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DIELS-ALDER CYCLOADDITION REACTIONS OF ENAMINOTHIONS WITH NITROALKENES

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Abstract : Diels-Alder cycloaddition reactions of enaminothiones (1) with nitroalkenes (2) result in very good yields (78-90%) of (2R,3S,4R)-6-aryl-2-aryl/furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyrans (3) as exclusive stereoisomers. The reactions of 3-N-arylamino-1-phenylpropene-1-thiones (5) with 2 leading to stereospecific formation of (2R,3S,4S)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyrans (6) and their conversions to thermodynamically more stable (2R,3S,4R)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyrans (7) is also reported.

Introduction :

The enaminothiones have been shown to participate as 4π component in Diels-Alder cycloaddition reactions with a large variety of carbon-carbon dienophiles[1-4]. The nitroalkenes have also been reported to effectively participate as 4π component in Diels-Alder cycloaddition reactions with enamines and related carbon-carbon dienophiles[5-10]. We have investigated the reactions of enaminothiones with nitroalkenes with a view to examine the nature of cycloaddition pathway followed in these cases.

Results and Discussions :

The treatment of 3-dimethylamino-1-arylpropene-1-thione (1) with β-nitroalkenes in methylene chloride at room temperature, resulted in very good yields of stereospecific (4+2) cycloadducts characterized as (2R,3S,4R)-6-aryl-2-aryl/furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyrans (3) (Scheme 1). To our knowledge these cycloadducts perhaps represent the only examples of enaminothiones cycloadditions where relative stereochemistry at C-2, C-3 and C-4 could be clearly assigned. It is because in almost all known cases of enaminothiones cycloadditions the initially formed cycloadducts undergo spontaneous elimination of neutral molecule like dimethylamine leading to the products having a C_3-C_4 double bond. The relative stereochemistry at C-2, C-3 and C-4 have been assigned on the basis of coupling constants between the protons attached to these carbon atoms. The ^1H n.m.r. spectrum ($CDCl_3$) of cycloadduct 3a, for example, showed two singlets at δ 2.33(3H) and δ 2.66(6H) assigned to H_3C-Ar and $N(CH_3)_2$ respectively. The doublet of doublet at δ 4.26($J_{3,4}$= ~11Hz, $J_{4,5}$= ~3Hz), the doublet at δ 4.79($J_{2,3}$= ~11Hz), another doublet of doublet at δ 5.26($J_{2,3}$= ~11Hz, $J_{3,4}$= ~11Hz) and the doublet at δ 6.00($J_{4,5}$= ~3Hz) are assigned to H_4, H_2, H_3 and H_5 respectively. The coupling constants $J_{2,3}$= ~11Hz and $J_{3,4}$= ~11Hz clearly indicate a trans diaxial arrangement for H_2H_3 and H_3H_4. Also, the

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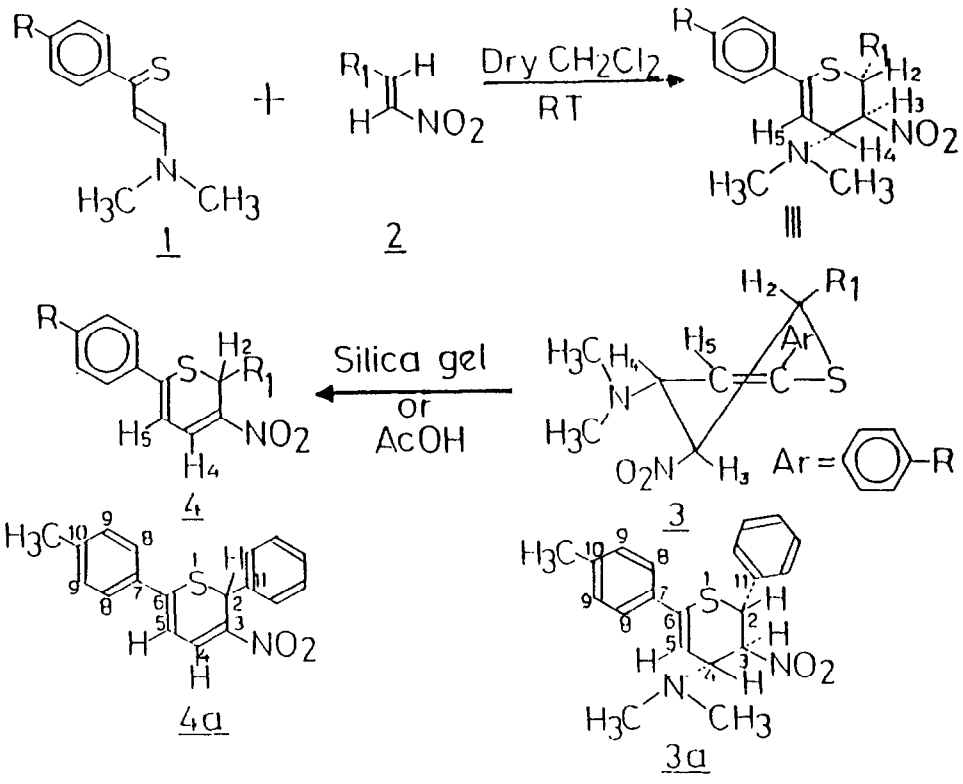


1–4	R	R_1	1–4	R	R_1
a	CH_3	C_6H_5	f	Cl	
b	CH_3	p-$OCH_3C_6H_4$	g	H	C_6H_5
c	CH_3		h	H	p-$OCH_3C_6H_4$
d	Cl	C_6H_5	i	H	
e	Cl	p-$OCH_3C_6H_4$			

Scheme 1

coupling constant value $J_{4,5}$ of about 3Hz indicates the quasiaxial orientation for H_4[11]. These values of coupling constants between $H_{2,3}$, $H_{3,4}$ and $H_{4,5}$ are consistent with a stereochemistry resulting from a concerted cycloaddition involving the endo approach of β-nitro styrene to the E-isomer of enaminothione (1). The theoretical calculations of Hoffmann and Woodward[12] support the predominance of endo approach products with dienophiles possessing a conjugated π system in a kinetically controlled

reaction. A preferred boat conformation has been proposed[13] for 3,6-dihydro-2H-thiopyran and established for a number of unsaturated six-membered sulphur heterocycles by X-ray studies[14]. On the contrary, the thiopyran derivatives 3 perhaps exist in half chair conformation in $COCl_3$ as was established by Vyas and Hay[15] for 3,6-dihydro-2H-thiopyrans on the basis of Garbisch equation[16]. Further proof for the structure of 3a was obtained from ^{13}C n.m.r. spectral assignments made with the help of off resonance decoupled spectrum which exhibited peaks at δ 21.07($\underline{C}H_3$-Ar), 40.51 [$N(\underline{C}H_3)_2$], 49.02(C-2), 65.99(C-4), 89.29(C-3), 115.54(C-5), 139.02(C-6/7), 138.20(C-7/6), 134.85(C-10/11) and 134.15(C-10/11). The other aromatic carbons are observed at δ 126.34, 127.34, 128.34, 128.29 and 129.28. Its mass spectrum showed the absence of molecular ion peak and exhibited strong peaks due to retro Diels-Alder fragments at m/z 205 and m/z 149.

The white cycloadducts 3 undergo facile elimination of dimethylamine either on eluting it through silica gel column or on stirring its methylene chloride solution with a few drops of acetic acid, resulting in good yields (65-80%) of hitherto unknown red crystalline 6-aryl-2-aryl/furyl-3-nitro-2H-thiopyrans (4). The thiopyran 4a for example analyzed satisfactorily for $C_{18}H_{15}NO_2S$. Its ^1H n.m.r. spectrum ($CDCl_3$) showed two singlets at δ 2.36 and 5.69 assigned to $\underline{H}_3C$-Ar and H_2 respectively. The vinylic protons H_5 and H_4 appeared as doublets at δ 6.63 and δ 8.00($J_{4,5}$ = ~8Hz) and nine aromatic protons are observed as a multiplet in the region δ 7.13-7.50. Its mass spectrum exhibited the molecular ion peak at m/z 309 (4) and base peak at m/z 263 corresponding to fragment (M^+-NO_2). Further structural proof for 4a was obtained from its off resonance decoupled ^{13}C n.m.r. spectrum which showed peaks at δ 21.31 ($H_3\underline{C}$-Ar), 39.98(C-2), 113.31(C-5), 147.42(C-3), 141.38(C-6/7), 139.79(C-7/6), 136.76 (C-10/11) and 133.09(C-11/10). Other aromatic carbons and C-4 are observed at δ 126.46, 127.57, 127.98, 128.39, 128.75, 129.51 and 131.15. It may be mentioned here that in presence of bases like triethylamine the benzene/methylene chloride solutions of 3 undergo very slow elimination of dimethylamine even under refluxing conditions. This fact probably also indicates cis arrangement for H_3 and $-N(CH_3)_2$ in thiopyran derivatives 3. It has also been observed that dissolution of white thiopyran derivatives 3 in methylene chloride result in deep red solution and the white thiopyran derivatives 3 are recovered unchanged on removal of solvent. It may either be due to the formation of a charge transfer complex between 1 & 2 or due to partial retro Diels-Alder reaction of 3. But thiopyran derivatives 3 definitely undergo retro Diels-Alder fragmentation on refluxing in methylene chloride as has been observed by formation of (4+2) cycloadduct of enaminothione and acrylamide on refluxing equimolar amounts of 3 and acrylic amide in methylene chloride.

In order to examine stereochemical influence on the course of these cycloaddition reactions we have investigated the reactions of nitroalkenes (2) with 3-N-arylamino-1-phenylpropene-1-thiones (5) which has preferred z-configuration because of

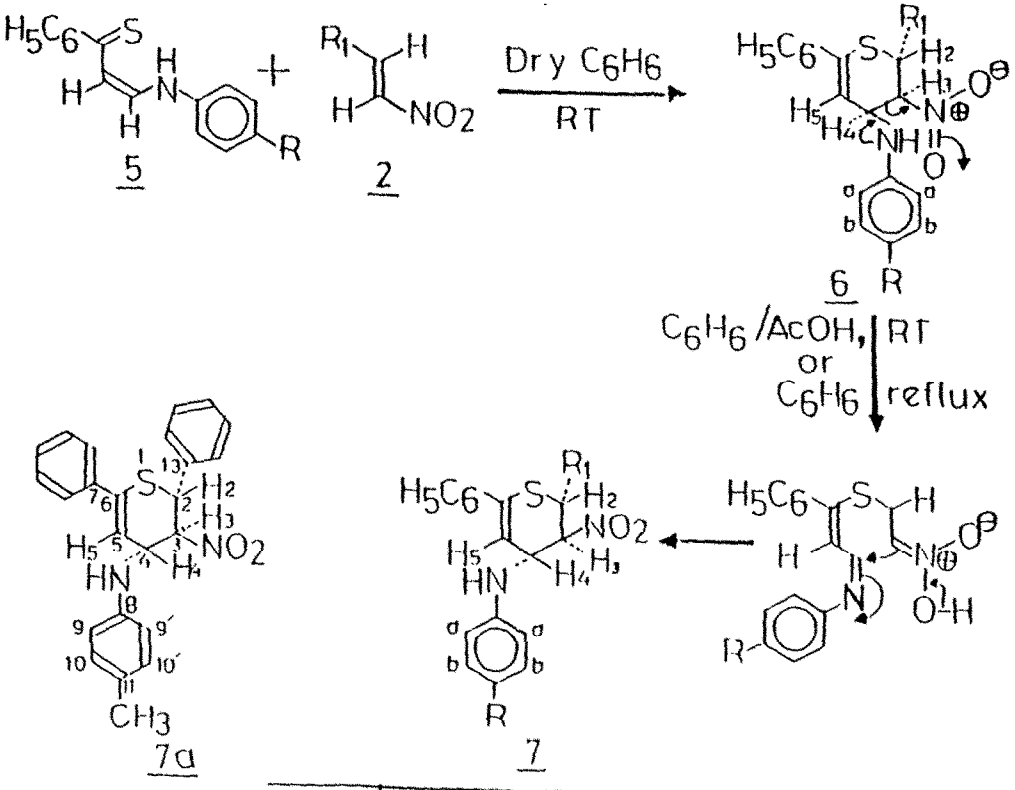
hydrogen bonding between NH and sulphur of thione. Thus, the treatment of enaminothione (5) with β-nitroalkenes (2) in anhydrous benzene yielded 70-78% of previously unknown (2R,3S,4S)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran(6) (Scheme 2). The structure 6 could be assigned to these thiopyran derivatives on the basis of analytical and spectral evidences. Compound 6a, for example, analyzed well for $C_{24}H_{22}N_2O_2S$ and its mass spectrum showed the absence of molecular ion peak but exhibited strong peaks at m/z 149 and m/z 253 corresponding to retro Diels-Alder fragments. Its ^1H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 2.20 corresponding to $\underline{H}_3C$-Ar and a broad doublet at δ 3.76 exchangeable with D_2O assigned to NH proton. A multiplet changing to a clear dd at δ 4.80 ($J_{3,4}$= ~4Hz, $J_{4,5}$= ~6Hz) could be assigned to H_4. The doublet at δ 5.00 ($J_{2,3}$= 10-11Hz), dd at δ 5.36($J_{2,3}$= 10-11Hz, $J_{3,4}$= ~4Hz) and another doublet at δ 6.18($J_{4,5}$= ~6Hz) are assigned to H_2,H_3 and H_5 respectively. The AA'BB' kind of splitting patterns at δ 6.50 and δ 6.90 (J_{ab}= ~8Hz) are assigned to protons Ha and Hb respectively. Other ten aromatic protons are observed as a multiplet in the region δ 7.13-7.60. The coupling constant values $J_{2,3}$=10-11Hz, $J_{3,4}$= ~4Hz, $J_{4,5}$= ~6Hz indicate trans diaxial arrangement for H_2,H_3 and quasi equatorial arrangement for H_4. These coupling constant values are consistent with a stereochemistry resulting from a cycloaddition of z-isomer of enaminothiones (5) involving an endo transition state. Hence it may be concluded that the cycloaddition of 5 and 2 proceeds in a concerted manner leading to the stereospecific formation of 6.

The solutions of kinetically controlled thiopyran derivatives 6 having equatorial NO_2 at C-3 and axial -NH-Ar at C-4 appear to undergo slow transformation to thermodynamically more stable thiopyran derivatives 7 in which NO_2 at C-3 and -NHAr at C-4 are equatorial. The transformations of 6 to their epimers 7 have been realized by

(i) stirring a solution of 6 in dry benzene containing few drops of acetic acid at room temperature for two hours.

(ii) refluxing a solution of 6 in dry benzene for five hours.

The structure 7 has been assigned to these products on the basis of analytical and spectral data. The analytical results indicated the compound 7a has molecular formula $C_{24}H_{22}N_2O_2S$. Its mass spectrum exhibited the molecular ion peak at m/z 402 and peaks due to retro Diels-Alder fragments at m/z 253 and m/z 149. Its i.r. spectrum showed the absorption bands at 3400 cm^{-1} (broad, ν_{NH}), 1610 cm^{-1} ($\nu_{C=C}$) and 1550 cm^{-1} (ν_{NO_2}). The characteristic evidence in support of assigned structure 7a was obtained from its ^1H n.m.r. spectrum. The singlet at δ 2.23 and a broad doublet at δ 3.63, exchangeable with D_2O, are assigned to the three methyl protons and NH proton respectively. The doublet at δ 4.95 ($J_{2,3}$= ~11Hz) is assigned to the proton H_2. A multiplet converting to a dd on D_2O exchange at δ 5.09 could be assigned to proton H_4



5-7	R	R_1
a	CH_3	C_6H_5
b	Cl	C_6H_5
c	H	C_6H_5
d	H	p-$OCH_3C_6H_4$
e	Cl	p-$OCH_3C_6H_4$

Scheme 2

$J_{4,5}$= ~ 3Hz, $J_{3,4}$= ~ 11Hz). Another doublet of doublet at δ 5.31 have been assigned to proton H_3($J_{2,3}$= $J_{3,4}$= ~11Hz). The vinylic proton H_5 appeared as a doublet at δ 6.03($J_{4,5}$= 3Hz) which in case of 6a appeared as a doublet at δ 6.18 ($J_{4,5}$= ~6Hz). The AA'BB' splitting patterns at δ 6.63 and 7.02 (J_{ab}= 8Hz) are assigned to protons Ha and Hb respectively. The multiplet in the region δ 7.13-7.53 is due to ten aromatic protons. The coupling constant value $J_{4,5}$ of 3Hz indicates a quasi axial orientation

of H_4. Further proof for the structure of 7a was obtained from its ^{13}C n.m.r.($CDCl_3$) δ ppm spectral assignments made with the help of off resonance decoupled spectrum. It showed peaks at δ 20.37 ($H_3\underline{C}$-Ar), 49.02(C-2), 57.01(C-4), 91.23(C-3), 115.12 (C-9/C-9'), 119.47(C-5), 129.98(C-11), 133.80(C-12), 136.73(C-6/C-7), 137.15(C-6/C-7) and 142.90(C-8). Other aromatic carbons are observed at δ 126.46, 128.48, 128.63, 129.16 and 129.34. The conversion of thiopyran derivatives 6 to its epimer 7 probably takes place by initial ring opening of 6 to give the intermediate 8 which undergoes ring closure leading to 7.

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Experimental Section :

M.Ps were determined on a Toshniwal melting point apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 297 spectrometer in KBr. ^1H n.m.r. spectra were obtained on Varian EM-390, 90 MHz instrument with $SiMe_4$ as internal standard in deuteriochloroform unless otherwise stated. Mass spectra were recorded on Jeol JMS D-300 spectrometer.

Starting Materials : 3-Dimethylamino-1-arylpropene-1-thione[17], 3-N-arylamino-1-phenylpropene-1-thione[18],[19], β-nitrostyrene[20], β-nitro-p-methoxystyrene[21] and β-nitro-α-(α-furyl)-ethylene[22] were prepared according to the known procedures.

General procedure for the preparation of (2R,3S,4R)-6-aryl-2-aryl/furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyrans (3a-i) :- The solution of a mixture of 3-dimethylamino-1-arylpropene-1-thione(1) (0.0048 mol) and β-nitroalkene (2) (0.0048 mol) in dry dichloromethane (20 ml) was stirred at room temperature for 20 minutes. The solvent was removed under reduced pressure and the product (3) thus obtained was recrystallized from benzene.

(2R,3S,4R)-p-Methylphenyl-2-phenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran(3a):- White crystals; (90%); m.p. 140°C; ν_{max} 1600, 1545, 1300 cm^{-1}; δ_H 2.33(3H,s,$C\underline{H}_3$), 2.66(6H,s,$N(C\underline{H}_3)_2$), 4.26(1H,dd,H_4,$J_{3,4}$= ~ 11Hz & $J_{4,5}$= ~3Hz), 4.79(1H,d,H_2,$J_{2,3}$= ~11Hz), 5.26(1H,dd,H_3,$J_{2,3}$= 11Hz & $J_{3,4}$= ~11Hz), 6.00(1H,d,H_5,$J_{4,5}$= ~3Hz), 7.06-7.40(9H,m,Ar$\underline{H}$); δ_C 21.07($\underline{C}H_3$), 40.51($N(\underline{C}H_3)_2$), 49.02(C-2), 65.99(C-4), 89.29(C-3), 115.54(C-5), 139.02(C-6/7), 138.20(C-7/6), 134.85(C-10/11), 134.15(C-11/19), 126.34, 127.34, 128.34, 128.98, 129.28($\underline{C}H$,ArH). (Found : C,68.27; H,6.45; N,7.90. $C_{20}H_{22}N_2O_2S$ requires : C,67.80; H,6.21; N,7.91%): m/z 205(M^+-149), 149(M^+-205).

(2R,3S,4R)-6-p-Methylphenyl-2-p-methoxyphenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran(3b) :- White crystals; (90%); m.p. 114°C; ν_{max} 1610, 1545, 1300 cm^{-1}; δ_H 2.33(3H,s,$C\underline{H}_3$), 2.46(6H,s,$N(C\underline{H}_3)_2$), 3.76(3H,s,$OC\underline{H}_3$), 4.23(1H,dd,H_4,$J_{3,4}$= 11Hz & $J_{4,5}$= 3Hz), 4.73(1H,d,H_2,$J_{2,3}$= 11Hz), 5.17(1H,dd,H_3,$J_{2,3}$= 11Hz & $J_{3,4}$= 11Hz),

5.92(1H,d,H_5,$J_{4,5}$= 3Hz), 6.72-7.30(8H,m,ArH). (Found: C,66.12; H,6.01; N,7.11. $C_{21}H_{24}N_2O_3S$ requires: C,65.63; H,6.25; N,7.29%);m/z 205(M^+-179), 179(M^+-205).

(2R,3S,4R)-6-p-Methylphenyl-2-furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran (3c) : White crystals; (78%); m.p. 101°C;ν_{max}1620,1600,1500,1310 cm^{-1};δ_H2.43(3H,s,CH_3), 2.53(6H,s,$N(CH_3)_2$), 4.26(1H,dd,H_4,$J_{3,4}$= 11Hz & $J_{4,5}$= 3Hz), 4.90(1H,d,$H_2$$J_{2,3}$= 11Hz), 5.23(1H,dd,$H_3$$J_{2,3}$= 11Hz & $J_{3,4}$= 11Hz), 6.00(1H,d,H_5,$J_{4,5}$= 3Hz), 6.30-6.66(2H,m, ), 7.00-7.80(5H,m,ArH & ). (Found: C,63.09; H,6.14; N,8.09. $C_{18}H_{20}N_2O_3S$ requires: C,62.79; H,5.81; N,8.14%).

(2R,3S,4R)-6-p-Chlorophenyl-2-phenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran (3d):- White crystals; (90%) ;m.p. 118°C;ν_{max} 1600, 1555, 1310 cm^{-1};δ_H2.43(6H,s, $N(CH_3)_2$) 4.26(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 4.76(1H,d,H_2,$J_{2,3}$=11Hz), 5.19(1H,dd, H_3,$J_{2,3}$= 11Hz & $J_{3,4}$= 11Hz), 6.00(1H,d,H_5,$J_{4,5}$= 3Hz), 7.2-7.4(9H,m,Ar-H). (Found: C,61.32; H,4.97; N,7.22. $C_{19}H_{19}ClN_2O_2S$ requires : C,60.88; H,5.07; N,7.48%).

(2R,3S,4R)-6-p-Chlorophenyl-2-p-methoxyphenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran (3e):- White crystals; (85%); m.p. 132°C;ν_{max} 1620,1550, 1300 cm^{-1}; δ_H 2.43(6H,s,$N(CH_3)_2$), 3.76(3H,s,OCH_3), 4.23(1H,dd,H_4,$J_{3,4}$= 11Hz & $J_{4,5}$= 3Hz), 4.73 (1H,d,$H_2$$J_{2,3}$= 11Hz), 5.17(1H,dd,$H_3$,$J_{2,3}$= 11Hz & $J_{3,4}$= 11Hz), 5.92(1H,d,H_5,$J_{4,5}$=3Hz), 6.72-7.30(8H,m,ArH). (Found: C,59.82; H,5.12; N,6.51. $C_{20}H_{21}N_2ClO_3S$ requires : C,59.33; H,5.19; N,6.92%).

(2R,3S,4R)-6-p-Chlorophenyl-2-furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran (3f):- White crystals; (81%); m.p.95°C; ν_{max} 1600, 1550, 1310 cm^{-1}; δ_H2.43(6H,s, $N(CH_3)_2$) , 4.27(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 5.10(1H,d,H_2,$J_{2,3}$=11Hz), 5.36(1H,dd, H_3,$J_{2,3}$=11Hz & $J_{3,4}$=11Hz), 6.03(1H,d,H_5,$J_{4,5}$=3Hz), 6.2-6.7(2H,m,), 7.20-7.90 (5H,m,ArH &). (Found: C,56.35; H,5.05; N,7.55. $C_{17}H_{17}ClN_2O_3S$ requires: C,55.97; H,4.66; N,7.68%).

(2R,3S,4R)-6-Phenyl-2-phenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran (3g):- White crystals (85%); m.p. 146°C; ν_{max} 1600, 1540, 1300 cm^{-1}; δ_H 2.45(6H,s,$N(CH_3)_2$), 4.30(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 4.85(1H,d,H_2,$J_{2,3}$=11Hz), 5.30(1H,dd,H_3,$J_{2,3}$=11Hz & $J_{3,4}$=11Hz), 6.03(1H,d,H_5,$J_{4,5}$=3Hz), 7.21-7.50(10H,m,ArH). (Found: C,67.52; H,5.67; N,7.92.$C_{19}H_{20}N_2O_2S$ requires C,67.06 ; H,5.88; N,8.23%): M/z 191(M^+-149), 149(M^+-191).

(2R,3S,4R)-6-Phenyl-2-p-methoxyphenyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran(3h):- White crystals; (83%); m.p. 131°C; ν_{max}1610, 1550, 1305 cm^{-1}; δ_H 2.40 (6H,s,$N(CH_3)_2$), 3.69(3H,s,OCH_3), 4.17(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 4.66(1H,d,H_2, $J_{2,3}$=11Hz), 5.13(1H,dd, H_3,$J_{2,3}$=11Hz & $J_{3,4}$=11Hz), 5.92(1H,d,H_5,$J_{4,5}$=3Hz), 6.70-7.33(9H,m,ArH). (Found: C,65.45; H,6.27; N,7.54. $C_{20}H_{22}N_2O_3S$ requires: C,64.86; H,5.94; N,7.57%).

(2R,3S,4R)-6-Phenyl-2-furyl-3,4-dihydro-4-dimethylamino-3-nitro-2H-thiopyran(3i):- white crystals; (80%); m.p. 104°C; ν_{max} 1600, 1545, 1305 cm^{-1}; δ_H 2.43(6H,s,N(CH_3)$_2$), 4.20(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz); 4.90(1H,d,H_2,$J_{2,3}$=11Hz), 5.16(1H,dd,H_3,$J_{2,3}$= 11Hz & $J_{3,4}$=11Hz), 5.92(1H,d,H_5,$J_{4,5}$=3Hz), 6.17-6.56(2H,m, ), 7.20-7.80(6H,m,ArH & ).(Found: C,61.98; H,5.52; N,8.37. $C_{17}H_{18}N_2O_3S$ requires C,61.82; H,5.45; N,8.48%).

General procedure for the preparation of 6-aryl-2-aryl/furyl-3-nitro-2H-thiopyrans (4a-i):- A solution of compound (3) (0.0028 mol) in dichloromethane (20 ml) and acetic acid (2 ml) was stirred at room temperature for one hour. The reaction mixture was then washed with a saturated solution of sodium bicarbonate, water and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue so obtained was chromatographed over silica gel column. Elution of the column with hexane gave compound 4 which was recrystallized from petroleum ether.

6-p-Methylphenyl-2-phenyl-3-nitro-2H-thiopyrans (4a):- red crystals (80%); m.p. 108°C; ν_{max} 1625, 1500, 1300 cm^{-1}; δ_H 2.36(3H,s,CH_3); 5.69(1H,s,H_2); 6.63(1H,d,H_5, J= 8Hz), 7.13-7.50(9H,m,ArH), 8.00(1H,d,H_4,J= ~8Hz).(Found: C,70.26; H,4.99; N,4.60. $C_{18}H_{15}NO_2S$ requires: C,69.90; H,4.85; N,4.53%): m/z 309(M^+).

6-p-Methylphenyl-2-p-methoxyphenyl-3-nitro-2H-thiopyrans (4b):- red crystals; (75%); m.p. 95°C; ν_{max} 1600, 1500, 1300 cm^{-1}; δ_H 2.42(3H,s,CH_3), 3.76(3H,s,OCH_3), 5.59(1H,s,H_2), 6.53(1H,d,H_5,J= ~8Hz), 6.80-7.50(8H,m,ArH), 7.83(1H,d,H_4,J= ~8Hz). (Found: C,67.86; H,4.96; N,4.02. $C_{19}H_{17}NO_3S$ requires C,67.25; H,5.01; N,4.13%): m/z 339(M^+).

6-p-Methylphenyl-2-furyl-3-nitro-2H-thiopyrans (4c):- red crystals; (69%); m.p. 80°C; ν_{max} 1625, 1605, 1500, 1300 cm^{-1}; δ_H 2.25(3H,s,CH_3), 5.70(1H,s,H_2), 6.00-6.13 (2H,m,),6.53(1H,d,H_5,J=8Hz), 7.00-7.43(5H,m,ArH &), 7.78(1H,d,H_4J=8Hz). (Found: C,64.85; H,4.25; N,4.56. $C_{16}H_{13}NO_3S$ requires C,64.21; H,4.35; N,4.68%): m/z 299(M^+).

6-p-Chlorophenyl-2-phenyl-3-nitro-2H-thiopyran (4d):- red crystals; (78%); m.p. 170°C; ν_{max} 1630, 1500, 1300 cm^{-1}; δ_H 5.66(1H,s,H_2), 6.59(1H,d,H_5J= ~8Hz), 7.16-7.50(9H,m,ArH), 7.82(1H,d,H_4,J= ~8Hz). (Found: C,62.33; H,3.57; N,4.16. $C_{17}H_{12}ClNO_2S$ requires C,61.91; H,3.64; N,4.25%): m/z 329(M^+).

6-p-Chlorophenyl-2-p-methoxyphenyl-3-nitro-2H-thiopyran (4e):- red crystals; (76%); m.p. 70°C; ν_{max} 1600, 1500, 1300 cm^{-1}; δ_H 3.69(3H,s,OCH_3); 5.59(1H,s,H_2); 6.50(1H,d, H_5,J= ~8Hz), 6.70-7.50(8H,m,ArH), 7.85(1H,d,H_4,J= ~8Hz).(Found: C,60.63; H,3.84; N,3.78. $C_{18}H_{14}ClNO_3S$ requires C,60.08; H,3.89; N,3.89%): m/z 359(M^+).

6-p-Chlorophenyl-2-furyl-3-nitro-2H-thiopyran (4f):- red crystals; (70%); m.p. 114°C; ν_{max} 1615, 1510, 1300 cm^{-1}; δ_H 5.85(1H,s,H_2), 6.10-6.29(2H,m,), 6.69(1H,d, H_5,J= ~8Hz), 7.06-7.52(5H,m,ArH &), 7.82(1H,d,H_4,J= ~8Hz). (Found: C,56.86; H,3.07; N,4.33. $C_{15}H_{10}ClNO_3S$ requires C,56.34; H,3.13; N,4.38%): m/z 319(M^+).

6-Phenyl-2-phenyl-3-nitro-2H-thiopyran (4g):- red crystals; (81%); m.p. 85°C; ν_{max} 1620, 1500, 1300 cm^{-1}; δ_H 5.71(1H,s,H_2), 6.66(1H,d,H_5,J= ~8Hz), 7.22-7.96(10H,m,ArH), 8.04(1H,d,H_4,J= ~8Hz). (Found: C,69.73; H,4.55; N,4.90. $C_{17}H_{13}NO_2S$ requires C,69.15; H,4.41; N,4.74%): m/z 295(M^+).

6-Phenyl-2-p-methoxyphenyl-3-nitro-2H-thiopyran (4h):- red crystals; (79%); m.p. 63°C; ν_{max} 1610, 1500, 1315 cm^{-1}; δ_H 3.73(3H,s,OCH_3), 5.59(1H,s,H_2), 6.50(1H,d,H_5, J= ~ 8Hz), 7.03-7.63(9H,m,ArH), 7.90(1H,d,H_4,J= ~ 8Hz). (Found: C,67.03; H,4.60; N,4.29. $C_{18}H_{15}NO_3S$ requires C,66.46; H,4.62; N,4.31%): m/z 325(M^+).

6-Phenyl-2-furyl-3-nitro-2H-thiopyran (4i):- red crystals; (65%); m.p. 65°C; ν_{max} 1625, 1500, 1300 cm^{-1}; δ_H 5.69(1H,s,H_2), 6.00-6.20(2H,m, ), 6.59(1H,d,H_5,J= ~8Hz), 7.00-7.56(5H,m,ArH & ), 7.69(1H,d,H_4,J= ~8Hz). (Found: C,63.73; H,3.85; N,4.83. $C_{15}H_{11}NO_3S$ requires C,63.16; H,3.86; N,4.91%): m/z 285(M^+).

General procedure for the preparation of (2R,3S,4S)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyrans (6a-e):-

A mixture of 3-N-arylamino-1-phenylpropene-1-thione (5) (0.0039 mol) and β-nitroalkene (2) (0.0040 mol) was dissoloved in dry benzene (25ml) and the reaction mixture was stirred at room temperature for 20 minutes. The solvent was removed under reduced pressure and the solid so obtained (6) was recrystallized from a mixture (1:1) of benzene and hexane.

(2R,3S,4S)-2-Phenyl-4-p-methylphenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran(6a):- yellow crystals; (75%); m.p. 116°C; ν_{max} 3400, 1610, 1545 cm^{-1}; δ_H 2.20(3H,s,CH_3), 3.76(1H,bd,NH), 4.80(1H,dd,H_4,$J_{3,4}$= 4Hz; $J_{4,5}$= 6Hz), 5.00(H_2d,$J_{2,3}$= ~11Hz), 5.36 (1H,dd,H_3,$J_{2,3}$= 11Hz & $J_{3,4}$= 4Hz), 6.18(1H,d,H_5,$J_{4,5}$= 6Hz), 6.50(2H,d,Ha), 6.96 (2H,d,Hb,$J_{a,b}$=8Hz), 7.13-7.60(10H,m,ArH). (Found: C,72.08; H,5.59; N,7.06. $C_{24}H_{22}N_2O_2S$ requires C,71.64; H,5.47; N,6.96%): m/z 149(M^+-253), 253(M^+-149).

(2R,3S,4S)-2-Phenyl-4-p-chlorophenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran(6b):- yellow crystals; (78%), m.p. 132°C; ν_{max} 3395, 1595, 1550 cm^{-1}; δ_H 3.95(1H,bd, NH), 4.80(1H,dd,H_4,$J_{3,4}$=4Hz & $J_{4,5}$=6Hz), 5.38(1H,dd,H_3,$J_{2,3}$=11Hz & $J_{3,4}$=4Hz), 6.15 (1H,d,H_5,$J_{4,5}$= 6Hz), 6.53(2H,d,Ha), 7.10(2H,d,Hb,J_{ab}=8Hz), 7.26-7.65(10H,m,ArH). (Found: C,65.92; H,4.21; N,6.39: $C_{23}H_{19}ClN_2O_2S$ requires C,65.32; H, 4.49; N,6.63%): m/z 149(M^+-273), 273(M^+-149).

(2R,3S,4S)-2-Phenyl-4-anilino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (6c):- yellow crystals; (74%); m.p. 147°C; ν_{max} 3390, 1600, 1545 cm^{-1}; δ_H 3.93(1H,bd,NH), 4.86 (1H,dd,H_4,$J_{3,4}$= 4Hz & $J_{4,5}$= 5Hz), 5.00(1H,d,H_2,$J_{2,3}$= 11Hz), 5.40(1H,dd,H_3,$J_{2,3}$= 11Hz & $J_{3,4}$= 4Hz), 6.20(1H,d,H_5,$J_{4,5}$= 6Hz), 6.60(2H,d,Ha), 6.82(2H,d,Hb,J_{ab}=8Hz), 7.00-7.60(11H,m,ArH). (Found: C,71.64; H,5.20; N,7.00. $C_{23}H_{20}N_2O_2S$ requires C,71.13; H,5.15; N,7.21%): m/z 149(M^+-239), 239(M^+-149).

(2R,3S,4S)-2-p-Methoxyphenyl-4-anilino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (6d):- yellow crystals; (72%); m.p. 96°C; ν_{max} 3395, 1600, 1550 cm^{-1}; δ_H 3.76(3H,s,OCH_3), 3.90(1H,bd,NH), 4.82(1H,dd,H_4,$J_{3,4}$=4Hz & $J_{4,5}$=6Hz), 4.93(1H,d,H_2,$J_{2,3}$=11Hz), 5.35 (1H,dd,H_3,$J_{2,3}$=11Hz & $J_{3,4}$=4Hz), 6.15(1H,d,H_5,$J_{4,5}$=6Hz), 6.56(2H,d,Ha), 6.78(2H,d,Hb, J_{ab}=8Hz), 6.93-7.53(10H,m,ArH). (Found: C,69.05; H,5.17; N,6.45. $C_{24}H_{22}N_2O_3S$ requires C,68.90; H,5.26; N,6.69%): m/z 179(M^+-239), 239(M^+-179).

(2R,3S,4S)-2-p-Methoxyphenyl-4-p-chlorophenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (6e):- yellow crystals; (70%); m.p. 77°C; ν_{max} 3400, 1600, 1550 cm^{-1}; δ_H 3.73(3H,s,OCH_3), 3.90(1H,bd,NH), 4.73(1H,dd,H_4,$J_{3,4}$=4Hz & $J_{4,5}$=6Hz), 4.90 (1H,d,H_2,$J_{2,3}$=11Hz), 5.23(1H,dd,H_3,$J_{2,3}$=11Hz & $J_{3,4}$=4Hz), 6.08(1H,d,H_5,$J_{4,5}$=6Hz), 6.46(2H,d,Ha), 6.85(2H,d,Hb,J_{ab}=8Hz), 7.05-7.60(9H,m,ArH). (Found: C,64.03; H,4.35; N,6.38. $C_{24}H_{21}ClN_2O_3S$ requires C,63.64; H,4.64; N,6.19%): m/z 179(M^+-273), 273(M^+-179).

Conversion of (2R,3S,4S)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyrans (6) to (2R,3S,4R)-2-aryl-4-arylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyrans (7): A General Procedure:- A solution of compound 6 (0.0012 mol) in benzene (20 ml) was treated with glacial acetic acid (1 ml) and the reaction mixture was stirred at room temperature for two hours. The reaction mixture was then washed with saturated sodium bicarbonate solution, water and dried over anhydrous sodium sulfate. The removal of the solvent resulted in 7 which was recrystallized from benzene.

(2R,3S,4R)-2-phenyl-4-p-methylphenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran(7a):- yellow crystals; (80%); m.p. 128°C; ν_{max} 3400, 1610, 1550 cm^{-1}; δ_H 2.23(3H,s,CH_3), 3.63(1H,bd,NH), 4.95(1H,d,H_2,$J_{2,3}$=11Hz), 5.09(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 5.31 (1H,dd,H_3,$J_{2,3}$=$J_{3,4}$=11Hz), 6.03(1H,d,H_5,$J_{4,5}$=3Hz), 6.63(2H,d,Ha), 7.02(2H,d,Hb,J_{ab}=8Hz), 7.13-7.53(10H,m,ArH); δ_C 20.37(CH_3), 49.02(C-2), 57.01(C-4), 91.23(C-3), 115.12 (C-9/9'), 119.47(C-5), 129.98(C-11), 133.80(C-12), 136.73(C-6/7), 137.15(C-7/6), 142.90(C-8), 126.46, 128.48, 128.63, 129.16, 129.34(CH,ArH). (Found: C,72.18; H,5.63; N,6.80. $C_{24}H_{22}N_2O_2S$ requires C,71.64; H,5.47; N,6.96%): m/z 402(M^+), 149(M^+-253), 253(M^+-149).

(2R,3S,4R)-2-phenyl-4-p-chlorophenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran(7b):- light yellow crystals; (76%); m.p. 142°C; ν_{max} 3400, 1610, 1550 cm^{-1}; δ_H($CDCl_3$/ D_3CCOCD_3), 3.73(1H,bd,NH), 4.95(1H,d,H_2,$J_{2,3}$=11Hz), 5.05(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$= 3Hz), 5.43(1H,dd,H_3 . $J_{2,3}$=$J_{3,4}$=11Hz), 5.98(1H,d,H_5,$J_{4,5}$= 3Hz), 6.65(2H,d,Ha), 7.13 (2H,d,Hb,J_{ab}=8Hz), 7.25-7.65(10H,m,ArH). (Found : C,65.71; H,4.38: N,6.52. $C_{23}H_{19}ClN_2O_2S$ requires C,65.32; H,4.49; N,6.63%): m/z 422(M^+), 149(M^+-273), 273 (M^+-149).

(2R,3S,4R)-2-Phenyl-4-anilino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (7c):- light yellow crystals; (74%); m.p. 167°C; ν_{max} 3340, 1600, 1550 cm^{-1}; δ_H 3.73(1H,bd,NH), 4.98(1H,d,H_2,$J_{2,3}$=11Hz), 5.08(1H,dd,H_4,$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 5.34(1H,dd,H_3,$J_{2,3}$= 11Hz), 6.03(1H,d,H_5,$J_{4,5}$=3Hz), 6.72(3H,m,Ha & Hc), 6.83(2H,d,Hb,J_{ab}=8Hz), 7.10-7.53 (10H,m,ArH). (Found : C,71.64; H,5.20; N,7.00. $C_{23}H_{20}N_2O_2S$ requires: C,71.13; H,5.15; N,7.21%): m/z 388(M^+), 149(M^+-239), 239(M^+-149).

(2R,3S,4R)-2-p-Methoxyphenyl-4-anilino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (7d):- light yellow crystals; (70%), m.p. 145°C; ν_{max} 3400, 1600, 1550 cm^{-1}; δ_H 3.76(3H,s, OCH_3); 3.80(1H,bd,NH), 4.92(1H,d,H_2,$J_{2,3}$=11Hz), 5.06(1H,dd,$H_4$$J_{3,4}$=11Hz & $J_{4,5}$=3Hz), 5.30(1H,dd,H_3,$J_{2,3}$=$J_{3,4}$=11Hz), 6.00(1H,d,H_5,$J_{4,5}$=3Hz), 6.70(2H,d,Ha),6.86(2H,d,Hb, J_{ab}=8Hz), 7.00-7.50(10H,m,ArH). (Found : C,69.30; H,5.08; N,6.44. $C_{24}H_{22}N_2O_2S$ requires C,68.90; H,5.26; N,6.69%): m/z 418(M^+), 179(M^+-239), 239(M^+-179).

(2R,3S,4R)-2-p Methoxyphenyl-4-p-chlorophenylamino-3-nitro-6-phenyl-3,4-dihydro-2H-thiopyran (7e):- light yellow crystal; (71%); m.p. 164°C; ν_{max} 3400, 1600, 1550 cm^{-1}; δ_H 3.77(3H,s,OCH_3), 3.93(1H,bd,NH), 4.93(1H,d,H_2,$J_{2,3}$=11Hz), 5.10(1H,dd,H_4,$J_{3,4}$= 11Hz, $J_{4,5}$=3Hz), 5.35(1H,dd,H_3,$J_{2,3}$=$J_{3,4}$=11Hz), 5.96(1H,d,H_5,$J_{4,5}$=3Hz), 6.63(2H,d,Ha), 6.87(2H,d,Hb,J_{ab}=8Hz), 7.00-7.66(10H,m,ArH). (Found : C,64.08; H,4.18; N,6.07. $C_{24}H_{21}ClN_2O_2S$ requires C,63.64; H,4.64; N,6.19%): m/z 452(M^+), 179(M^+-273), 273 (M^+-179).

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