Synthesis and Spectral Properties of 2-Methylthio-3*H*-4-(*para*-substituted-phenyl)-7-[(*o*-, and *p*-substituted)-phenylthio]-1,5-benzodiazepines

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A series of twelve new 2-methylthio-3*H*-4-(*p*-substituted phenyl)-7-[(*o*-, and *p*-substituted)phenylthio]-1,5-benzodiazepines, which have potentially useful pharmacological properties, has been synthesized by condensing the 3,3-dimercapto-1-(*para*-substituted-phenyl)-2-propen-1-one with 3,4-diamino phenyl-R-phenylthio ethers, and subsequently the 1*H*-1,5-benzodiazepine-2-thiones obtained were treated with sodium hydride and methyl iodide. The structure of all products was corroborated by ir, ^{1}H-nmr, ^{13}C-nmr and ms.

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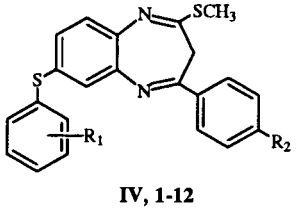
In the course of synthesis and spectral properties studies of compounds with possible pharmacological activity, we have previously reported the synthesis of 7-(*o*-, *m*-, and *p*-substituted-phenoxy-1*H*-1,5-benzodiazepine-2-thiones [3,4]. There have been several reports concerning pharmacological activity of benzodiazepines with chloro-substituents in the position C-7 of the benzene ring of the benzodiazepine derivatives [5-8]. As a part of a program directed towards the synthesis and spectral property determination of 1,5-benzodiazepine derivatives with possible pharmacological activity, we describe in this report the synthesis of the novel compounds 2-methylthio-3*H*-4-(*p*-substituted-phenyl)-7-[(*o*-, and *p*-substituted)phenylthio]-1,5-benzodiazepines **IV, 1-12** (Scheme 1) as shown in Scheme 2. The reaction of Compounds **I** with **II**, has been performed in anhydrous ortho-xylene at reflux for six hours. The 1*H*-1,5-benzodiazepine-2-thiones **III**, have been obtained in 35-65% yield. Treatment of the compounds **III**, with sodium hydride and methyl iodide at reflux in anhydrous *ortho*-xylene for four hours afforded the compounds 2-methylthio-3*H*-4-(*para*-substituted-phenyl)-7-[(*o*-, and *p*-substituted)phenylthio]-1,5-benzodiazepines **IV, 1-12** in 57-91% yield.

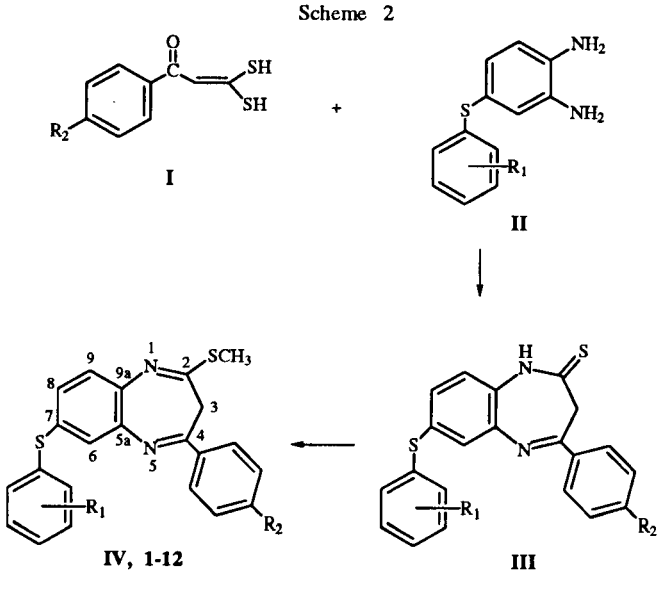
Scheme 1



IV, 1-12

	R_1	R_2
1	H	H
2	H	CH_3
3	H	OCH_3
4	H	Br
5	*o*-OCH_3	H
6	*o*-OCH_3	CH_3
7	*o*-OCH_3	OCH_3
8	*o*-OCH_3	Br
9	*p*-OCH_3	H
10	*p*-OCH_3	CH_3
11	*p*-OCH_3	OCH_3
12	*p*-OCH_3	Br

Scheme 2

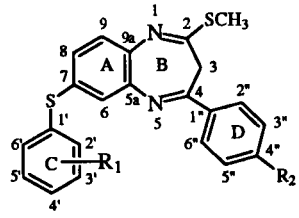


I **II** **III** **IV, 1-12**

The infrared spectrum of Compounds **1-12** displayed absorptions at 1584-1598 cm^{-1} for C=N stretching; at 1270-1292 and 1176-1185 cm^{-1} for C-N stretching; at 1015-1031 and 1242-1254 cm^{-1} for C-O stretching and the corresponding absorptions for aromatic and R-substituents. In the ^{1}H-nmr spectra the presence of three protons signals at δ 2.35-2.38 singlet were assigned to the methylthio protons joined at C-2, the presence of two proton signals at δ 3.48-3.55 broad was consistent with the methylene protons of the C-3. The presence of three proton signals at δ 7.41-7.04 multiplet was assigned to the aromatic protons of C-6, C-8 and C-9 of the benzodiazepine framework. The other aromatic protons appeared as a multiplet and AA'BB' system at δ 6.93-8.10; the presence of three proton signals at δ 3.77-3.83

Table 1

^{13}C NMR Spectral Data for Compounds **1-12**



IV, 1-12

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
R_1	H	H	H	H	*o*-OCH_3	*o*-OCH3	*o*-OCH_3	*o*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3
R_2	H	*p*-CH_3	*p*-OCH_3	*p*-Br	H	*p*-CH_3	*p*-OCH_3	*p*-Br	H	*p*-CH_3	*p*-OCH_3	*p*-Br
C-2	157.6	157.6	158.3	158.1	157.3	157.5	158.1	158.0	157.0	157.0	157.9	158.0
C-3	39.0	39.0	38.8	38.9	38.1	39.0	38.8	38.9	39.0	37.1	39.0	38.9
C-4	154.7	154.5	153.6	153.6	154.0	153.9	153.4	152.9	154.4	154.3	153.8	153.6
C-5a	140.0	141.2	140.3	139.8	140.5	141.2	140.3	140.4	140.0	140.1	140.2	140.5
C-6	127.5	127.5	127.4	127.5	128.7	127.5	128.9	128.3	128.1	128.2	128.5	126.6
C-7	130.4	131.0	128.8	130.8	130.9	130.0	130.0	130.0	131.0	133.2	133.4	133.9
C-8	127.4	127.3	127.1	126.2	126.5	126.6	126.7	126.3	124.9	124.7	126.5	125.2
C-9	128.1	127.6	128.5	128.5	129.5	129.4	129.3	129.4	126.5	126.5	129.2	129.4
C-9a	135.9	139.2	139.1	138.3	138.6	138.7	138.9	138.2	138.2	138.2	138.1	139.9
C-1'	128.1	126.4	126.5	125.1	122.2	122.6	122.6	121.9	122.7	122.8	122.8	122.7
C-2'	128.6	130.9	130.8	131.0	158.2	158.1	161.6	157.4	135.4	135.4	135.4	135.6
C-3'	129.5	129.5	130.1	130.5	111.7	111.7	111.6	111.7	115.4	115.4	114.0	115.5
C-4'	129.8	128.5	130.9	131.3	129.2	129.4	129.0	129.0	159.7	159.7	159.7	159.9
C-5'	129.5	129.5	130.1	130.5	121.3	121.2	121.2	121.3	115.4	115.4	114.0	115.5
C-6'	128.6	130.9	130.8	131.0	131.8	131.6	131.4	122.9	135.4	135.4	135.4	135.6
C-1"	134.5	134.6	134.6	135.1	136.1	128.4	138.5	135.2	133.6	133.5	134.0	135.3
C-2"-C-6"	128.1	128.2	129.5	129.5	130.9	128.1	130.0	129.4	128.1	128.2	130.0	130.1
C-3"-C-5"	130.9	129.2	114.0	131.6	131.1	129.2	114.0	131.7	128.6	129.2	115.3	131.8
C-4"	128.3	139.1	153.6	125.9	128.6	138.6	153.8	125.7	128.0	138.4	153.8	124.0
S-CH_3	13.3	13.3	13.2	13.3	13.3	13.2	13.3	13.2	13.2	13.2	13.2	13.4
R_1	-	-	-	-	55.8	55.8	55.4	55.8	55.2	55.2	55.3	55.4
R_2	-	20.9	55.3	-	-	20.9	55.8	-	-	20.9	55.2	-

Note: The numbering of the phenyl ring is only for the assignment of the chemical shifts of the carbon in ^{13}C nmr spectra.

singlet were assigned to the methoxy protons for the R_1,R_2-substituents; the presence of three proton signals at δ 2.36-2.38 singlet was consistent with the methyl protons of the R_2-substituents. The ^{13}C-nmr spectra of the compounds **1-12** are given in Table 1, and the signals were confirmed by using HETCOR, long range HETCOR, COSY and NOESY nmr experiments operating at 500 MHz.

The mass spectra of the compounds **1-12** include ions at m/z $[M-15]^+$, $[M-33]^+$, $[M-47]^+$, $[M-62]^+$, $[M-72]^+$, $[M-87]^+$, $[270+R_1]^+$, $[238+R_1]^+$, $[217+R_2]^+$, and 139. The molecular ion is the base peak, and the main fragmentation was consistent with the assigned structures. The proposed fragmentation pathways leading to the formation of a number of important daughter ions have been confirmed of the corresponding parent ion spectra by collision-induced dissociation (CID) experiments. The elemental composition of the molecular ion and the principal fragment ion was determined by exact mass measurements.

EXPERIMENTAL

The ir spectra were recorded on a Nicolet Magna TR-750 spectrophotometer. The ^{1}H-nmr spectra were recorded on a Varian Unity 300 spectrometer operating at 300 MHz and the ^{13}C-nmr spectra were recorded on a Varian Unity Plus-500 spectrometer operating at 500 MHz in deuteriochloroform solution or deuteriodimethyl sulfoxide solution containing tetramethylsilane as the internal standard with chemical shifts δ (ppm) expressed downfield from tetramethylsilane. The mass spectra were measured on a Jeol JMS-AX505 and Jeol MS-SX 102A high resolution mass spectrometer with accurate mass determination of the molecular ion and the principal fragments ions, using the direct inlet system. The spectra were recorded by electron impact at an ionization chamber temperature of 190° and ionizing electron energy of 70eV.

Compounds **I** and **II** have been prepared following literature methods with modifications [9-11].

General Procedure for the Synthesis of the 2,3-Dihydro-4-(*para*-substituted-phenyl)-7-[(*o*-, and *p*-substituted)phenylthio]-1*H*-1,5-benzodiazepine-2-thiones, **III**.

A mixture of 0.024 mole of 3,3-dimercapto-1-(*p*-substituted-phenyl)-2-propen-1-one, **II**, 0.024 mole of 3,4-diaminophenyl-R_1-phenylthio ether, **II**, in 150 ml of dry *ortho*-xylene was heated at reflux for 6-9 hours. After cooling, the crystals were collected and washed with hexane-acetone (80:20) to yield the compounds **III** (35-60%).

General Procedure for the Synthesis of the 2-Methylthio-3*H*-4-(*para*-substituted-phenyl)-7-[(*o*-, and *p*-substituted)phenylthio]-1,5-benzodiazepines **IV**, **1-12**.

A mixture of 0.005 mole of 1*H*-1,5-benzodiazepine-2-thiones, **III**, 0.015 mole of sodium hydride in 150 ml of dry *ortho*-xylene was heated at reflux for one hour. After the reaction mixture was cooled at room temperature, subsequently was added dropwise over a few minutes 0.014 mole of methyl iodide and the reflux continued for 2-3 hours. The reaction mixture was cooled to room temperature, filtered and the organic solution was dried (sodium sulfate) and evaporated *in vacuo* to yield a semisolid. The residual semisolid was purified on a silica gel chromatography column and elution with hexane-ethyl acetate (98:2) to yield the compounds **IV**, **1-12** (57-91%).

2-Methylthio-3*H*-4-phenyl-7-phenylthio-1,5-benzodiazepine (**1**).

This compound was obtained as yellow needles in 74% yield, mp 132°; ir (nujol mull): ν C=N 1595, C-N 1286 and 1183 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.38 (s, 3H, S-CH_3), 3.55 (bs, 2H, 3-H), 7.21 (d, d, 1H, J = 2.1, 8.1 Hz, 8-H), 7.32 (d, 1H, J = 1.8 Hz, 6-H), 7.35 (d, 1H, J = 8.7 Hz, 9-H), 7.38-7.41 (m, 5H, phenyl protons of "C" ring), 7.49-7.54 (m, 1H, 4"-H), 7.51 and 8.08 (AA'BB', 4H, J = 7.8 Hz, phenyl protons of "D" ring, 2"-H, 3"-H, 5"-H, 6"-H); ms: m/z 374 (M^+), m/z 376 $[M+2]^+$, m/z 378 $[M+4]^+$.

Anal. Calcd. for $C_{22}H_{18}N_2S_2$: C, 70.55; H, 4.84; N, 7.48. Found: C, 70.67; H, 4.90; N, 7.40.

2-Methylthio-3*H*-4-(*para*-methylphenyl)-7-phenylthio-1,5-benzodiazepine (**2**).

This compound was obtained as yellow needles in 60% yield, mp 134°; ir (nujol mull): ν C=N 1593; C-N 1279 and 1189 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 2.38 (s, 3H, $C_{4''}$-CH_3), 3.53 (bs, 2H, 3-H), 7.19 (d, d, 1H, J = 2.1, 8.3 Hz, 8-H), 7.22 (d, 1H, J = 2.1 Hz, 6-H), 7.30 (d, 1H, J = 8.7 Hz, 9-H), 7.28 and 7.43 (m, 5H, phenyl protons of "C" ring), 7.31 and 7.97 (AA'BB', 4H, J = 8.4 Hz, phenyl protons of "D" ring); ms: m/z 388 (M^+), 390 $[M+2]^+$, 392 $[M+4]^+$.

Anal. Calcd. for $C_{23}H_{20}N_2S_2$: C, 71.10; H, 5.19; N, 7.21. Found: C, 71.02; H, 5.25; N, 7.16.

2-Methylthio-3*H*-4-(*para*-methoxyphenyl)-7-phenylthio-1,5-benzodiazepine (**3**).

This compound was obtained as yellow needles in 72% yield, mp 130°; ir (nujol mull): ν C=N 1593; C-N 1291 and 1178; C-O 1254 and 1030 cm^{-1}; ^1H-nmr (deuterio dimethyl sulfoxide): δ 2.36 (s, 3H, S-CH_3), 3.52 (bs, 2H, 3-H), 3.82 (s, 3H, $C_{4''}$-OCH_3), 7.03 and 8.04 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "D" ring), 7.17 (d, d, 1H, J = 2.1, 8.4 Hz, 8-H), 7.23 (d, 1H, J = 2.4 Hz, 6-H), 7.34 (d, 1H, J = 8.4 Hz, 9-H), 7.38 and 7.42 (m, 5H, phenyl protons of "C" ring); ms: m/z 404 (M^+), 406 $[M+2]^+$, 408 $[M+4]^+$.

Anal. Calcd. for $C_{23}H_{20}N_2OS_2$: C, 68.28; H, 4.98; N, 6.93. Found: C, 68.22; H, 4.91; N, 6.85.

2-Methylthio-3*H*,4-(*para*-bromophenyl)-7-phenylthio-1,5-benzodiazepine (**4**).

This compound was obtained as yellow needles in 61% yield, mp 135°; ir (nujol mull): ν C=N 1589; C-N 1283 and 1180 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 3.53 (bs, CH_2, 3-H), 7.16 (d, d, 1H, J = 2.0, 8.4 Hz, 8-H), 7.22 (d, 1H, J = 2.0 Hz, 6-H), 7.34 (d, 1H, J = 8.7 Hz, 9-H), 7.37-7.44 (m, 5H, phenyl protons of "C" ring), 7.70 and 8.04 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring); ms: m/z 452 (M^+), 454 $[M+2]^+$, 456 $[M+4]^+$, 458 $[M+6]^+$.

Anal. Calcd. for $C_{22}H_{17}BrN_2S_2$: C, 58.28; H, 3.78; N, 6.18. Found: C, 58.18; H, 3.85; N, 6.23.

2-Methylthio-3*H*-4-phenyl-7-(*ortho*-methoxyphenylthio)-1,5-benzodiazepine (**5**).

This compound was obtained as yellow needles in 67% yield, mp 90°, ir (nujol mull): ν C=N 1597; C-N 1272 and 1182; C-O 1243 and 1025 cm^{-1}; ^1H nmr (deuterio dimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 3.55 (bs, 2H, 3-H), 3.81 (s, 3H, $C_{2'}$-OCH_3), 6.73 (d, t, 1H, J = 1.3, 7.5 Hz, 5'-H), 7.10 (d, d, 1H, J = 2.1, 7.5 Hz, 3'-H), 7.13 (d, d, 1H, J = 2.1, 8.6 Hz, 8-H), 7.14 (d, 1H, J = 2.1 Hz, 6-H), 7.17 (d, d, 1H, J = 2.1, 7.5 Hz, 6'-H), 7.32 (d, t, 1H, J = 1.5, 7.6 Hz, 4'-H), 7.41 (d, 1H, J = 8.7 Hz, 9-H), 7.48-7.54 (m, 1H, 4"-H), 7.52 and 8.10 (AA'BB', 4H, J = 7.5 Hz, phenyl protons of "D" ring; 2"-H, 3"-H, 5"-H, 6"-H); ms: m/z 404 (M^+), 406 $[M+2]^+$, 408 $[M+4]^+$.

Anal. Calcd. for $C_{23}H_{20}N_2OS_2$: C, 68.28; H, 4.98; N, 6.93. Found: C, 68.34; H, 4.89; N, 7.00.

2-Methylthio-3*H*-4-(*para*-methylphenyl)-7-(*ortho*-methoxyphenylthio)-1,5-benzodiazepine (**6**).

This compound was obtained as yellow needles in 66% yield, mp 97°; ir (nujol mull): ν C=N 1596; C-N 1273 and 1184, C-O 1245 and 1023 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 2.36 (s, 3H, $C_{4''}$-CH_3), 3.52 (bs, 2H, 3-H), 3.81 (s, 3H, $C_{2'}$-OCH_3), 6.93 (d, t, 1H, J = 1.2, 7.5 Hz, 5'-H), 7.09 (d, d, 1H, J = 2.1, 7.4 Hz, 3'-H), 7.12 (d, d, 1H, J = 2.1, 8.5 Hz, 8-H), 7.15 (d, d, 1H, J = 2.1, 7.4 Hz, 6'-H), 7.19 (d, 1H, J = 2.1 Hz, 6-H), 7.31 (d, t, 1H, J = 2.1, 7.5 Hz, 4'-H), 7.31-8.00 (AA'BB', 4H, J = 8.4 Hz, phenyl protons of "D" ring), 7.41 (d, 1H, J = 8.4 Hz, 9-H); ms: m/z 418 (M^+), 420 $[M+2]^+$, 422 $[M+4]^+$.

Anal. Calcd. for $C_{24}H_{22}N_2OS_2$: C, 68.87; H, 5.30; N, 6.69. Found: C, 68.81; H, 5.37; N, 6.60.

2-Methylthio-3*H*-4-(*para*-methoxyphenyl)-7-(*ortho*-methoxyphenylthio)-1,5-benzodiazepine (**7**).

This compound was obtained as yellow needles in 68% yield, mp 95°; ir (nujol mull): ν C=N 1598, C-N 1287 and 1182, C-O 1242 and 1025 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 3.52 (bs, 2H, 3-H), 3.81 (s, 3H, $C_{2'}$-OCH_3), 3.83 (s, 3H, $C_{4''}$-OCH_3), 6.93 (d, t, 1H, J = 1.5, 7.5 Hz, 5'-H), 7.05 and 8.06 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring), 7.09 (d, d, 1H, J = 1.2, 7.5 Hz, 3'-H), 7.11 (d, d, 1H, J = 1.5, 7.6 Hz, 6'-H), 7.12 (d, d, 1H, J = 2.1, 8.7 Hz, 8-H), 7.19 (d, 1H, J = 2.1 Hz, 6-H), 7.31 (d, t, 1H, J = 1.2, 7.5 Hz, 4'-H), 7.39 (d, 1H, J = 8.4 Hz, 9-H); ms: m/z 434 (M^+), 436 $[M+2]^+$, 438 $[M+4]^+$.

Anal. Calcd. for $C_{24}H_{22}N_2O_2S_2$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.41; H, 5.01; N, 6.49.

2-Methylthio-3*H*-4-(*para*-bromophenyl)-7-(*ortho*-methoxyphenylthio)-1,5-benzodiazepine (**8**).

This compound was obtained as yellow needles in 63% yield, mp 101°; ir (nujol mull): ν C=N 1584; C-N 1270 and 1185; C-O 1246 and 1015 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 3.53 (bs, 2H, 3-H), 3.82 (s, 3H, $C_{2'}$-OCH_3), 6.95 (d, t, 1H, J = 1.2, 7.5 Hz, 5'-H), 7.11 (d, d, 1H, J = 2.1, 7.6 Hz, 3'-H), 7.12 (d, d, J = 1.7, 7.5 Hz, 6'-H), 7.14 (d, d, 1H, J = 2.1, 8.5 Hz, 8-H), 7.16 (d, 1H, J = 2.2 Hz, 6-H), 7.34 (d, t, 1H, J = 1.8, 7.5 Hz, 4'-H), 7.41 (d, 1H, J = 8.4 Hz, 9-H), 7.72 and 8.04 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring); ms: m/z 482 (M^+), 484 $[M+2]^+$, 486 $[M+4]^+$, 488 $[M+6]^+$.

Anal. Calcd. for $C_{23}H_{19}BrN_2OS_2$: C, 57.14; H, 3.96; N, 5.80. Found: C, 57.24; H, 3.90; N, 5.85.

2-Methylthio-3*H*-4-phenyl-7-(*para*-methoxyphenylthio)-1,5-benzodiazepine (**9**).

This compound was obtained as yellow needles in 78% yield, mp 108°, ir (nujol mull): ν C=N 1596; C-N 1288 and 1179; C-O 1248 and 1030 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.37 (s, 3H, S-CH_3), 3.53 (bs, 2H, 3-H), 3.77 (s, 3H, $C_{4'}$-OCH_3), 7.02 and 8.06 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "C" ring), 7.07 (d, d, 1H, J = 2.1, 8.4 Hz, 8-H), 7.09 (d, 1H, J = 1.8 Hz, 6-H), 7.28 (d, 1H, J = 8.4 Hz, 9-H), 7.45 and 7.54 (m, 5H, phenyl protons of "D" ring); ms: m/z 404 (M^+), 406 $[M+2]^+$, 408 $[M+4]^+$.

Anal. Calcd. for $C_{23}H_{20}N_2OS_2$: C, 68.28; H, 4.98; N, 6.93. Found: C, 68.15; H, 5.05; N, 6.99.

2-methylthio-3*H*-4-(*para*-methyl phenyl)-7-(*para*-methoxyphenylthio)-1,5-benzodiazepine (**10**).

This compound was obtained as yellow needles in 57% yield, mp 114°; ir (nujol mull): ν C=N 1595; C-N 1292 and 1182; C-O 1248 and 1030 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 2.36 (s, 3H, $C_{4''}$-CH_3), 3.50 (bs, 2H, 3-H), 3.78 (s, 3H, $C_{4'}$-OCH_3), 7.02 and 7.42 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "C" ring), 7.05 (d, d, 1H, J = 2.1, 8.3 Hz, 8-H), 7.07 (d, 1H, J = 2.1 Hz, 6-H), 7.27 (d, 1H, J = 8.4 Hz, 9-H), 7.29 and 7.95 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "D" ring); ms: m/z 418 (M^+), 420 $[M+2]^+$, 422 $[M+4]^+$.

Anal. Calcd. for $C_{24}H_{22}N_2OS_2$: C, 68.87; H, 5.30; N, 6.69. Found: C, 68.79; H, 5.22; N, 6.57.

2-Methylthio-3*H*-4-(*para*-methoxyphenyl)-7-(*para*-methoxyphenylthio)-1,5-benzodiazepine (**11**).

This compound was obtained as yellow needles in 62% yield, mp 120°; ir (nujol mull): ν C=N 1593; C-N 1288 and 1176; C-O 1250 and 1031 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.36 (s, 3H, S-CH_3), 3.48 (bs, 2H, 3-H), 3.79 (s, 3H, $C_{4'}$-OCH_3), 3.81 (s, 3H, $C_{4''}$-OCH_3), 7.02 and 8.05 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring), 7.03 and 7.46 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "C" ring), 7.04 (d, d, 1H, J = 2.1, 8.4 Hz, 8-H), 7.07 (d, 1H, J = 2.1 Hz, 6-H), 7.34 (d, 1H, J = 8.4 Hz, 9-H); ms: m/z 434 (M^+), 436 $[M+2]^+$, 438 $[M+4]^+$.

Anal. Calcd. for $C_{24}H_{22}N_2O_2S_2$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.23; H, 5.18; N, 6.51.

2-Methylthio-3*H*-4-(*para*-bromophenyl)-7-(*para*-methoxyphenylthio)-1,5-benzodiazepine (**12**).

This compound was obtained as yellow needles in 91% yield, mp 128°; ir (nujol mull): ν C=N 1593; C-N 1289 and 1180; C-O 1248 and 1030 cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 2.35 (s, 3H, S-CH_3), 3.52 (bs, 2H, 3-H), 3.77 (s, 3H, $C_{4'}$-OCH_3, 7.01 and 7.45 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "C" ring), 7.07 (d, d, 1H, J = 2.1, 8.3 Hz, 8-H), 7.09 (d, 1H, J = 2.1 Hz, 6-H), 7.34 (d, 1H, J = 8.7 Hz, 9-H), 7.67 and 7.98 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring); ms: m/z 482 (M^+), 484 $[M+2]^+$, 486 $[M+4]^+$, 488 $[M+6]^+$.

Anal. Calcd. for $C_{23}H_{19}BrN_2OS_2$: C, 57.14; H, 3.96; N, 5.80. Found: C, 57.23; H, 3.90; N, 5.72.

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