Syntheses of [1,2,3]Selenadiazolo[4,5-*e*]benzofuran or Benzothiophene, [1,2,3]Thiadiazolo[4,5-*e*]benzofuran or Benzothiophene, and 2-Benzofuranyl-1,3,4-oxodiazole Derivatives

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Dehydrogenation of ethyl 3-methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylate **1** with 2,2′-azobisisobutyronitrile and *N*-bromosuccinimide gave ethyl 4-hydroxy-3-methylbenzofuran-2-carboxylate **3**. Reaction of compounds **3-4** with hydrazine hydrate afforded the corresponding hydrazides **5a-b**. The reaction of **5a-b** with aldehydes yielded substituted hydrazones **6a-l**. Compounds **7a-d** were prepared from compounds **6a-d** and bromine in acetic acid. Lead tetraacetate oxidation of compounds **6e-l** afforded substituted oxadiazoles **8e-l**. Selenium dioxide oxidation of 4-oxo-4,5,6,7-tetrahydrobenzofuran semicarbazones **9**, **14a** and 4-oxo-4,5,6,7-tetrahydrobenzothiophene **14b** gave the tricyclic 1,2,3-selenadiazoles **10**, **15a** and **15b** respectively. Reaction of semicarbazones **9**, **14a** and **14b** with thionyl chloride afforded the corresponding 1,2,3-thiadiazoles **12**, **16a** and **16b** respectively.

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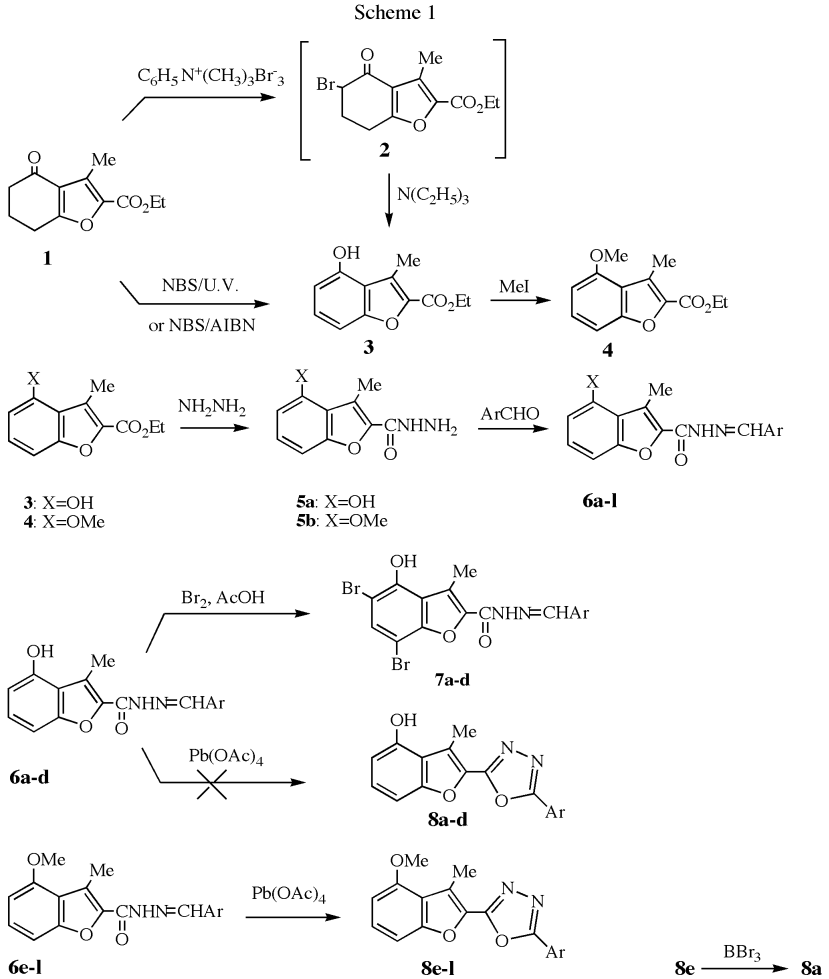
The risk of opportunistic fungal infection has been greatly increased due to the increasing number of immunocompromised patient, such as those infected with HIV-1, organ-transplants and those under cancer chemotherapy [1]. On the other hand the rising incidence of microbial resistance to conventionally utilized antimicrobial drugs has diverted scientist attention toward new compounds [2-3].

In view of the potential biochemical and physiological activity of benzo[*b*]furan, benzo[*b*]thiophene, oxadiazole, selendiazole and thiadiazole derivatives [4-10], it was

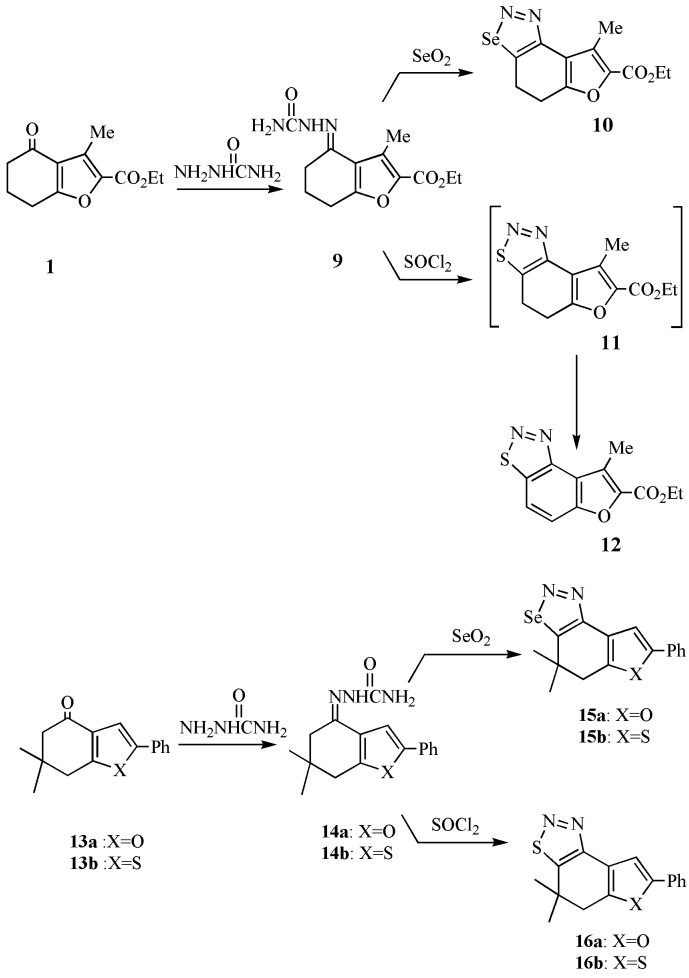
Scheme 1



thought worthwhile to prepare some fused derivatives of these structures as possible effective drugs against tropical diseases [11].

The desired compounds were synthesized according to Schemes 1 and 2.

Scheme 2



According to previous reports dehydrogenation of 4-oxo-4,5,6,7-tetrahydrobenzofurans has been achieved by heating with sulfur or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[12]. Alternatively bromination followed by dehydrobromination can give 4-hydroxybenzofuran [13]. In the present work the transformation of 4-oxo-4,5,6,7-tetrahydrobenzofuran into 4-hydroxybenzofuran was achieved by α-bromination of compound **1** with phenyltrimethylammonium perbromide in dry tetrahydrofuran and subsequent dehydrobromination with a weak base like triethylamine in 35% yield (method A) [14]. Also, heating compound **1** with *N*-bromosuccinimide in carbon tetrachloride in the presence of U.V. light gave compound **3** in one step and in 80% yield. Modification of the latter reaction by using 2,2′-azobisisobutyronitrile (AIBN) instead of U.V. light increased the reaction yield to 98% (method B) [15]. Methylation of compound **3** with equivalent iodomethane gave compound **4**. Addition of hydrazine hydrate to esters **3** and **4** gave the corresponding hydrazides **5a** and **5b** in high yield. Condensation of compounds **5a** and **5b** with different aldehydes in the presence of concentrated sulfuric acid afforded the corresponding hydrazones **6a-l**. The attempted cyclization of **6a-d** with bromine in glacial acetic acid containing anhydrous sodium acetate according to the literature [16], did not give the expected 1,3,4-oxadiazoles **8a-d** but rather gave predominately the arylaldehyde 5,7-dibromo-4-hydroxy-3-methylbenzofuran-2-carboxy hydrazones **7a-d**. In addition, refluxing 4-hydroxybenzofurans **6a-d** with lead tetraacetate in glacial acetic acid [17] resulted in decomposition of the starting material. However the reaction of 4-methoxybenzofurans **6e-l** under the latter condition gave the desired 1,3,4-oxadiazoles **8e-l** in good yield. In addition compound **8e** could be demethylated to the desired compound **8a** with boron tribromide in dichloromethane [18].

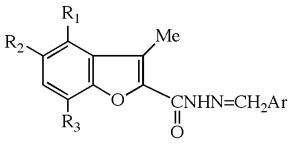
The reaction of compound **1** with semicarbazide hydrochloride afforded the corresponding semicarbazone **9** which was oxidized with selenium dioxide to give 4,5-dihydro-1,2,3-selenadiazolo[4,5-*e*]benzofuran (**10**). The reaction of compound **9** with thionyl chloride did not give 4,5-dihydro-[1,2,3]thiadiazolo[4,5-*e*]benzofuran **11**, but this compound was oxidized under the experimental condition and ethyl 8-methyl-[1,2,3]thiadiazolo[4,5-*e*]benzofuran-7-carboxylate (**12**) was obtained [19,20].

Semicarbazones of 6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzofuran and benzothiophene (**14a** and **14b**) were obtained from the reaction of related 4-oxobenzofuran and benzothiophene **13a** and **13b** [21-23], with semicarbazide hydrochloride. These compounds **14a** and **14b** were reacted with either selenium dioxide or thionyl chloride to afford the corresponding 4,5-dihydro-4,4-dimethyl-7-phenyl-[1,2,3]selenadiazolo[4,5-*e*]benzofuran (**15a**), 4,5-dihydro-4,4-dimthyl-7-phenyl-[1,2,3]selenadiazolo[4,5-*e*]benzothiophene (**15b**), 4,5-dihydro-4,4-dimethyl-7-pheyl-[1,2,3]thiadiazolo[4,5-*e*]benzofuran (**16a**), 4,5-dihydro-4,4-dimethyl-7-phenyl-[1,2,3]thiadiazolo[4,5-*e*]benzothiophene (**16b**) respectively.

EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ^{1}H nmr spectra were recorded on a Brucker FT-80 spectrometer. Tetramethylsilane was used as an internal standard. The infrared spectra were acquired on a Nicolet 550-FT spectrometer. The mass spectra were run on a Finnigan TSQ 70 spectrometer at 70 eV. Elemental analyses were carried out with a Perkin-Elmer Model 240-C apparatus. The results of elemental analyses (C, H, N) were within ±0.4% of the calculated values.

Table 1



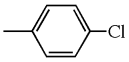
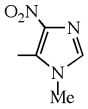
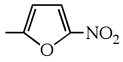
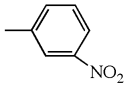
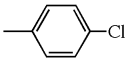
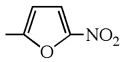
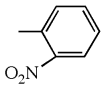
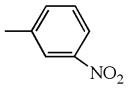
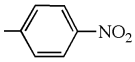
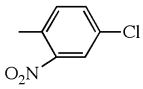
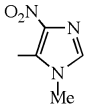
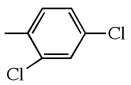
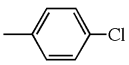
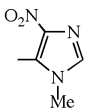
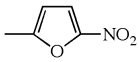
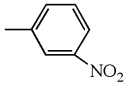
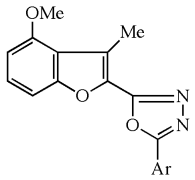
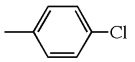
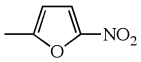
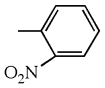
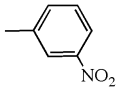
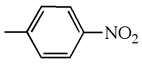
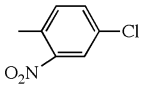
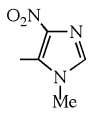
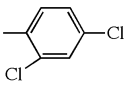
Comp.	R_1	R_2	R_3	**Ar**	Mp °C	Yield (%)	Formula	Calcd. C	Found C	Calcd. H	Found H	Calcd. N	Found N
6a	OH	H	H		313-315	85	$C_{17}H_{13}ClN_2O_3$	62.11	62.30	3.98	3.71	8.52	8.68
6b	OH	H	H		348-350	67	$C_{15}H_{13}N_5O_5$	52.48	52.61	3.82	3.73	20.40	20.28
6c	OH	H	H		315-316	72	$C_{15}H_{11}N_3O_6$	54.72	54.92	3.37	3.54	12.76	12.53
6d	OH	H	H		358-359	55	$C_{17}H_{13}N_3O_5$	60.18	60.48	3.86	3.63	12.38	12.18
6e	OMe	H	H		190-192	83	$C_{18}H_{15}ClN_2O_3$	63.07	63.38	4.41	4.11	8.17	8.31
6f	OMe	H	H		243-246	78	$C_{16}H_{13}N_3O_6$	56.05	56.32	3.81	3.68	12.22	12.45
6g	OMe	H	H		278-280	68	$C_{18}H_{15}N_3O_5$	61.19	61.37	4.28	4.46	11.89	11.63
6h	OMe	H	H		256-258	65	$C_{18}H_{15}N_3O_5$	61.19	61.49	4.28	4.58	11.89	11.94
6i	OMe	H	H		282-284	58	$C_{18}H_{15}N_3O_5$	61.19	61.39	4.28	4.58	11.89	11.93
6j	OMe	H	H		244-246	75	$C_{18}H_{14}ClN_3O_5$	55.75	55.93	3.64	3.82	10.84	10.59
6k	OMe	H	H		296-298	81	$C_{16}H_{15}N_5O_5$	53.78	53.46	4.23	4.56	19.61	19.42
6l	OMe	H	H		264-266	78	$C_{18}H_{17}Cl_2N_2O_3$	57.31	57.51	3.74	3.63	7.43	7.65
7a	OH	Br	Br		324-326	76	$C_{17}H_{11}Br_2ClN_2O_3$	41.97	41.73	2.28	2.41	5.76	5.53
7b	OH	Br	Br		358-360	73	$C_{15}H_{11}Br_2N_5O_5$	35.95	35.75	2.21	2.45	13.98	13.71
7c	OH	Br	Br		230-232	79	$C_{15}H_9Br_2N_3O_6$	36.99	36.78	1.86	1.63	8.63	8.41
7d	OH	Br	Br		337-339	58	$C_{17}H_{11}Br_2N_3O_5$	41.07	41.31	2.23	2.57	8.45	8.68

Table 2



Comp.	Ar	mp°C	Yield %	Formula	Calcd. C	Found	Calcd. H	Found	Calcd. N	Found
8e		210-212	83	$C_{18}H_{13}ClN_2O_3$	63.45	63.27	3.84	3.98	8.22	8.45
8f		244-246	87	$C_{16}H_{11}N_3O_6$	56.31	56.68	3.25	3.59	12.31	12.59
8g		216-220	82	$C_{18}H_{13}N_3O_5$	61.54	61.73	3.73	3.43	12.00	12.32
8h		219-221	78	$C_{18}H_{13}N_3O_5$	61.54	61.69	3.73	3.65	12.00	12.21
8i		249-252	69	$C_{18}H_{13}N_3O_5$	61.54	61.38	3.73	3.48	12.00	12.31
8j		294-296	65	$C_{18}H_{12}ClN_3O_5$	56.04	56.29	3.14	3.31	10.90	10.68
8k		284-286	70	$C_{16}H_{13}N_5O_5$	54.09	54.32	3.70	3.43	19.71	19.89
8l		251-253	88	$C_{18}H_{12}Cl_2N_2O_3$	57.62	57.31	3.22	3.45	7.50	7.79

Ethyl 3-Methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylate (**1**).

Compound **1** was prepared according to the reported methods [12] in 90% yield, mp 88-90 °C; ir (potassium bromide): ν 2985, 1735, 1655, 1460, 1352 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 4.38 (q, 2H, CH_2), 2.92 (t, 2H, CH_2), 2.55 (s, 3H, CH_3), 2.51 (t, 2H, CH_2), 2.18 (m, 2H, CH_2), 1.39 ppm (t, 3H, CH_3); ms: m/z (%) 222 (M^+, 100), 194 (69), 177 (41), 166 (44), 150 (25).

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.73; H, 6.59.

Ethyl 4-Hydroxy-3-methylbenzofuran-2-carboxylate (**3**).

Method A.

To a stirring solution of compound **1** (2.22 g, 10 mmoles) in THF (20 ml) a solution of phenyltrimethylammonium perbromide (3.75 g, 10 mmoles) in THF (20 ml) was added. The mixture was stirred at room temperature for 48 hours and filtered. The filtrate was evaporated under reduced pressure. The residue was dissolved in dichloromethane and washed with sodium bicarbonate solution, dried (sodium sulfate) and evaporated under reduced pressure. A solution of crude yellow oil, ethyl 5-bromo-3-methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylate (**2**), methanol (20 ml) and triethylamine (0.4 g, 20 mmoles) was refluxed for two hours. The methanol was removed, water was added and the precipitate was crystallized from carbon tetrachloride to give 0.77g (35%) of compound **3**, mp 138-140 °C; ir (potassium bromide): ν 3340, 2919, 1710, 1516, 1444, 1275 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.13 (m, 2H, aromatic), 6.57 (m, 1H, aromatic), 4.45 (q, 2H, CH_2), 2.77 (s, 3H, CH_3), 1.43 ppm (t, 3H, CH_3); ms: m/z (%) 220 (M^+, 100), 191 (60), 175 (43), 147 (37), 118 (20), 91 (19), 65 (10).

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.53; H, 5.49. Found: C, 65.32; H, 5.51.

Method B.

A solution of compound **1** (2.22 g, 10 mmoles) in wet carbon tetrachloride (40 ml) was heated to reflux and NBS (1.87 g, 10 mmoles) and AIBN (40 mg) were added in one portion to the refluxing solution under N_2 atmosphere. When all the NBS was converted to succinimide the reaction mixture was cooled to room temperature. The succinimide was removed by filtration and washed with CCl_4 (2×4 ml). The solvent was evaporated under reduced pressure to give the crude product which was

crystallized from carbon tetrachloride to give 2.15 g (98%) of compound **3**, mp and mixed melting point with an authentic sample (see method A) was 138-140 °C. It is worthy to mention that when dry carbon tetrachloride was used the reaction did not go to completion.

Ethyl 4-Methoxy-3-methylbenzofuran-2-carboxylate (**4**).

To a solution of compound **3** (2.2 g, 10 mmoles), iodomethane (1.42 g, 10 mmoles) in dry acetone (30 ml) and potassium carbonate (1.38 g, 10 mmoles) were added and the mixture was refluxed for 10 hours. The solvent was removed under reduced pressure and the residue was treated with 50 ml of water. The mixture was extracted with diethyl ether (3× 20 ml). The combined organic layers were dried (sodium sulfate) and evaporated under reduced pressure to give the crude product which was crystallized from methanol to give 1.64g (70%) of compound **4** as a white solid, mp 85-87 °C; ir (potassium bromide): ν 3075, 2955,1710, 1680, 1444, 1326, 1214 cm^{-1}; ^{1}H-nmr (deuteriochlorform): δ 7.14 (m, 2H, aromatic), 6.61 (m, 1H, aromatic), 4.43 (q, 2H, CH_2), 3.91 (s, 3H, OCH_3), 2.72 (s, 3H, CH_3), 1.42 ppm (t, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.88; H, 6.12.

4-Hydroxy-3-methylbenzofuran-2-carboxylic Acid Hydrazide (**5a**).

To a solution of compound **4** (2.2 g, 10 mmoles) in methanol (15 ml) hydrazine hydrate (2.5 g, 20 mmoles) was added and stirred at room temperature for 48 hours. The mixture was filtered and crystallized from water:methanol (1:1) to give 1.65 g (80%) of compound **5a**, mp 149-150 °C; ir (potassium bromide):ν 3344, 3108, 1634, 1291, 1050, 947, 717 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 7.69 (brs, 1H, NHCO), 7.15 (m, 2H, aromatic), 6.63 (d, 1H, aromatic), 2.71 ppm (s, 3H, Me); ms:m/z (%) 206 (M^+, 17), 175 (56), 119 (19), 91 (42), 65 (79), 39 (100).

Anal. Calcd. for C_{10} H_{10} N_2O_3: C, 58.00; H, 4.90; N, 13.59. Found: C, 58.25; H, 4.83; N, 13.37.

4-Methoxy-3-methylbenzofuran-2-carboxylic Acid Hydrazid (**5b**).

This compound was obtained from **4**, similarly to **5a**, mp 160-162 °C; ir (potassium bromide):ν 3324, 3216, 1654, 1603, 1495, 1280 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.69 (brs, 1H, NHCO), 7.26 (q, 1H, aromatic), 7.00 (d, 1H, aromatic), 6.63 (d, 1H, aromatic), 4.01 (brs, 2H, NH_2), 3.92 (s, 3H, OCH_3), 2.77 ppm (s, 3H, CH_3).

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.75; H, 5.65; N, 12.95.

p-Chlorobenzaldehyde 4-Hydroxy-3-methylbenzofuran-2-carboxyhydrazone (**6a**).

To a solution of compound **5a** (2.06 g, 10 mmoles) in methanol (50 ml) *p*-chlorobenzaldehyde (2.81 g, 20 mmoles) and sulfuric acid (1 ml) were added. The mixture was stirred at room temperature for 2 hours. The precipitate was collected by filtration and crystallized from ethanol to give 2.71 g (85%) of compound **6a**, mp 313-315 °C; ir (potassium bromide): ν 3247, 1680, 1603, 1480, 1337, 1147 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d_6): δ 11.92 (brs, 1H, NHCO), 10.25 (brs, 1H, OH), 8.15 (s, 1H, N=CH), 7.19 (m, 7H, aromatic), 2.71 (s, 3H, CH_3); ms: m/z (%) 328 (M^+, 5), 181 (15), 121 (10), 91 (100).

Anal. Calcd. for $C_{17}H_{13}ClN_2O_3$; C, 62.11; H, 3.98; N, 8.52. Found: C, 62.30; H, 3.71; N, 8.68.

Compounds **6b-l** were prepared similarly (see Table 1).

p-Chlorobenzaldehyde 5,7-Dibromo-4-hydroxy-3-methyl-benzofuran-2-carboxy hydrazone (**7a**).

To a solution of compound **6a** (1.64 g, 5 mmoles) and anhydrous sodium acetate (1.64 g, 20 mmoles) in galcial acetic acid (10 ml), bromine (0.44 g, 5.5 mmoles) was added under an atmosphere of argon and stirred at room temperature for 1 hour. The mixture was poured into water (40 ml). The crude product was collected by filtration and crystallized from methanol: diethyl ether (7:3) to give 1.84 g (76%) of compound **7a**, mp 323-325 °C; ir (potassium bromide): ν 3581, 3247, 1680, 1603, 1480, 1337, 1050, 748 cm^{-1}; ^{1}H-nmr (dimethyl-sulfoxide-d_6): δ 11.9 (brs, 1H, NHCO), 8.52 (s, 1H, -N=CH-), 7.69 (m, 5H, aromatic), 2.68 (s, 3H, Me); ms: m/z (%) 486 (M^+, 37), 432 (18), 348 (100), 219 (52).

Anal. Calcd. for $C_{17}H_{11}Br_2ClN_2O_3$: C, 41.97; H, 2.28; N, 5.76. Found: C, 41.73; H, 2.41; N, 5.53.

Compounds **7b-7d** were prepared similarly (see Table 1).

2-[3-Methyl-4-methoxybenzofuran-2-yl]-5-[4-chlorophenyl]-1,3,4-oxodiazole (**8e**).

A suspension of compound **6e** (1.71 g, 5 mmoles) and lead tetraacetate (4.43 g, 10 mmoles) in glacial acetic acid (50 ml) was refluxed for 4 hours. After cooling the precipitate was collected by filtration and washed with 4 *N* HCl (50 ml) to remove any lead compounds and crystallized from ethyl acetate:diethyl ether (7:3) to give 1.4 g (83%) of compound **8e**, mp 210-212 °C; ir (potassium bromide): ν 2914, 1603, 1485, 1280 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.66 (m, 6H, aromatic), 6.72 (m, 1H, aromatic) 3.96 (s, 3H, OCH_3), 2.84 (s, 3H, CH3); ms: m/z (%) 340 (M^+, 100), 324 (22), 267 (10), 234 (20), 138 (62).

Anal. Calcd. for $C_{18}H_{13}ClN_2O_3$: C, 63.45, H, 3.84; N, 8.22. Found: C, 63.27; H, 3.98; N, 8.45.

Compounds **8f-l** were prepared similarly (see Table 2).

2-[4-Hydroxy-3-methyl-benzofuran-2-yl]-5-[4-chlorophenyl]-1,3,4-oxadiazole (**8a**).

To a suspension of compound **8e** (3.41 g, 10 mmoles) in dry dichloromethane (30 ml), a solution of boron tribromide (2.5 g, 10 mmoles) in dichloromethane (10 ml) was added at 0-5 °C and stirred for 48 hours. The solvent was removed under reduced pressure. The residue was stirred with water (20 ml) to hydrolyze excess reagent and boron complexes. The product was collected by filtration to give the crude product which was crystallized from methanol:diethyl ether (7:3) to give 2.21 g (65%) of compound **8a** , mp 289-290 °C; ir (potassium bromide): ν 3347, 2919, 1603, 1480, 1337 cm^{-1}; ^{1}H-nmr (dimethyl sulfoxide-d6): δ 10.37 (s, 1H, OH), 8.38 (m, 4H, aromatic), 7.23 (m, 2H, aromatic), 6.73 (m, 1H, aromatic), 2.79 ppm (s, 3H, CH_3); ms: m/z (%) 328 (7), 326 (M^+, 46), 291 (60), 188 (100).

Anal. Calcd. for $C_{17}H_{11}ClN_2O_3$: C, 62.49; H, 3.39; N, 8.57. Found: C, 62.41; H, 3.32; N, 8. 53.

Ethyl 3-Methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylate Semicarbazone (**9**).

This compound was prepared accoriding to the reported methods [19] in 85% yield; mp 232-235 °C; ir (potassium bromide): ν 3520, 3404, 3222, 1704, 1680, 1564, 1434 cm^{-1}; ^{1}H-nmr

(dimethyl sulfoxide-d_6): δ 9.66 (s, 1H, NH), 6.47 (brs, 2H, NH_2), 4.41 (q, 2H, CH_2), 2.97 (t, 2H, CH_2), 2.57 (s, 3H, CH_3), 2.55 (t, 2H, CH_2), 2.22 (m, 2H, CH_2), 1.48 ppm (t, 3H, CH_3); ms: m/z (%) 279 (M^+, 70), 262 (45), 236 (30), 206 (15), 163 (25), 105 (60), 91 (100).

Anal. Calcd. for: $C_{13}H_{17}N_3O_4$: C, 55.91; H, 6.14; N, 15.05. Found: C, 56.01; H, 6.21; N, 15.21.

Ethyl 4,5-Dihydro-7-methyl[1,2,3]selenadiazolo[4,5-*e*]benzofuran-7-carboxylate (**10**).

To a stirring mixture of compound **9** (1.00 g, 3.6 mmoles) in glacial acetic acid, selenium dioxide (400 mg, 3.6 mmoles) was added slowly. The mixture was refluxed in a hot water bath for 3 hours. The mixture was cooled, filtered and water (15 ml) was added to the filtrate. The filtrate was extracted with chloroform (3×15 ml), dried (sodium sulfate) and the solvent was evaporated. The residue was purified by preparative tlc on silica gel using chloroform:methanol (40:1) as eluent. The desired compound was crystallized from petroleum ether to give 111 mg (10%) of **10**, mp 139-140 °C; ir (potassium bromide): ν 2919, 1710, 1516, 1444, 1275 cm^{-1}; ^{1}H- nmr (deuteriochloroform): δ 4.41 (q, 2H, CO_2CH_2), 3.34 (m, 4H, CH_2-CH_2), 2.75 (s, 3H, CH_3), 1.41 ppm (t, 3H, CH_3); ms: m/z (%) 313 (62), 312 (M^+, 60), 284 (100), 282 (55), 280 (22), 211 (10), 102 (25), 91 (35), 65 (24).

Anal. Calcd. for $C_{12}H_{12}N_2O_3Se$: C, 46.32; H, 3.89; N, 9.00. Found: C, 46.50; H, 3.78; N, 8.84.

Ethyl 8-Methyl[1,2,3]thiadiazolo[4,5-*e*]benzofuran-7-carboxylate (**12**).

A mixture of compound **9** (1.00 g, 3.6 mmoles) and thionyl chloride (20 ml) was heated on a steam bath for 2 hours. After cooling, water was added and the mixture was neutralized with 10% sodium carbonate solution, extracted with chloroform (2 × 20 ml) and dried (sodium sulfate). The solvent was removed under reduced pressure. The residue was purified by preparative tlc on silica gel using chloroform:methanol (30:1) as eluent. The desired compound was crystallized from petroleum ether to give 130 mg (14%) of compound **12**, mp 86-88 °C; ir (potassium bromide): ν 3078, 2919, 1716, 1557, 1449, 1270 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.98 (ABq, J=8.9 Hz, 2H, aromatic), 4.52 (q, 2H, CO_2CH_2), 3.12 (s, 3H, CH_3), 1.49 ppm (t, 3H, CH_3); ms: m/z (%) 263 (100), 262 (M^+, 98), 234 (90), 206 (85), 189 (70), 162 (100), 133 (78), 107 (60), 89 (80), 69 (60), 63 (45).

Anal. Calcd. for $C_{12}H_{10}N_2O_3S$: C, 54.95; H, 3.84; N. 10.68. Found: C, 54.79; H, 4.01; N, 10.39.

6,6-Dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (**13a**).

This compound was prepared according to the reported methods [23] in 41% yield, mp 83-85 °C; ir (potassium bromide): ν 3028, 2949,1665, 1580, 1370, 1360 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.51 (m, 5H, aromatic), 6.67 (s, 1H, aromatic), 2.81 (s, 2H, CH_2), 2.40 (s, 2H, CH_2), 1.17 ppm (s, 6H, 2×CH_3); ms: m/z (%) 240 (M^+, 40), 184 (87), 156 (40), 128 (10), 112 (25), 105 (100), 83 (95).

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.94; H, 6.61.

6,6-Dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzothiophene (**13b**).

This compound was prepared according to the reported methods [21,23] in 66% yield, mp 73-75 °C; ir (potassium bromide): ν 3054, 2930, 1670, 1564, 1375 cm^1; ^{1}H-nmr (deuteriochloroform): δ 7.63 (m, 5H, aromatic), 6.81 (s, 1H, aromatic), 2,81 (s, 2H, CH_2), 2.39 (s, 2H, CH_2), 1.18 ppm (s, 6H, 2×CH_3); ms: m/z (%) 256 (M^+, 70), 239 (23), 183 (30), 127 (30), 82 (100), 62 (40).

Anal. Calcd. for $C_{16}H_{16}OS$: C, 74.96; H, 6.29. Found: C, 74.92; H, 6.32.

6,6-Dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzofuran Semicarbazone (**14a**).

This compound was prepared according to the reported method [21] in 83% yield, mp 189-191 °C; ir (potassium bromide): ν 3449, 1645, 1564, 1415 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.15 (s, 2H, NH_2), 7.51 (m, 5H, aromatic), 6.85 (s, 1H, aromatic), 2.67 (s, 2H, CH_2), 2.29 (s, 2H, CH_2), 1.14 ppm (s, 6H, 2×CH_3); ms: m/z (%) 297 (M^+, 38), 254 (100), 222 (40), 182 (25), 105 (20), 97 (40), 69 (42), 55 (60), 43 (100).

Anal. Calcd. for $C_{17}H_{19}N_3O_2$: C, 68.67; H, 6.44; N, 14.13. Found: C, 68.51; H, 6.21; N, 14.23.

6,6-Dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydrobenzothiophene Semicarbazone (**14b**).

This compound was prepared according to the reported methods [21] in 76% yield, mp180-183 °C; ir (potassium bromide): ν 3409, 3311, 1681, 1606, 1485 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.84 (s, 1H, NH), 7.55 (m, 5H, aromatic), 6.99 (s, 1H, aromatic), 2.77 (s, 2H, CH_2), 2.30 (s, 2H, CH_2), 1.14 ppm (s, 6H, 2×CH_3); ms: m/z (%) 313 (M^+, 28), 268 (100), 224 (19), 195 (69), 180 (28), 111 (29), 97 (45), 55 (65).

Anal. Calcd. for $C_{17}H_{19}N_3OS$: C, 65.15; H, 6.11; N, 13.41. Found: C, 65.28; H, 6.08; N, 13.39.

4,5-Dihydro-4,4-dimethyl-7-phenyl-[1,2,3]selenadiazolo[4,5-*e*]-benzofuran (**15a**).

This compound was obtained from **14a**, similar to **10** mp 115-117 °C (from chloroform); ^{1}H-nmr (deuteriochloroform);:δ 7.59 (m, 6H, aromatic), 3.02 (s, 2H, CH_2), 1.52 ppm (s, 6H, 2×CH_3); ms: m/z (%) 329 (M^+, 2), 273 (10), 139 (100).

Anal. Calcd. for $C_{16}H_{14}N_2OSe$: C, 58.36; H, 4.28; N, 8.51. Found: C, 58.12; H, 4.21; N, 8.66.

4,5-Dihydro-4,4-dimethyl-7-phenyl-[1,2,3]selenadiazolo[4,5-*e*]-benzothiophene (**15b**).

This compond was obtained from **14b**, similar to **10**; mp 122-125 °C (chloroform); ^{1}H-nmr (deuteriochloroform): δ 7.61 (m, 6H, aromatic), 2.99 (s, 2H, CH_2), 1.50 ppm (s, 6H, 2×CH_3); ms: m/z (%) 345 (M^+, 65), 317 (40), 238 (57), 104 (100), 77 (65).

Anal. Calcd. for $C_{16}H_{14}N_2SSe$: C, 55.65; H, 4.09; N, 8.11. Found: C, 55.87; H, 3.92; N, 8.32

4,5-Dihyro-4,4-dimethyl-7-phenyl-[1,2,3]thiadiazolo[4,5-*e*]-benzofuran (**16a**).

This compound was obtained from **14a**, similar to **12**; mp 108-110 °C (methanol); ^{1}H-nmr (deuteriochloroform): δ 7.47 (m, 6H, aromatic), 3.00 (s, 2H, CH_2), 1.51 ppm (s, 6H, 2×CH_3); ms: m/z (%) 282 (M^+, 8), 254 (7), 178 (15), 149 (25), 105 (100), 77 (42), 51 (25).

Anal. Calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 4.00; N, 9.92. Found: C, 68.28; H, 4.24; N, 9.80.

4,5-Dihydro-4,4-dimethyl-7-phenyl-[1,2,3]thiadiazolo[4,5-*e*]-benzothiophene (**16b**).

This compound was obtained from **14b**, similar to **12**; mp 104-106 °C (methanol): ^{1}H-nmr (deuteriochloroform): δ 7.56 (m, 6H, aromatic), 3.01 (s, 2H, CH_2), 1.48 ppm (s, 6H, 2×CH_3); ms: m/z (%) 298 (M^+, 37), 267 (100), 237 (100), 208 (35), 148 (80), 104 (100), 77 (60).

Anal. Calcd. for $C_{16}H_{14}N_2S_2$; C, 64.40; H, 4.73; N, 9.39. Found: C, 64.29; H, 4.64; N, 9.27.

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