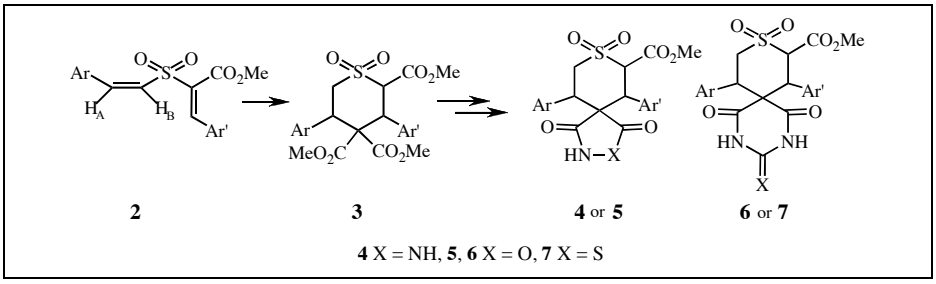
Venkatapuram Padmavathi,* Kaveti Sudheer, Dandu Rangayapalle Chinna
Venkata Subbaiah and Konda Mahesh

Department of Chemistry, Sri Venkateswara University, Tirupati – 517 502, A.P., India.
(Phone: +91-877-2249666-303; Fax: +91-877-2248499)
E-mail: vkpuram2001@yahoo.com
Received July 25, 2007



A new class of spiro heterocycles *viz*., spiropyrazolidinediones, isoxazolidinediones, pyrimidinetriones or thioxopyrimidinediones are developed from methyl 3-aryl-2-(*Z*-arylethenylsulfonyl)acrylate by double Michael addition reaction with dimethyl malonate followed by cyclocondensation with appropriate nucleophiles.

J. Heterocyclic Chem., **45**, 513 (2008).

INTRODUCTION

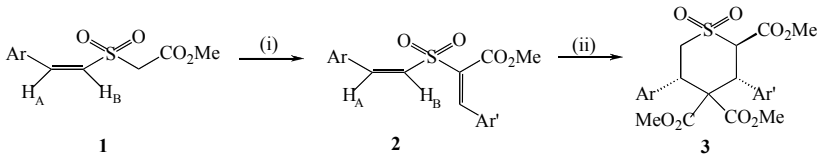
Amongst different heterocyclic systems, the chemistry of barbituric acid and their derivatives has drawn much attention due to their broad spectrum of chemotherapeutic properties such as hypnotic, antitumor, antiviral, anticonvulsant, analgesic and toxic [1,2]. A number of pyrazole derivatives also possess bacteriostatic, antidiabetic, analgesic, antiarrhythmic, anti-inflammatory, antiviral and antifungal [3-6]. In fact, celecoxib, a pyrazole derivative and valdecoxib, an isoxazole derivative are now widely used in the market as anti-inflammatory drugs [7]. A number of barbiturate and thio-barbiturate derivatives exhibit anticonvulsant, anaesthetic, sedative and hypnotic properties [8,9]. In fact, pheno-barbital and mephobarbital [10] are used for clinical treatment of epilepsy. Barbiturates still are used world wide in hospitals as injection narcotics [11,12]. During the last one and half decades we have been actively involved in the synthesis of spiro heterocycles [13]. In continuation of our sustained interest in this field, we herein report a new class of spiro heterocycles exploiting *gem* diester functionality with different nucleophiles.

RESULTS AND DISCUSSION

The synthetic scheme involves the preparation of 2,4,4-tricarbomethoxy-3,5-diaryltetrahydrothiopyran-1,1-dioxide (**3**) from methyl 3-aryl-2-(*Z*-arylethenylsulfonyl)acrylate (**2**). The compound **2** is prepared by the Knovenagel condensation of *Z*-styrylsulfonylacetic acid methyl ester (**1**) with araldehydes in the presence of piperidine in absolute ethanol (Scheme I & Table 1).

The double Michael addition of dimethyl malonate to **2** in the presence of Triton-B in toluene produced 2,4,4-tricarbomethoxy-3,5-diaryltetrahydrothiopyran-1,1-dioxide (**3**). The compound **3** is utilized as synthetic intermediate for the preparation of spiro-heterocycles. Cyclocondensation of **3** with hydrazine hydrate and hydroxylamine hydrochloride in the presence of sodium methoxide and methanol gave 6,10-diaryl-7-carbomethoxy-8-thia-2,3-diaza-spiro[4.5]decane-1,4-dione-8,8-dioxide (**4**) and 6,10-diaryl-7-carbomethoxy-8-thia-2-oxa-3-aza-spiro-

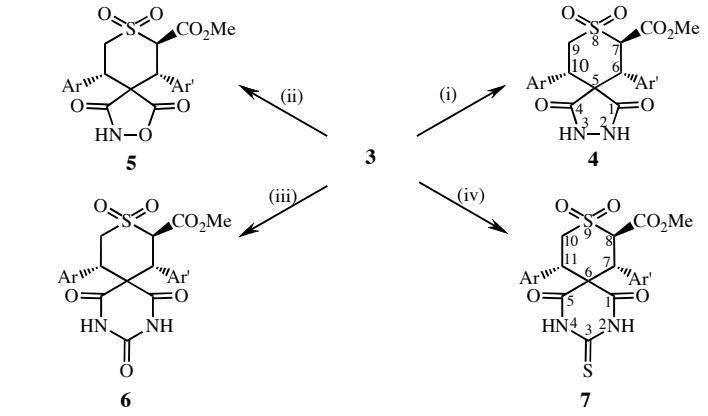
Scheme I



Ar = a) C_6H_5 Ar'= a) C_6H_5
Ar = b) *p*-$CH_3C_6H_4$ Ar'= b) *p*-$CH_3C_6H_4$
Ar = c) *p*-ClC_6H_4 Ar'= c) *p*-ClC_6H_4
Ar = d) C_6H_5 Ar'= d) *p*-$CH_3C_6H_4$
Ar = e) *p*-$CH_3C_6H_4$ Ar'= e) *p*-ClC_6H_4

(i) Ar'CHO / piperidine / EtOH
(ii) $CH_2(CO_2Me)_2$ /Triton-B/ Toluene

Scheme-II

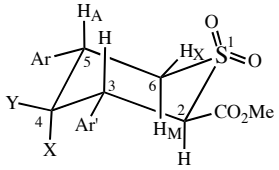


Ar = a) C_6H_5 Ar' = a) C_6H_5
Ar = b) *p*-$CH_3C_6H_4$ Ar' = b) *p*-$CH_3C_6H_4$
Ar = c) *p*-ClC_6H_4 Ar' = c) *p*-ClC_6H_4
Ar = d) C_6H_5 Ar' = d) *p*-$CH_3C_6H_4$
Ar = e) *p*-$CH_3C_6H_4$ Ar' = e) *p*-ClC_6H_4

(i) $NH_2NH_2.H_2O$ / NaOMe / MeOH
(ii) $NH_2OH.HCl$ / NaOMe / MeOH
(iii) NH_2CONH_2 / NaOMe / MeOH
(iv) NH_2CSNH_2 / NaOMe / MeOH

[4.5]decane-1,4-dione-8,8-dioxide (**5**). Similarly, the reaction of **3** with urea and thiourea resulted in 7,11-diaryl-8-carbomethoxy-9-thia-2,4-diaza-spiro[5.5]undecane-1,3,5-trione-9,9-dioxide (**6**) and 7,11-diaryl-8-carbomethoxy-9-thia-3-thioxo-2,4-diaza-spiro[5.5]undecane-1,5-dione-9,9-dioxide (**7**) (Scheme II & Table 1).

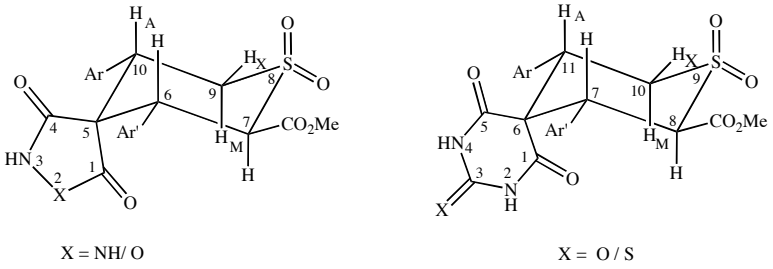
The IR spectra of **2** showed absorption bands in the regions 1120-1140 and 1325-1340 (SO_2), 1640-1655 (C=C) and 1730-1750 cm^{-1} (CO_2Me) (Table 2). The ^1H NMR spectrum of **2a** exhibited two singlets at 8.10 for Ar′C*H* and at 3.62 ppm for methoxy protons of carbomethoxy group and two doublets at 7.61, and 6.62 ppm for H_A and H_B protons. The coupling constant values (J = 9.7 Hz) indicate that they possess *cis* geometry. The IR spectra of **3** showed absorption bands at 1130-1150 and 1330-1340 (SO_2), 1735-1750 cm^{-1} (CO_2Me). The ^1H NMR spectrum of **3a** showed three double doublets for methylene and methine protons thus exhibiting an AMX splitting pattern. The axial methylene proton, H_M, due to the deshielding effect of sulfonyl group absorb farther downfield than the equatorial methylene proton, H_X. Thus three double doublets observed at 4.31, 4.11, 3.09 ppm in **3a** are assigned to H_A, H_M and H_X, respectively. The coupling constant values are found to be J_{AM} = 10.6 Hz, J_{MX} =15.2 Hz, J_{AX} = 5.6 Hz. Besides, two doublets are observed at 4.61, (C_3-H), 4.11 ppm (C_2-H) in **3a**. The coupling constant values (J = 10.6 Hz) indicates that they possess *trans* geometry (Table 3). Hence, it is presumed that the two aryl groups at C-3 and C-5 positions are in *cis* orientation of the chair conformation of 4,4- disubstituted thiandioxide ring, while the carbomethoxy group at C-2 is in equatorial position (Figure I). In fact, Otto and Yamamura have pointed out that in 3,5-diaryl-4,4-dialkoxycarbonyl-1,1-dioxides the two aryl groups at 3 and 5 positions have diequatorial arrangement based on the NMR spectra [14].



X = Y = CO_2Me; X = CO_2Et, Y = CN; X = Y = CN

Figure I

The IR spectra of **4**-**7** displayed absorption bands at 1735-1745 (CO_2Me), 1125-1140 and 1330-1345 (SO_2), 1655-1670 (*CO*NH), 3315-3340 cm^{-1} (NH) (Table 2). The ^1H NMR spectra of **4**-**7** can be rationalized by presuming that the two aryl groups at C-6 and C-10 in **4** and **5** and at C-7 and at C-11 in **6** and **7** are in true *cis* 1,3-arrangement in the preferred rigid chair conformation of thiandioxide moiety whereas the pyrimidine, pyrazole and isoxazole rings which are nearly planar would be perpendicular to the average plane of the thiandioxide ring [13a] (Figure II). The ^1H NMR spectra of **4a** and **5a** showed three double doublets at 4.21, 4.24 (H_A) 3.71, 3.65 (H_M) and 3.24, 3.26 (H_X) protons, two doublets at 4.11, 4.16 (C_7-H), 4.62, 4.56 (C_6-H). Apart from these a singlet is observed at 3.50 (**4a**) and at 3.57 (**5a**) whose integration accounts for the methoxy protons. A broad singlet is observed at 10.91 (**4a**) and 10.82 ppm (**5a**) for NH, which disappeared on deuteration. The ^1H NMR spectra of **6a** and **7a** exhibited three double doublets at 4.37, 4.46 (H_A) 3.69, 3.76 (H_M) and 3.23, 3.26 (H_X), two doublets at 4.62, 4.73 (C_7-H), 4.17, 4.14 (C_8-H) and a singlet at 3.51, 3.61 ppm (-COOMe), respectively. Apart from these, a broad singlet is observed at 10.79 and 10.83 for NH in **6a** and **7a**, which disappeared on deuteration. The structures of **4-7** are further confirmed by ^{13}C NMR spectra (Table 3).



X = NH/ O X = O / S

Figure II

CONCLUSION

A new class of spiro heterocylcles *viz*., spiro pyrazolidinediones, isoxazolidinediones, pyrimidinetriones and thioxopyrimidinediones are developed from bis unsaturated sulfone adopting simple, elegant and well versed methodology.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 1:3). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^1H NMR spectra were recorded

Table 1

Physical and Analytical Data of Compounds **2-7**

Compound	Mp (°C)	Ar	Ar′	Yield%	Molecular Formula	Analysis % Calcd. /Found		
						C	H	N
2a	79-80	Ph	Ph	69	$C_{18}H_{16}O_4S$	65.79 65.84	4.84 4.91	-
2b	104-106	4-MePh	4-MePh	66	$C_{20}H_{20}O_4S$	67.28 67.39	5.57 5.66	-
2c	98-99	4-ClPh	4-ClPh	72	$C_{18}H_{14}Cl_2O_4S$	54.36 54.42	3.48 3.55	-
2d	117-119	Ph	4-Me.Ph	65	$C_{19}H_{18}O_4S$	66.58 66.65	5.29 5.30	-
2e	126-128	4-MePh	4-ClPh	70	$C_{19}H_{17}ClO_4S$	60.43 60.55	4.36 4.55	-
3a	122-124	Ph	Ph	75	$C_{23}H_{24}O_8S$	59.87 59.99	5.31 5.25	-
3b	143-145	4-MePh	4-MePh	79	$C_{25}H_{28}O_8S$	61.55 61.46	5.66 5.78	-
3c	149-151	4-Cl.Ph	4-Cl.Ph	76	$C_{23}H_{22}Cl_2O_8S$	52.14 52.18	4.17 4.19	-
3d	136-138	Ph	4-Me.Ph	72	$C_{24}H_{26}O_8S$	60.69 60.75	5.55 5.52	-
3e	129-131	4-MePh	4-ClPh	74	$C_{24}H_{25}ClO_8S$	56.69 56.64	4.99 4.95	-
4a	222-224	Ph	Ph	65	$C_{21}H_{20}N_2O_6S$	58.82 58.87	4.72 4.70	6.70 6.54
4b	252-254	4-MePh	4-MePh	70	$C_{23}H_{24}N_2O_6S$	60.66 60.51	5.35 5.30	6.21 6.14
4c	248-250	4-ClPh	4-ClPh	75	$C_{21}H_{18}Cl_2N_2O_6S$	50.65 50.71	3.62 3.65	5.58 5.63
4d	228-230	Ph	4-MePh	62	$C_{22}H_{22}N_2O_6S$	59.84 59.72	4.98 5.01	6.44 6.33
4e	230-232	4-MePh	4-ClPh	74	$C_{22}H_{21}ClN_2O_6S$	55.50 55.40	4.49 4.44	5.98 5.87
5a	214-216	Ph	Ph	65	$C_{21}H_{19}NO_7S$	58.65 58.73	4.42 4.46	3.34 3.26
5b	240-242	4-Me.Ph	4-Me.Ph	68	$C_{23}H_{23}NO_7S$	60.51 60.38	5.10 5.07	3.12 3.06
5c	235-238	4-ClPh	4-ClPh	70	$C_{21}H_{17}Cl_2NO_7S$	50.58 50.61	3.41 3.44	2.77 2.81

Table 1 (continued)

Compound	Mp (°C)	Ar	Ar′	Yield%	Molecular Formula	Analysis % Calcd. /Found		
						C	H	N
5d	226-228	Ph	4-MePh	62	$C_{22}H_{21}NO_7S$	59.67 59.58	4.85 4.77	3.23 3.16
5e	222-224	4-MePh	4-ClPh	73	$C_{22}H_{20}ClNO_7S$	55.36 55.29	4.25 4.22	2.98 2.93
6a	290-292	Ph	Ph	68	$C_{22}H_{20}N_2O_6S_2$	55.80 55.92	4.25 4.27	6.00 5.93
6b	285-287	4-MePh	4-MePh	71	$C_{24}H_{24}N_2O_6S_2$	57.65 57.58	4.88 4.83	5.65 5.60
6c	274-276	4-Cl.Ph	4-Cl.Ph	65	$C_{22}H_{18}Cl_2N_2O_6S_2$	48.88 48.80	3.30 3.35	5.12 5.17
6d	280-282	Ph	4-Me.Ph	72	$C_{23}H_{22}N_2O_6S_2$	56.72 56.78	4.60 4.56	5.74 5.76
6e	270-272	4-MePh	4-Cl.Ph	69	$C_{23}H_{21}ClN_2O_6S_2$	53.15 53.02	4.08 4.06	5.43 5.38
7a	294-296	Ph	Ph	63	$C_{22}H_{20}N_2O_7S$	57.98 57.89	4.47 4.42	6.17 6.14
7b	285-287	4-MePh	4-MePh	68	$C_{24}H_{24}N_2O_7S$	59.55 59.49	5.01 4.99	5.72 5.78
7c	276-278	4-ClPh	4-ClPh	71	$C_{22}H_{18}Cl_2N_2O_7S$	50.25 50.30	3.48 3.45	5.38 5.33
7d	290-292	Ph	4-MePh	74	$C_{23}H_{22}N_2O_7S$	58.80 58.71	4.68 4.71	5.91 5.95
7e	282-284	4-MePh	4-ClPh	69	$C_{23}H_{21}ClN_2O_7S$	54.76 54.71	4.23 4.19	5.62 5.55

Table 2

IR Data of Compounds **2-7**

Compound	IR (cm^{-1})						
	SO_2		C=C	C=S	*CO*NH	CO_2Me	NH
2a	1131	1327	1652	--	-	1730	-
2b	1124	1329	1642	-	-	1743	-
2c	1139	1338	1648	-	-	1739	-
2d	1132	1331	1643	-	-	1736	-
2e	1135	1334	1641	-	-	1742	-
3a	1148	1339	-	-	-	1748	-
3b	1141	1330	-	-		1745	-
3c	1134	1332	-	-	-	1736	-
3d	1136	1336	-	-	-	1741	-
3e	1142	1333	-	-	-	1738	-
4a	1146	1338	-	-	1663	1742	3321
4b	1138	1336	-	-	1666	1748	3328
4c	1142	1339	-	-	1658	1739	3330
4d	1146	1335	-	-	1654	1742	3324
4e	1141	1346	-	-	1660	1736	3327
5a	1139	1342	-	-	1665	1738	3321
5b	1136	1339	-	-	1662	1742	3319
5c	1132	1338	-	-	1668	1731	3325
5d	1134	1332	-	-	1664	1738	3320
5e	1138	1340	-	-	1667	1731	3326
6a	1131	1338	-	-	1665	1736	3331
6b	1136	1335	-	-	1662	1734	3329
6c	1133	1332	-	-	1668	1737	3323
6d	1137	1339	-	-	1664	1732	3332
6e	1134	1331	-	-	1669	1735	3334
7a	1136	1334	-	1496	1663	1738	3336
7b	1131	1330	-	1501	1660	1741	3338
7c	1138	1336	-	1497	1665	1737	3327
7d	1134	1332	-	1499	1668	1734	3330
7e	1138	1335	-	1504	1662	1739	3333

Table 3

^{1}H and ^{13}C NMR Data of Compounds **2-7**

Compound	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
2a	3.62 (s, 3H, OCH_3), 6.62 (d, 1H, H_B, J = 9.7 Hz), 7.61 (d, 1H, H_A, J = 9.7 Hz), 8.10 (s, 1H, Ar′-CH), 7.12-7.48 (m, 10H, Ar-H)	53.1 (OCH_3), 125.4 (=$CHSO_2$), 129.7 (SO_2-*C*=(CO_2Me), 142.1 (=CH-Ar′), 145.4 (=CH-Ar), 176.1 (C=O), 128.2, 128.9, 129.4, 130.2, 130.8, 131.4, 131.6, 131.9 (aromatic carbons)
2b	2.28 (s, 6H, Ar-CH_3 & Ar′-CH_3), 3.58 (s, 3H, OCH_3), 6.60 (d, 1H, H_B, J = 9.6 Hz), 7.58 (d, 1H, H_A, J=9.6 Hz), 8.09 (s, 1H, Ar′-CH), 7.10-7.45 (m, 8H, Ar-H)	21.2 (Ar-CH_3 & Ar′-CH_3), 53.8 (OCH_3), 125.9 (=$CHSO_2$), 129.1 (SO_2-*C*=(CO_2Me), 141.8 (=CH-Ar′), 144.9 (=CH-Ar), 174.8 (C=O), 128.6, 129.1, 129.7, 130.4, 130.9, 131.2, 131.9, 132.4 (aromatic carbons)
2c	3.60 (s, 3H, OCH_3), 6.64 (d, 1H, H_B, J = 9.9 Hz), 7.63 (d, 1H, H_A, J = 9.9 Hz), 7.90 (s, 1H, Ar′-CH), 7.32-7.53 (m, 8H, Ar-H)	51.7 (OCH_3), 124.7 (=$CHSO_2$), 129.3 (SO_2-*C*=(CO_2Me), 142.8 (=CH-Ar′), 145.6 (=CH-Ar), 174.1 (C=O), 128.8, 129.4, 129.9, 131.4, 131.8, 132.0, 132.4, 132.8 (aromatic carbons)
2d	2.35 (s, Ar′-CH_3), 3.56 (s, 3H, OCH_3), 6.65 (d, 1H, H_B, J = 9.8 Hz), 7.64 (d, 1H, H_A, J = 9.8 Hz), 7.96 (s, 1H, Ar′-CH), 7.28-7.50 (m, 9H, Ar-H)	22.4 (Ar′-CH_3), 52.1 (OCH_3), 125.3 (=$CHSO_2$), 128.9 (SO_2-*C*=(CO_2Me), 142.1 (=CH-Ar′), 145.2 (=CH-Ar), 173.9 (C=O), 128.5, 129.1, 129.8, 130.6, 131.1, 131.7, 132.1, 132.5 (aromatic carbons)
2e	2.29 (s, Ar-CH_3), 3.59 (s, 3H, OCH_3), 6.63 (d, 1H, H_B, J = 9.6 Hz), 7.60 (d, 1H, H_A, J = 9.6 Hz), 7.92 (s, 1H, Ar′-CH), 7.24-7.51 (m, 8H, Ar-H)	21.8 (Ar-CH_3), 53.4 (O*C*H_3), 126.1 (=$CHSO_2$), 129.2 (SO_2-*C*=(CO_2Me), 142.6 (=CH-Ar′), 146.4 (=CH-Ar), 174.6 (C=O), 128.8, 129.6, 130.4, 130.8, 131.6, 131.9, 132.7, 133.2 (aromatic carbons)
3a	3.09 (dd, 1H, H_X, J_{AX} =5.6 Hz, J_{MX} =15.2 Hz), 3.58 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.11 (d, 1H, C_2-H), 3.37 (dd, 1H, H_M), 4.31 (dd, 1H, H_A, J_{AM}=10.2 Hz), 4.61 (d, 1H, C_3-H, J=10.6 Hz), 7.03-7.27 (m, 10H, Ar-H)	24.6 (C-3), 27.3 (C-5), 51.3, 54.6, 55.9 (3 -OCH_3), 58.6 (C-6), 59.9 (C-2), 67.3 (C-4), 173.9, 176.6, 179.3 (C=O), 126.6, 127.9, 128.6, 129.3, 129.9, 136.6, 139.3 (aromatic carbons)
3b	2.31 (s, 6H, Ar-CH_3 & Ar′-CH_3), 3.12 (dd, 1H, H_X, J_{AX}=5.8 Hz, J_{MX}=15.5 Hz), 3.52 (s, 3H, OCH_3), 3.68, (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.14 (d, 1H, C_2-H), 3.34 (dd, 1H, H_M), 4.26 (dd, 1H, H_A, J_{AM}=10.4 Hz), 4.65 (d, 1H, C_3-H, J=10.8 Hz), 7.08-7.36 (m, 8H, Ar-H)	20.9 (Ar-CH_3 & Ar′-CH_3), 24.2 (C-3), 27.9 (C-5), 50.7, 53.2, 54.7 (3-OCH_3), 56.8 (C-6), 59.5 (C-2), 67.7 (C-4), 174.7, 175.6, 177.8 (C=O), 127.9, 127.7, 128.1, 128.9, 129.1, 129.6, 137.5, 138.7 (aromatic carbons)
3c	3.08 (dd, 1H, H_X, J_{AX}=5.8 Hz, J_{MX}=15.5 Hz), 3.58 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.12 (d, 1H, C_2-H), 3.36 (dd, 1H, H_M), 4.22 (dd, 1H, H_A, J_{AM} =10.6 Hz), 4.64 (d, 1H, C_3-H, J=10.7 Hz), 7.02-7.31 (m, 8H, Ar-H)	24.7 (C-3), 27.1 (C-5), 50.2, 51.4, 53.4, (3-OCH_3), 56.4 (C-6), 58.6 (C-2), 66.9 (C-4), 173.9, 175.1, 178.4 (C=O), 128.5, 129.4, 129.8, 130.4 131.2, 132.7, 134.4, 138.9 (aromatic carbons)
3d	2.35 (s, 3H, Ar′-CH_3), 3.11 (dd, 1H, H_X, J_{AX} = 5.7 Hz, J_{MX} =15.8 Hz), 3.54 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 4.12 (d, 1H, C_2-H), 3.38 (dd, 1H, H_M), 4.28 (dd, 1H, H_A, J_{AM}=10.6 Hz), 4.59 (d, 1H, C_3-H, J=10.5 Hz), 7.10-7.39 (m, 9H, Ar-H)	22.7 (Ar′-CH_3), 24.2 (C-3), 27.8 (C-5), 50.6, 51.2, 51.6 (3-OCH_3), 56.7 (C-6), 59.5 (C-2), 67.4 (C-4), 174.0, 175.6, 177.8 (C=O), 128.2, 129.0, 129.2, 129.5, 131.4, 132.3, 134.8, 135.5 (aromatic carbons)
3e	2.33 (s, 3H, Ar-CH_3), 3.13 (dd, 1H, H_X, J_{AX}=5.5 Hz, J_{MX}=15.6 Hz), 3.49 (s,3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.11 (d, 1H, C_2-H), 3.41 (dd, 1H, H_M), 4.27 (dd, 1H, H_A, J_{AM}=10.6 Hz), 4.62 (d, 1H, C_3-H, J=10.7 Hz), 7.11-7.42 (m, 8H, Ar-H)	21.3 (Ar-CH_3), 24.2 (C-3), 28.4 (C-5), 50.6, 52.9, 55.7 (3-OCH_3), 56.2 (C-6), 59.2 (C-2), 67.2 (C-4), 174.3, 175.5 & 177.2 (C=O), 127.1, 127.4, 128.4, 128.8, 129.6, 130.1, 137.1, 138.5 (aromatic carbons)
4a	3.24 (dd, 1H, H_X, J_{AX}=5.3 Hz, J_{MX} =15.1 Hz), 3.50 (s, 3H, OCH_3), 3.71 (dd, 1H, H_M), 4.11 (d, 1H, C_7-H), 4.21 (dd, 1H, H_A, J_{AM}=10.1 Hz), 4.62 (d, 1H, C_6-H, J=10.8 Hz), 7.08-7.66 (m, 10H, Ar-H), 10.91 (bs, 2H, NH)	24.2 (C-6), 27.4 (C-10), 51.5 (CO_2CH_3), 56.2 (C-9), 59.2 (C-7), 67.2 (C-5), 172.5, 171.2 (C-1 & C-4), 174.3 (C=O), 128.6, 129.1, 129.5, 129.8, 131.1, 132.4, 134.7, 134.9 (aromatic carbons)
4b	2.29 (s, 6H, Ar-CH_3 & Ar′-CH_3), 3.22 (dd, 1H, H_X, J_{AX}=5.4 Hz, J_{MX} =15.3 Hz), 3.53 (s, 3H, OCH_3), 3.67 (dd, 1H, H_M), 4.14 (d, 1H, C_7-H), 4.23 (dd, 1H, H_A, J_{AM}=10.2 Hz), 4.59 (d, 1H, C_6-H, J=10.6 Hz), 7.10-7.64 (m, 8H, Ar-H), 10.98 (bs, 2H, NH)	20.4 (Ar-CH_3 & Ar′CH_3), 24.8 (C-6), 27.6 (C-10), 51.1 (CO_2CH_3), 56.6 (C-9), 59.6 (C-7), 67.0 (C-5), 170.4, 172.6 (C-1 & C-4), 174.5 (C=O), 128.2, 129.2, 129.4, 129.6, 131.4, 132.7, 134.3, 134.6 (aromatic carbons)
4c	3.25 (dd, 1H, H_X, J_{AX} = 5.7 Hz, J_{MX} =15.6 Hz), 3.56 (s, 3H, OCH_3), 3.65 (dd, 1H, H_M), 4.17 (d, 1H, C_7-H), 4.24 (dd, 1H, H_A, J_{AM} =10.5 Hz), 4.57 (d, 1H, C_6-H, J=10.5 Hz), 7.15-7.68 (m, 8H, Ar-H), 10.94 (bs, 2H, NH)	24.6 (C-6), 28.1 (C-10), 52.1 (CO_2CH_3), 56.9 (C-9), 59.7 (C-7), 67.6 (C-5), 171.4, 172.9 (C-1 & C-4), 174.5 (C=O), 128.4, 129.5, 129.9, 131.0, 131.5, 132.6, 134.9, 135.7 (aromatic carbons)
4d	2.36 (s, 3H, Ar′-CH_3), 3.23 (dd, 1H, H_X, J_{AX}=5.6 Hz, J_{MX}=15.4 Hz), 3.52 (s, 3H, OCH_3), 3.63 (dd, 1H, H_M), 4.13 (d, 1H, C_7-H), 4.21 (dd, 1H, H_A, J_{AM}=10.2 Hz), 4.52 (d, 1H, C_6-H, J=10.4 Hz), 7.08-7.62 (m, 9H, Ar-H), 10.89 (bs, 2H, NH)	22.3 (Ar′-CH_3), 24.1 (C-6), 28.6 (C-10), 52.7 (CO_2CH_3), 57.1 (C-9), 59.9 (C-7), 67.2 (C-5), 171.7, 172.3 (C-1 & C-4), 174.8 (C=O), 128.1, 129.4, 131.4, 131.9, 132.4, 133.1, 134.1, 134.8 (aromatic carbons)
4e	2.26 (s, 3H, Ar-CH_3), 3.24 (dd, 1H, H_X, J_{AX}=5.8 Hz, J_{MX}=15.3 Hz), 3.54 (s, 3H, OCH_3), 3.66 (dd, 1H, H_M), 4.15 (d, 1H, C_7-H), 4.23 (dd, 1H, H_A, J_{AM}=10.3 Hz), 4.54 (d, 1H, C_6-H, J=10.6 Hz), 7.11-7.67 (m, 8H, Ar-H), 10.86 (bs, 2H, NH)	21.7 (Ar-CH_3), 24.8 (C-6), 28.2 (C-10), 52.9 (CO_2CH_3), 57.7 (C-9), 59.2 (C-7), 67.7 (C-5), 172.1, 172.9 (C-1 & C-4), 174.2 (C=O), 128.4, 129.0, 131.6, 132.5, 133.2, 133.7, 134.6, 137.8 (aromatic carbons)

Table 3 (continued)'

Compound	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
5a	3.26 (dd, 1H, H_X, J_{AX}=5.9 Hz, J_{MX}=15.7 Hz), 3.57 (s, 3H, OCH_3), 3.65 (dd, 1H, H_M), 4.16 (d, 1H, C_7-H), 4.24 (dd, 1H, H_A, J_{AM}=10.4 Hz), 4.56 (d, 1H, C_6-H, *J*=10.7 Hz), 7.12-7.69 (m, 10H, Ar-H), 10.82 (bs, 1H, NH)	24.8 (C-6), 27.7 (C-10), 51.9 (CO_2CH_3), 56.4 (C-9), 59.6 (C-7), 67.3 (C-5), 169.8 (C-4), 172.2 (C-1), 174.3 (C=O), 128.6, 129.1, 129.8, 131.1, 132.4, 133.3, 134.7, 134.9 (aromatic carbons)
5b	2.24 (s, 6H, Ar-CH_3 & Ar′-CH_3), 3.22 (dd, 1H, H_X, J_{AX}=5.6 Hz, J_{MX} =15.6 Hz), 3.55 (s, 3H, OCH_3), 3.62 (dd, 1H, H_M), 4.13 (d, 1H, C_7-H), 4.21 (dd, 1H, H_A, J_{AM}=10.2 Hz), 4.52 (d, 1H, C_6-H, *J*=10.5 Hz), 7.12-7.69 (m, 8H, Ar-H), 10.85 (bs, 1H, NH)	20.7 (Ar-CH_3 & Ar′CH_3), 24.1 (C-6), 27.2 (C-10), 51.3 (CO_2CH_3), 56.0 (C-9), 59.1 (C-7), 67.5 (C-5), 169.2 (C-4), 171.6 (C-1), 174.0 (C=O), 128.2, 129.2, 129.8, 131.4, 132.0, 133.1, 134.2, 134.7 (aromatic carbons)
5c	3.19 (dd, 1H, H_X, J_{AX}=5.4 Hz, J_{MX}=15.5 Hz), 3.52 (s, 3H, OCH_3), 3.60 (dd, 1H, H_M), 4.11 (d, 1H, C_7-H), 4.18 (dd, 1H, H_A, J_{AM}=10.1Hz), 4.51 (d, 1H, C_6-H, *J*=10.4 Hz), 7.08-7.72 (m, 8H, Ar-H), 10.82 (bs, 1H, NH)	24.6 (C-6), 27.9 (C-10), 51.8 (CO_2CH_3), 56.4 (C-9), 59.9 (C-7), 67.8 (C-5), 170.1 (C-4), 171.9 (C-1), 174.7 (C=O), 128.4, 129.0, 129.6, 131.8, 132.6, 133.4, 134.5, 137.7 (aromatic carbons)
5d	2.32 (s, 3H, Ar′-CH_3), 3.24 (dd, 1H, H_X, J_{AX}=5.5 Hz, J_{MX}=15.8 Hz), 3.57 (s, 3H, OCH_3), 3.65 (dd, 1H, H_M), 4.16 (d, 1H, C_7-H), 4.23 (dd, 1H, H_A, J_{AM}=10.3 Hz), 4.53 (d, 1H, C_6-H, *J*=10.5 Hz), 7.14-7.70 (m, 9H, Ar-H), 10.88 (bs, 1H, NH)	23.1 (Ar′-CH_3), 24.4 (C-6), 27.7 (C-10), 51.2 (CO_2CH_3), 56.4 (C-9), 59.5 (C-7), 67.1 (C-5), 170.7 (C-4), 172.2 (C-1), 174.2 (C=O), 128.5, 129.1, 129.6, 129.9, 131.2, 132.3, 134.1, 134.8 (aromatic carbons)
5e	2.24 (s, 3H, Ar-CH_3), 3.22 (dd, 1H, H_X, J_{AX}=5.4 Hz, J_{MX}=15.7 Hz), 3.54 (s, 3H, OCH_3), 3.62 (dd, 1H, H_M), 4.14 (d, 1H, C_7-H), 4.22 (dd, 1H, H_A, J_{AM}=10.1 Hz), 4.56 (d, 1H, C_6-H, *J*=10.6 Hz), 7.11-7.71 (m, 8H, Ar-H), 10.85 (bs, 1H, NH)	20.8 (Ar-CH_3), 24.8 (C-6), 27.5 (C-10), 51.6 (CO_2CH_3), 56.8 (C-9), 59.2 (C-7), 67.5 (C-5), 169.6 (C-4), 171.4 (C-1), 174.4 (C=O), 128.2, 129.4, 129.6, 129.9, 131.1, 132.0, 134.4, 134.6 (aromatic carbons)
6a	3.23 (dd, 1H, H_X, J_{AX}=5.7 Hz, J_{MX} =15.6 Hz), 3.51 (s, 3H, OCH_3), 3.69 (dd, 1H, H_M), 4.17 (d, 1H, C_8-H), 4.37 (dd, 1H, H_A, J_{AM}=10.2 Hz), 4.62 (d, 1H, C_7-H, *J*=10.6 Hz), 7.11-7.70 (m, 10H, Ar-H), 10.79 (bs, 2H, NH)	24.2 (C-7), 27.1 (C-11), 51.4 (CO_2CH_3), 56.4 (C-10), 59.4 (C-8), 67.1 (C-6), 157.4 (C-3), 174.6 (C=O), 175.9 (C-5), 177.5 (C-1), 128.0, 129.7, 129.9, 131.2, 132.1, 134.1, 134.2, 134.5 (aromatic carbons)
6b	2.25 (s, 3H, Ar-CH_3 & Ar′-CH_3), 3.22 (dd, 1H, H_X, J_{AX}=5.5 Hz, J_{MX} =15.5 Hz), 3.52 (s, 3H, OCH_3), 3.62 (dd, 1H, H_M), 4.15 (d, 1H, C_8-H), 4.20 (dd, 1H, H_A, J_{AM}=10.1 Hz), 4.51 (d, 1H, C_7-H, *J*=10.4 Hz), 7.12-7.74 (m, 8H, Ar-H), 10.81 (bs, 2H, NH)	21.1 (Ar-CH_3 & Ar′CH_3), 24.9 (C-7), 27.6 (C-11), 51.8 (CO_2CH_3), 56.1 (C-10), 60.1 (C-8), 67.7 (C-6), 157.9 (C-3), 174.4 (C=O), 175.3 (C-5), 177.9 (C-1), 128.1, 129.2, 129.5, 130.2, 131.3, 132.1, 133.9, 134.7 (aromatic carbons)
6c	3.20 (dd, 1H, H_X, J_{AX}=5.4 Hz, J_{MX} =15.3 Hz), 3.50 (s, 3H, OCH_3), 3.61 (dd, 1H, H_M), 4.13 (d, 1H, C_8-H), 4.22 (dd, 1H, H_A, J_{AM} =10.2 Hz), 4.53 (d, 1H, C_7-H), 7.09-7.81 (m, 8H, Ar-H), 10.84 (bs, 2H, NH)	24.7 (C-7), 27.4 (C-11), 51.2 (CO_2CH_3), 56.1 (C-10), 59.7 (C-8), 67.4 (C-6), 157.9 (C-3), 168.4 (C-5), 170.2 (C-1), 174.7 (C=O), 128.3, 129.2, 129.6, 129.9, 131.3, 132.4, 134.4, 134.7 (aromatic carbons)
6d	2.35 (s, 3H, Ar′-CH_3), 3.24 (dd, 1H, H_X, J_{AX}=5.6 Hz, J_{MX}=15.7 Hz), 3.55 (s, 3H, OCH_3), 3.61 (dd, 1H, H_M), 4.17 (d, 1H, C_8-H), 4.22 (dd, 1H, H_A, J_{AM} =10.2 Hz), 4.53 (d, 1H, C_7-H, *J*=10.5 Hz), 7.11-7.69 (m, 9H, Ar-H), 10.81 (bs, 2H, NH)	22.6 (Ar′-CH_3), 24.2 (C-7), 27.2 (C-11), 51.0 (CO_2CH_3), 56.4 (C-10), 59.3 (C-8), 67.6 (C-6), 158.1 (C-3), 169.3 (C-5), 171.3 (C-1), 174.2 (C=O), 128.1, 129.0, 129.3, 129.6, 131.5, 132.7, 134.5, 134.9 (aromatic carbons)
6e	2.23 (s, 3H, Ar-CH_3), 3.21 (dd, 1H, H_X, J_{AX}=5.3 Hz, J_{MX}=15.4 Hz), 3.49 (s, 3H, OCH_3), 3.60 (dd, 1H, H_M), 4.12 (d, 1H, C_8-H), 4.19 (dd, 1H, H_A, J_{AM} =10.1 Hz), 4.55 (d, 1H, C_7-H, *J*=10.6 Hz), 7.10-7.77 (m, 8H, Ar-H), 10.83 (bs, 2H, NH)	21.4 (Ar-CH_3), 24.9 (C-7), 27.7 (C-11), 51.8 (CO_2CH_3), 56.9 (C-10), 60.1 (C-8), 67.9 (C-6), 158.8 (C-3), 170.3 (C-5), 171.7 (C-1), 174.0 (C=O), 128.7, 129.6, 130.4, 131.9, 132.3, 133.6, 134.0, 136.9 (aromatic carbons)
7a	3.26 (dd, 1H, H_X, J_{AX}=5.4 Hz, J_{MX}=15.3 Hz), 3.61 (s, 3H, OCH_3), 3.76 (dd, 1H, H_M), 4.14 (d, 1H, C_8-H), 4.46 (dd, 1H, H_A, J_{AM}=10.1 Hz), 4.73 (d, 1H, C_7-H, *J*=10.5 Hz), 7.08-7.49 (m, 10H, Ar-H), 10.83 (bs, 2H, NH)	24.1 (C-7), 26.4 (C-11), 52.3 (CO_2CH_3), 57.6 (C-10), 59.4 (C-8), 66.4 (C-6), 164.7 (C-3), 167.6 (C-5), 171.1 (C-1), 175.2 (C=O), 128.1, 129.4, 129.8, 131.4, 134.3, 134.7, 135.8 (aromatic carbons)
7b	2.23 (s, 3H, Ar-CH_3 & Ar′-CH_3), 3.24 (dd, 1H, H_X, J_{AX} = 5.5 Hz, J_{MX} =15.5 Hz), 3.51 (s, 3H, OCH_3), 3.62 (dd, 1H, H_M), 4.18 (d, 1H, C_8-H), 4.42 (dd, 1H, H_A, J_{AM} =10.3 Hz), 4.65 (d, 1H, C_7-H, *J*=10.7 Hz), 7.10-7.72 (m, 8H, Ar-H), 10.86 (bs, 2H, NH)	20.6 (Ar-CH_3 & Ar′-CH_3), 24.5 (C-7), 26.6 (C-11), 51.6 (CO_2CH_3), 58.4 (C-10), 59.8 (C-8), 67.8 (C-6), 165.9 (C-3), 168.2 (C-5), 170.8 (C-1), 174.8 (C=O), 128.4, 129.1, 129.4, 129.7, 131.8, 134.2, 135.2 (aromatic carbons)
7c	3.26 (dd, 1H, H_X, J_{AX}=5.6 Hz, J_{MX} =15.7 Hz), 3.54 (s, 3H, OCH_3), 3.68 (dd, 1H, H_M), 4.16 (d, 1H, C_8-H), 4.49 (dd, 1H, H_A, J_{AM}=10.3 Hz), 4.70 (d, 1H, C_7-H, *J*=10.4 Hz), 7.12-7.78 (m, 8H, Ar-H), 10.84 (bs, 2H, NH)	24.9 (C-7), 25.9 (C-11), 51.2 (CO_2CH_3), 58.1 (C-10), 60.1 (C-8), 67.2 (C-6), 166.3 (C-3), 168.9 (C-5), 170.1 (C-1), 174.0 (C=O), 128.9, 129.6, 129.9, 130.4 132.6, 133.4, 134.8, 135.8 (aromatic carbons)-
7d	2.33 (s, 3H, Ar′-CH_3), 3.22 (dd, 1H, H_X, J_{AX} = 5.4 Hz, J_{MX} =15.5 Hz), 3.58 (s, 3H, OCH_3), 3.66 (dd, 1H, H_M), 4.17 (d, 1H, C_8-H), 4.42 (dd, 1H, H_A, J_{AM} =10.5 Hz), 4.74 (d, 1H, C_7-H, *J*=10.5 Hz), 7.15-7.72 (m, 9H, Ar-H), 10.91 (bs, 2H, NH)	22.1 (Ar′-CH_3), 24.2 (C-7), 25.5 (C-11), 51.5 (CO_2CH_3), 58.4 (C-10), 60.6 (C-8), 68.8 (C-6), 166.1 (C-3), 168.2 (C-5), 169.8 (C-1), 173.6 (C=O), 128.4, 129.7, 130.0, 130.6 131.4, 132.7, 133.0, 133.6. (aromatic carbons)
7e	2.22 (s, 3H, Ar-CH_3), 3.25 (dd, 1H, H_X, J_{AX}=5.6 Hz, J_{MX}=15.7 Hz), 3.56 (s, 3H, OCH_3), 3.67 (dd, 1H, H_M), 4.19 (d, 1H, C_8-H), 4.38 (dd, 1H, H_A, J_{AM}=10.6 Hz), 4.75 (d, 1H, C_7-H, *J*=10.6 Hz), 7.12-7.81 (m, 8H, Ar-H), 10.92 (bs, 2H, NH)	20.9 (Ar-CH_3), 24.2 (C-7), 26.5 (C-11), 51.4 (CO_2CH_3), 57.9 (C-10), 59.4 (C-8), 67.6 (C-6), 166.2 (C-3), 167.8 (C-5), 171.1 (C-1), 174.3 (C=O), 128.2, 129.2, 129.3, 131.6, 131.9, 132.4, 133.4 (aromatic carbons)

in $CDCl_3$/DMSO-d_6 on a Varian EM-360 spectrometer (300 MHz). The ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Varian VXR spectrometer operating at 75.5 MHz. All chemical shifts were reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer. The starting compound *Z*-styrylsulfonylacetic acid methyl ester (**1**) was prepared by the literature procedure [15].

Methyl 3-aryl-2-(*Z*-arylethenylsulfonyl)acrylate (2). General Procedure. A mixture of Z-styrylsulfonylacetic acid methyl ester **1** (1 mmol), araldehyde (1 mmol) in absolute ethanol (10 mL) was taken and to this piperidine (0.3 mL) was added. The contents were refluxed for 6-8 hours, cooled and poured into ice-cold water (100 mL) containing concentrated hydrochloric acid (5 mL). The resulting mixture was extracted with ethyl acetate and the organic layer was washed with saturated sodium bisulfite solution, brine and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the crude substance was recrystallized from 2-propanol.

2,4,4,-Tricarbomethoxy-3,5-diaryltetrahydrothiopyran-1,1-dioxide (3). General Procedure. A mixture of **2** (1 mmol), dimethyl malonate (1.5 mmol) and catalytic amount of Triton-B (0.3 mL) in toluene (10 mL) was taken and refluxed for 3-4 hours. The reaction mixture was cooled and the solvent was removed under reduced pressure. The solid obtained was recrystallized from 2-propanol.

6,10-Diaryl-7-carbomethoxy-8-thia-2,3-diaza-spiro[4.5]-decane-1,4-dione-8,8-dioxide (4) / 6,10-diaryl-7-carbomethoxy-8-thia-2-oxa-3-aza-spiro[4.5]decane-1,4-dione-8,8-dioxide (5). General Procedure. To a solution of **3** (1 mmol), hydrazine hydrate (1.5 mmol) / hydroxylamine hydrochloride (1.2 mmol) in MeOH (20 mL), 10% NaOMe (3 mL) was added and refluxed for 6–8 hours. The solution was cooled and poured into crushed ice (100 g) containing concentrated hydrochloric acid (5 mL). The solid obtained was filtered, dried, and recrystallized from MeOH.

7,11-Diaryl-8-carbomethoxy-9-thia-2,4-diaza-spiro[5.5]-undecane-1,3,5-trione-9,9-dioxide / 7,11-Diaryl-8-carbomethoxy-9-thia-3-thioxo-2,4-diaza-spiro[5.5]undecane-1,5-dione-9,9-dioxide (6/7). General Procedure. The compound **3** (1 mmol) was dissolved in MeOH (10 mL). To this, urea / thiourea (1.5 mmol) in MeOH (10 mL) was added and refluxed for 8-12 hours. The contents were cooled and poured into crushed ice (100 g) containing concentrated hydrochloric acid (5 mL). The separated solid was collected by filtration and recrystallized from MeOH.

REFERENCES

[1] Voronin, V. G.; Polevaya, O. Yu.; Makhanova, V. G.; Landau, M. A.; Kolbanov, V. M.; Priovol' neva, T. P.; Chugunov, V. V.; Lavertskaya, E. F. *Khim-Farm Zh*. **1976**, *10*, 43.

[2] Aboul-Enein, M. N.; El-Azzouny, A. A. *Acta Pharm sue*. **1986**, *23*, 107.

[3] Dannahardt, G.; Kiefer, W.; Kramer, G.; Maehrlein, S.; Nowe, U.; B. Fiebich. *Eur. J. Med. Chem.* **1998**, *41*, 63.

[4] Heinemann, H.; Wolfgang, K.; Owe, S.; Gerd, B.; Ulrich, K.; Ger Offen DE, 3424586, 1986, *Chem. Abstr*. **1986,** *105*, 42788e.

[5] Varmini, G. L.; Gluseppe, D.; Paolo, G. *Mycopathol.* **1976,** *58*, 39.

[6] Gerald, L. G.; Scriven, F. V. E.; James, G. K.; Lowell, M. Eur. Patent, 1988, 269308, *Chem. Abstr*. **1988**, *109*, 211058g.

[7] Dannhardt, G.; Kiefer, W.; Kramer, G.; Maehrlein, S.; Nowe,U.; Fiebich,B. *Eur. J. Med. Chem.* **2000**, *35*, 499.

[8] Goodman, L. S.; Gilman, A. *The Pharmacological Basis of Therapeutics*, Mc Graw-Hill, New Delhi, **1991**, pp 358-360.

[9] Meyers, F. H.; Jawetz, E.; Goldfien, A. *Review of Medical Pharmacology*, Lange Medical Publications, Los Altos, California, **1976**, pp 222.

[10] Hardman, J. G.; Limbird, L. E. *Goodman & Gilman's The Pharmacological Basis of Therapeutics,* Mc Graw-Hill: New York, **1996**, pp 471 & 472.

[11] Cope, A. C.; Kovacic, P.; Burg, M. *J. Am. Chem. Soc*. **1949**, *71*, 3656.

[12] Geigy, J. R.; Swiss, A. G. 230367, 1944; *Chem. Abstr*. **1949**, *43*, 3472i.

[13a] Bhaskar Reddy, D.; Padmavathi, V.; Ramana Reddy, P V. *Indian J Chem*. **1992**, *31B*, 774; [b] Bhaskar Reddy, D.; Padmavathi, V.; Seenaiah, B.; Padmaja, A. *Heteroatom Chem*. **1993**, *4*, 55; [c] Bhaskar Reddy, D.; Chandrasekhar Babu, N.; Padmavathi, V. *J. Heterocycl. Chem*. **2001**, *38*, 769; [d] Bhaskar Reddy, D.; Chandrasekhar Babu, N.; Padmavathi, V. *Heteroatom Chem*. **2001**, *12*, 131; [e] Padmavathi, V.; Venkata Subbaiah, D R C.; Rajagopala Sarma, M.; Balaiah, A. *Heteroatom Chem*. **2004**, *7*, 477.

[14] Bhaskar Reddy, D.; Padmavathi, V.; Reddy, S.; *Sulfur Lett*. **1991**, 13, 123.

[15] Bhaskar reddy, D.; Muralidhar Reddy, M.; Subbaraju, G. V. *Indian J. Chem*. **1995**, *34B*, 816.