Synthesis and Spectral Properties of 11-[(*o*-; and *p*-substituted)-phenyl]-8-[(*o*-; *m*-; *p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones

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The preparation of twelve novel 2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*] [1,4]diazepin-1-ones which have potentially useful pharmacological properties; by condensation and cyclization between 3-{[4-(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone with (*o*-; and *p*-substituted)benzaldehyde. The structure of all final products were corroborated by ir, ^{1}H-nmr, ^{13}C-nmr and ms.

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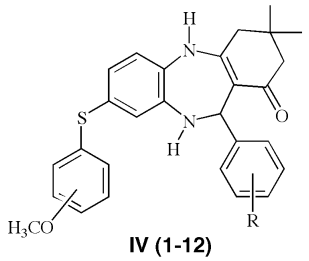
A piperidine derivative of the dibenzodiazepine family is the clozapine that is an atypical antipsychotic agent with proven efficacy in the management of refractory schizophrenia [3-4]. Currently there is considerable interest in the synthesis of new benzodiazepines with pharmacological activity [5-7]. We have previously reported the synthesis of 2,3-dihydro-2-[o-; and p-substituted)anilinylidene]-1*H*-4-(*p*-methylphenyl)-7-[(*o*-; and *p*-methyl)phenoxy]-1,5-benzodiazepines [8]; 2-[(*o*-; and *p*-substituted)-aminophenyl]-3*H*-5-[(*o*-; and *p*-substituted)phenyl]-7-chloro-1,4-benzodiazepines [9] and 2-methylthio-7-[(*o*-; *p*-substituted)phenylthio]-1,5-benzodiazepines [10].

As a part of a program directed towards the synthesis and the spectral property determination of dibenzo-[*b,e*][1,4]diazepin-1-ones derivatives. We describe in this report the synthesis of novel compounds 11-[(*o*-; and *p*-substituted)phenyl]-8-[(*o*-; *m*-; *p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*]-[1,4]diazepin-1-ones **IV, 1-12**, (Scheme 1) as shown in Scheme 2.

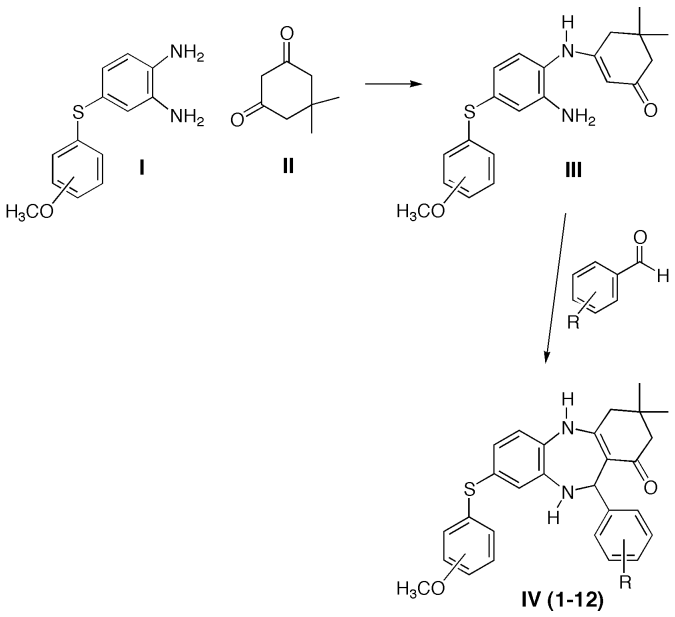
Scheme 1



IV (1-12)

		R
1	*o*-OCH_3	*o*-Cl
2	*o*-OCH_3	*p*-Cl
3	*o*-OCH_3	*o*-OCH_3
4	*o*-OCH_3	*p*-OCH_3
5	*m*-OCH_3	*o*-Cl
6	*m*-OCH_3	*p*-Cl
7	*m*-OCH_3	*o*-OCH_3
8	*m*-OCH_3	*p*-OCH_3
9	*p*-OCH_3	*o*-Cl
10	*p*-OCH_3	*p*-Cl
11	*p*-OCH_3	*o*-OCH_3
12	*p*-OCH_3	*p*-OCH_3

Scheme 2



I **II** **III** **IV (1-12)**

Treatment of 4-[(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamines **I** with 5,5-dimethyl-1,3-cyclohexanedione **II** at reflux in anhydrous benzene with a Dean-Stark apparatus were performed for 24 hours to obtain the 3-{[4-(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone **III**, which have been obtained in 55-60% yields. A mixture of 0.001 mole of compounds **III**, 0.001 mole of the corresponding (*o*-; and *p*-substituted)benzaldehyde in the presence of a few drops of acetic acid at reflux in ethanol for 1.5 hours afforded the 11-[(*o*-; and *p*-substituted)phenyl]-8-[(*o*-; *m*-; *p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-ones **IV, 1-12** in 45-70% yields.

The infrared spectrum of compounds **1-12**, displayed absorptions at 3410-3412 cm^{-1} for N-H stretching, at

1597-1616 cm^{-1} for C=O stretching, at 1387-1393 and 1273-1365 cm^{-1} for C-N stretching, at 1177-1151 and 1028-1094 cm^{-1} for C-O stretching and the corresponding absorptions for aromatic and R-substituents.

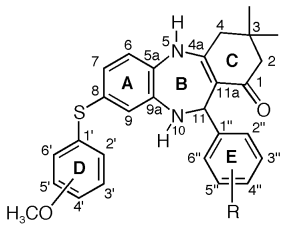
In the ^{1}H-nmr spectra the presence of two singlet signals at δ 1.01-1.16 were assigned to the methyl protons at C-3. The presence of a doublet at δ 2.23-2.25 and 2.30-2.32 was consistent with the methylene protons at C-2. The presence of a doublet at δ 2.40-2.49 and 2.54-2.62 was consistent with the methylene protons at C-4. The presence of a doublet at δ 5.83-6.22 was consistent with the methyne proton at C-11. The presence of a broad proton signal at δ 6.27-6.59 was consistent with N-H, deuterium oxide exchangeable. The presence of a three proton multiplet signal at δ 6.28-6.80 was assigned to the aromatic protons at C-6, C-7 and C-9 of the dibenzodiazepine framework. The other aromatic protons appeared as a multiplet and an AA'BB' system at δ 6.58-7.30 and with the signal for the R-substituents.

The ^{13}C-nmr spectra data for compounds **1-12** are given in Table 1. The signals were confirmed by using HETCOR, COSY, FLOCK, and NOESY nmr experiments operating at 300 and 500 MHz.

The mass spectra for compounds **1-12** include ions of m/z corresponding to molecular ion $[M]^+$; $[M-CH_3]^+$; $[M-CH_4]^+$; $[M-R]^+$; $[M-(HR)]^+$; $[M-(R+CH_4)]^+$; $[M-47]^+$; $[M-57]^+$; $[M-84]^+$; $[M-85]^+$; $[M-(76+R)]^+$; m/z 363; 351; 311; 275; 240; 83. The ion at m/z $[M-(76+R)]^+$ is the base peak; except for

Table 1

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



IV (1-12)

Compounds	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
OCH_3	*o*-OCH_3	*o*-OCH_3	*o*-OCH_3	*o*-OCH_3	*m*-OCH_3	*m*-OCH_3	*m*-OCH_3	*m*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3
R	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3
C-1	193.9	193.9	193.9	194.0	193.9	193.9	193.9	194.0	193.7	193.9	193.7	193.8
C-2	49.7	49.7	49.7	49.7	49.7	49.6	49.7	49.7	49.7	49.7	49.8	49.7
C-3	32.4	32.4	32.2	32.3	32.4	32.3	32.3	32.3	32.3	32.4	32.3	32.3
C-4	46.0	46.3	46.0	46.1	46.1	46.3	46.2	46.0	46.1	46.4	46.4	46.5
C-4a	154.5	152.8	154.6	153.2	154.4	152.7	156.6	153.2	154.4	152.7	153.8	152.4
C-5a	126.0	125.7	125.8	125.9	125.9	125.8	125.2	126.3	125.9	126.0	126.5	126.6
C-6	128.1	128.3	127.8	128.5	122.2	123.3	121.9	122.4	123.7	123.4	123.5	123.5
C-7	127.4	126.5	126.7	126.8	120.4	120.3	119.8	120.1	120.4	120.5	120.1	120.4
C-8	131.6	131.6	131.5	131.8	131.8	131.5	130.1	131.7	131.7	132.0	131.4	131.3
C-9	126.5	126.4	126.7	126.9	123.7	123.6	121.9	123.7	122.9	123.6	123.2	123.6
C-9a	139.7	137.7	139.1	138.2	137.9	137.4	139.6	138.0	139.7	142.2	138.9	137.9
C-11	55.7	57.4	53.7	57.4	55.9	58.0	57.7	57.2	55.9	57.5	55.3	57.4
C-11a	110.2	111.4	110.4	111.9	110.1	111.9	110.4	112.1	109.9	111.3	110.5	111.9
C-1'	138.0	137.5	139.1	138.1	139.6	142.1	139.8	139.9	137.9	137.5	138.0	135.9
C-2'	155.6	156.1	155.6	155.8	114.8	114.8	112.7	114.8	133.0	133.0	132.8	132.7
C-3'	110.3	110.5	110.3	110.3	159.9	159.2	159.9	159.9	114.7	114.8	114.7	114.8
C-4'	126.7	126.8	126.5	126.6	129.6	129.6	129.1	129.6	159.1	159.2	158.9	159.1
C-5'	120.6	121.2	119.7	121.2	129.6	129.7	129.9	129.7	114.7	114.8	114.7	114.8
C-6'	129.8	129.0	129.9	130.0	132.8	133.0	132.2	132.7	133.0	133.0	132.8	132.7
C-1"	133.6	132.3	130.3	131.5	133.7	132.4	133.8	131.6	133.6	132.3	130.1	130.1
C-2"	132.1	128.4	156.7	128.2	132.0	128.3	156.6	128.1	130.3	128.4	156.7	128.1
C-3"	110.4	128.5	110.3	113.5	111.5	128.4	110.3	113.6	114.7	128.5	110.2	113.6
C-4"	126.1	129.9	126.4	158.1	126.2	129.8	126.7	158.1	126.6	129.9	126.7	158.2
C-5"	128.5	128.5	121.2	113.5	128.3	128.4	120.5	128.1	122.0	128.5	119.8	113.6
C-6"	129.7	128.4	127.7	128.2	129.6	128.3	126.9	113.6	129.7	128.4	128.0	128.1
C-3(CH_3)	28.0	27.8	28.0	27.8	28.1	27.7	28.0	27.6	28.0	27.8	28.1	27.8
	28.5	28.8	28.7	28.8	28.5	28.7	28.4	28.8	28.6	28.7	28.9	28.8
C-2'-OCH_3	56.0	55.8	55.6	55.8	-	-	-	-	-	-	-	-
C-3'-OCH_3	-	-	-	-	50.1	55.0	55.2	55.2	-	-	-	-

Table 1 (Continued)

Compounds	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
OCH_3	*o*-OCH_3	*o*-OCH_3	*o*-OCH_3	*o*-OCH_3	*m*-OCH_3	*m*-OCH_3	*m*-OCH_3	*m*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3
R	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3
C-4'-OCH_3	-	-	-	-	-	-	-	-	55.3	55.4	53.7	55.3
C-2"-OCH_3	-	-	55.3	-	-	-	55.2	-	-	-	53.6	-
C-4"-OCH_3	-	-	-	55.0	-	-	-	55.0	-	-	-	55.1

11-[(*o*-methoxy)phenyl]-8-[(*m*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo [b,e][1,4]diazepin-1-ones and 11-[(*o*-methoxy)phenyl]-8-[(*p*-methoxy)phenylthio]- 3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[b,e][1,4]diazepin-1-ones in which the base peak corresponds to the fragment ion $[M-47]^+$. The mass spectra of the compounds exhibit a stable molecular ion; 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 by the corresponding parent ion spectra using collision-induced dissociation experiments. The elemental composition of the molecular ion and the principal fragment ion was determined by 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 500 spectrometer operating at 125 MHz in deuteriochloroform 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 70 eV.

The 4-[(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamines **I** was prepared following literature methods with modifications [11].

General Procedure for the Synthesis of the 3-{4-[(*o*-; *m*-; *p*-Methoxy)phenylthio]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone **III**.

A mixture of 0.01 mole of 4-[(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamines **I**, 0.01 mole of 5,5-dimethyl-1,3-cyclohexanedione **II** in 10 ml of dry benzene was heated at reflux with a Dean-Stark apparatus for 24 hours. The reaction mixture was cooled to room temperature 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 (1:9) to yield the compounds **III**, with 55-60% yield.

General Procedure for the Synthesis of the 11-[(*o*-; and *p*-Substituted)phenyl]-8-[(*o*-; *m*-; *p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[b,e][1,4]-diazepin-1-ones **IV, 1-12**.

A mixture of 0.001 mole of 3-{4-[(*o*-; *m*-; *p*-methoxy)phenylthio]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone **III**, 0.001 mole of corresponding (*o*-; and *p*-substituted)benzaldehyde, 0.5 ml of acetic acid in 5 ml ethanol was heated at reflux for 1.5 hours. The reaction mixture was cooled to room temperature and evaporated *in vacuo* to yield a semisolid. The residual semisolid was purified by crystallization from hexane-ethyl acetate to yield compounds **IV, 1-12** (45-70%).

11-[(*o*-Chloro)phenyl]-8-[(*o*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones (**1**).

This compound was obtained as a yellow solid in 60% yield, mp 110°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1387 and 1273, C-O 1153 and 1066 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.06 and 1.13 (s, 6H, C_2-CH_3), 2.23 (d, 1H, J = 16.5 Hz, 2-H_a), and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.49 (d, 1H, J = 15.9 Hz, 4-H_a) and 2.62 (d, 1H, J = 15.9 Hz, 4-H_b), 3.81 (s, 3H, $C_{2'}$-OCH_3), 6.22 (d, 1H, J = 6.5 Hz, 11-H), 6.45 (d, 1H, J = 8.1, 6-H), 6.46 (bs, 2H, -NH, deuterium oxide exchangeable), 6.53 (d, 1H, J = 1.8 Hz, 9-H), 6.70 (dt, 1H, J = 2.0, 8.4 Hz, 5'-H), 6.73 (dd, 1H, J = 1.5, 7.8 Hz, 3"-H), 6.76 (dd, 1H, J = 3.3, 8.1 Hz, 7-H), 6.81 (dd, 1H, J = 1.8, 8.1 Hz, 3'-H), 6.92 (dt, 1H, J = 2.1, 7.5 Hz, 4"-H), 6.92 (dt, 1H, J = 2.1, 7.8 Hz, 5"-H), 6.93 (dt, 1H, J = 1.5, 7.5 Hz, 4'-H), 7.26 (dd, 1H, J = 1.8, 8.1 Hz, 6"-H), 7.30 (dd, 1H, J = 1.5, 7.5 Hz, 6'-H); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.40; H, 5.43; N, 5.82.

11-[(*p*-Chloro)phenyl]-8-[(*o*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones (**2**).

This compound was obtained as an orange solid in 70% yield, mp 123°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1392 and 1365, C-O 1153 and 1028 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.07 and 1.14 (s, 6H, C_2-CH_3), 2.23 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.42 (d, 1H, J = 15.9 Hz, 4-H_a) and 2.60 (d, 1H, J = 15.9 Hz, 4-H_b), 3.80 (s, 3H, $C_{2'}$-OCH_3), 5.88 (d, 1H, J = 6.5 Hz, 11-H), 6.42 (d, 1H, J = 8.1, 6-H), 6.50 (d, 1H, J = 2.1 Hz, 9-H), 6.55 (bs, 2H, -NH, deuterium oxide exchangeable), 6.71 (dd, 1H, J = 2.3, 7.8 Hz, 7-H), 6.82 (dd, 1H, J = 1.8, 8.1 Hz, 3'-H), 6.82 (dt, 1H, J = 1.2, 8.4 Hz, 5'-H), 7.00 and 7.11 (AA'BB', 4H, J = 8.6 Hz, phenyl protons of "E" ring), 7.17 (dt, 1H, J = 1.5, 7.3 Hz, 4'-H), 7.17 (dd, 1H, J = 1.5, 7.2 Hz, 6'-H); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.59; H, 5.61; N, 5.62.

11-[(*o*-Methoxy)phenyl]-8-[(*o*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones (**3**).

This compound was obtained as a yellow solid in 60% yield, mp 85°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1393 and 1273, C-O 1153 and 1028 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.03 and

1.09 (s, 6H, C_2-CH_3), 2.25 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.42 (d, 1H, J = 16.2 Hz, 4-H_a) and 2.56 (d, 1H, J = 16.2 Hz, 4-H_b), 3.78 (s, 3H, $C_{2'}$-OCH_3), 3.85 (s, 3H, $C_{2''}$-OCH_3), 6.15 (d, 1H, J = 6.5 Hz, 11-H), 6.36 (d, 1H, J = 8.1, 6-H), 6.47 (d, 1H, J = 1.8 Hz, 9-H), 6.59 (bs, 2H, -NH, deuterium oxide exchangeable), 6.62 (dt, 1H, J = 1.8, 8.1 Hz, 5'-H), 6.64 (dt, 1H, J = 1.8, 7.8 Hz, 4"-H), 6.72 (dd, 1H, J = 1.8, 7.2 Hz, 3"-H), 6.73 (dt, 1H, J = 2.1, 7.8 Hz, 5"-H), 6.77 (dd, 1H, J = 2.7, 8.4 Hz, 7-H), 6.79 (dd, 1H, J = 1.8, 8.1 Hz, 3'-H), 7.08 (dd, 1H, J = 1.5, 7.4 Hz, 6'-H), 7.08 (dd, 1H, J = 1.8, 8.1 Hz, 6"-H), 7.10 (dt, 1H, J = 1.5, 7.2 Hz, 4'-H); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.45; H, 6.28; N, 5.70.

11-[(*p*-Methoxy)phenyl]-8-[(*o*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]-diazepin-1-ones (**4**).

This compound was obtained as an orange solid in 55% yield, mp 117°; ir (chloroform): ν N-H 3412, C=O 1614, C-N 1393 and 1288, C-O 1177 and 1028 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.02 and 1.08 (s, 6H, C_2-CH_3), 2.22 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.30 (d, 1H, J = 16.5 Hz, 2-H_b), 2.40 (d, 1H, J = 15.6 Hz, 4-H_a) and 2.54 (d, 1H, J = 15.6 Hz, 4-H_b), 3.68 (s, 3H, $C_{2'}$-OCH_3), 3.82 (s, 3H, $C_{4''}$-OCH_3), 5.87 (d, 1H, J = 6.6 Hz, 11-H), 6.42 (d, 1H, J = 8.1, 6-H), 6.42 (d, 1H, J = 1.8 Hz, 9-H), 6.48 (bs, 2H, -NH, deuterium oxide exchangeable), 6.73 (dt, 1H, J = 1.2, 8.1 Hz, 5'-H), 6.80 (dd, 1H, J = 2.7, 8.1 Hz, 7-H), 6.80 (dd, 1H, J = 1.8, 8.1 Hz, 3'-H), 6.97 and 7.09 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "E" ring), 7.09 (dt, 1H, J = 1.5, 7.2 Hz, 4'-H), 7.10 (dd, 1H, J = 1.5, 7.2 Hz, 6'-H); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.50; H, 6.29; N, 5.87.

11-[(*o*-Chloro)phenyl]-8-[(*m*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]-diazepin-1-ones (**5**).

This compound was obtained as an orange solid in 60% yield, mp 115°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1390 and 1286, C-O 1153 and 1036 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.11 and 1.14 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.30 (d, 1H, J = 16.5 Hz, 2-H_b), 2.46 (d, 1H, J = 15.9 Hz, 4-H_a) and 2.59 (d, 1H, J = 15.9 Hz, 4-H_b), 3.79 (s, 3H, $C_{3'}$-OCH_3), 6.19 (d, 1H, J = 6.0 Hz, 11-H), 6.34 (d, 1H, J = 1.5 Hz, 9-H), 6.37 (bs, 2H, -NH, deuterium oxide exchangeable), 6.43 (d, 1H, J = 8.4 Hz, 6-H), 6.63 (dd, 1H, J = 2.7, 7.0 Hz, 7-H), 6.70 (dd, 1H, J = 2.1, 8.2 Hz, 3"-H), 6.78 (dt, 1H, J = 1.8, 7.9 Hz, 5"-H), 6.79 (d, 1H, J= 2.4 Hz, 2'-H), 6.86 (dd, 1H, J = 2.1, 7.5 Hz, 4'-H), 6.90 (dt, 1H, J = 1.8, 7.2 Hz, 4"-H), 7.03 (dd, 1H, J = 2.1, 7.7 Hz, 6'-H), 7.11 (t, 1H, J = 7.9 Hz, 5'-H), 7.28 (dd, 1H, J = 1.8, 7.6 Hz, 6"-H); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.61; H, 5.42; N, 5.60.

11-[(*p*-Chloro)phenyl]-8-[(*m*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones (**6**).

This compound was obtained as a dark brown solid in 50% yield, mp 125°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1387 and 1285, C-O 1153 and 1094 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.06 and 1.14 (s, 6H, C_2-CH_3), 2.22 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.42 (d, 1H, J = 16.2 Hz, 4-H_a) and 2.58 (d, 1H, J = 16.2 Hz, 4-H_b), 3.80 (s, 3H, $C_{3'}$-OCH_3), 5.86 (d, 1H, J = 5.4 Hz, 11-H), 6.33 (d, 1H, J = 1.5 Hz, 9-H), 6.35 (d, 1H, J = 8.4, 6-H), 6.37 (bs, 2H, -NH, deuterium oxide exchangeable), 6.68 (dd, 1H, J = 2.4, 7.3 Hz, 7-H), 6.83 (d, 1H, J = 2.1 Hz, 2'-H), 6.84 (dd, 1H, J = 2.1, 7.8 Hz, 4'-H), 6.92 (dd, 1H, J = 1.8, 7.8 Hz, 6'-H), 6.97 and 7.08 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "E" ring), 7.11 (t, 1H, J = 7.8 Hz, 5'-H); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.39; H, 5.62; N, 5.81.

11-[(*o*-Methoxy)phenyl]-8-[(*m*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]-diazepin-1-ones (**7**).

This compound was obtained as a dark brown solid in 50% yield, mp 95°; ir (chloroform): ν N-H 3410, C=O 1612, C-N 1389 and 1283, C-O 1151 and 1094 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.05 and 1.14 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.44 (d, 1H, J = 15.6 Hz, 4-H_a) and 2.58 (d, 2H, J = 15.6 Hz, 4-H_b), 3.71 (s, 3H, $C_{3'}$-OCH_3), 3.91 (s, 3H, $C_{2''}$-OCH_3), 6.19 (d, 1H, J = 5.4 Hz, 11-H), 6.36 (d, 1H, J = 8.1, 6-H), 6.38 (bs, 2H, -NH, deuterium oxide exchangeable), 6.49 (d, 1H, J = 1.5 Hz, 9-H), 6.63 (dt, 1H, J = 1.8, 7.9 Hz, 5"-H), 6.65 (dt, 1H, J = 1.8, 7.2 Hz, 4"-H), 6.57 (dd, 1H, J = 2.0, 7.5 Hz, 7-H), 6.75 (d, 1H, J = 2.1 Hz, 2'-H), 6.76 (dd, 1H, J = 1.9, 8.4 Hz, 3"-H), 6.78 (dd, 1H, J = 2.1, 7.8 Hz, 4'-H), 6.90 (dd, 1H, J = 2.1, 7.8 Hz, 6'-H), 7.06 (dd, 1H, J = 1.8, 8.1 Hz, 6"-H), 7.12 (t, 1H, J = 7.8 Hz, 5'-H); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.69; H, 6.30; N, 5.70.

11-[(*p*-Methoxy)phenyl]-8-[(*m*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]-diazepin-1-ones (**8**).

This compound was obtained as an orange solid in 45% yield, mp 90°; ir (chloroform): ν N-H 3412, C=O 1612, C-N 1389 and 1273, C-O 1175 and 1035 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.01 and 1.13 (s, 6H, C_2-CH_3), 2.24 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.31 (d, 1H, J = 16.5 Hz, 2-H_b), 2.46 (d, 1H, J = 16.2 Hz, 4-H_a) and 2.59 (d, 1H, J = 16.2 Hz, 4-H_b), 3.65 (s, 3H, $C_{3'}$-OCH_3), 3.75 (s, 3H, $C_{4''}$-OCH_3), 5.83 (d, 1H, J = 5.4 Hz, 11-H), 6.33 (d, 1H, J = 1.5 Hz, 9-H), 6.34 (d, 1H, J = 8.5, 6-H), 6.35 (bs, 2H, -NH, deuterium oxide exchangeable), 6.66 and 6.94 (AA'BB', 4H, J = 8.5 Hz, phenyl protons of "E" ring), 6.66 (dd, 1H, J = 2.0, 7.5 Hz, 7-H), 6.78 (d, 1H, J = 2.5 Hz, 2'-H), 6.84 (dd, 1H, J = 2.0, 7.5 Hz, 4'-H), 7.05 (dd, 1H, J = 2.0, 8.0 Hz, 6'-H), 7.12 (t, 1H, J = 8.0 Hz, 5'-H); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.70; H, 6.10; N, 5.83.

11-[(*o*-Chloro)phenyl]-8-[(*p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (**9**).

This compound was obtained as an orange solid in 51% yield, mp 85°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1389 and 1286, C-O 1174 and 1034 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.05 and 1.12 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.30 (d, 1H, J = 16.5 Hz, 2-H_b), 2.45 (d, 1H, J = 15.9 Hz, 4-H_a) and 2.58 (d, 1H, J = 15.9 Hz, 4-H_b), 3.79 (s, 3H, $C_{4'}$-OCH_3), 6.19 (d, 1H, J = 3.6 Hz, 11-H), 6.34 (d, 1H, J = 1.5 Hz, 9-H), 6.37 (bs, 2H, -NH, deuterium oxide exchangeable), 6.57 (dd, 1H, J = 1.8, 8.3 Hz, 7-H), 6.62 (d, 1H,

J = 8.1, 6-H), 6.73 (dt, 1H, J = 1.4, 7.9 Hz, 5''-H), 6.74 (dd, 1H, J = 1.2, 7.9 Hz, 3''-H), 6.78 and 7.03 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "D" ring), 6.89 (dt, 1H, J = 1.2, 7.3 Hz, 4''-H), 7.12 (dd, 1H, J = 1.8, 8.7 Hz, 6''-H); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.39; H, 5.65; N, 5.84.

11-[(*p*-Chloro)phenyl]-8-[(*p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones (**10**).

This compound was obtained as an orange solid in 53% yield, mp 119°; ir (chloroform): ν N-H 3412, C=O 1616, C-N 1389 and 1317, C-O 1176 and 1032 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.09 and 1.10 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.31 (d, 1H, J = 16.5 Hz, 2-H_b), 2.40 (d, 1H, J = 15.6 Hz, 4-H_a) and 2.58 (d, 1H, J = 15.6 Hz, 4-H_b), 3.80 (s, 3H, $C_{4'}$-OCH_3), 5.84 (d, 1H, J = 3.6 Hz, 11-H), 6.32 (d, 1H, J = 2.1 Hz, 9-H), 6.36 (d, 1H, J = 8.1, 6-H), 6.43 (bs, 2H, -NH, deuterium oxide exchangeable), 6.67 (dd, 1H, J = 1.8, 8.7 Hz, 7-H), 6.84 and 7.08 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "D" ring), 6.97 and 7.10 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "E" ring); ms: m/z 490 $(M)^+$; 492 $[M+2]^+$; 494 $[M+4]^+$.

Anal. Calcd. for $C_{28}H_{27}ClN_2O_2S$: C, 68.49; H, 5.54; N, 5.70. Found: C, 68.56; H, 5.43; N, 5.78.

11-[(*o*-Methoxy)phenyl]-8-[(*p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-ones (**11**).

This compound was obtained as an orange solid in 60% yield, mp 85°; ir. (chloroform): ν N-H 3412, C=O 1597, C-N 1390 and 1286, C-O 1177 and 1035 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.14 and 1.16 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.5 Hz, 2-H_a) and 2.32 (d, 1H, J = 16.5 Hz, 2-H_b), 2.44 (d, 1H, J = 15.6 Hz, 4-H_a) and 2.58 (d, 1H, J = 15.6 Hz, 4-H_b), 3.80 (s, 3H, $C_{4'}$-OCH_3), 3.81 (s, 3H, $C_{2''}$-OCH_3), 6.12 (d, 1H, J = 3.6 Hz, 11-H), 6.28 (d, 1H, J = 1.8 Hz, 9-H), 6.40 (bs, 2H, -NH, deuterium oxide exchangeable), 6.58 (d, 1H, J = 7.5, 6-H), 6.58 (dt, 1H, J = 1.5, 8.1 Hz, 5''-H), 6.59 (dd, 1H, J = 1.8, 8.6 Hz, 7-H), 6.61 (dt, 1H, J = 2.1, 6.2 Hz, 4''-H), 6.73 (dd, 1H, J = 1.2, 7.6 Hz, 3''-H), 6.79 and 7.01 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "D" ring), 7.09 (dd, 1H, J = 1.8, 8.7 Hz, 6''-H); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.48; H, 6.28; N, 5.65.

11-[(*p*- Methoxy)phenyl]-8-[(*p*-methoxy)phenylthio]-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-ones (**12**).

This compound was obtained as an orange solid in 65% yield, mp 85°; ir (chloroform): ν N-H 3412, C=O 1614, C-N 1389 and 1317, C-O 1177 and 1034 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.06 and 1.13 (s, 6H, C_2-CH_3), 2.21 (d, 1H, J = 16.2 Hz, 2-H_a) and 2.31 (d, 1H, J = 16.2 Hz, 2-H_b), 2.40 (d, 1H, J = 15.9 Hz, 4-H_a) and 2.59 (d, 1H, J = 15.9 Hz, 4-H_b), 3.69 (s, 3H, $C_{4'}$-OCH_3), 3.75 (s, 3H, $C_{4''}$-OCH_3), 5.84 (d, 1H, J = 3.6 Hz, 11-H), 6.27 (bs, 2H, -NH, deuterium oxide exchangeable), 6.35 (d, 1H, J = 8.1, 6-H), 6.36 (d, 1H, J = 1.8 Hz, 9-H), 6.66 (dd, 1H, J = 1.8, 8.7 Hz, 7-H), 6.66 and 6.93 (AA'BB', 4H, J = 9.0 Hz, phenyl protons of "E" ring), 6.79 and 7.06 (AA'BB', 4H, J = 8.7 Hz, phenyl protons of "D" ring); ms: m/z 486 $(M)^+$; 488 $[M+2]^+$.

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.57; H, 6.21; N, 5.76. Found: C, 71.49; H, 6.32; N, 5.82.

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