 (br, s, 1H, C_3H), 2.33 - 2.24 (br, m, *N* - CH_3 protons), 2.05 – 1.93 (m, 1H, *N*-CH proton), 1.74 – 1.32 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 87 (C_5), 73 (C_3), 58 (C_4), 56, 55 (2 x CH_3 carbons), 39 – 28 (6 cyclohexyl carbons); MS *(m/z)*: 334 (M^+), 292, 252, 222, 153, 152, 139, 113, 111, 83, 82, 44; HRMS – EI: Calcd. for $C_{11}H_{18}N_2OCl_4$, (M) 336.0240, Found; M^+, 336.0231.

Reaction type III

General procedure for the preparation of *N*-phenyl-α-aminonitrone[8a] (nitrone 3):



Scheme 37

N-phenyl hydroxylamine (0.5161 gm, 4.7 mmol) was added to dry distilled *N,N*-dimethyl formamide (9 mL, 1 equivalent) in presence of anhydrous $MgSO_4$. The reaction mixture was kept at RT with constant stirring with a magnetic stirrer under N_2 atmosphere for 24 hour. The formation of nitrone **3** was monitored by TLC (R_f = 0.32, silica gel; ethyl acetate : benzene = 1 : 10). The nitrone **3** was isolated by extraction with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over sodium sulphate and concentrated on a rotary evaporator and finally obtained as faint yellow crystals (m.p 52^0C,uncorrected). The nitrone decomposes when kept at room temperature for a longer period and hence it was either used right after its synthesis (for aqueous phase synthesis) or as *in-situ* for other cycloaddition reactions.

Spectral data of (*Z*)-*N*-((dimethylamino)methylene)aniline oxide:

Pale yellow crystals, 94%; IR ($CHCl_3$): 3410 (m), 1660 (s), 1610 (s), 1440 (m), 1300 (m), 1180 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.73 - 7.26 (m, 5H, C_6H_5 protons), 1.90 (br, 6H, *N*-methyl protons), 1.42 (s, 1H, $CH{=}N^+$); ^{13}C NMR ($CDCl_3$): δ 142.00

(CH=N+), 132.90, 131.00, 129.65, 127.40 (aromatic carbons), 47.42, 44.84 (methyl carbons); HRMS – EI: Calcd. for $C_9H_{12}N_2O$, (M) 164.2066, Found; M^+, 164.2052.

General Procedure for 1,3-dipolar cycloaddition reaction in aqueous phase

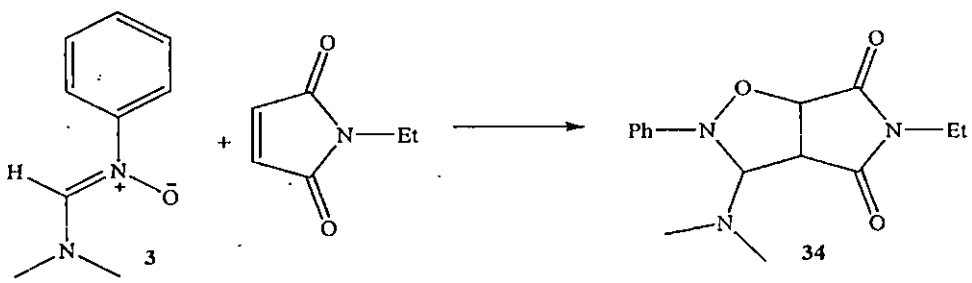
Since nitrone (**3**) decomposes when kept for longer period therefore all the cycloaddition reactions are performed with freshly prepared nitrone **3**. In a 50 mL conical flask, nitrone **3** (1 mmol), dipolarophile (1 equivalent) and water (10 mL) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 5 - 6 hour. The progress of the reaction was monitored by TLC. After completion of the reaction the product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The product was purified by column chromatography using ethyl acetate – hexane. This procedure was followed for all the substrates listed in **Table 4**

Table 4: List of dipolarophiles used for cycloaddition reaction

Alkenes

- *N*-ethyl maleimide
- *p*-OMe-*N*-phenyl maleimide
- Acenaphthylene
- Ethyl acrylate
- Methyl vinyl ketone

34. Synthesis of 3-(dimethylamino)-5-ethyl-2-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (Ethyl maleimide cycloadduct):



Scheme 38

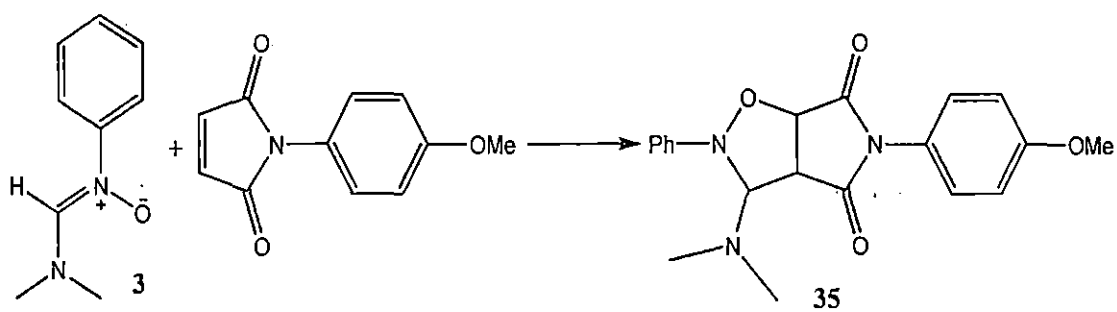
To a stirred solution of nitrone **3** (1 mmol) in 15 mL water was added *N*-ethyl maleimide (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 4 hr. The progress of the reaction was monitored by TLC (R_f = 0.44). The product was extracted with ether (2 x 25 mL), the organic layer was washed with

brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as yellow solid.

Spectral data:

Yellow solid, 94%; IR ($CHCl_3$): 3165 - 3082 (br), 3013 (m), 2865 (m), 1760 (s), 1660 (m), 1445 (s), 1280 (m), 778 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.45 – 7.31 (m, 5H, C_6H_5), 5.26 (d, 1H, J = 8.20 Hz, C_5H), 3.62 (d, 1H, J = 7.20 Hz, C_3H), 3.38 (dd, 1H, J = 6.16, 6.32 Hz, C_4H), 2.90 – 2.78 (br, 6H, NMe_2), 2.66 (q, 2H, J = 6.12, 6.80 Hz, $\underline{CH_2}CH_3$), 1.34 (t, 3H, J = 7.10 Hz, $CH_2\underline{CH_3}$); ^{13}C NMR ($CDCl_3$): δ 200.40, 197.80 (carbonyl carbons), 136.50, 135.00, 133.20, 131.80 (phenyl carbons), 86.20 (C_5), 78.40 (C_3), 55.00 (C_4), 41.70, 39.64 (NMe_2), 23.50 ($\underline{CH_2}CH_3$), 14.00 ($CH_2\underline{CH_3}$); MS (*m/z*): 289 (M^+), 260, 212, 182, 168, 148, 141 (B.P), 107, 77 ; HRMS – EI: Calcd. for $C_{15}H_{19}O_3N_3$ (M) 289.3350, Found; M^+ 289.3334.

35. Synthesis of 3-(dimethylamino)-5-(4-methoxyphenyl)-2-phenyldihydro-2*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (*p*-OMe-*N*-phenyl maleimide cycloadduct):



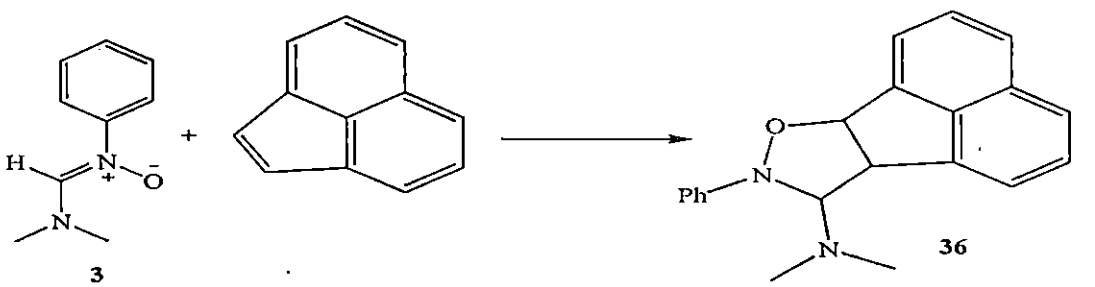
Scheme 39

To a stirred solution of nitrone **3** (1 mmol) in 15 mL water was added 4-methoxy-*N*-phenyl maleimide (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.39). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as dark yellow crystals.

Spectral data:

Dark yellow crystals, 94 %; IR ($CHCl_3$): 3084 – 3022 (br), 2880 (m), 1765 (s), 1650 (s), 1472 (m), 1365 (m), 795 (s), 775 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 - 7.40 (m, 5H, C_6H_5 protons), 6.90 – 6.78 (m, 4H, phenyl protons), 5.40 (d, 1H, J = 8.24 Hz, C_5H), 3.82 (d, 1H, J = 7.28 Hz, C_3H), 3.54 (dd, 1H, J = 9.24, 6.08 Hz, C_4H), 3.30 (s, 3H, OCH_3), 2.70 – 2.56 (br, 6H, NMe_2); ^{13}C NMR ($CDCl_3$): δ 204.50, 198.65 (carbonyl carbons), 138.00, 137.00, 135.64, 134.32, 133.70, 132.00, 131.46, 130.00 (aromatic carbons), 85.50 (C_5), 76.00 (C_3), 59.42 (C_4), 54.60 (OCH_3), 40.75, 38.20 (NMe_2); MS (*m/z*): 351(M^+), 320, 274, 244, 230, 167, 148, 107, 77; HRMS – EI: Calcd. for $C_{20}H_{21}O_4N_3$ (M), 351.4060, Found; M^+, 351.4044.

36. Synthesis of *N,N*-dimethyl-8-phenyl-6b,8,9,9a-tetrahydroacenaphtho[1,2-*d*]isoxazol-9-amine (acenaphthylene cycloadduct)



Scheme 40

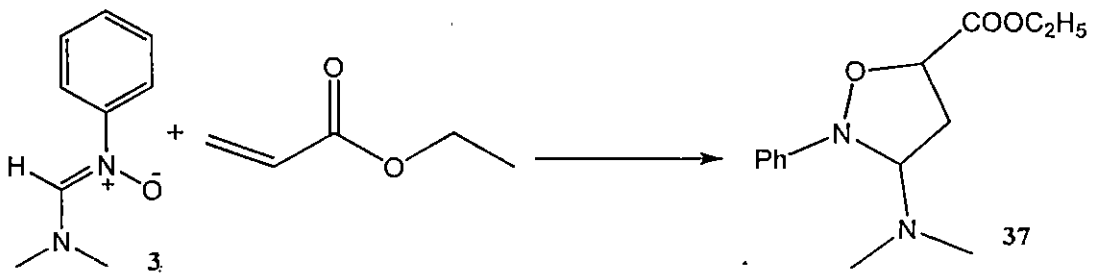
To a stirred solution of nitrone **3** (1 mmol) in 15 mL water was added 4-methoxy-*N*-phenyl maleimide (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.54). The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate-hexane and finally obtained under reduced pressure as bright yellow crystals.

Spectral data:

Yellow crystals, 89%; IR ($CHCl_3$): 3084 - 3022 (br), 2848 (m), 2472 (m), 1710 (s), 1523 (m), 1523 (m), 1394 (s), 1145 (m), 1022 (m), 831 (m), 776 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.46 – 7.35 (m, 5H, phenyl protons), 7.12 – 6.96 (m, 6H, napthylene protons), 4.88 (d, 1H, J = 6.76 Hz, C_5H), 3.76 (d, 1H, J = 7 Hz, C_3H), 3.52 (dd, 1H, J

= 8.30, 8.0 Hz, C_4H), 2.58 – 2.43 (br, 6H, NMe_2); ^{13}C NMR ($CDCl_3$): δ 137.00, 135.08, 134.60, 133.00, 132.80, 131.25, 130.10, 129.45, 128.00, 126.90 (aromatic carbons), 88.70 (C_5), 76.46 (C_3), 58.00 (C_4), 36.00, 35.00 (NMe_2); MS (*m/z*): 316 (M^+), 239, 209, 195, 168, 162, 154 (B. P), 148, 107, 73; HRMS-EI: Calcd. for $C_{14}H_{26}O_3N_2$ (M) 316.1814, Found M^+, 316.1811.

37. Synthesis of ethyl 3-(dimethylamino)-2-phenylisoxazolidine-5-carboxylate (Ethyl acrylate cycloadduct):



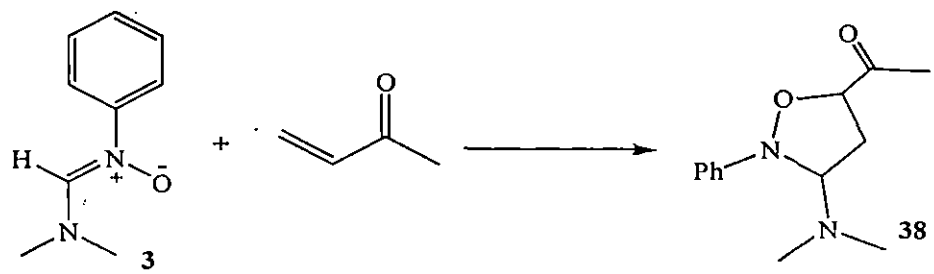
Scheme 41

To a stirred solution of nitrone **3** (1 mmol) in 15 mL water was added ethyl acrylate (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 5 hr. The progress of the reaction was monitored by TLC (R_f = 0.48).The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as white gummy liquid.

Spectral data:

White gummy liquid, 93%; IR ($CHCl_3$): 3155 – 3060 (br), 2930 (s), 2856 (m), 1750 (s), 1445 (s), 1340 (m), 770 (s) cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 7.20 - 7.12 (m, 5H, C_6H_5), 4.80 (t, 1H, *J* = 8.2 Hz, C_5H), 4.26 (q, 2H, *J* = 6, 6.02 Hz, $-OCH_2CH_3$), 3.58 (t, 1H, *J* = 7.22 Hz, C_3H), 3.24 (dd, 2H, *J* = 8.40, 7.08 Hz, C_4 2H), 2.76 – 2.65 (br, 6H, NMe_2), 1.24 (t, 3H, *J* = 7.50 Hz, $-OCH_2CH_3$); ^{13}C NMR ($CDCl_3$): δ 170.40 (carbonyl carbon), 135.00, 134.00, 132.25, 130.60 (aromatic carbons), 87.50 (C_5), 76.30 (C_3), 70.40 (CH_2 carbon of $-OCH_2CH_3$), 57.00 (C_4), 44.50, 42.80 (NMe_2), 20.00 (CH_3 carbon of OCH_2CH_3); MS (*m/z*): 264 (M^+), 190, 187, 157, 148, 143, 116, 107, 77; HRMS - EI: Calcd. for $C_{14}H_{20}O_3N_2$ (M) 264.3250, Found M^+, 264.3239.

38. Synthesis of methyl 3-(dimethylamino)-2,5-diphenylisoxazolidine-4-carboxylate (Methyl vinyl ketone cycloadduct):



Scheme 42

To a stirred solution of nitrone **3** (1 mmol) in 15 mL water was added methyl vinyl ketone (1 equivalent) at RT under nitrogen atmosphere and the reaction mixture was stirred for 8 hr. The progress of the reaction was monitored by TLC (R_f = 0.44).The product was extracted with ether (2 x 25 mL), the organic layer was washed with brine water (2 x 15 mL), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using ethyl acetate - hexane and finally obtained under reduced pressure as pale yellow oil.

Spectral data:

Pale yellow oil, 91%; IR ($CHCl_3$): 3172 – 3033 (br), 2936 (s), 1720 (s), 1442 (m), 1235 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.80 – 6.58 (m, 5H, C_6H_5), 4.86 (t, 1H, *J* = 7.14 Hz, C_5H), 3.74 (t, 1H, *J* = 6.80 Hz, C_3H), 3.38 (dd, 2H, *J* = 8.80, 7.40 Hz, C_4H), 2.82 – 2.70 (br, 6H, NMe_2), 2.16 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$): δ 202.50 (carbonyl carbon), 133.55, 132.00, 130.86, 129.20 (aromatic carbons), 88.70 (C_5), 76.00 (C_3), 58.45 (C_4), 42.40, 40.00 (NMe_2), 31.20 (methyl carbon of $COCH_3$); FAB - MS (*m/z*): 234 (M^+), 233, 219, 191, 157, 148 (B.P), 113, 107, 86, 77; HRMS-EI: Calcd for $C_{13}H_{18}O_2N_2$ (M) 234.2990, Found M^+, 234.2978.

General Procedure for 1,3-dipolar cycloaddition reaction with alkynes at RT:

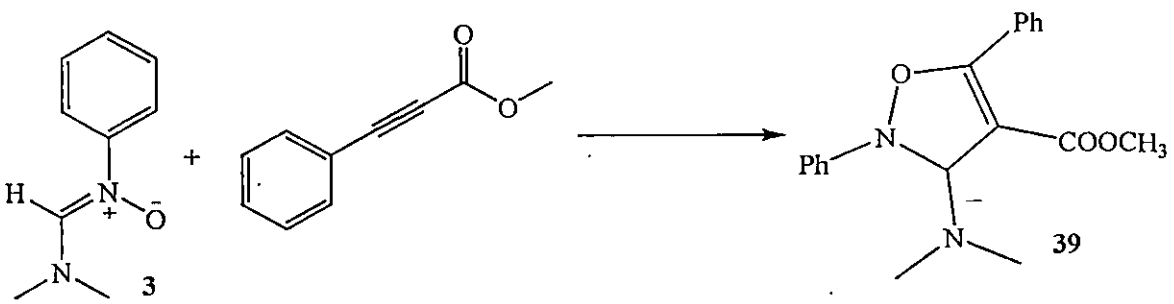
N-phenyl-α-amino nitrone (**3**) decomposes slowly at RT and hence after isolation of nitrone immediately cycloaddition reaction with alkynes were performed with 1:1 ratio. In a 100 mL conical flask, nitrone **3** (2.20 mmol), alkyne (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 12 hour. The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was concentrated on a rotary evaporator and

the products were purified and separated by silica gel column chromatography using ethyl acetate - hexane to furnish pure cycloadducts. This procedure was followed for the substrates mentioned below.

Alkynes

- Phenyl methyl propiolate
- Dimethyl acetylene dicarboxylate

39. Synthesis of methyl 3-(dimethylamino)-2,5-diphenyl-2,3-dihydroisoxazole-4-carboxylate (phenyl methyl propiolate cycloadduct):



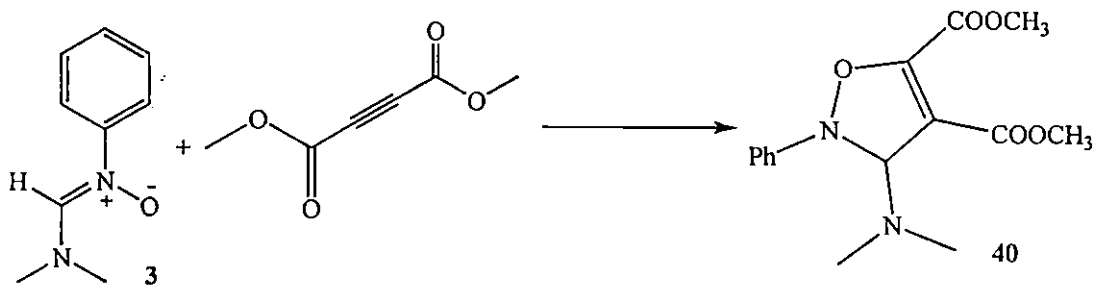
Scheme 43

In a 100 mL conical flask, nitrone **3** (2.20 mmol), phenyl methyl propiolate (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 10 hour. The progress of the reaction was monitored by TLC (R_f = 0.73). After completion of the reaction the solvent was concentrated on a rotary evaporator and the crude product was purified by silica gel column chromatography using ethyl acetate-hexane combinations to furnish white viscous liquid (73 mg, 70%).

Spectral data:

White viscous liquid, 70%; IR ($CHCl_3$): 3155 (m), 1750 (s), 1665 (m), 1430 (m), 1360 (m), 778 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.70 – 7.04 (m, 10H, C_6H_5 protons), 4.06 (s, 1H, C_3H), 3.32 (s, 3H, - $COOCH_3$), 2.40 (br, 6H, NMe_2); ^{13}C NMR ($CDCl_3$): δ 172.50 (carbonyl carbon), 137.00, 135.40, 134.00, 132.60, 131.43, 129.65, 128.00, 127.28 (aromatic carbons), 88.00 (C_5), 73.40 (C_3), 57.40 (C_4), 45.20 (-$COOCH_3$), 33.42, 29.50 (*N* - CH_3 carbons); MS (*m/z*): 324 (M^+), 296, 266, 219, 189, 188, 111. 105, 83, 77; HRMS – EI: Calcd. for $C_{19}H_{20}O_3N_2$ (M) 324.1910, Found M^+, 324.1891.

40. Synthesis of dimethyl 3-(dimethylamino)-2-phenyl-2,3-dihydroisoxazole-4,5-dicarboxylate (dimethyl acetylene dicarboxylate):



Scheme 44

In a 100 mL conical flask nitrone **3** (2.20 mmol), dimethyl acetylene dicarboxylate (1 equivalent) was added to 50 mL dry ether and stirred at RT with a magnetic stirrer under N_2 atmosphere for 13 hour. The progress of the reaction was monitored by TLC (R_f = 0.64). After completion of the reaction the solvent was concentrated on a rotary evaporator and the crude product was purified by silica gel column chromatography using ethyl acetate-hexane combinations to furnish red liquid (64 mg, 68%).

Spectral data:

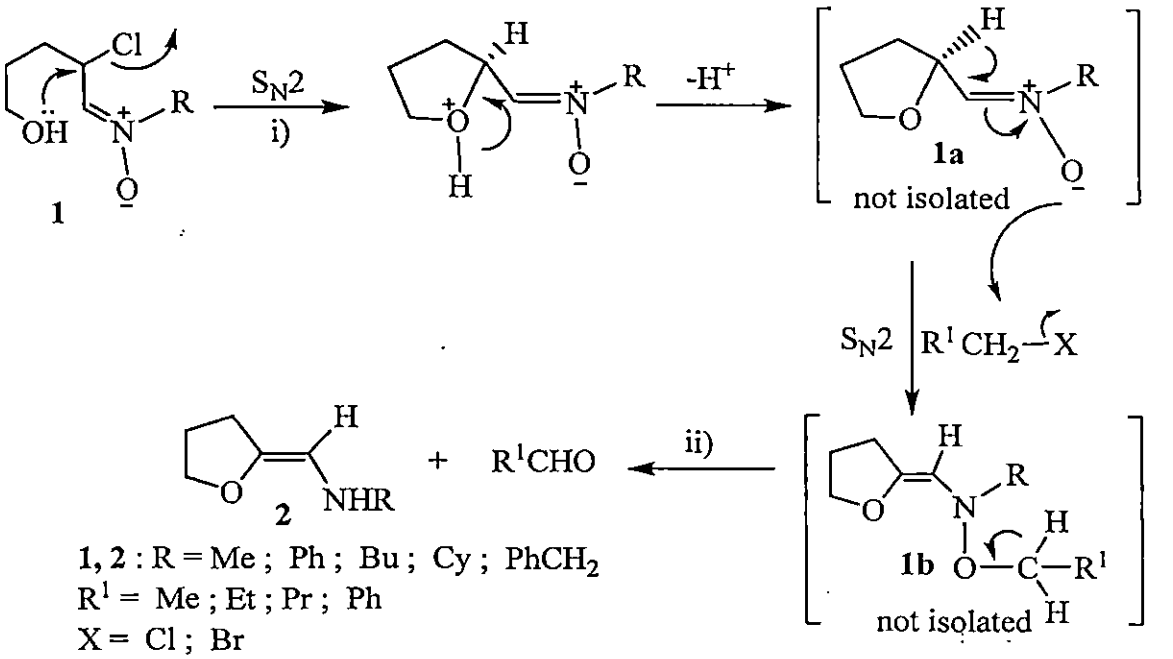
Red liquid, 68%; IR ($CHCl_3$): 3145 (m), 2820 (m), 1745 (s), 1700 (m), 1670 (m), 1420 (s), 1260 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.86 - 6.77 (m, 5H, C_6H_5 protons), 4.75 (s, 1H, C_3H), 3.66 (s, 3H, -$COOCH_3$), 3.60 (s, 3H, -$COOCH_3$), 2.68 (br, 6H, NMe_2); ^{13}C NMR ($CDCl_3$): δ 169.00, 167.48 (carbonyl carbons), 87.50 (C_5), 76.64 (C_3), 59.47 (C_4), 44.65, 43.72 ($COO\underline{C}H_3$), 31.00, 29.43 (*N* - CH_3 carbons); MS (*m/z*): 306 (M^+), 275, 262, 229, 219, 203, 188, 111, 87, 59; HRMS – EI: Calcd. for $C_{15}H_{24}O_5N_2$ (M) 306.1670, Found M^+, 312.1652.

Reaction type IV

Special type aldehyde synthesis using α-chloro and α-amino nitrones as oxidizing agents

Using the tremendous synthetic potentiality of α-chloro and α-amino nitrones we have synthesized a variety of aldehydes[11] with a very good yield and the most important fact during the aldehyde synthesis is the use of side product as efficient dipolarophile making the reaction atom efficient[12]. Similarly in case of amino nitrones, the side

product can be hydrolyzed under acidic medium to furnish the starting material along with imines[13].



1, 2 : R = Me ; Ph ; Bu ; Cy ; $PhCH_2$
R^1 = Me ; Et ; Pr ; Ph
X = Cl ; Br

Reagents and conditions : i) Dry ether, pyridine, r.t , N_2 atmosphere
ii) Dry ether, Na_2CO_3, r.t , N_2 atmosphere

Scheme 1

In a 100 ml conical flask *N*-phenyl-α-chloro nitrone (500mg, 2.3086 mmol), pyridine (1 equivalent) and diethyl ether (25 ml) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 1 hour and the formation of transient nitrone (not isolated) was monitored by TLC (R_f = 0.34). Benzyl chloride (292.1002mg, 1 equivalent) was added at this stage and the reaction mixture was stirred for another 2 hours till the intermediate compound (not isolated) was developed (monitored by TLC; R_f = 0.37). 2 gms of solid Na_2CO_3 was added at this stage and the reaction mixture was stirred for further 1 hr while the progress of the reaction was again monitored by TLC (R_f = 0.40, 0.46). The reaction was typically completed when the N–O bond was cleaved[14]. Basic workup, removal of pyridine hydrochloride and silica gel column chromatographic purification provided desired benzaldehyde as colourless liquid (712mg, 90%; R_f = 0.40) and furan derivative as pale yellow gummy liquid (Scheme **1**; 78 mg, 10%; R_f = 0.46).

Spectral data for benzaldehyde

Colourless liquid, 90%, IR ($CHCl_3$): 1695 (s), 1320 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.80 (s, 1H, CHO), 7.30 – 7.16 (m, 5H, C_6H_5); ^{13}CNMR ($CDCl_3$): δ 198

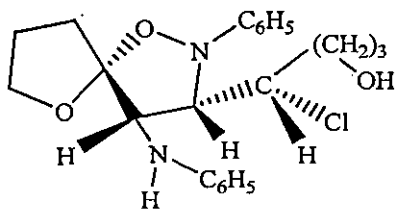
(CHO), 136, 134, 132, 131 (aromatic carbons); FAB - MS (*m/z*): 106 (M^+), 105 (B.P), 77, 51, 28; HRMS-EI: Calcd. for C_6H_5CHO (M), 106.0417, Found M^+ 106.0408.

Spectroscopic data for 2 (R = Ph) [(*E*)-1-(dihydrofuran-2-(3H)-ylidene)-*N*-phenyl methanamine (α-*N*-phenyl furan derivative)]

Pale yellow gummy liquid, 10%, IR ($CHCl_3$): 3150-3060 (br), 2860 (m), 1640 (s), 1430 (m), 1140 (m), 776 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.43 – 7.28 (m, 5H, C_6H_5), 5.16 (br, 1H, N-H), 4.72 (s, 1H, C=CH), 2.95-2.34 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 137.20, 135.65, 134.00, 132.15 (aromatic carbons), 106.24, 104.18 (double bonded carbons), 28.46, 27.10, 24.84 (3 CH_2 carbons); FAB - MS (*m/z*): 175 (M^+), 98, 97, 77. HRMS-EI: Calcd. for $C_{11}H_{13}ON$ (M), 175.0993, Found M^+ 175.0981.

Cycloaddition reaction of side product (2) with *N*-phenyl-α-chloro nitrone

To a stirred solution of *N*–phenyl-α-chloro nitrone **1** (R = Ph, 61.8375 mg, 0.2855 mmol) in 25 mL dry ether was added **2** (R = Ph, 50 mg, 0.2855 mmol, 1 equivalent) and stirred at RT with a magnetic stirrer under N_2 atmosphere for 6 hr. The progress of the reaction was monitored by TLC (R_f = 0.52). After completion of the reaction, the solvent was evaporated under a rotary evaporator to afford crude cycloadduct (**3**: R=Ph) which was purified by column chromatography using ethyl acetate-hexane and was obtained as pale yellow viscous liquid (R=Ph, 95 mg, 85%).



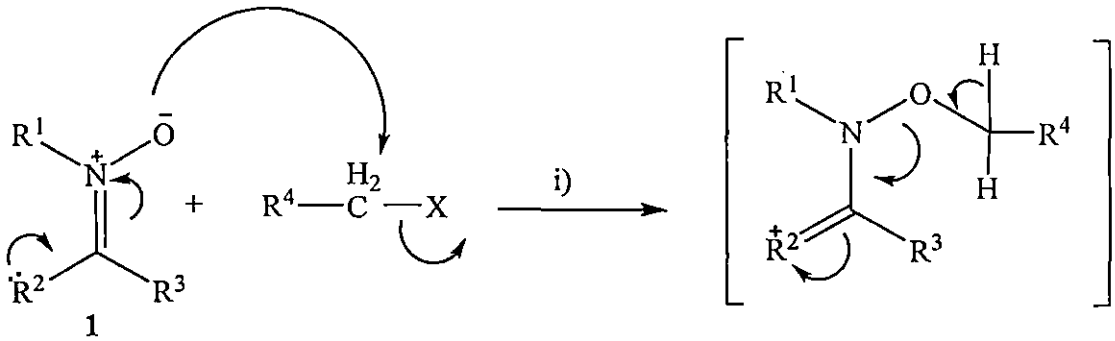
3

Spectral data:

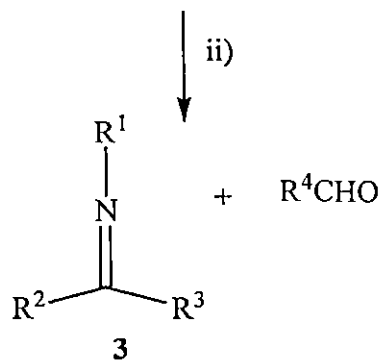
IR (KBr): 3485 – 3290 (br), 2962 (m), 2425 (m), 1620 (s), 1490 (s), 1260 (m), 1040 (m), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.98 - 6.92 (m, 10H, 2 x C_6H_5), 5.84 (dd, 1H, *J* = 8.55, 8.20 Hz, C_3H), 5.00 (br, 1H, CH_2OH, exchanged in D_2O), 3.60 (dt, 1H, *J* = 9.34, 7.88 Hz, C_4H), 3.40 (s, 1H, N – H proton of NHPh), 2.68 (dt~m, 1H, CHCl), 1.90 (dt, 1H, *J* = 6.82, 6.64 Hz, C_3·H), 1.50 – 1.12 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 138.00, 136.50, 134.30, 133.80, 131.75, 130.42, 129.46, 128.64 (aromatic carbons), 95.10 (CHCl), 86.40 (C_5), 73.75 (C_3), 53.30 (C_4), 30.20, 28.55, 27.34, 26.22, 25.73,

24.37 (6 CH_2 carbons); MS (*m/z*): 404 (M^++2), 402 (M^+), 325, 310, 309, 218 (B.P), 107, 91, 77. HRMS-EI: Calcd. for $C_{22}H_{27}O_3N_2Cl$ (M), 402.7130, Found M^+, 402.7122.

Scheme for aldehyde synthesis from α-amino nitrone



1 : R^1 = Ph, Cy
R^2 = NH_2, NMe_2
R^3 = H, CH_2, CH_3CH_2, $CH_3CH_2CH_2$, $CH_3CH_2CH_2CH_2$, Ph
X = Cl / Br / I



Scheme 2

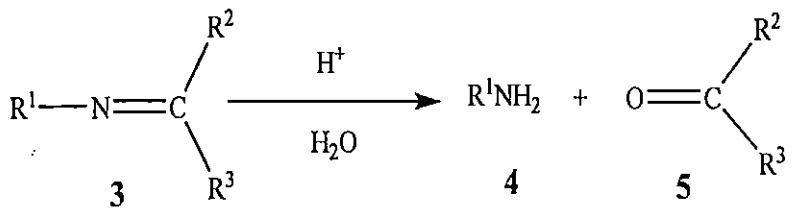
In a 100 ml conical flask, *N*-phenyl-α-amino nitrone (500 mg, 2.3570 mmol), benzyl chloride (295.8670 mg, 1 equivalent) and diethyl ether (25 ml) was added and stirred at RT with a magnetic stirrer under N_2 atmosphere for 1 hour. During this process nitrone underwent S_N2 reaction very quickly with benzyl chloride and developed an intermediate compound which was not isolated. The progress of the reaction was monitored by TLC (R_f = 0.38). 2 gms of solid Na_2CO_3 was added at this stage and the reaction mixture was stirred for further 3 hour and monitored by TLC. The N-O bond was easily cleaved under basic medium in a Kornblum type mechanism and developed benzaldehyde (R_f = 0.43) and imine derivative (R_f = 0.54) respectively (**Scheme 2**). The reaction mixture was filtered and concentrated on a rotary evaporator. Basic work-up followed by silica gel column chromatography using ethyl acetate – hexane results benzaldehyde as colourless liquid (706 mg, 88 %) and imine derivative (**3**) as pale yellow gummy liquid (**Scheme 2**; 84 mg, 11 %).

Spectral data:

Colourless liquid, 88%, IR ($CHCl_3$): 2824 (s), 1695 (s), 1320 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.80 (s, 1H, CHO), 7.30 – 7.16 (m, 5H, C_6H_5); $^{13}CNMR$ ($CDCl_3$): δ 198 (CHO), 136.00, 134.00, 132.50, 131.00 (aromatic carbons). MS-FAB (m/z): 106 (M^+), 105 (B.P), 77, 51; HRMS-EI: Calcd. for C_6H_5CHO (M) 106.1240, Found M^+ 106.1228.

Pale yellow gummy liquid, 11 %, IR ($CHCl_3$): 3450 (m), 1680 (s), 785 (s); ^1H NMR ($CDCl_3$): δ 7.32 – 7.25 (m, 5H, C_6H_5), 6.76 – 6.68 (m, 5H, C_6H_5), 3.75 – 3.62 (br, 2H, NH_2); $^{13}CNMR$ ($CDCl_3$): δ 136.84, 135.24, 134.25, 132.80, 131.25, 130.00, 128.50, 127.45 (phenyl carbons), 86.86 (C=N); FAB – MS (*m/z*): 196 (M^+), 119, 103 (B.P), 77. HRMS-EI: Calcd. for $C_{13}H_{12}N_2$ (M) 196.2530, Found M^+ 196.2519.

General procedure of acid hydrolysis of imine 3



a: R^1 = Ph; Cy
b: R^2 = NH_2; NMe_2
c: R^3 = H; CH_3; Ph

Scheme 3

In a 100 mL R.B flux, imine derivative 3 (70 mg), 20 mL 10% HCl was taken and refluxed in water bath for 30 minutes. The formation of the desired hydrolysed products were monitored by TLC. During the hydrolysis process, the double bond between carbon and nitrogen of the imine derivative was cleaved and benzamide (R^2 = NH_2; R^3 = Ph; R_f = 0.42) and aniline (R^1 = Ph; R_f = 0.64) was developed[15]. The products were extracted with ether (2 x 25 mL) when aniline passes into organic layer while benzamide remains in aqueous phase. The ether extract containing aniline was dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator and finally purified by silica gel column chromatography using ethyl acetate – hexane as pale yellow liquid (24 mg, 34%). Benzamide was obtained as white crystalline solid when aqueous part of the solution was evaporated in a temperature controlled water bath

and was crystallized from ethanol (**Scheme 3**; 42 mg, 60%; m.p. 126^{0}C). This general hydrolysis procedure was followed for all the imine derivatives.

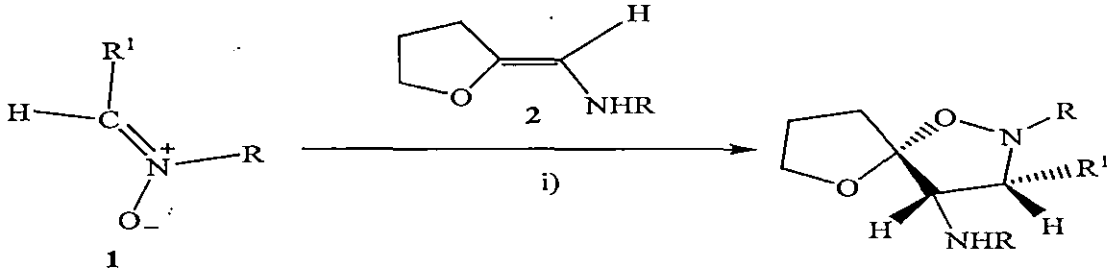
Spectroscopic data for product 4

IR ($CHCl_3$): 3440 (m), 3205 (s), 1635 (s), 1280 (m), 778 (s); ^{1}H NMR ($CDCl_3$): δ 6.88 – 6.76 (m, 5H, C_6H_5), 3.82 – 3.66 (br, 2H, NH_2); ^{13}CNMR ($CDCl_3$): δ 135.50, 134.00, 132.00, 129.20 (phenyl carbons); FAB – MS (*m/z*): 93 (M^+). HRMS-EI: Calcd. for C_6H_7N (M) 93.0690, Found; M^+ 93.0683.

Spectral data for product 5

White crystalline solid, 60%, m.p.126^{0}C, IR ($CHCl_3$): 3455 (s), 1675 (s), 1630 (m), 780 (s); ^{1}H NMR ($CDCl_3$): δ 7.14 – 7.08 (m, 5H, C_6H_5), 6.94 – 6.76 (br, $CONH_2$); ^{13}CNMR ($CDCl_3$): δ 177.50 (C=O), 130.50, 129.00, 128.00, 127.20 (phenyl carbons); FAB – MS (*m/z*): 121 (M^+), 77; HRMS-EI: Calcd. for C_7H_7NO (M) 121.0690, Found; M^+ 121.0681.

General procedure for cycloaddition (for regioselective *spiro* cycloadducts)



R = C_6H_5
R^1 = C_6H_5 ; $CHCl(CH_2)_3OH$; NH_2
Reagents and conditions: i) Dry ether, RT, N_2 atmosphere, 4 - 6 hr

Scheme 4

To a well stirred solution of nitrone **1** (**R = Ph**; 1 mmole) in diethyl ether (20 mL) taken in a 50 mL conical flask, was added α-*N*-methyl furan derivative [(*E*)-1-(dihydrofuran-2-(3*H*)-ylidene)-*N*-methyl methanamine)] (1 equivalent) and was stirred at RT with a magnetic stirrer under N_2 atmosphere for 4 hr. The progress of the reaction was monitored by TLC (R_f = 0.53). After completion of the reaction and work-up, the crude spiro cycloadduct was concentrated in a rotary evaporator and finally purified by column chromatography using ethyl acetate - hexane to afford pure spiro cycloadduct **3**[16] (**Scheme 4**). This procedure was followed for the reaction of nitrone **1** (**R = Ph**) with α-*N*-methyl/phenyl furan derivatives **2** [(*E*)-1-(dihydrofuran-

2-(3*H*)-ylidene)-*N*-methyl methanamine) / (*E*)-1-(dihydrofuran-2-(3*H*)-ylidene)-*N*-phenyl methanamine)].

Spectroscopic data for 2 (R=Ph; α-*N*-phenyl furan derivative) [(*E*)-1-(dihydrofuran-2-(3*H*)-ylidene)-*N*-phenyl methanamine)]

IR (KBr): 3150-3060 (br), 2860 (m), 1640 (s), 1430 (m), 1140 (m), 778 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.83 (m, 5*H*, C_6H_5), 6.29 (br, 1H, *N-H*), 2.17 (s, 1H, C=CH), 1.79 - 1.18 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 137.20, 135.65, 134.00, 132.15 (aromatic carbons), 106.24, 104.18 (double bonded carbons), 28.46, 27.10, 24.84 (3 CH_2 carbons); FAB - MS (*m/z*): 175 (M^+), 98, 97, 77. HRMS-EI: Calcd. for $C_{11}H_{13}ON$ (M) 175.0993, Found M^+, 175.0981.

3: Spectral data of (*S*)-4-chloro-4-((3*S*,4*S*,5*R*)-2methyl-4-(methylamino)-1,6-dioxa-2-azaspiro[4.4]nonan-3-yl)butan-1-ol

Pale yellow gummy liquid. Yield 88%, R_f = 0.53; IR (KBr): 3460 – 3326 (br), 2948 (m), 2420 (m), 1485 (s), 1325 (m), 810 (m), 774 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.83 (br, 1H, CH_2OH, exchanged in D_2O), 4.60 (s, 1H, $NHCH_3$), 3.37 (s, 6H, 2 x *N*-CH_3), 3.12 (dd, 1H, *J* = 9.20, 8.32 Hz, C_3H), 2.70 (dt, 1H, *J* = 8.10, 7.88 Hz, C_4H), 2.35 (dt~m, 1H, CHCl), 1.88 – 1.42 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 93.00 (CHCl), 87.55 (C_5), 76.20 (C_3), 55.20 (C_4), 41.97 (N-CH_3), 40.24 (NH-CH_3), 33.37, 31.50, 28.68, 26.00, 25.12, 23.40 (6 CH_2 carbons); MS (*m/z*): 280 (M^++2), 278 (M^+), 263, 248, 156 (B.P), 141, 107; HRMS-EI: Calcd. for $C_{12}H_{23}O_3N_2Cl$ (M) 278.6710, Found M^+, 278.6698.

4: Spectral data of (*S*)-4-chloro-4-((3*S*,4*S*,5*R*)-2-phenyl-4-(phenylamino)-1,6-dioxa-2-azaspiro[4.4]nonan-3-yl)butan-1-ol

Dark red viscous liquid. Yield 86%, R_f = 0.48; IR (KBr): 3485 – 3290 (br), 2962 (m), 2425 (m), 1620 (s), 1490 (s), 1260 (m), 1040 (m), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.98 - 6.92 (m, 10H, 2 x C_6H_5), 5.84 (dd, 1H, *J* = 8.55, 8.20 Hz, C_3H), 5.00 (br, 1H, CH_2OH, exchanged in D_2O), 3.60 (dt, 1H, *J* = 9.34, 7.88 Hz, C_4H), 3.40 (s, 1H, N – H proton of NHPh), 2.68 (dt~m, 1H, CHCl), 1.90 (dt, 1H, *J* = 6.82, 6.64 Hz, C_3-H), 1.50 – 1.12 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 138.00, 136.50, 134.30, 133.80, 131.75, 130.42, 129.46, 128.64 (aromatic carbons), 95.10 (CHCl), 86.40 (C_5), 73.75 (C_3), 53.30 (C_4), 30.20, 28.55, 27.34, 26.22, 25.73, 24.37 (6 CH_2 carbons); MS (*m/z*): 404 (M^++2), 402

(M^+), 325, 310, 309, 218 (B.P), 107, 91, 77; HRMS-EI: Calcd. for $C_{22}H_{27}O_3N_2Cl$ (M), 402.7130, Found M^+, 402.7122.

5. Spectral data of *(S)*-3-amino-(3*S*,4*S*,5*S*)-2-methyl-4-(methylamino)-1,6-dioxa-2-azaspiroisoxazole

Gray viscous liquid. Yield 84%, R_f = 0.52; IR (KBr): 3430 - 3380 (br), 3033 (m), 2955 (m), 1773 (s), 1662 (s), 1480 (s), 1282 (m), 1178 (s), 806 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.90 (br, s, 2H, NH_2, exchanged in D_2O), 4.60 (br, 1H, $NHCH_3$), 3.36 (s, 6H, 2 x *N*-CH_3), 3.00 (d, 1H, *J* = 7.54 Hz, C_3H), 2.70 (dt, 2H, *J* = 6.24, 6.28 Hz, $C_3'2H$), 2.38 (dt, 1H, *J* = 7.12, 6.70 Hz, C_4H), 1.70 – 1.48 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 88.50 (C_5/C_2'), 77.12 (C_3), 56.26 (C_4), 40.94 (N-CH_3), 38.13 (NH-CH_3), 32.07, 31.22, 29.34 (3',4',5' CH_2 carbons); MS (*m/z*): 187 (M^+), 172, 157, 156 (B.P), 141. HRMS-EI: Calcd. for $C_8H_{17}O_2N_3$ (M) 187.1633, Found M^+, 187.1613.

6: Spectral data of (*S*)-3-amino-(3*S*,4*S*,5*S*)-2-phenyl-4-(phenylamino)-1,6-dioxa-2-azaspiroisoxazole

Dark gray viscous liquid, Yield 81%, R_f= 0.48; IR (KBr): 3436 - 3390 (br), 3030 (m), 2952 (m), 1780 (s), 1674 (s), 1480 (m), 1276 (m), 815 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.02 - 6.90 (m, 10H, 2 x C_6H_5), 5.86 (d, 1H, *J* = 6.30 Hz, C_3H), 5.00 (br, s, 2H, NH_2, exchanged in D_2O), 3.50 (dt, 2H, *J*= 6.74, 6.06 Hz, $C_3'2H$), 3.38 (br,s,1H, NHC_6H_5), 2.70 (dt, 1H, *J* = 7.20, 6.18 Hz,C_4H), 1.52 – 1.28 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 137.21, 135.44, 134.00, 133.10, 130.66, 129.40, 128.32, 127.84 (aromatic carbons), 86.94 (C_5/C_2'), 74.24 (C_3), 55.70 (C_4), 27.87, 25.63, 24.00 (3',4',5' CH_2 carbons); MS (*m/z*): 311 (M^+), 295, 218, 203 (B.P), 202, 92, 77; HRMS-EI: Calcd. for $C_{18}H_{21}O_2N_3$ (M), 311.2054, Found; M^+, 311.2037.

7: Spectral data of (*S*)-3-phenyl-(3*S*,4*S*,5*S*)-2-methyl-4-(methylamino)-1,6-dioxa-2-azaspiroisoxazole

Colourless gummy liquid, Yield 78%, R_f= 0.52; IR (KBr): 3040 (m), 2965 (m), 1760 (s), 1685 (m), 1464 (s), 1290 (m), 1084 (s), 808 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.81 (s, 5H, C_6H_5), 4.67 (s, 1H, $NHCH_3$), 3.36 (s, 6H, 2 x N-CH_3), 3.00 (d, 1H, *J* = 5.74 Hz, C_3H), 2.74 (dt, 1H, *J* = 6.64, 6.30 Hz, C_4H), 2.30 (dt, 2H, *J* = 5.10, 4.92 Hz, $C_3'2H$), 1.80 – 1.55 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 129.05, 128.53, 128.27, 127.22 (aromatic carbons), 80.28 (C_5/C_2'), 70.36 (C_3), 59.70 (C_4), 45.17 (N-CH_3), 41.64 (NH-CH_3), 32.07, 31.22, 29.34 (3',4',5' CH_2 carbons); MS (*m/z*): 248 (M^+), 218, 171, 156

(B.P), 141, 77. HRMS-EI: Calcd. for $C_{14}H_{20}O_2N_2$ (M) 248.1862, Found M^+, 248.1853.

8: Spectral data of (*S*)-3-phenyl-(3*S*,4*S*,5*S*)-2-phenyl-4-(phenylamino)-1,6-dioxa-2-azaspiroisoxazole

Colourless gummy liquid. Yield 78%, R_f= 0.48; IR (KBr): 3024 (m), 2950 (m), 1772 (s), 1670 (s), 1468 (m), 1382 (m), 805 (m), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50 - 6.62 (m, 15H, 3 x C_6H_5), 5.84 (s, 1H, NHC_6H_5), 4.63 (d, 1H, *J* = 6.06 Hz, C_3H), 4.02 (dt, 1H, *J* = 6.18, 6.20 Hz, C_4H), 2.64 (dt, 2H, *J* = 5.28, 4.10 Hz,C_3'2H), 2.00 – 1.26 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 136.76, 136.53, 136.24, 135.15, 134.90, 134.62, 134.30, 133.78, 132.44, 132.18, 130.92, 130.37 (aromatic carbons), 83.22 ($C_5/C_{2'}$), 71.52 (C_3), 52.89 (C_4), 23.61, 22.57, 21.14 (3',4',5' CH_2 carbons); MS (*m/z*): 372 (M^+), 295, 280, 218, 203 (B.P), 92, 77; HRMS-EI: Calcd. for $C_{24}H_{24}O_2N_2$ (M) 372.2286, Found M^+, 372.2270.

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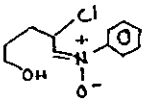
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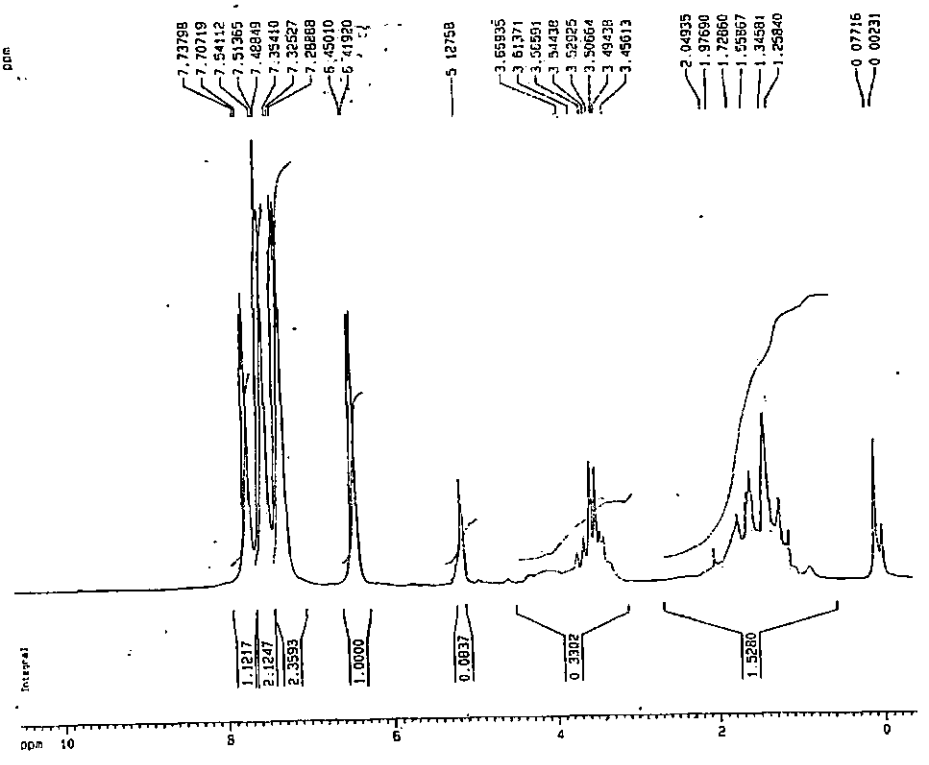
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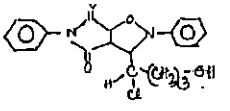
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PROCNO 1

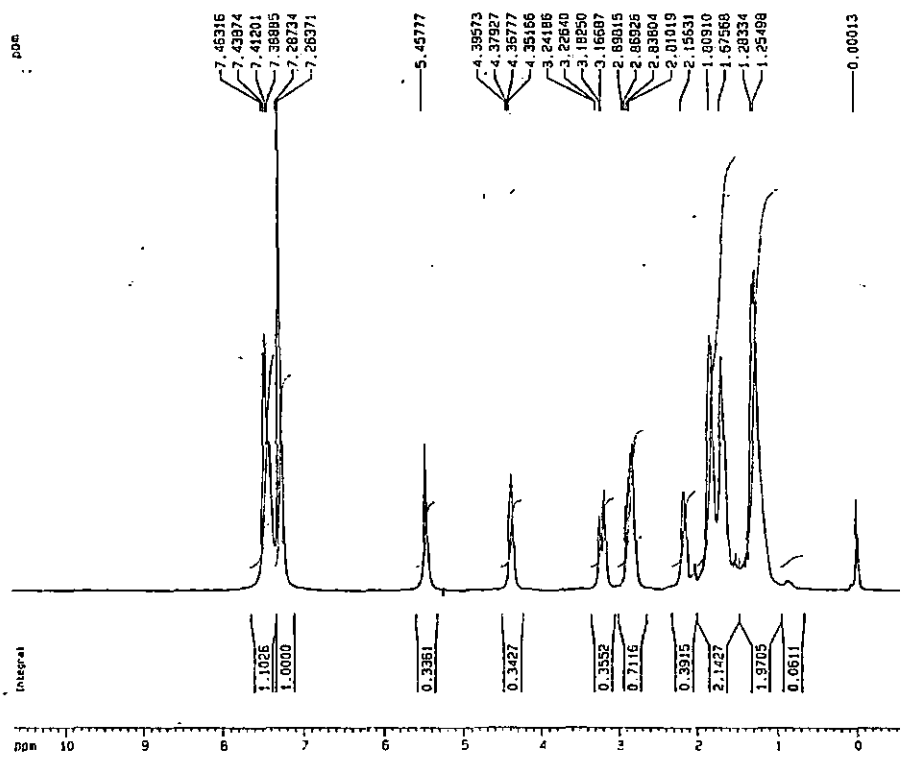
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Time 15.55
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 6172.839 Hz
FIDRES 0.094193 Hz
AQ 5.3084660 sec
RG 362
DW 81.000 usec
DE 6.00 usec
TE 510.3 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 6.88 usec
PL1 -3.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300016 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 10.580 ppm
F1 3175.41 Hz
F2P -0.363 ppm
F2 -108.94 Hz
PPMCM 0.54715 ppm/cm
HZCM 164.21732 Hz/cm





Current Data Parameters
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EXPNO 1
PROCNO 1

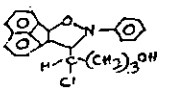
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SOLVENT CDCl3
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DS 2
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FIDRES 0.109618 Hz
AQ 4.5613556 sec
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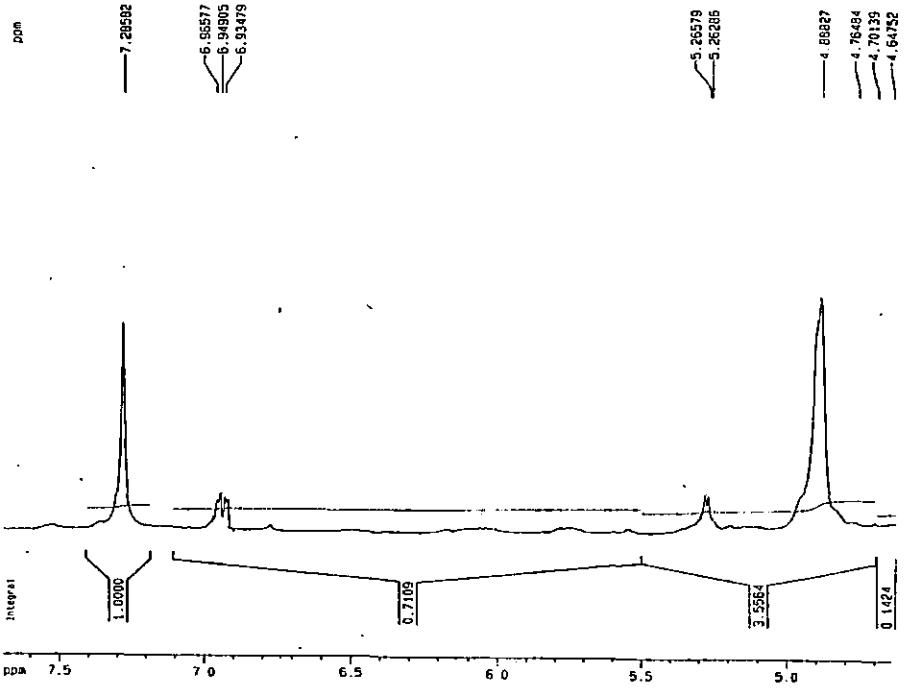
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PL1 -3.00 dB
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SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 7.00 cm
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F1 3205.81 Hz
F2P -0.540 ppm
F2 -162.00 Hz
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HZCM 168.44034 Hz/cm

S-22






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Current Data Parameters
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PROCNO                       1

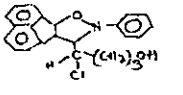
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TD                     65536
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NS                         32
DS                          2
SWH                 7183.908 Hz
FIDRES              0.109618 Hz
AQ                  4.5613556 sec
RG                        128
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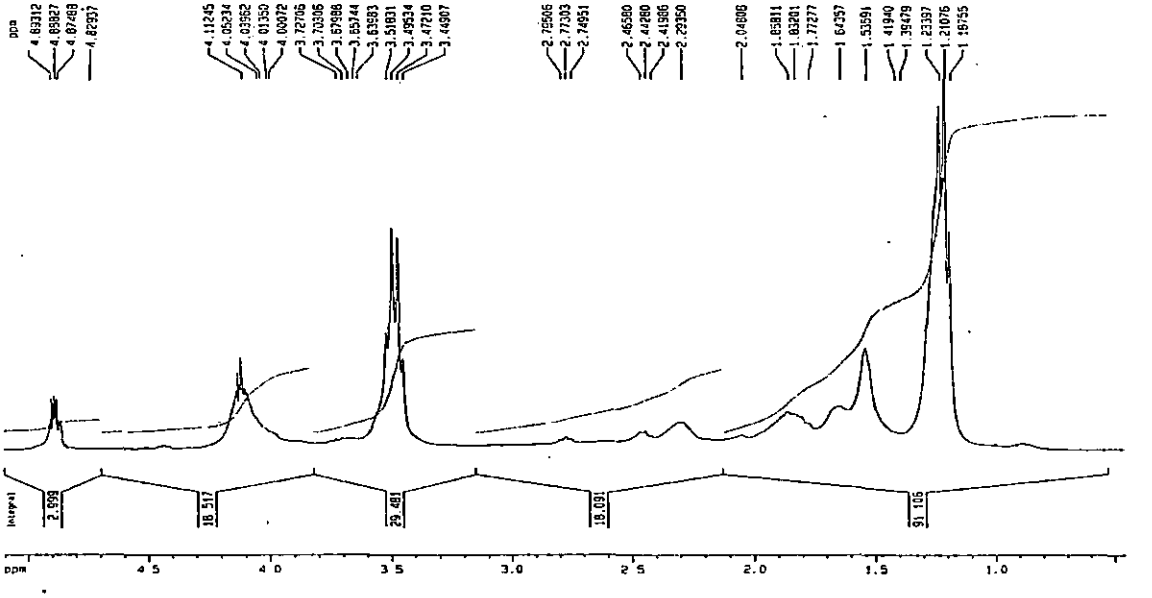
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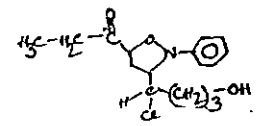
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LB                   0.30 Hz
GB                          0
PC                       1.00

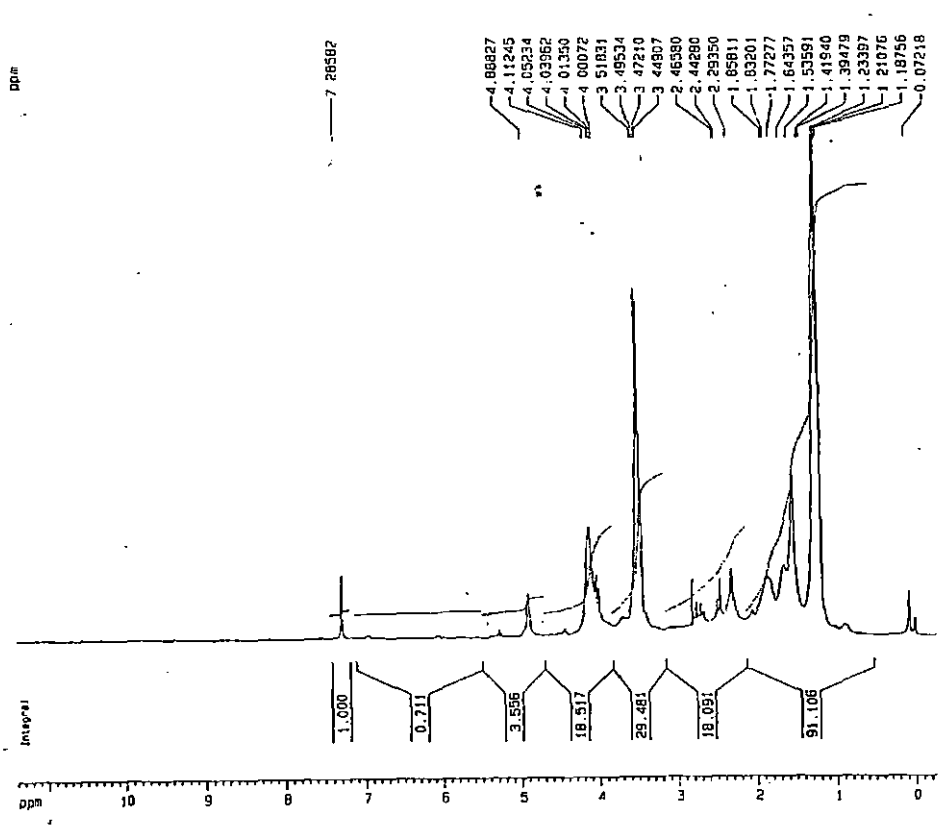
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F2                 1389.22 Hz
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HZCM              46.01505 Hz/cm
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S-22









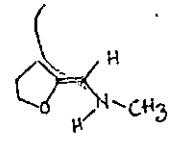

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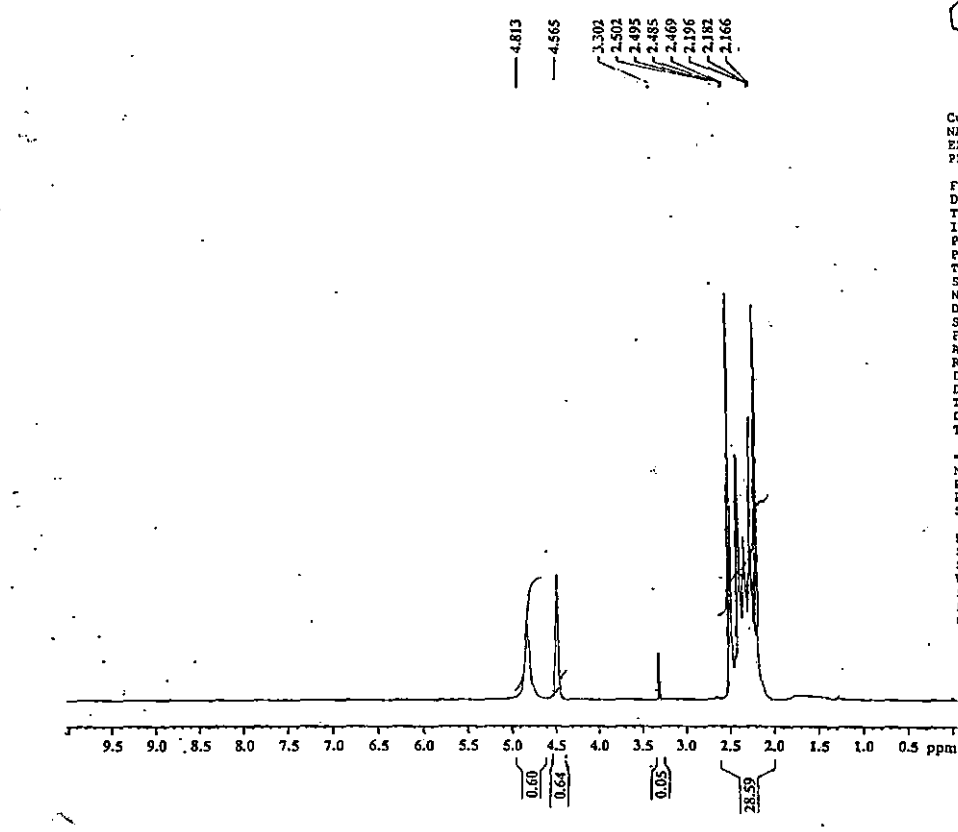
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TD                     65536
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DS                          2
SWH                7183.908 Hz
FIDRES             0.109616 Hz
AQ                 4.5613556 sec
RG                        128
DW                     69.600 usec
DE                      6.00 usec
TE                     310.3 K
D1                 1.00000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                      6.86 usec
PL1                    -3.00 dB
SFO1          300.1315782 MHz

F2 - Processing parameters
SI                        32768
SF          300.1299979 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
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CY                      14.00 cm
F1P                    11.405 ppm
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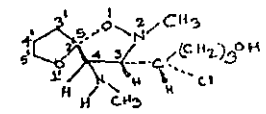

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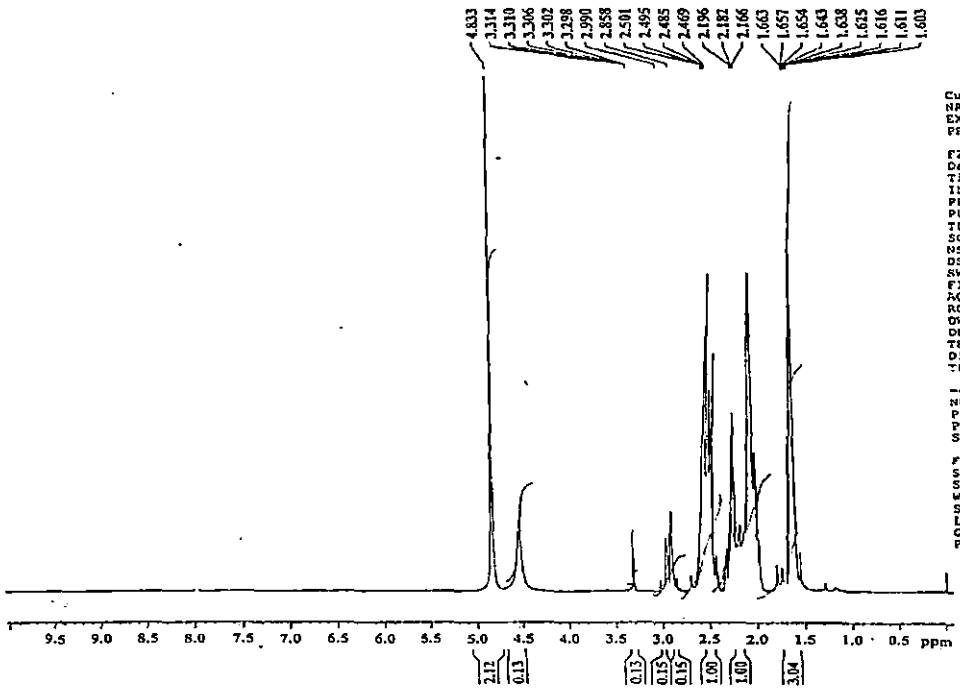
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SOLVENT                 MeOD
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DS                          0
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FIDRES             0.097563 Hz
AQ                 5.1249652 sec
RG                         16
DW                    78.200 usec
DE                     6.00 usec
TE                     300.0 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      7.00 usec
PL1                     2.50 dB
SFO1          400.1324008 MHz

F2 - Processing parameters
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SF          400.1300091 MHz
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25





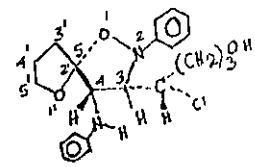
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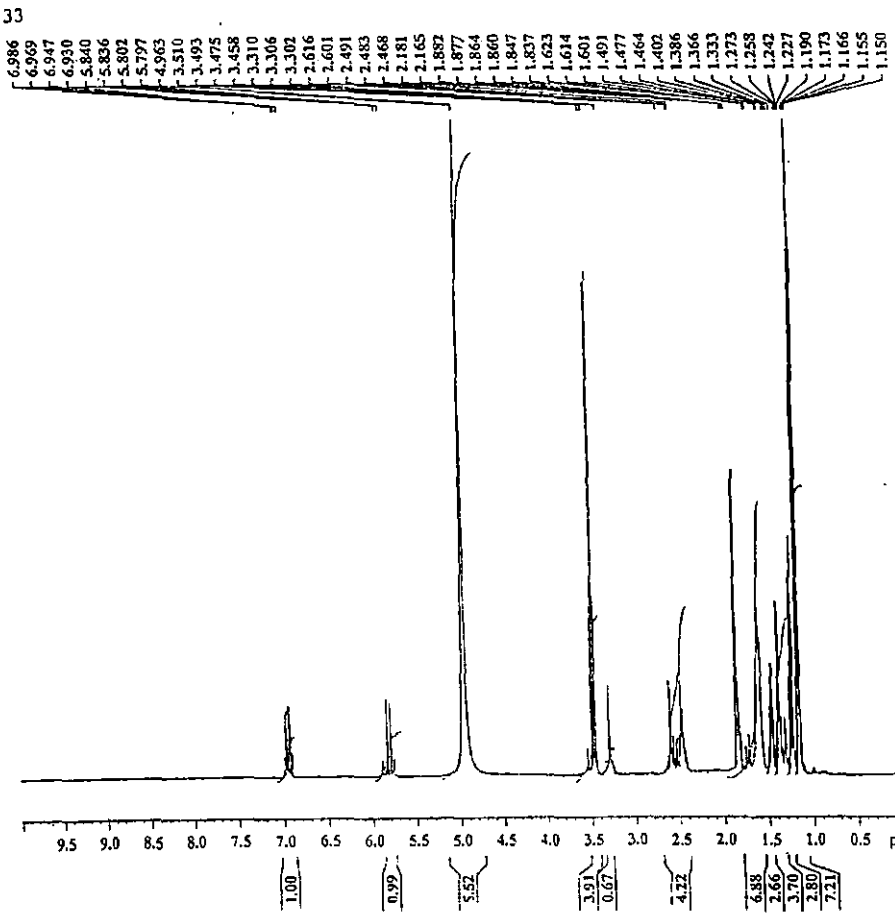
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SOLVENT MeOD
NS 16
DS 0
SWH 6393.862 Hz
FIDRES 0.097563 Hz
AQ 5.1249652 sec
RG 45.2
DW 78.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

---------- CHANNEL f1 ----------
NUC1 1H
P1 7.00 usec
PL1 2.50 dB
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F2 - Processing parameters
SI 32768
SF 400.1300091 MHz
WDW EM
SSB 0
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GB 0
PC 1.00

33





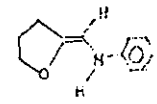
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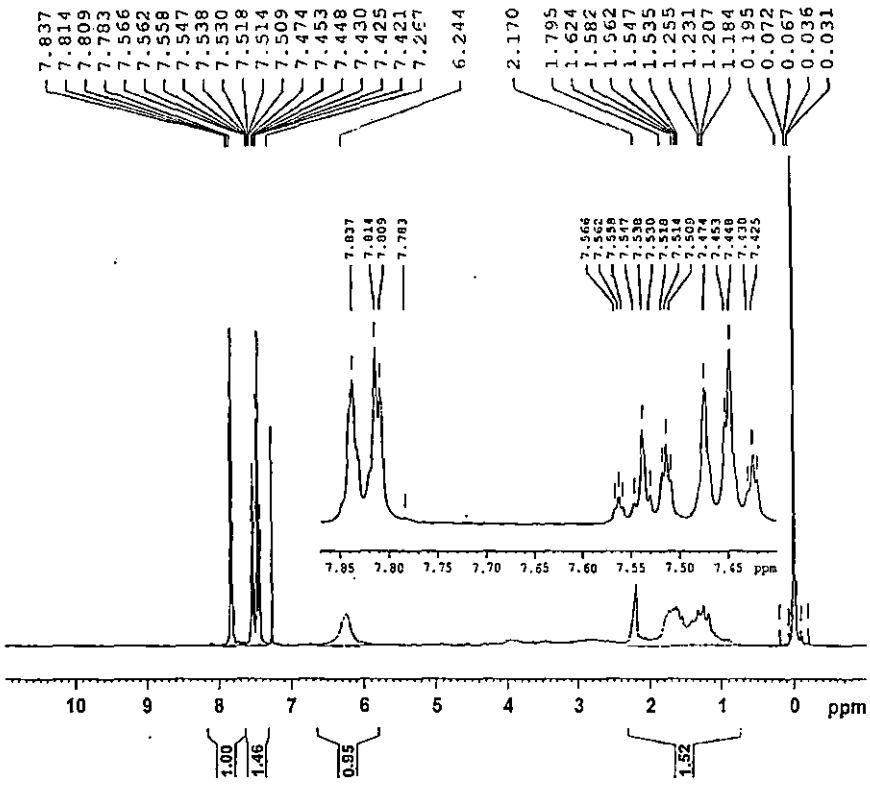
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NS 16
DS 0
SWH 6393.862 Hz
FIDRES 0.097563 Hz
AQ 5.1249652 sec
RG 20.2
DW 78.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

---------- CHANNEL f1 ----------
NUC1 1H
P1 7.00 usec
PL1 2.50 dB
SFO1 400.1324009 MHz

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SF 400.1300091 MHz
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PC 1.00

Bhskar-4





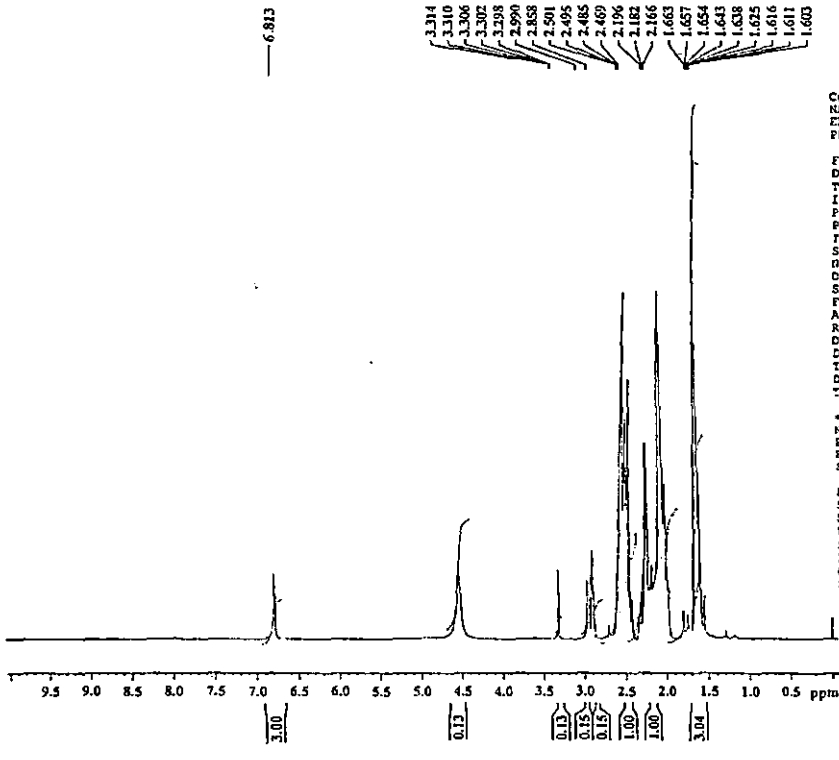
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TE 0.0 K
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MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
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P1 13.10 usec
PL1 0.00 dB
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Bha-1

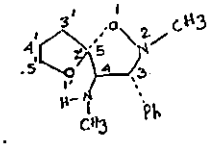


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PROCNO 1

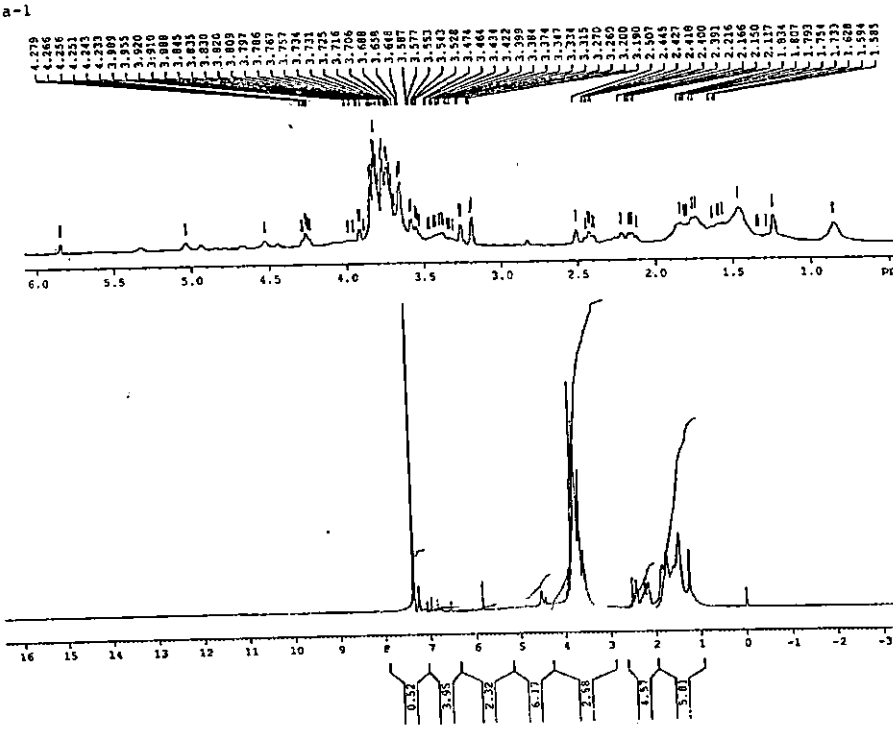
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NS 16
DS 0
SWH 6393.862 Hz
FIDRES 0.097563 Hz
AQ 5.1249652 sec
RG 45.2
DW 78.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 2.50 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
SF 400.1300091 MHz
WDW EM
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GB 0
PC 1.00



Bha-1

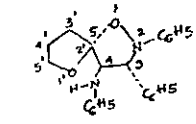


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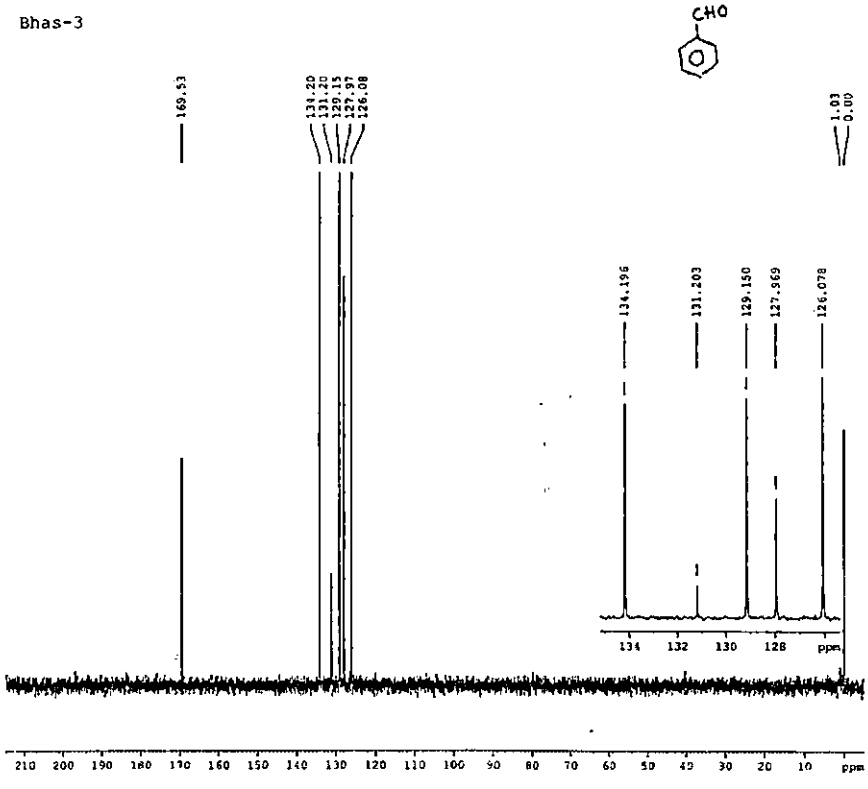
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SOLVENT               DMSO
NS                        16
DS                         0
SWH                6172.839 Hz
FIDRES             0.094150 Hz
AQ                 5.3084650 sec
RG                      45.3
DW                 81.000 usec
DE                      6.00 usec
TE                    0.0 K
D1                 2.00000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                     12.25 usec
PL1                    -2.00 dB
SFO1           300.1318536 MHz

F2 - Processing parameters
SI                        32768
SF                 300.1300002 MHz
WDW                       EM
SSB                        0
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Bhas-3



```
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PROCNO                     2

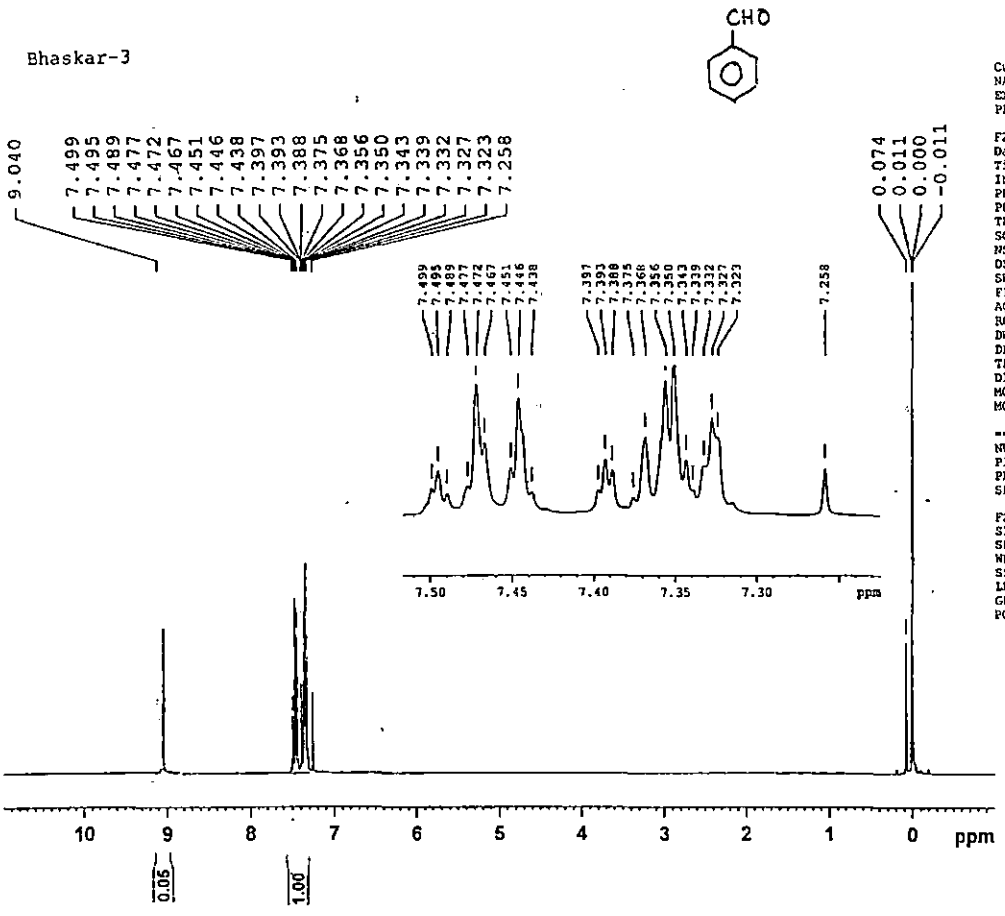
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SOLVENT               CDCl3
NS                       512
DS                         4
SWH               17985.611 Hz
FIDRES             0.274439 Hz
AQ                 1.8219508 sec
RG                     32768
DW                 27.800 usec
DE                      6.00 usec
TE                    0.0 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                     12.25 usec
PL1                     0.00 dB
SFO1           75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL2                    -2.00 dB
PL12                   15.00 dB
PL13                   19.00 dB
SFO2           300.1312005 MHz

F2 - Processing parameters
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Bhaskar-3

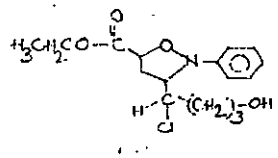


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EXPNO 3
PROCNO 1

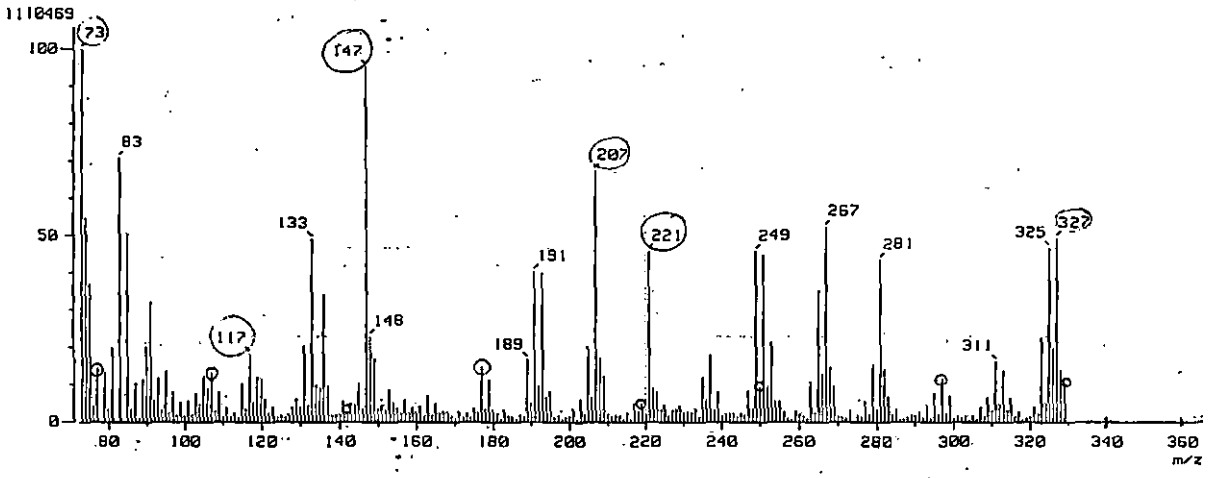
F2 - Acquisition Parameters
Date_ 20081005
Time 11.16
INSTRUM av300
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 64
DS 0
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 181
DW 81.000 usec
DE 6.00 usec
TE 0.0 K
D1 2.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

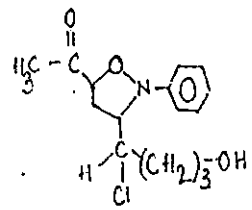
-------- CHANNEL f1 --------
NUC1 1H
P1 13.10 usec
PL1 0.00 dB
SFO1 300.1321909 MHz

F2 - Processing parameters
SI 32768
SF 300.1300068 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40

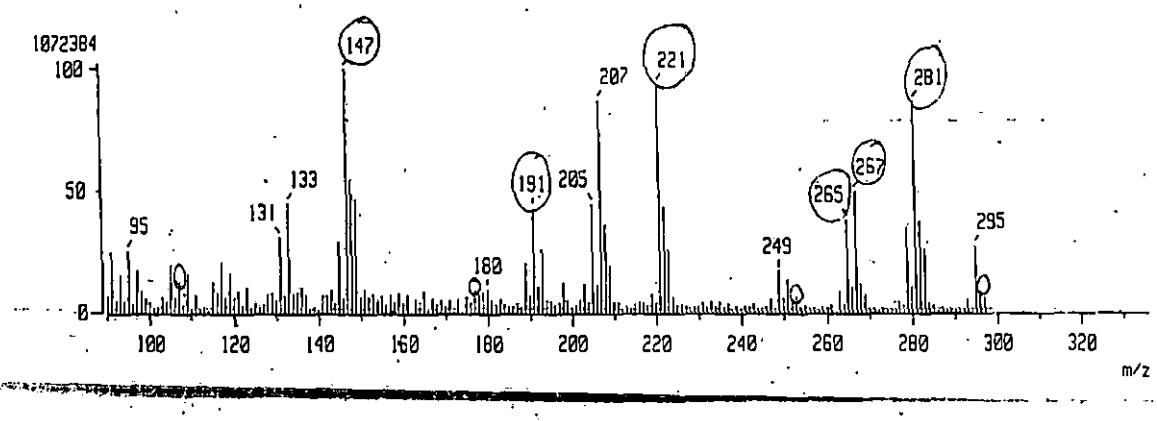


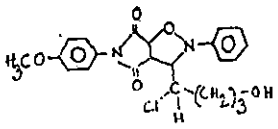
[Mass Spectrum]
Data : BE30APR196 Date : 30-Apr-2008 15:01
Sample: S-21 DR B CHAKRABORTY SIKKIM GOVT COLL. #2719
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.00 min Scan# : 1
BP : m/z 73.0000 Int. : 100.00



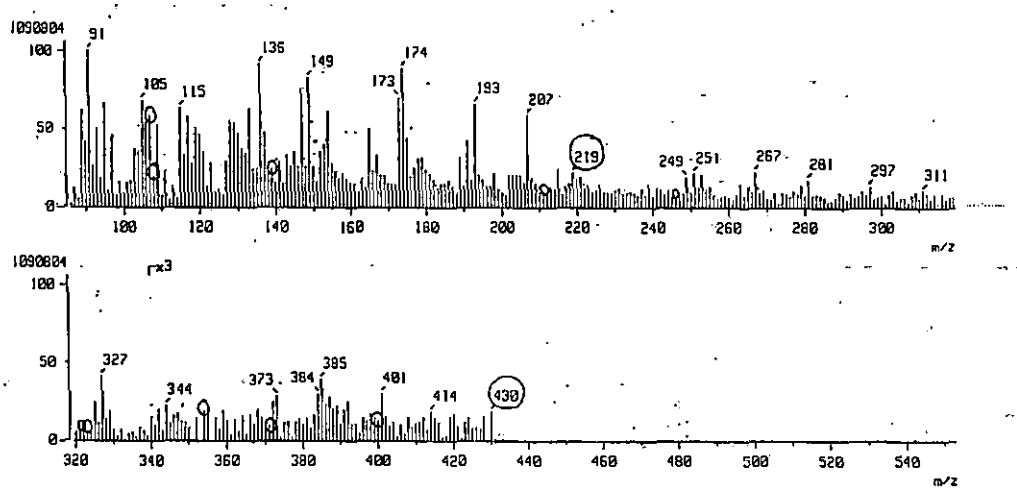


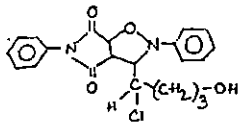
[Mass Spectrum]
Data : 7E16NOV123 Date : 16-Nov-2007 14:44
Sample: D-51 DR B CHAKRABORTY GANGATOK #2173
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.98 min Scan# : (8,10)
BP : m/z 147.0000 Int. : 100.00



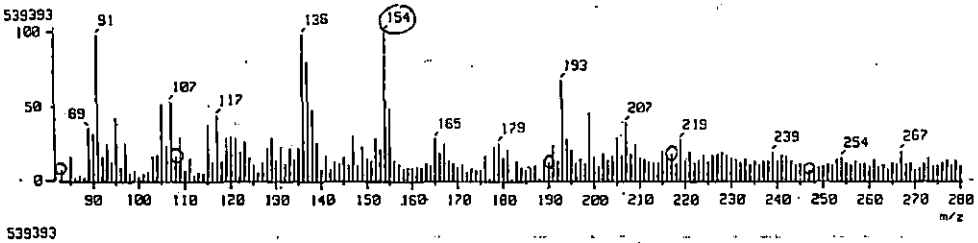


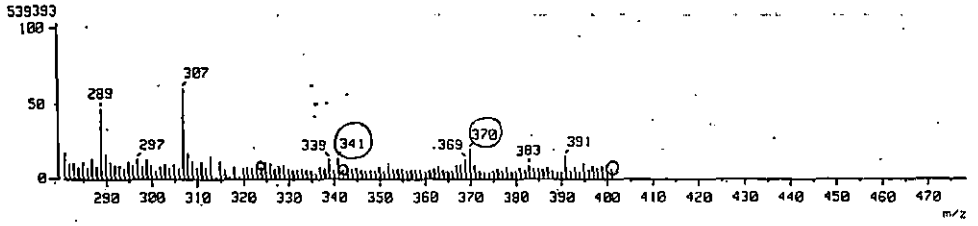
[Mass Spectrum]
Data : 7E21SEPT181 Date : 21-Sep-2007 10:56
Sample: S5 DR B CHAKRABORTY SIKKIM GOVT COLL TADONG #2081
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.00 min Scan# : (1,2)
BP : m/z 91.0000 Int. : 98.55

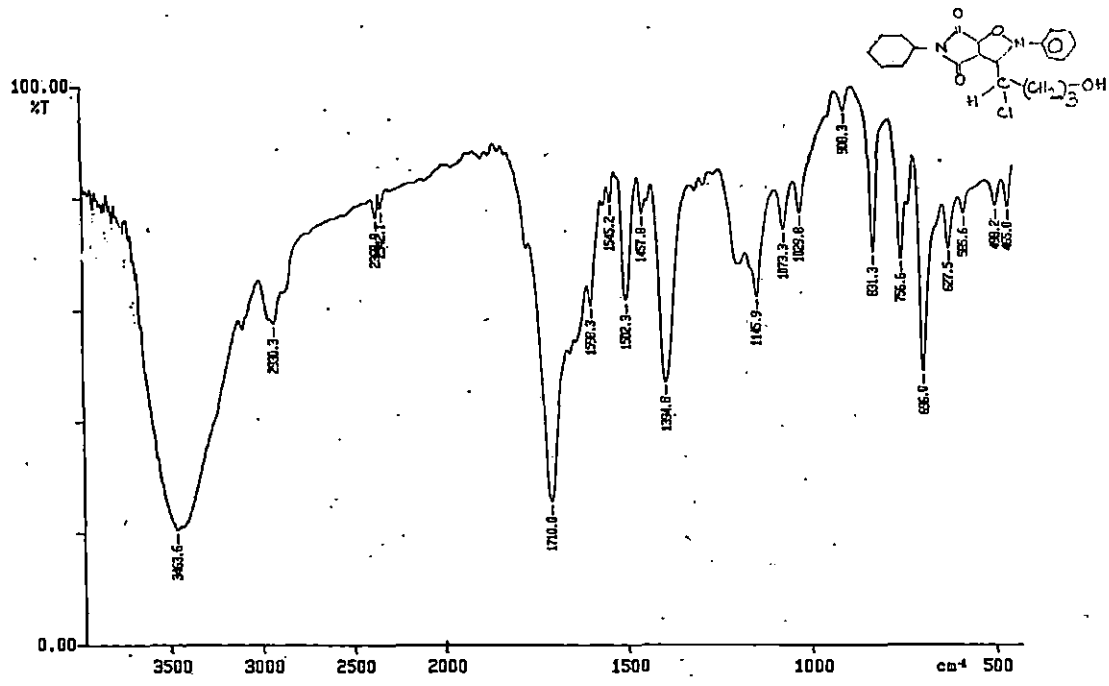




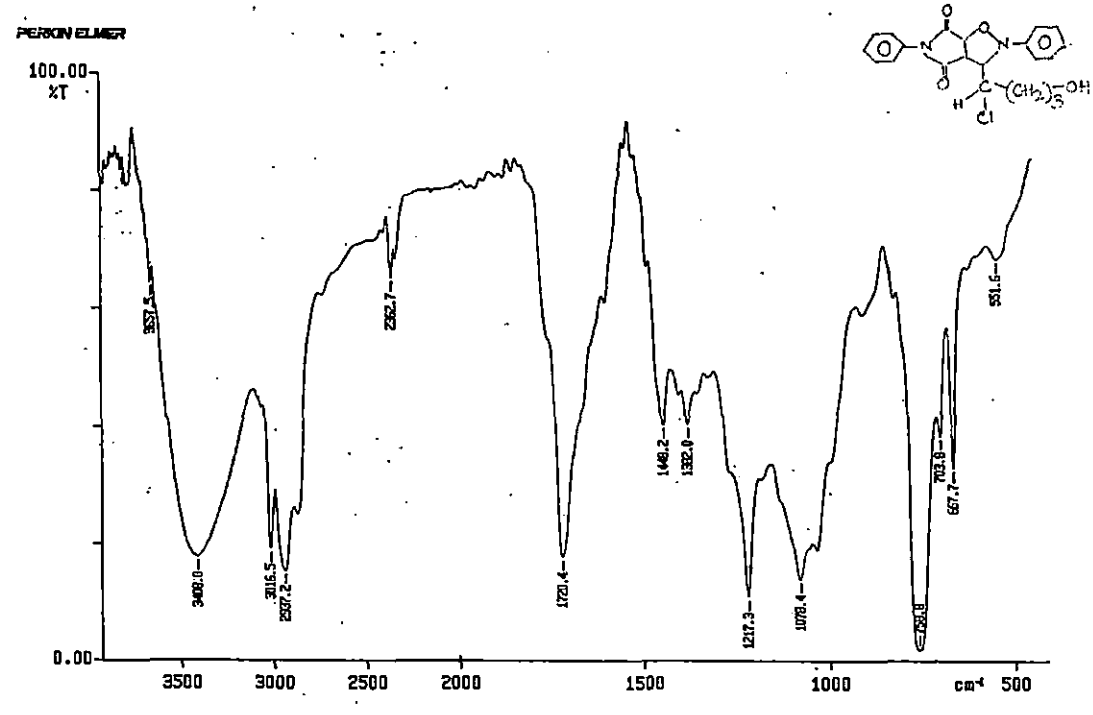
[Mass Spectrum]
Data : 7E10AUG117 Date : 13-Aug-2007 15:05
Sample: BOTTLE-37 DR B CHAKRABORTY SIKKIM GOVT COLL TADONG #1946
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.12 min Scan# : (1,3)
BP : m/z 154.0000 Int. : 49.99



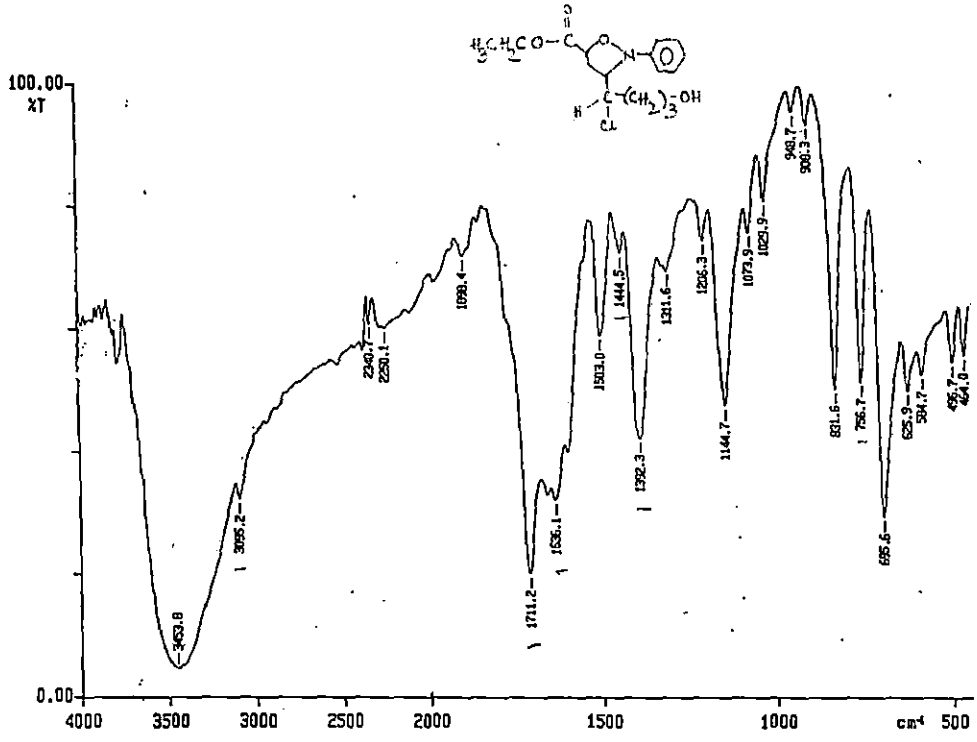




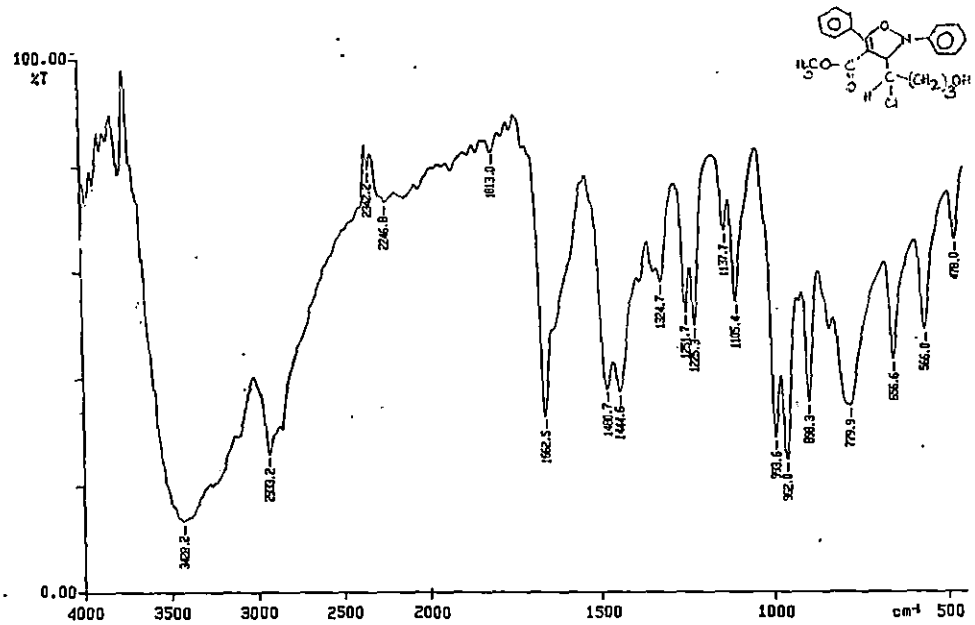
07/09/19 10:39 AH, CODE- S5
X: 4 scans, 4.0cm-1, flat, smooth, abex



07/10/24 10:44 PKA CODE- S-13
X: 4 scans, 4.0cm-1, flat, smooth, abex
SAIF No.-2173

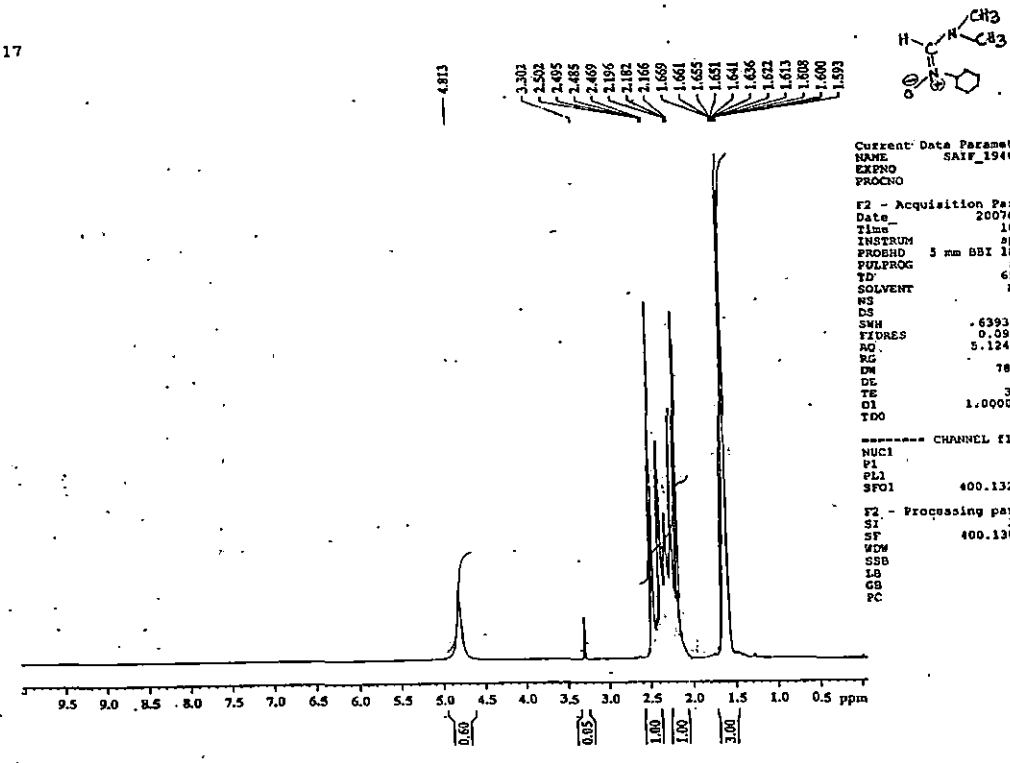


07/08/17 16:07 AH, CODE-32
X: 4 scans, 4.0cm-1, flat, smooth, abex
SAIF NO – 1946



07/08/17 16:08 AH, CODE-28
X: 4 scans, 4.0cm-1, flat, smooth, abex
SAIF NO – 1946

17



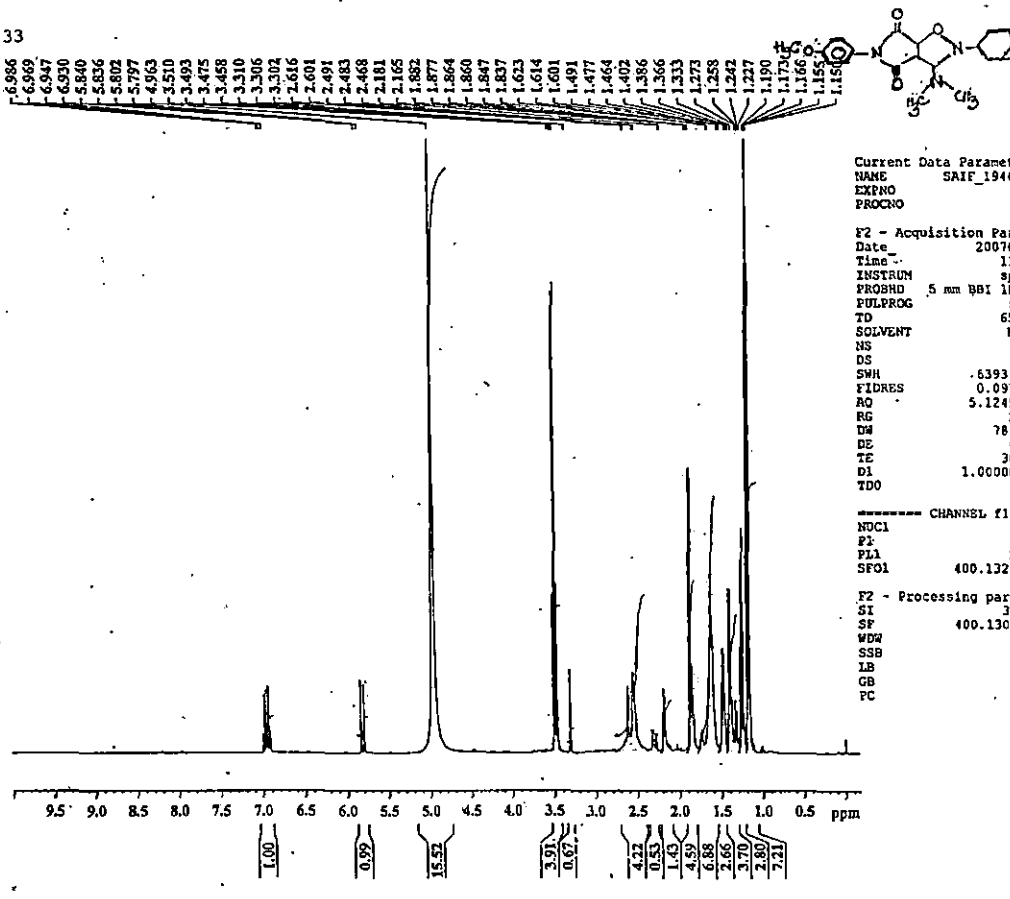
Current Data Parameters
NAME SAIF_1946_17
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070829
Time 10.43
INSTRUM spect
PROBHD 5 mm BBI 1H/D-
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 0
SWH 6393.862 Hz
FIDRES 0.097563 Hz
AQ 5.1249652 sec
RG 16
DW 78.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 2.50 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
SF 400.1300091 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

33

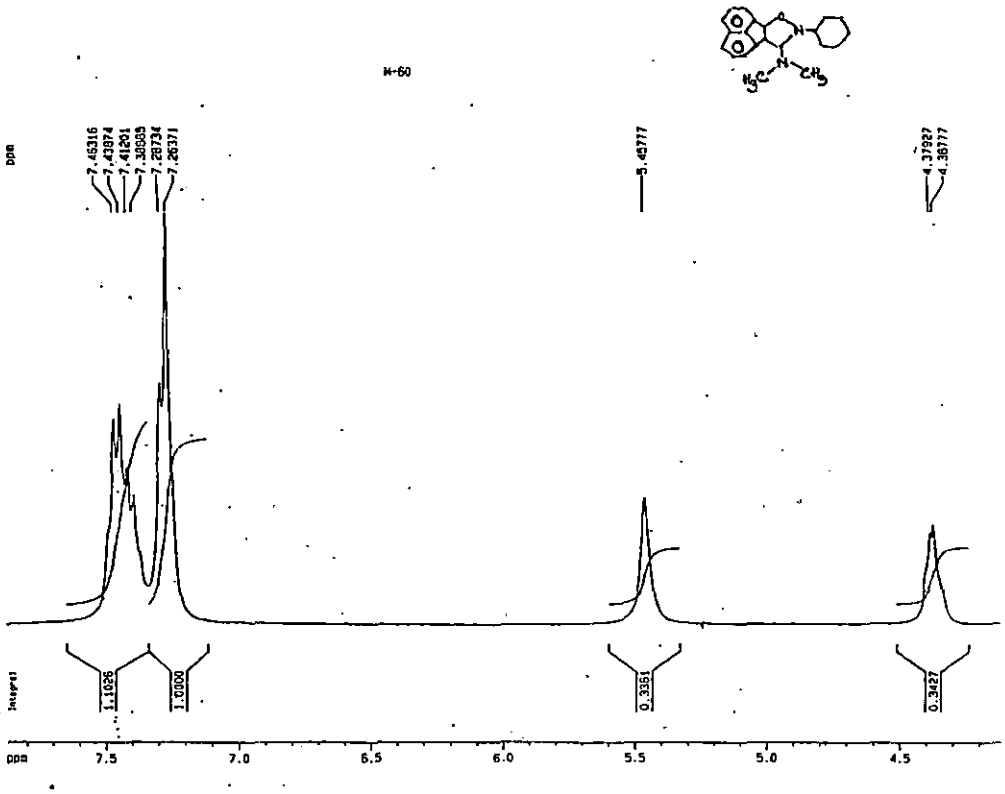


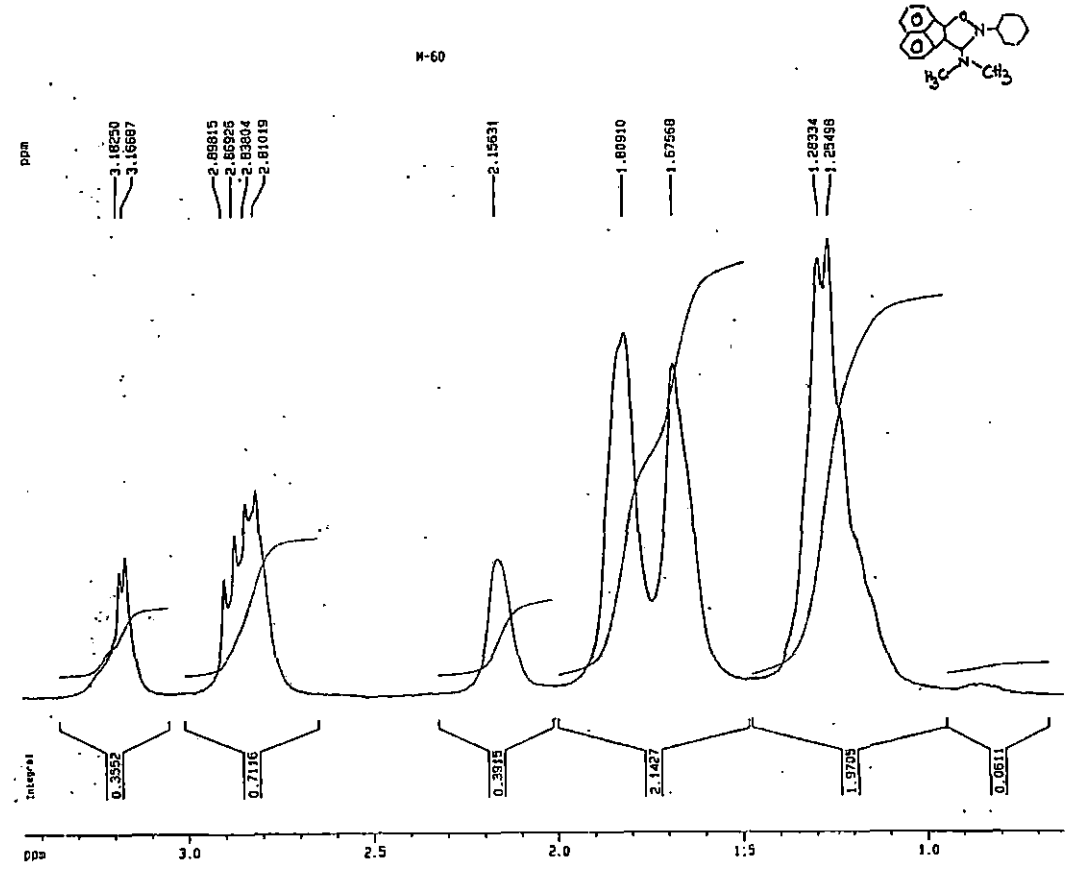
Current Data Parameters
NAME SAIF_1946_33
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070829
Time 11.20
INSTRUM spect
PROBHD 5 mm BBI 1H/D-
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 0
SWH 6393.862 Hz
FIDRES 0.097563 Hz
AQ 5.1249652 sec
RG 20.2
DW 78.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

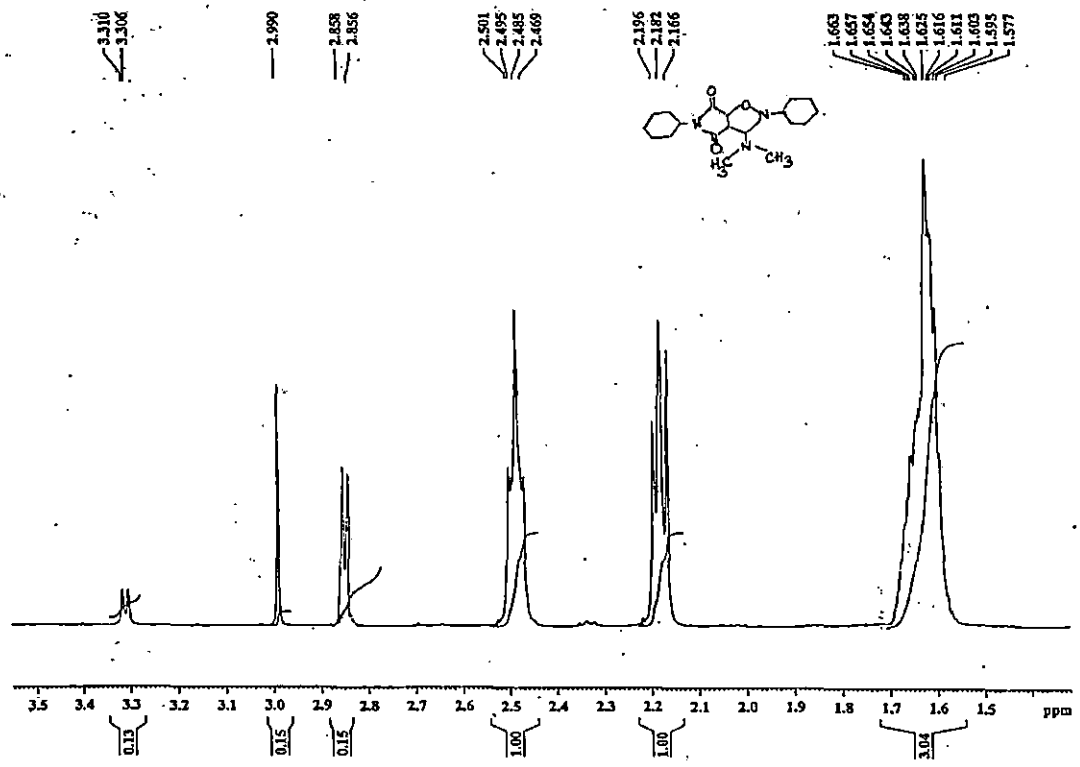
======== CHANNEL f1 ========
NUC1 1H
P1 7.00 usec
PL1 2.50 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
SF 400.1300091 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

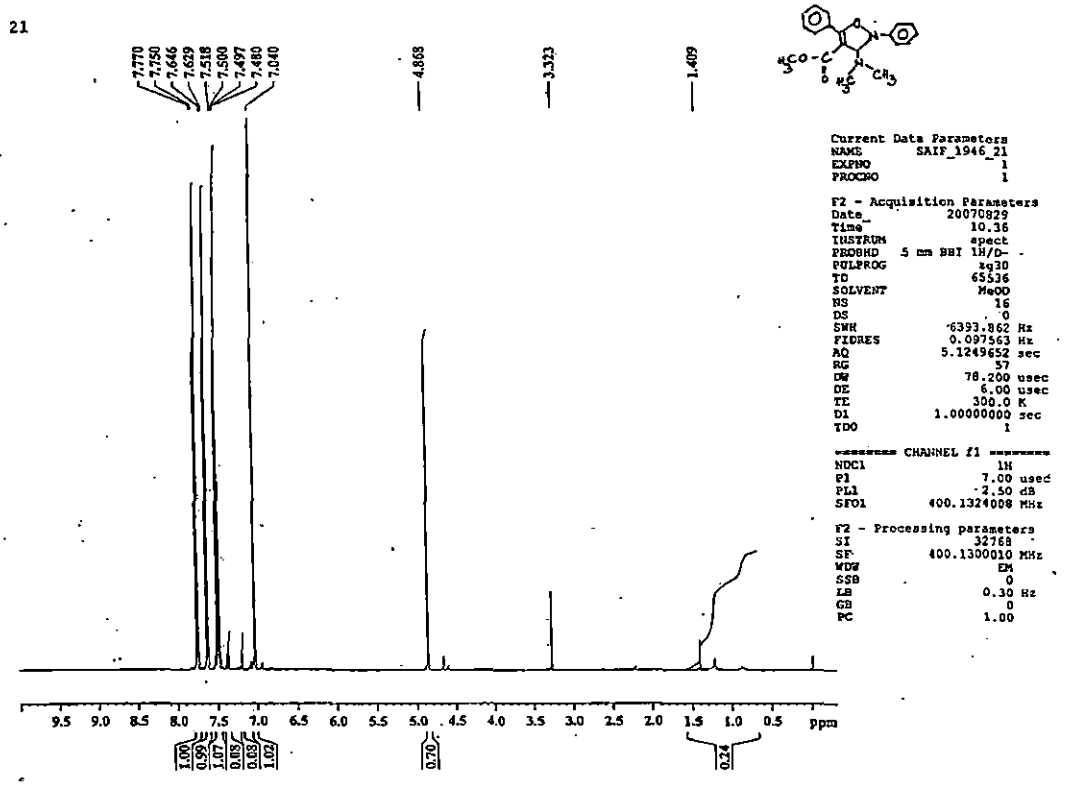

M-60
ppm
7.46316
7.43974
7.41201
7.30695
7.28734
7.26371
5.45777
4.37922
4.36177
Integral
1.1026
1.0000
0.3361
0.3427
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5


M-60
ppm
3.18250
3.16687
2.89815
2.86926
2.83804
2.81019
2.15631
1.80910
1.67568
1.28334
1.25498
Integral
0.3552
0.7116
0.3915
2.1427
1.9705
0.0611
ppm
3.0
2.5
2.0
1.5
1.0

25



21

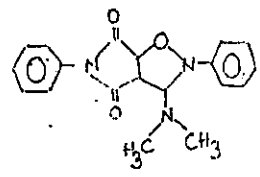



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Current Data Parameters
NAME          SAIF_1946_21
EXPNO                    1
PROCNO                   1

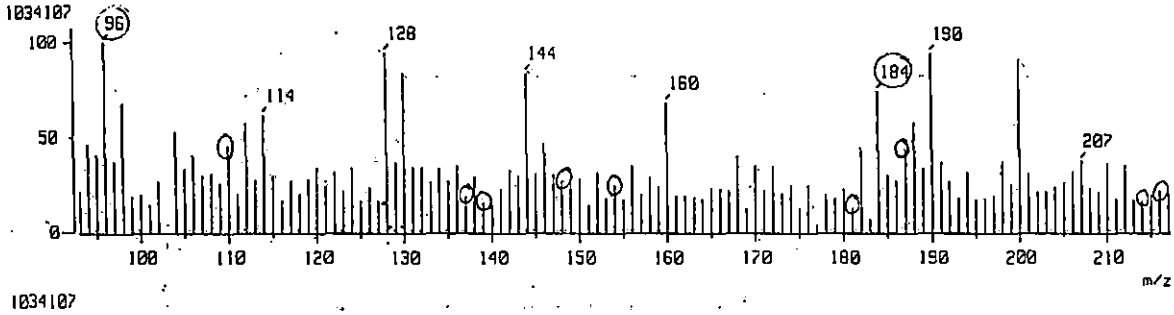
F2 - Acquisition Parameters
Date_             20070829
Time                 10.36
INSTRUM              spect
PROBHD   5 mm BBI 1H/D- -
PULPROG              zg30
TD                  65536
SOLVENT              MeOD
NS                      16
DS                       0
SWH              6393.862 Hz
FIDRES           0.097563 Hz
AQ               5.1249652 sec
RG                      57
DW                78.200 usec
DE                 6.00 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                      1

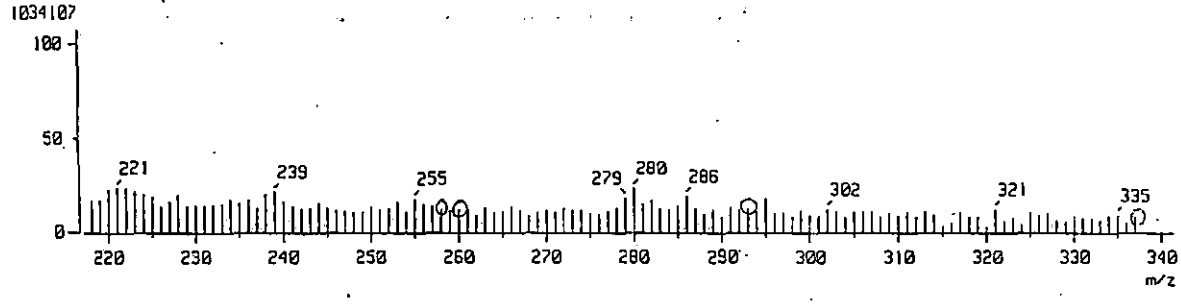
======== CHANNEL f1 ========
NUC1                    1H
P1                 7.00 usec
PL1               -2.50 dB
SFO1         400.1324008 MHz

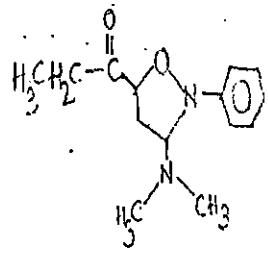
F2 - Processing parameters
SI                   32768
SF           400.1300010 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```



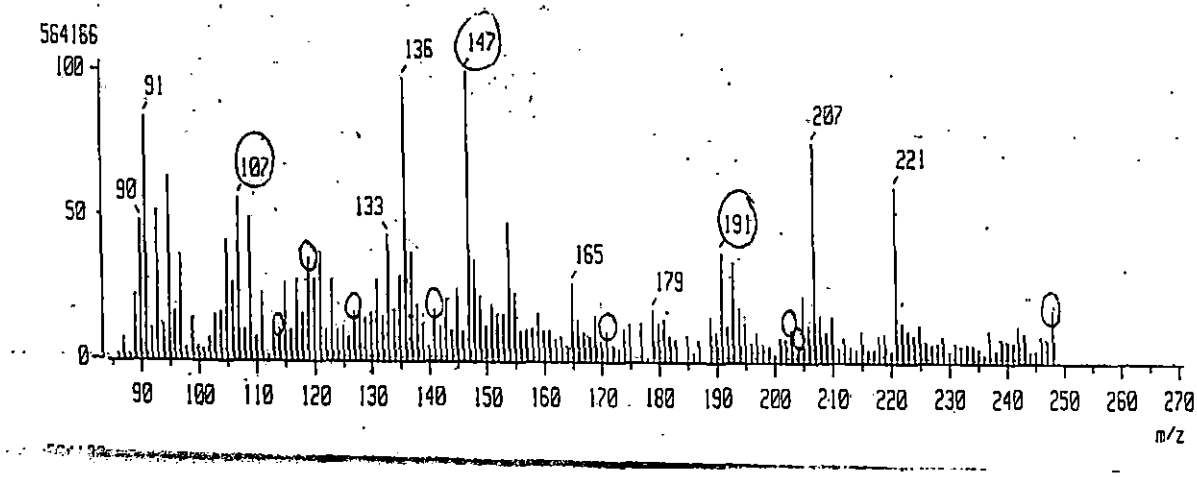
[Mass Spectrum]
Data : 7E10AUG116 Date : 13-Aug-2007 14:58
Sample: BOTTLE-35 DR B CHAKRABORTY SIKKIM GOVT COLL TADONG #1946
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.12 min Scan# : (1,3)
BP : m/z 96.0000 Int. : 91.91

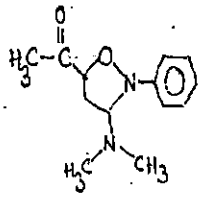




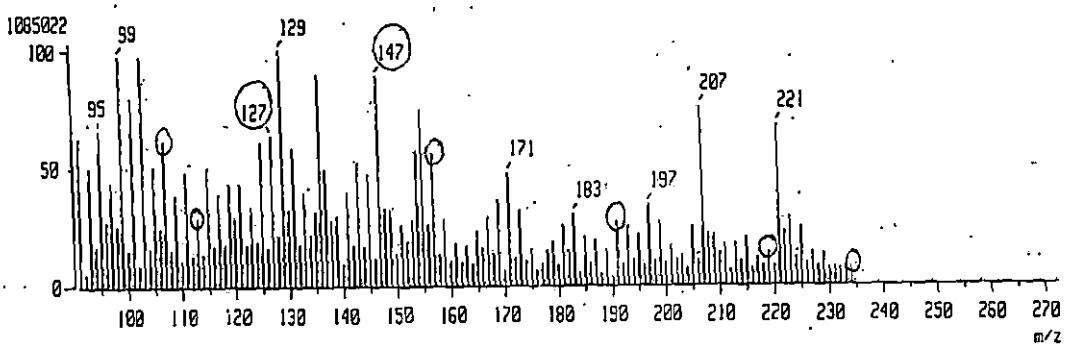


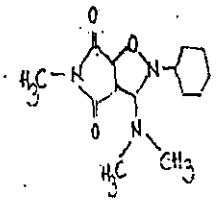
[Mass Spectrum]
Data : 7E12JULY099 Date : 12-Jul-2007 14:20
Sample: BOTTLE-15 DR BHASKAR CHAKRABORTY TADONG #1840
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.12 min Scan# : (2,3)
BP : m/z 147.0000 Int. : 52.28



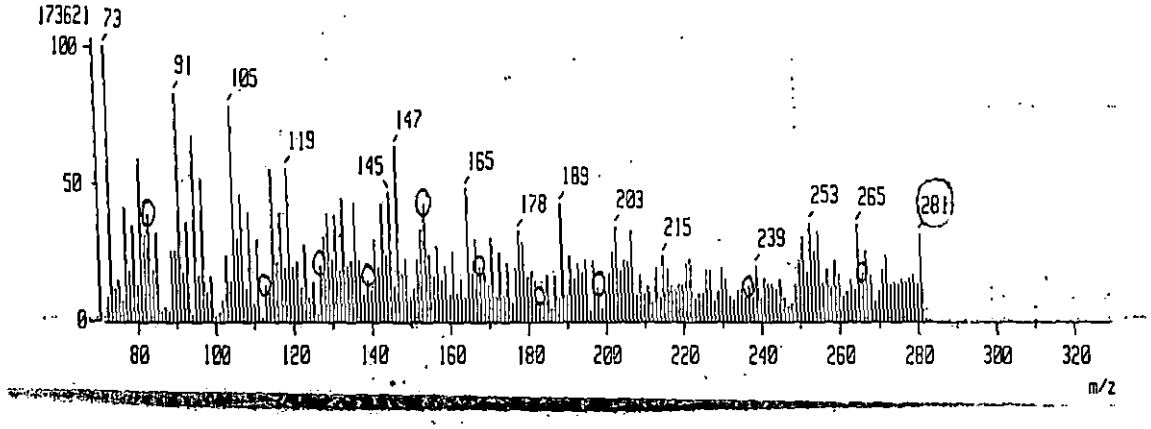


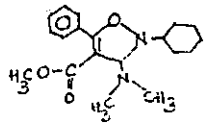
[Mass Spectrum]
Data : 7E10AUG114 Date : 13-Aug-2007 14:46
Sample: BOTTLE-27 DR B CHAKRABORTY SIKKIM GOVT COLL TADONG #1946
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.00 min Scan# : (1,2)
BP : m/z 129.0000 Int. : 100.00



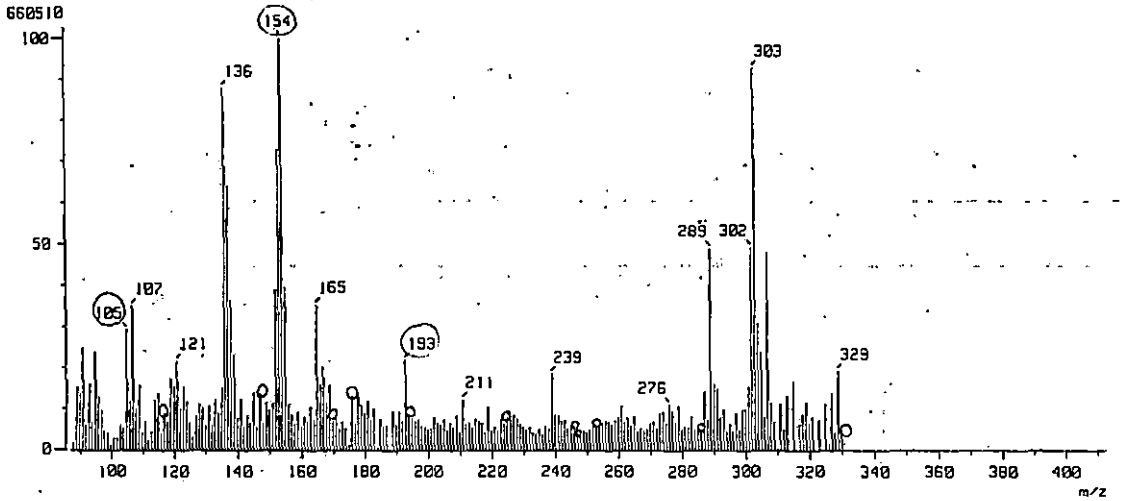


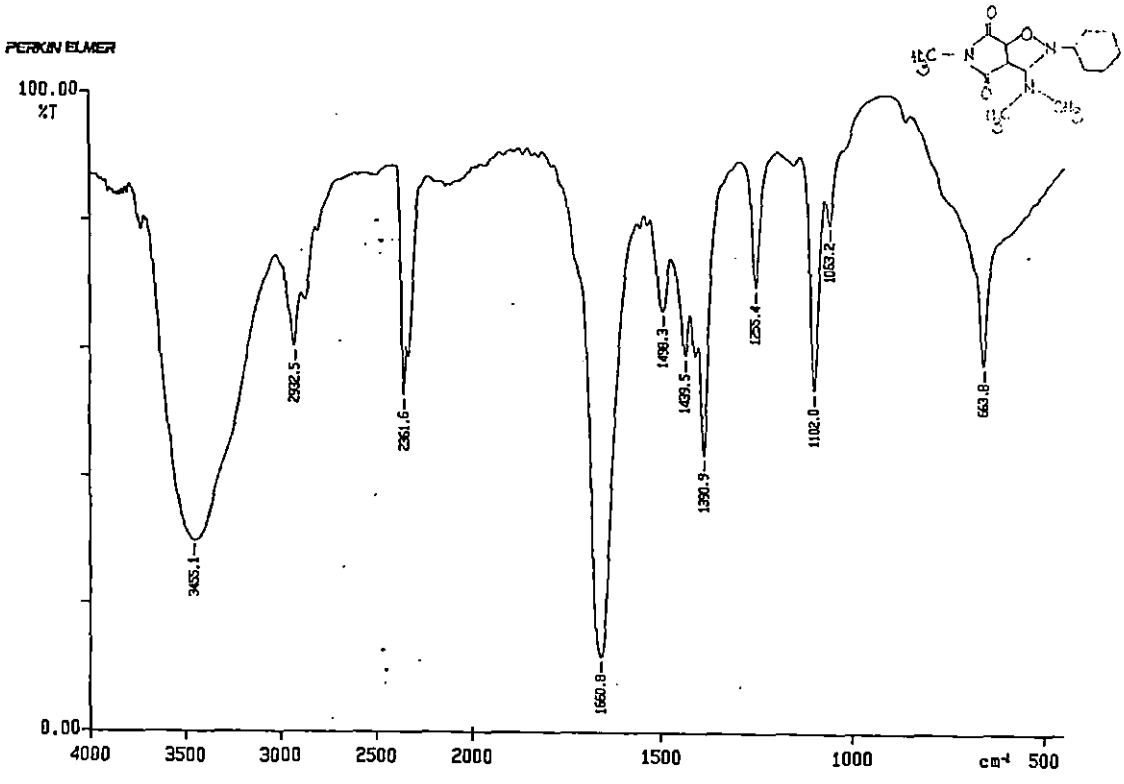
[Mass Spectrum]
Data : 7E12JULY097 Date : 12-Jul-2007 14:04
Sample: BOTTLE-7 DR BHASKAR CHAKRABORTY TADONG #1840
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.00 min Scan# : (1,2)
BP : m/z 73.0000 Int. : 16.09



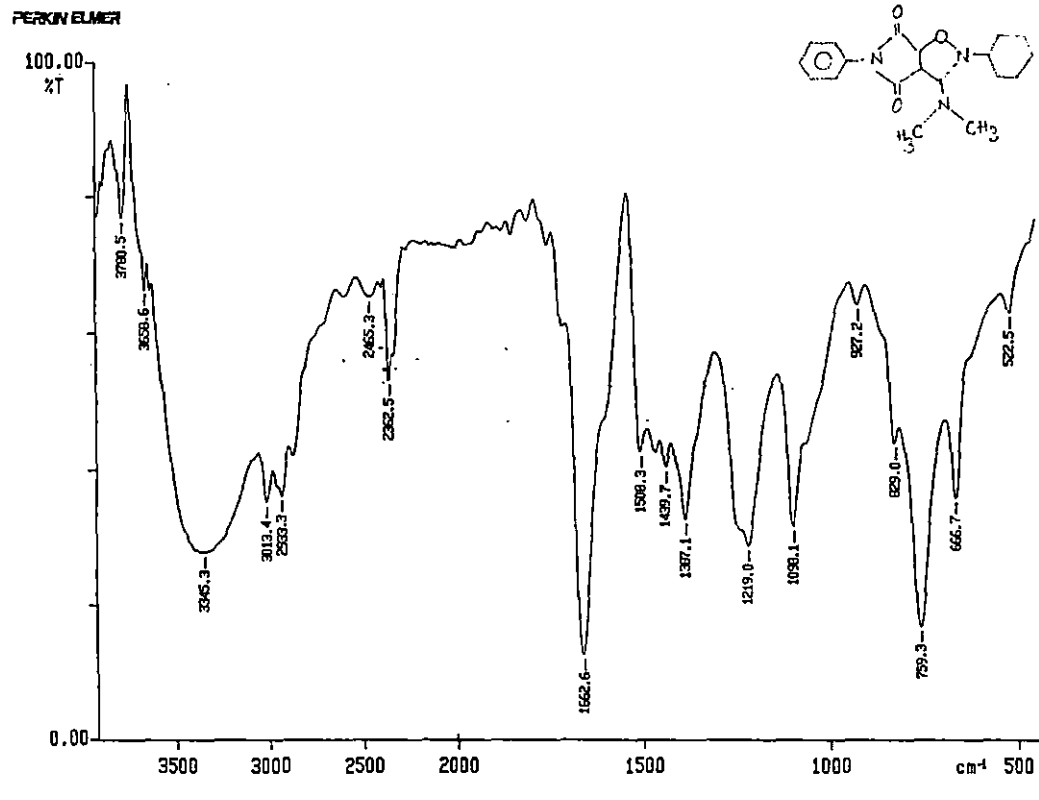


[Mass Spectrum]
Data : 7E10AUG112 Date : 13-Aug-2007 14:30
Sample: BOTTLE-19 DR B CHAKRABORTY SIKKIM GOVT COLL TADONG #1946
Note : -
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion (MF-Linear)
RT : 0.49 min Scan# : (5,6)
BP : m/z 154.0000 Int. : 61.39



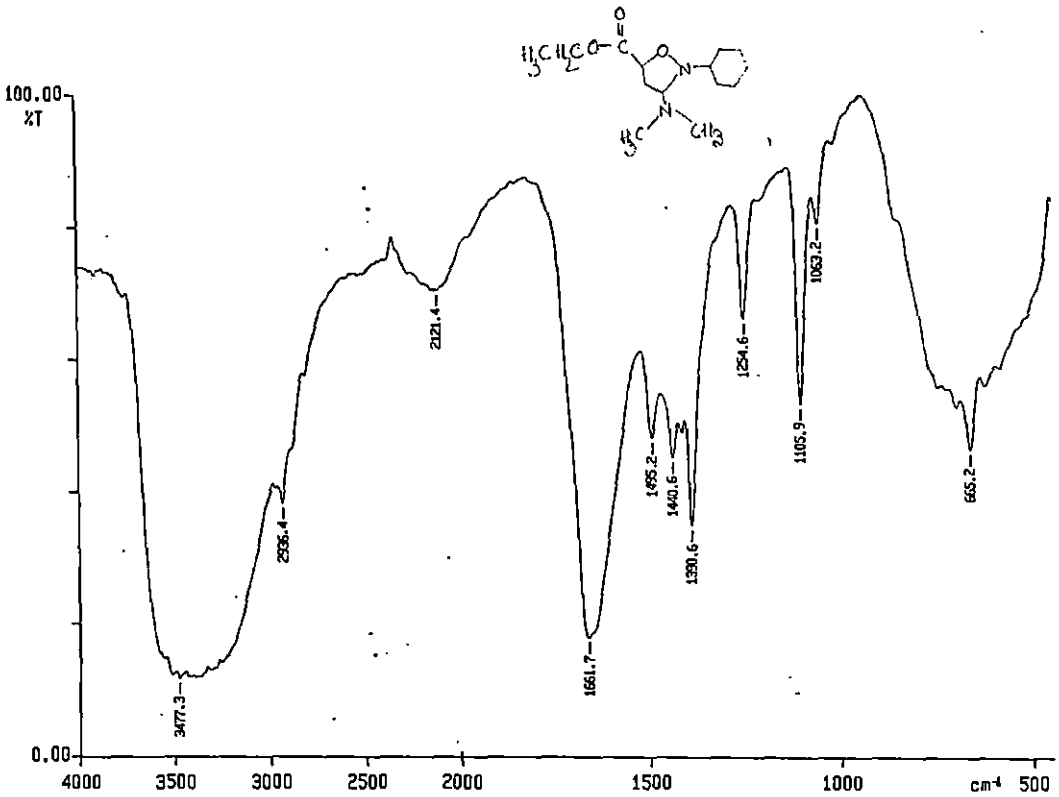


08/04/28 09:31 AH, CODE- M-64
X: 4 scans, 4.0cm-1, flat, smooth, abex



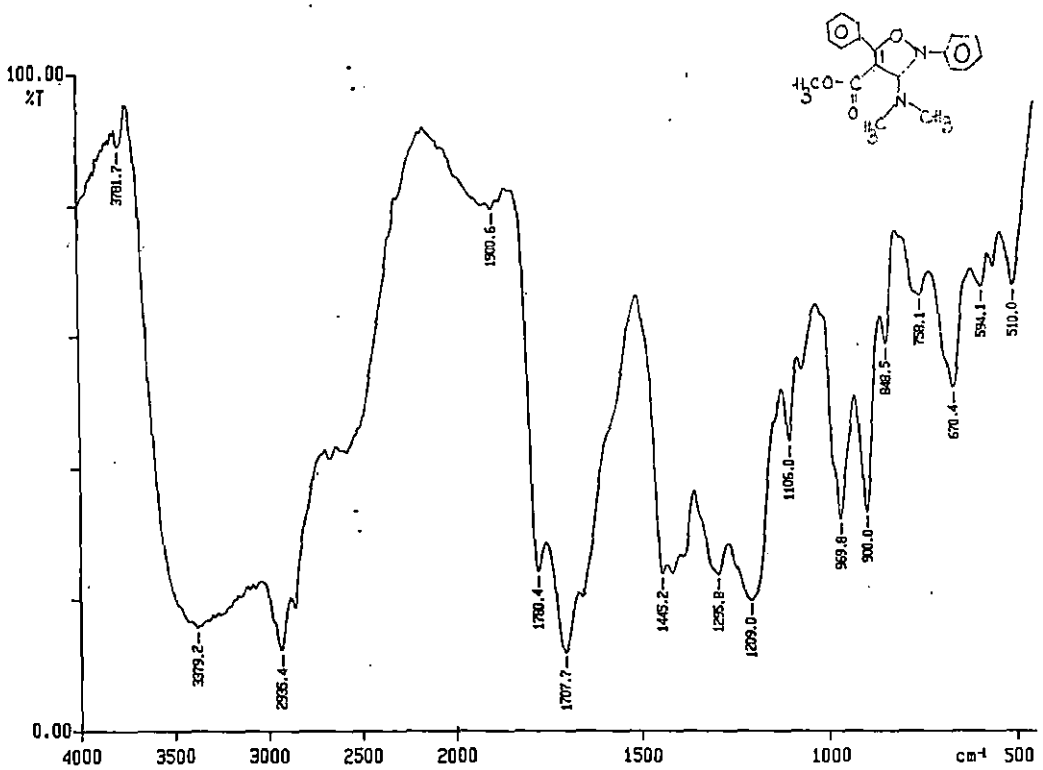
07/10/24 10:41 PKA CODE- 46
X: 4 scans, 4.0cm-1, flat, smooth, abex

SAIF No.- 2173



07/08/17 16:02 AH, CODE-39
X: 4 scans, 4.0cm-1, flat, smooth, abex

SAIF NO - 1946



07/08/17 16:05 AH, CODE-34
X: 4 scans, 4.0cm-1, flat, smooth, abex

SAIF NO - 1946