The Synthesis of N,S-Substituted compounds from the reactions of 2-Nitrohalobuta-1,3-diene with Mercaptocoumarin

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Summary: 4-Bromo-1,3,4-trichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1,3-butadiene **(3),** and 4-Bromo-3,4-dichloro-2-nitro-1,1-bis (7-coumarinthio-4-methyl)-1,3-butadiene **(4)** were synthesized from the reactions of 4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene **(1)** with 7-mercapto-4-methylcoumarin **(2)**. Afterwards, new N,S- substituted dienes**(6a-j**, **8a-d, 10 and 12)** were obtained by the reactions of derivatives of piperazine [4-(fluorophenyl) piperazine, phenyl piperazine, 1-(2-methoxyphenyl)-piperazine, ethoxycarbonyl piperazine, formylpiperazine,2-(fluorophenyl)-piperazine, 4-(nitrophenyl)-piperazine, diphenylmethyl piperazine, 4-(hydroxyphenyl)- piperazine, 4-(hydroxyphenyl)- piperazine]; piperidine [4-methyl piperidinyl, 4-benzyl piperidinyl, 4-hydroxy piperidinyl]; morpholin and 1,4-dioxoazospiro [4,5] decan with the mono(thio)substituted nitrodien compound **3**.
Structures of the novel compounds were characterized by using microanalysis, FT-IR, UV-Vis, ^{1}H-NMR, APT and MS spectroscopy methods.

Introductıon

In recent years, the photophysics, photochemistry [1] and photodimer of aromatic thioketones have shown many interesting and unusual features, which makes this class of molecules quite different from the corresponding aromatic ketones. The spectroscopic and photophysical parameters of the second excited singlet states of several thiocoumarin derivatives have been measured in inert perfluoroalkane solvents [2-5]. Reactions of derivatives of dicyanobenzene with the 7-mercapto-4-methylcoumarin were explored and phthalocyanines compounds were obtained . The novel chromogenic compounds were characterized [6]. Nitro-substituted polyhalogeno-1,3-butadienes are useful and valuable precursor for versatile synthetic applications which became the subject of last decade investigations due to rich chemical [7, 8] as well as biological properties [9-11]

It is well known that the reaction of **1** with nucleophiles such as thiols and piperazine derivatives follows a classical nucleophilic vinylic substitution (S_NVin) [9-11] pathway via the addition-elimination route that leads to the formation of new products. In compound **1**, the electrophilic character of the C-1 position is profound due to the powerful electron withdrawing properties which the α-nitro group allows and regioselective substitution of these either one or two terminal vinylic chlorine substituents in the nitrodichlorovinyl moiety of the dienes.

We previously reported that N,S-substituted diene compounds were prepared from the reaction of some mono(thio)substituted compounds with some amines [12-20]. The present work describes the synthesis of new N,S- substituted compounds from the reactions of 2-Nitrohalobuta-1,3-diene with mercaptocoumarin.

Results and Discussion

In the present paper, the interaction of 4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene [9,10-29] **1** with 7-mercapto-4-methylcoumarin **2** has been found to lead to the substituted products 4-bromo-1,3,4-trichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1,3-butadiene **3** and 4-bromo-3,4-dichloro-2-nitro-1,1-bis (7-coumarinthio-4-methyl)-1,3-butadiene **4** under mild conditions. Furthermore, we attempted some subsequent reactions of the 1-(aryl)thio-perhalo-2-nitro-1,3-butadienes namely with **3** as the exemplary starting compounds. Similarly, the subsequent vinylic substitution of **3** in dichloromethane by means of hard nucleophiles, piperazine **(5)**, piperidine **(7)** derivatives, morpholine **9** and 1,4-dioxoazospiro [5, 6] decan **11** gave N,S-substituted nitrodiene compounds **(6a-j**, **8a-d, 10 and 12)** (Fig. 1).

In the ^{1}H-NMR spectra of **(3,4,6a-j**, **8a-d, 10 and 12)** methyl protons of coumarin compound have shown as singlet 2.42 ppm, vinily protons of coumarin compound have been observed as singlet

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6.20 ppm, the aromatic protons have shown typical ppm values within the range 6.88-7.70 ppm. The piperazine protons of the substituted product **6a-j** have been observed as multiplets around 3.00-3.80 ppm. The piperidine protons of the substituted product **6a-j** have been observed as multiplets around 2.60-4.40 ppm.

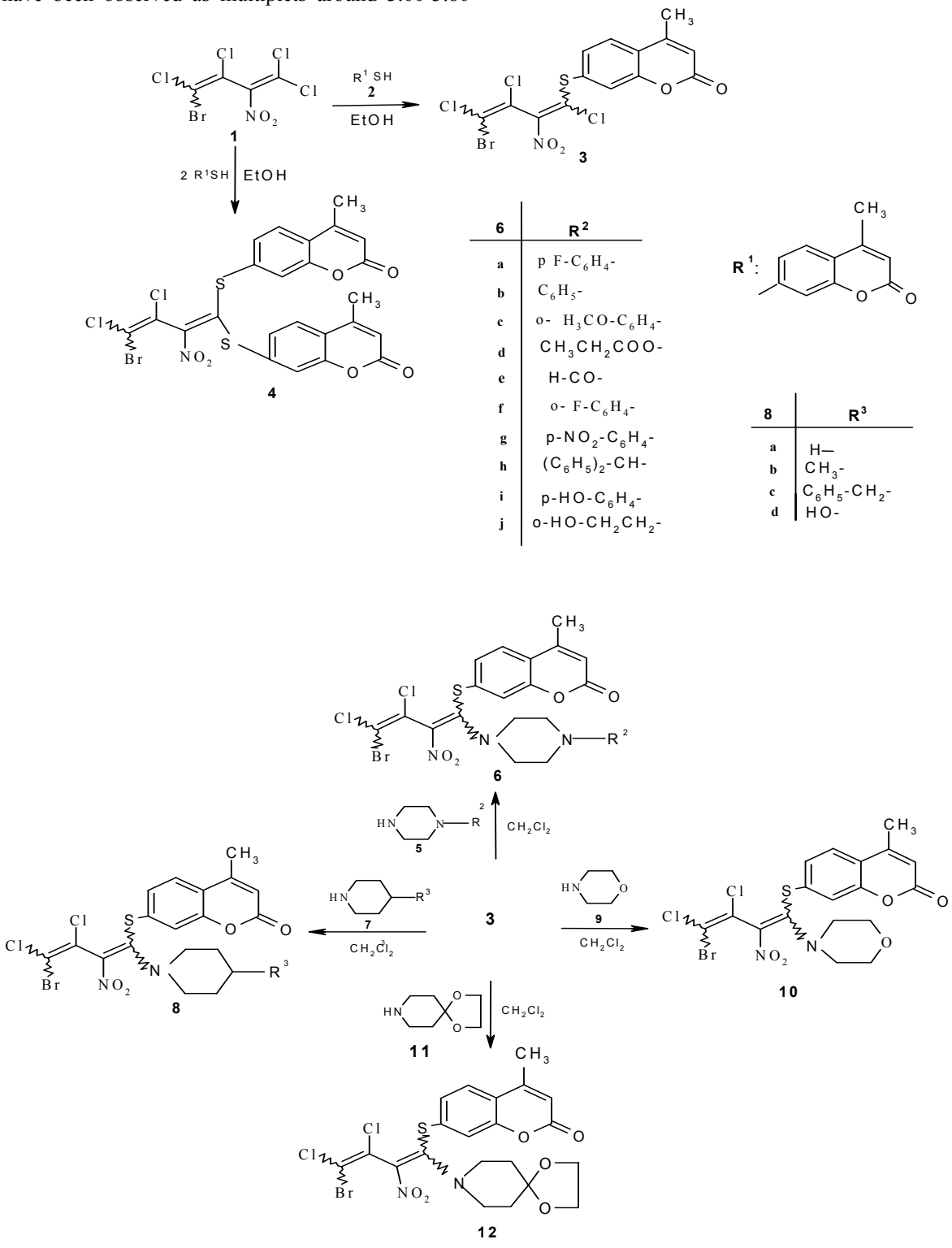

Fig. 1: The synthesis of S- and N,S- substituted compounds from 2-Nitrohalobuta-1,3-diene.

In the APT spectra of compounds **(3,4,6a-j**, **8a-d, 10 and 12)** methyl carbons of coumarin compound have shown 18 ppm, vinily carbons of coumarin compound have been observed 116.1 ppm and 152.2 ppm, carbonyl carbons of coumarin compound have shown 152.4 ppm, the aromatic carbons have shown typical ppm values within the range 122.6-150.1 ppm and butadiene carbons have shown within the range 114.6-121.4 ppm. The piperazine carbons of the substituted product **6a-j** have been observed around 42.1-46.8 ppm. The piperidine carbons of the substituted product **6a-j** have been observed around 29.0-42.0 ppm.

Some characteristic bands in the IR spectra of the compounds should be mentioned: asymmetric stretching of the NO_2 groups have been observed range from 1520 to 1540 cm^{-1}, and symmetric stretching of the NO_2 groups range from 1270 to 1310 cm^{-1}. The IR spectra of the molecules **(3,4,6a-j**, **8a-d, 10 and 12)** have shown the characteristic C-H band at 2900 and 3020 cm^{-1} , C=O band at 1725 and 1745 cm^{-1}, C=C band at 1590 and 1600 cm^{-1}respectively.

The MS experiment for **6e** was performed in positive ion mode for ESI. The molecular ion peak (M^+) is detected at m/z 549.83 with strong abundance (100 %). Fragmentation of m/z 549.83 has yielded fragment rich product ions.The loss of a nitro group from **6e** occurs readly with 100% at m/z 502.97. Notably , the other strong relative abundance of fragment ion of compound **6b** at m/z 517.70 appeared to be characteristic ion corresponding (M^+-Br) being showed at m/z 597.82 molecular ion peak.

The coumarins showed maximum absorption with a single band at 270-310 nm [6]. The UV-vis spectra of compounds **6d, 8b and 12** in $CHCl_3$ showed broad 275, 276 and 273 nm respectively.

Several coumarin derivatives revealed pronounced medicinal value as antibacterial and antifungal agents. Others diplayed antitubercular activity and some have insecticidal properties [21-28]. In the next part of the study will be investigated biological properties of new synthesized compounds.

Experimental

Elemental analyses were carried out using a Carlo Erba 1106 analyzer. Melting points were determined on a Buchi B-540 capillary apparatus and were uncorrected. Infrared spectra were recorded on a Shimadzu FTIR-8101 spectrometer in KBr discs. ^{1}H-NMR and APT spectra were obtained on a Varian^{UNITY} INOVA spectrometer at 500 MHz. Mass spectra was obtained using Finnigan LCQ Advantage Max. LC/MS spectrometer according to ESI techniques. UV spectra were recorded on a UV-VIS spectrometer TU-3200. Thin-layer chromatography was performed on 0.5 mm X 20 cm X 20 cm E. Merck silica gel plates (60 F-254). Column chromatography was conducted over Silica gel (63-200 μm), available from E. Merck. All chemicals were reagent grade and used without further purification. Moisture was also excluded from the glass apparatus using $CaCl_2$ drying tubes.

Preparation of Mono Substituted Compound General Procedure

Equimolar amount of 4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene **1** (2 gr, 6.3 mmol) and 7-mercapto-4-methylcoumarin **2** (1.22 gr, 6.3 mmol) were stirred in ethanol at room temperature until completion of the reaction. The mixture was stirred for 24 h. Then, chloroform (3x50 mL) was added to the reaction mixture. The organic layer was separated, washed with water several times and dried over anhydrous $CaCl_2$ or $MgSO_4$. After evaporation of the solvent, the products were either crystallized or purified by column chromatography over silica gel [9, 10].

Preparation of Di-(Thio)Substituted Compound General Procedure

4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene **1**(2 gr, 6.3 mmol) and 7-mercapto-4-methylcoumarin **2** (2.44 gr, 12.6 mmol) were stirred in ethanol at room temperature until completion of the reaction. The mixture was stirred for 24 h. Then, chloroform (3x50 mL) was added to the reaction mixture. The organic layer was separated, washed with water several times and dried over anhydrous $CaCl_2$ or $MgSO_4$. After evaporation of the solvent, the products were either crystallized or purified by column chromatography over silica gel [9,10].

Preparation of N,S- Substituted Polyhalonitrodiene Compounds General Procedure

A suspension of amine derivatives of piperazine, piperidine and morfiline , 1,4-dioxoazospirol (4,5) decan in 25 ml dichloromethane was added to a solution of 4- Bromo-1,3,4 tricholoro-2-nitro-1-(7-coumarinthio-4-methyl)-1,3-butadiene **3** in 25 ml dichloromethane at the same molar ratio.The mixture was stirred at room temperature until completion of the reaction. Then, chloroform (3x50 mL) was added to the reaction mixture. The organic

layer was separated and washed with water several times and dried over anhydrous $CaCl_2$ or $MgSO_4$. After evaporation of the solvent, the products were either crystallized or purified by column chromatography over silica gel. [9, 10].

The products were purified by column chromatography with solvent systems (Table-1)

Table-1: Column chromatography data for S- and N,S- substituted compounds.

Compound	Solvent system	Ratio (v/v)
(3)	**$CHCl_3$/PET**	**1:3**
(4)	**$CHCl_3$/PET**	**1:3**
(6a)	**EtAc/PET**	**1:2**
(6b)	**EtAc/PET**	**1:2**
(6c)	**EtAc/PET**	**1:1**
(6d)	**$CHCl_3$/PET**	**2:1**
(6e)	**EtAc/ EtAc**	**1:1**
(6f)	**$CHCl_3$/$CHCl_3$**	**1:1**
(6g)	**$CHCl_3$/$CHCl_3$**	**1:1**
(6h)	**$CHCl_3$/$CHCl_3$**	**1:1**
(6i)	**EtAc/PET**	**2:1**
(6j)	**EtAc/ EtAc**	**1:1**
(8a)	**EtAc/PET**	**2:1**
(8b)	**EtAc/PET**	**1:2**
(8c)	**$CHCl_3$/$CHCl_3$**	**1:1**
(8d)	**EtAc/ EtAc**	**1:1**
(10)	**EtAc/PET**	**2:1**
(12)	**EtAc/PET**	**2:1**

4-Bromo-1,3,4-trichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1,3-butadiene **(3)**

Yield: 1.45 gr (49 %); m.p. 181-183 ^{0}C. R_f ($CHCl_3$):0.50; IR (KBr, cm^{-1}): 2987, 3050 (C-H), 1600, 1610 (C=C), 1741 (C=O), 1300, 1530 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.00-7.81 (3H, *m*, H_{arom}), 6.30-6.51 (1H, *s*, COCH), 2.50 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 114.1, 116.0, 116.1, 121.2, 121.4, 122.6, 122.7, 124.2, 130.0, 132.0, 150.1, 152.2, 158.4; MS (+ESI) (m/z) : 471.78 (M^+), 425.53 (M-NO_2), 390.43 (M-Br) ;$C_{14}H_7BrCl_3NO_4S$ (M,471.54). Calcd.: C, 35.66; H, 1.50; N, 2.97 % . Found: C, 35.90; H, 1.62; N, 3.02 %; UV-Vis ($CHCI_3$) (λmax / nm): 250, 275, 300, 345 .

4-Bromo-3,4-dichloro-2-nitro-1,1-bis (7-coumarinthio-4-methyl)-1,3-butadiene **(4)**

Yield: 1.23 gr (30 %); m.p. 176-178^{0}C. R_f ($CHCl_3$):0.25; IR (KBr, cm^{-1}): 2900, 3055 (C-H), 1600, 1610 (C=C), 1737 (C=O), 1290, 1300, 1520 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.00-7.81 (6H, *m*, H_{arom}), 6.30-6.51 (2H, *s*, 2COCH), 2.44 (6H, *s,* $2CH_3$); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 114.1, 116.0, 116.1, 121.2, 121.4, 122.6, 122.7, 124.2, 130.0, 132.0, 150.1, 152.2, 152.4; MS (+ESI) (m/z) :627.93 (M^+) ,581.40 (M-NO_2); $C_{24}H_{14}BrCl_2NO_6S_2$ (M, 627.32). Calcd.: C, 45.94; H, 2.25; N, 2.30 %. Found: C, 47.05; H, 2.81; N, 2.30 %; UV-Vis ($CHCI_3$) (λmax / nm): 247, 300, 342.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^I-[4-fluorophenyl]-piperazine **(6a)**

Yield: 0.12gr (46 %); m.p. 157-159 ^{0}C. R_f (EtAc): 0.83; IR (KBr, cm^{-1}): 2825, 3070 (C-H), 1590, 1600 (C=C), 1735 (C=O), 1320, 1535 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.88-7.70 (7H, *m*, H_{arom}), 3.10-3.98 (8H, *m,* H_{piper}) , 6.20 (1H, *s*, COCH), 2.42 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.4, 42.1, 46.8, 111.0, 114.0, 114.3, 114.7, 116.1, 118.9, 120.2, 120.3, 120.4, 122.2, 125.9, 136.0, 140.8, 151.8, 152.0, 154.0, 160.1 MS (+ESI) (m/z) : 615.80 (M^+), 534.65 (M-Br); $C_{24}H_{14}BrCl_2NO_6S_2$ (M, 615.51) .Calcd: C, 46.85; H, 3.44; N, 6.83 % . Found: C, 47.05; H, 3.49; N, 6.93 %;.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^I-phenyl piperazine **(6b)**

Yield: 0.15 gr(58 %); m.p. 151-153 ^{0}C. R_f (EtAc): 0.77; IR (KBr, cm^{-1}): 2852, 3010 (C-H), 1590, 1600 (C=C), 1725 (C=O), 1388, 1539 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.88-7.70 (8H, *m*, H_{arom}), 3.00-3.98 (8H, *m,* H_{piper}) , 6.22 (1H, *s*, COCH), 2.38 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 48.0, 52.0, 112.0, 112.8, 112.9, 115.9, 116.0, 119.8, 120.0, 121.7, 121.8, 124.0, 126.2, 134.0, 140.0, 152.0, 154.0, 159.0; MS (+ESI) (m/z) : 597.82 (M^+), 517.70 (M-Br); $C_{24}H_{20}BrCl_2N_3O_4S$ (M, 597.32). Calcd.: C, 48.26; H, 3.37; N, 7.03 %. Found: C, 48.97; H, 3.87; N, 7.55 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^I-[1-(2-methoxyphenyl)]-piperazine **(6c)**

Yield: 0.14 gr (51 %); m.p. 158-160 ^{0}C. R_f (EtAc): 0.76; IR (KBr, cm^{-1}): 2960, 3010 (C-H), 1595, 1600 (C=C), 1739 (C=O), 1525, 1530 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.80-7.82 (7H, *m*, H_{arom}), 3.10-3.60 (8H, *m,* H_{piper}) , 3.75 (3H, *s*, OCH_3), 6.20 (1H, *s*, COCH), 2.44 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 48.0, 52.2, 54.2, 112.0, 114.0, 114.2, 116.0, 116.2, 118.3, 120.0, 120.1, 122.8, 123.0, 126.0, 130.0, 134.0, 134.1, 150.0, 152.0, 152.8, 158.0; MS (+ESI) (m/z): 627.84 (M^+), 580.72 (M-NO_2) ,546.82 (M-Br) ;$C_{25}H_{22}BrCl_2N_3O_5S$ (M,627.35). Calcd. : C, 47.87; H,

3.53; N, 6.70 %. Found: C, 47.95; H, 3.60; N, 7.03 %;. UV-Vis ($CHCl_3$) (λmax / nm): 250, 275, 325, 375.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1-ethoxycarbonyl piperazine **(6d)**

Yield: 0.21 gr (85 %); m.p. 179-180^{0}C. R_f ($CHCl_3$):0.25; IR (KBr, cm^{-1}): 2940, 3575 (C-H), 1600, 1620 (C=C), 1725 (C=O), 1365, 1520 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.15-7.77 (3H, *m*, H_{arom}), 3.20-3.61 (8H, *m,* H_{piper}) , 4.15-4.20 (2H ,*q*, OCH_2, *J* = 6.35 Hz), 1.15-1.20 (3H, *t*, OCH_2CH_3, *J* = 6.35 Hz), 6.40 (1H ,*s*, CO-CH), 2.44 (3H,*s*, CH_3) ; APT (500 MHz, $CDCl_3$, δ/ ppm): 14.0, 18.0, 42.0, 45.2, 61.8, 112.1, 112.3, 115.3, 115.9, 116.1, 119.0, 120.0, 121.8, 123.2, 124.8, 126.0, 126.1, 128.1, 132.0, 133.3, 150.0, 152.6, 154.0, 158.2; MS (+ESI) (m/z) : 593.85(M^+), 546.80 (M-NO_2), 512.02 (M-Br); $C_{21}H_{20}BrCl_2N_3O_6S$ (M, 593.29). Calcd.: C, 42.51; H, 3.39; N, 7.08 %. Found: C, 42.87; H, 3.60; N, 7.88 %. UV-Vis ($CHCl_3$) (λmax / nm): 245, 275, 325, 375.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1-[formyl]-piperazine **(6e)**

Yield: 0.16gr (67 %); m.p. 150-152^{0}C. R_f (EtAc): 0.25; IR (KBr, cm^{-1}): 2940, 3500 (C-H), 1600, 1660 (C=C), 1725 (C=O), 1520, 1525 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.20-7.62 (3H, *m*, H_{arom}), 3.20-3.80 (8H, *m,* H_{piper}) ,7.99 (1H ,*s*, CHO), 6.20 (1H, *s*, COCH), 2.40 (3H, *s,* CH_3);APT (500 MHz, $CDCl_3$, δ/ ppm): 16.0, 18.0, 42.8, 52.0, 112.6, 115.9, 118.8, 119.8, 120.0, 122.0, 123.8, 124.0, 126.0, 132.0, 150.0, 152.6, 158.8; MS (+ESI) (m/z) : 549.83 (M^+), 502.97 (M-NO_2); $C_{19}H_{16}BrCl_2N_3O_5S$ (M, 549.23). Calcd.: C, 41.55; H, 2.94; N, 7.65 %. Found: C, 41.85; H, 3.05; N, 7.77 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo -3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1-[2-fluorophenyl]-piperazine **(6f)**

Yield:0.08 gr (32 %); m.p. 180-182^{0}C. R_f ($CHCl_3$):0.25; IR (KBr, cm^{-1}): 2900, 3055 (C-H), 1600, 1625 (C=C), 1738 (C=O), 1500, 1520 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.61-7.71 (7H, *m*, H_{arom}), 2.99-3.80 (8H, *m,* H_{piper}) , 6.25 (1H, *s*, COCH), 2.38 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.2, 50.0, 54.0, 113.6, 114.0, 115.8, 116.0, 116.2, 116.3, 119.8, 120.1, 120.2, 121.8, 124.6, 126.0, 136.0, 138.1, 152.0, 154.0, 156.0, 160.0; MS (+ESI) (m/z) : 615.82 (M^+); $C_{24}H_{19}BrCI_2FN_3O_4S$ (M, 615.31). Calcd. : C, 46.85; H, 3.44; N, 6.83 %. Found: C, 46.92; H, 3.85; N, 7.01 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1-[1-(4-nitrophenyl)]-piperazine **(6g)**

Yield:0.13 gr (55 %); m.p. 188-189^{0}C. R_f ($CHCl_3$):0.32; IR (KBr, cm^{-1}): 2923, 3071 (C-H), 1600, 1621 (C=C), 1735 (C=O), 1365, 1532 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.65-7.62 (7H, *m*, H_{arom}), 3.23-4.15 (8H, *m,* H_{piper}) , 6.25 (1H, *s*, COCH), 2.39 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 48.0, 50.1, 112.0, 112.6, 114.2, 116.1, 118.0, 118.8, 118.9, 121.1, 121.2, 124.8, 125.1, 134.1, 140.0, 150.1, 151.0, 153.9, 158.9; MS (+ESI) (m/z) : 642.32 (M^+); $C_{24}H_{19}BrCI_2N_4O_6S$ (M, 642.42). Calcd : C, 44.88; H, 2.98; N, 8.72 %. Found: C, 44.92; H, 3.01; N, 8.80 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1-[diphenylmethyl]- piperazine **(6h)**

Yield:0.12gr (43 %) ; m.p. 150-152^{0}C. R_f ($CHCl_3$):0.25; IR (KBr, cm^{-1}): 2920, 3059**,** 3422 (C-H), 1600, 1622 (C=C), 1735 (C=O), 1365, 1525 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.67-7.65 (13H, *m*, H_{arom}), 3.20-4.10 (8H, *m,* H_{piper}) , 4.25 (1H ,*s*, $(C_6H_5)_2CH$), 6.25 (1H, *s*, COCH), 2.38 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 50.2, 51.0, 62.0, 112.0, 114.1, 113.9, 115.9, 118.0, 121.1, 126.1, 121.2, 121.3, 124.0, 124.2, 125.8, 126.2, 126.8, 140.0, 142.0, 153.9, 160.0; MS (+ESI) (m/z): 673.92 (M^+); $C_{31}H_{26}BrCl_2N_2O_4S$ (M, 673.92). Calcd. : C, 55.29; H, 3.89; N, 4.16 %. Found: C, 55.47; H, 3.95; N, 4.21 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^1- [1-(4-hydroxyphenyl)]- piperazine **(6i)**

Yield:0.12 gr (54 %); m.p. 178-180^{0}C. R_f (EtAc): 0.42; IR (KBr, cm^{-1}): 2920, 3050 (C-H), 1590, 1610 (C=C), 1735 (C=O), 1510, 1535 (C-NO_2), 3510 (OH); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.86-7.68 (7H, *m*, H_{arom}), 2.98-3.86 (8H, *m,* H_{piper}) , 6.20 (1H, *s*, COCH), 2.38 (3H, *s,* CH_3) , 1.38 (1H, *s,* OH); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.2, 44.8, 48.4, 112.0, 113.8, 115.4, 115.8, 116.0, 119.0, 120.0, 120.4, 124.8, 124.9, 125.0, 135.7, 142.1, 151.2, 151.9, 153.8, 160.0; MS (+ESI) (m/z) : 613.32 (M^+), 595.43 (M-OH); $C_{24}H_{20}BrCI_2N_3O_5S$

(M, 613.32). Calcd. : C, 47.00; H, 3.29; N, 6.85 %. Found: C, 47.14; H, 3.33; N, 6.89 %.

N-[1-(7-coumarinthio-4-methyl)-4-bromo-3,4-dichloro-2-nitro-1,3-butadienyl)]-N^{1}-[1-(2-hydroxyethyl)]- piperazine **(6j)**

Yield:0.12 gr (47 %); m.p. 168-170^{0}C. R_f ($CH_3\hat{O}H$)): 0.72; IR (KBr, cm^{-1}): 2931, 3075 (C-H), 1600, 1615 (C=C), 1735 (C=O), 1520, 1536 (C-NO_2), 3515 (OH); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.18-7.66 (3H, *m*, H_{arom}), 3.10-3.65 (8H, *m,* H_{piper}) , 3.81-4.00 (2H ,*t*, CH_2OH, *J* = 6.32 Hz), 2.18-2.21 (2H, *t*, CH_2, *J* = 6.32 Hz), 6.25 (1H ,*s*, CO-CH), 2.40 (3H,*s*, CH_3) , 1.58 (1H ,*s*, OH);APT (500 MHz, $CDCl_3$, δ/ ppm): 18.2, 51.2, 53.4, 57.6, 58.8, 112.0, 113.8, 115.8, 119.0, 120.0, 120.4, 124.8, 124.9, 125.0, 130.3, 151.6, 153.8, 159.8; MS (+ESI) (m/z) : 568.30 (M^+); $C_{20}H_{23}BrCI_2N_3O_5S$ (M,568.31). Calcd. : C, 42.27; H, 4.08; N, 7.39 %. Found: 42.59; H, 4.14; N, 7.43 %.

4-Bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(piperidinyl)-1,3-butadiene **(8a)**

Yield:0.12 gr (55 %); m.p. 180-181^{0}C. R_f (CH_2Cl_2): 0.36; IR (KBr, cm^{-1}): 2940, 3071 (C-H), 1600, 1625 (C=C), 1745 (C=O), 1384, 1531 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.20-7.61 (3H, *m*, H_{arom}), 3.22-4.10 (9H, *m,* H_{piper}) , 6.25 (1H, *s*, COCH), 2.39 (3H, *s,* CH_3);APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 22.4, 26.0, 50.2, 114.6, 115.8, 116.2, 119.8, 119.9, 124.0, 124.1, 125.0, 125.2, 139.8, 151.0, 153.4, 159.2; MS (+ESI) (m/z) : 520.23 (M^+) ; $C_{19}H_{17}BrCI_2N_2O_4S$ (M, 520.50). Calcd. : C, 43.87; H, 3.29; N, 5.40 %. Found: C, 43.92; H, 3.51; N, 5.45 %.

4-Bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(4-methyl piperidinyl)-1,3-butadiene **(8b)**

Yield: 0.17 gr (75 %); m.p. 126-128^{0}C. R_f (EtAc): 0.78; IR (KBr, cm^{-1}): 2900, 3075 (C-H), 1600, 1625 (C=C), 1738 (C=O), 1360, 1545 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.20-7.80 (3H, *m*, H_{arom}), 3.21-4.00 (9H, *m,* H_{piper}) , 0.88 (3H ,*s*, $CH_{3\ piper}$), 6.25 (1H, *s*, COCH), 2.39 (3H, *s,* CH_3). APT (500 MHz, $CDCl_3$, δ/ ppm): 19.0, 21.8, 30.0, 30.1, 34.0, 113.0, 114.0, 116.1, 119.0, 120.1, 120.3, 122.2, 128.0, 130.2, 141.5 152.0, 154.0, 160.0; MS (+ESI) (m/z) : 534.83 (M^+), 487.95 (M-NO_2); $C_{20}H_{19}BrCI_2N_2O_4S$ (M, 534.26). Calcd.: C, 44.96; H, 3.58; N, 5.24 % . Found: C, 45.10; H, 3.91; N, 5.73 %. UV-Vis ($CHCI_3$) (λmax / nm): 244, 276, 323, 375.

4-Bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(4-benzyl piperidinyl)-1,3-butadiene **(8c)**

Yield: 0.11gr (44 %); m.p. 148-150^{0}C. R_f ($CHCl_3$): 0.32; IR (KBr, cm^{-1}): 2900, 3050 (C-H), 1600, 1625 (C=C), 1745 (C=O), 1360, 1530 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 6.99-7.60 (8H, *m*, H_{arom}), 2.60-4.40 (9H, *m,* H_{piper}) , 2.50-2.75 ppm (2H,*d*, CH_2), 6.25 (1H, *s*, COCH), 2.38 (3H, *s,* CH_3); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 29.0, 36.0, 42.0, 42.1, 112.0, 113.1, 115.7, 118.0, 119.2, 119.3, 121.1, 124.2, 125.0, 127.0, 127.2, 128.0, 134.0, 138.0, 150.2, 153.0, 159.0; MS (+ESI)(m/z) :610.88 (M^+); $C_{26}H_{23}BrCI_2N_2O_4S$ (M, 610.36). Calcd.: C, 51.16; H, 3.79; N, 4.59 %. Found: C, 51.64; H, 4.02; N, 4.82 %.

4-Bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(4-hydroxy piperidinyl)-1,3-butadiene **(8d)**

Yield:0.12 gr (54 %); m.p. 168-170^{0}C. R_f (EtAc): 0.32; IR (KBr, cm^{-1}): 2950, 3100 (C-H), 1600, 1620 (C=C), 1735 (C=O), 1365, 1540 (C-NO_2), 3455 (OH); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.20-7.62 (3H, *m*, H_{arom}), 3.15-3.68 (9H, *m,* H_{piper}) , 6.25 (1H, *s*, COCH), 2.39 (3H, *s,* CH_3), 3.88 (1H, s, OH); APT (500 MHz, $CDCl_3$, δ/ ppm): 18.0, 32.2, 48.6, 64.1, 112.0, 112.4, 115.8, 118.8, 119.0, 119.8, 123.8, 124.4, 126.0, 138.8, 151.0 153.9, 159.8; MS (+ESI) (m/z) : 536.95 (M^+); $C_{19}H_{17}BrCI_2N_2O_5S$ (M, 536.63). Calcd. : C, 42.56; H, 3.19; N, 5.22 %. Found: C, 42.62; H, 3.21; N, 5.30 %.

4-Bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(4-morpholinyl)-1,3-butadiene **(10)**

Yield:0.14 gr (62 %); m.p. 175-176^{0}C.R_f (CH_2Cl_2):0.22; IR (KBr, cm^{-1}): 2900, 3069 (C-H), 1600, 1625 (C=C), 1735 (C=O), 1386, 1531 (C-NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.11-7.60 (3H, *m*, H_{arom}), 3.25-3.62 (8H, *m,* $H_{morfo.}$) , 6.25 (1H, *s*, COCH), 2.40 (3H, *s,* CH_3);APT (500 MHz, $CDCl_3$, δ/ ppm): 19.0, 54.0, 68.1, 113.8, 114.0, 115.8, 119.8, 120.0, 120.3, 122.0, 122.2, 124.8, 140.1, 152.0, 154.1, 160.1; MS (+ESI) (m/z) : 522.21 (M^+); $C_{18}H_{15}BrCI_2N_2O_5S$ (M, 522.10).Calcd. : C, 41.40; H, 2.89; N, 5.36 %. Found: C, 41.47; H, 3.00; N, 5.49 %.

4-bromo-3,4-dichloro-2-nitro-1-(7-coumarinthio-4-methyl)-1-(1,4-dioxoazospiryl)-1,3-butadiene **(12)**

Yield:0.17 gr (68 %); m.p. 180-181^{0}C. R_f (EtAc): 0.60; IR (KBr, cm^{-1}): 2900, 3050 (C-H), 1600, 1620 (C=C), 1735 (C=O), 1360, 1545 (C-

NO_2); ^{1}H-NMR (500 MHz, $CDCl_3$, δ/ ppm): 7.20-7.70 (3H, *m*, H_{arom}), 3.20-3.68 (8H, *m,* H_{piper}) , 3.89 (4H,*s*, O-$(CH_2)_2$-O) , 6.25 (1H, *s*, COCH), 2.40 (3H, *s,* CH_3). APT (500 MHz, $CDCl_3$, δ/ ppm): 18.4, 34.0, 52.0, 64.3, 108.0, 113.1, 113.9, 116.2, 120.0, 121.8, 124.8, 122.2, 126.0, 128.0, 130.0 136.0, 152.0, 154.0, 160.0; MS (+ESI) (m/z): 578.86 (M^+); $C_{21}H_{19}BrCI_2N_2O_6S$ (M, 578.27). Calcd.: C, 43.62; H, 3.31; N, 4.84 %. Found: C, 43.78; H, 3.55; N, 4.89 %. UV-Vis ($CHCI_3$) (λmax / nm): 246, 273, 327, 377.

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