New Derivatives of Dibenzo[*b*,*e*][1,4]diazepin-1-ones by an Efficient Synthesis and Spectroscopy

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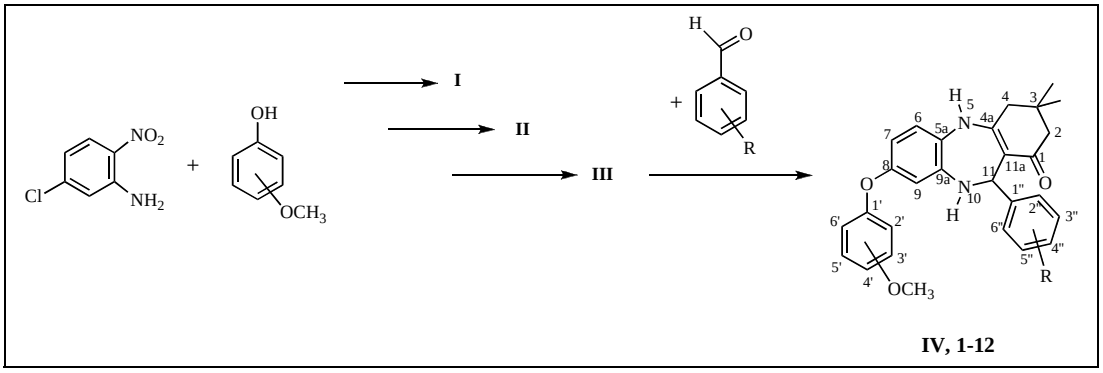
Received May 22, 2006



An efficient synthesis of four steps to obtain twelve new derivatives of 3,3-dimethyl-2,3,4,5,10,11-hexahydro-8-[(*o*-; and *p*-methoxy)phenoxy]-11-[(*o*-; and *p*-R)phenyl]-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones **IV**, **1**-**12** with possible biological and pharmacological activity as anticonvulsant and schizophrenia treatment in the central nervous system (CNS). The final products were obtained by condensation and cyclization between 3-{4-[(*o*-; and *p*-methoxy)phenoxy]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone with (*o*-; and *p*-R)benzaldehyde. The structure of all products was corroborated by spectroscopy of ir, ^{1}H-nmr, ^{13}C-nmr, with bidimensional experiments and MS in Low and high resolution with Collision-Induced Dissociation experiments (CID).

J. Heterocyclic Chem., **44**, 183 (2007).

INTRODUCTION

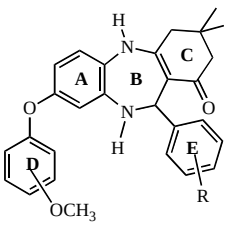
The Clozapine is the best representative example of the 1,4-dibenzodiazepine activity as an atypical antipsychotic agent with good efficiency in the treatment of schizophrenia [3,4]; and as an antipsychotic drug [5-10].

Our last report about the synthesis of 8-chloro derivates of 1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one, which have potentially useful pharmacological properties, was published in 2002 and 2004 [11-12].

RESULTS AND DISCUSSION

We described in this report the synthesis of twelve new derivatives and spectral properties 3,3-dimethyl-2,3,4,5,10,11-hexahydro-8-[(*o*-; and *p*-methoxy)phenyl]-11-[(*o*-; and *p*-R)phenyl]-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones **IV**, **1**-**12** (Figure 1). The synthesis of these compounds was carried out as shown in Scheme 1.

The reaction of 5-choro-2-nitroaniline with the (*o*-; and *p*-methoxy)phenol at reflux in anhydrous dimethylformamide in presence of anhydrous potassium carbonate, was heated for five hours. After cooling, the reaction mixture was diluted with water, the 3-amine-4-nitrophenyl-[(*o*-; and *p*-methoxy)phenyl]ether **I**, that was precipitated and was collected by filtration with suction and obtained in a 96-99% yield. The 3,4-diaminophenylether derivatives **II**, were obtained by hydrogenation of the derivatives **I** in



	R	
1	o-OCH_3	o-CH_3
2	o-OCH_3	p-CH_3
3	o-OCH_3	o-Cl
4	o-OCH_3	p-Cl
5	o-OCH_3	o-OCH_3
6	o-OCH_3	p-OCH_3
7	p-OCH_3	o-CH_3
8	p-OCH_3	p-CH_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

Figure 1

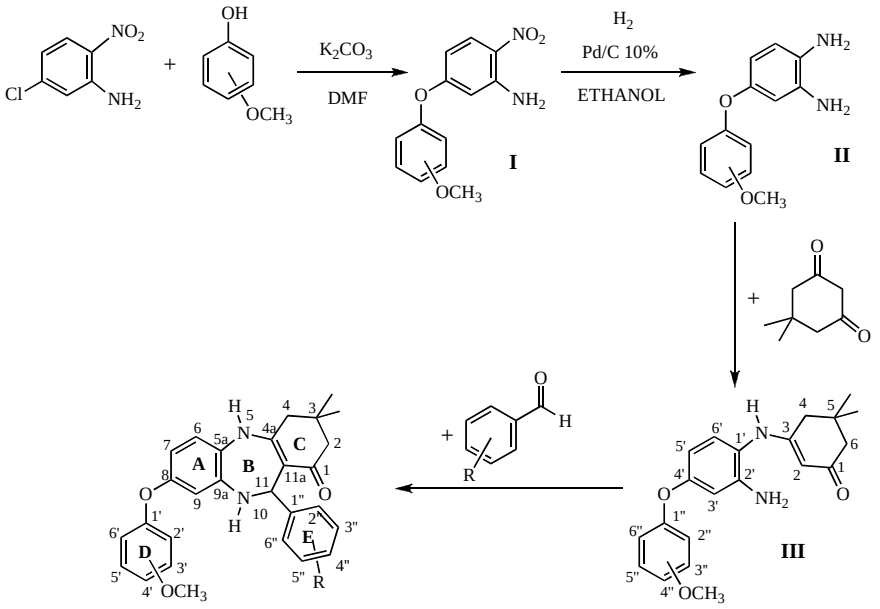
ethanol in presence of Pd/C 10% under a pressure of 60 pounds/inch^2 at room temperature with magnetic stirring for 24 hours. When the hydrogenation was finished the catalyst was removed by filtration and the solution was evaporated under reduced pressure; the 3,4-diaminophenyl-[(*o*-; and *p*-methoxy)phenyl]ether **II**, was obtained in a 72-85%.

Treatment of the derivatives **II** with the 5,5-dimethyl-1,3-cyclohexanedione at reflux in anhydrous benzene with

a Dean-Stark apparatus was performed for 24 hours to obtain the 3-{4-[(*o*- and *p*-methoxy)phenyl]-1,2-phenyl-enediamine}-5,5-dimethyl-2-cyclohexenone **III**, in 72-78% yield.

Treatment of 1 x 10^{-3} mole of compound **III**, with 1 x 10^{-3} mole of the corresponding (*o*-; and *p*-R)benzaldehyde in the presence of 0.5 mL of glacial acetic acid at reflux in 10 mL of ethanol for 2-4 hours afforded the 1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-ones **IV**, **1**-**12** in a 76-98% yield.

Scheme 1



The infrared spectrum of compounds **IV**, **1**-**12** displayed absorptions at 3409-4316 cm^{-1} for N-H stretching, at 1616-1620 cm^{-1} for C=O stretching, at 1368-1373 and 1309-1325 cm^{-1} for C-N stretching, at 1259-1268 and 1111-1117 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 (2 x 3H) at δ 1.03-1.12 and 1.08-1.15 were assigned to the methyl protons joined at C-3. The presence of a doublet at δ 2.11-2.27 and 2.20-2.32 was consistent with the methylene protons at C-2. Other doublet signals at δ 2.38-2.51 and 2.53-2.61 were assigned at the methylene protons on C-4. The presence of a singlet at δ 5.85-6.21 was consistent with the methine proton on C-11; the signal doublet at δ 5.93-6.10 was assigned at one aromatic protons on C-9; the presence of a signal doublet of doublet at δ 6.19-6.39 was consistent with the one aromatic proton on C-7; the signal doublet at δ 6.67-6.87 was assigned at one aromatic protons on C-6. The presence of a broad proton signal at δ 6.31-9.96 was consistent with N-H, deuterium oxide exchangeable. The others aromatic protons appears as a multiplet signal and AA'BB' systems at δ 6.45-7.50. The signals for the R= OCH_3 substituted were also observed in δ 3.69-3.85.

The ^{13}C-nmr spectra data for compounds **IV, 1**-**12** are given in Table 1. The signals were confirmed by using HETCOR, COSY, FLOCK, NOESY, and DEPT nmr experiments operating at 300 and 500 MHz. The mass spectra of compounds **IV, 1**-**12** exhibit a stable molecular ion with a relative abundance of 35-68%. The base peak is the ion at m/z $[M-(76+R)]^+$. The main fragmentation was consistent with the assigned structures and the mass spectra of the compound **IV, 1-12** includes ions of m/z corresponding to molecular ion $[M]^+$; $[M-1]^+$; $[M-CH_3]^+$; $[M-(NH_2)]^+$; $[M-R]^+$; $[M-HR]^+$; $[M-(R+NH_2)]^+$; $[M-(C_4H_9)]^+$; $[M-(C_5H_8O)]^+$; $[M-(C_5H_9O)]^+$ and m/z 83.

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 (CID) experiments. The elemental composition of the molecular ion and the principal fragment ion were 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 500

spectrometer operating at 125 MHz in deuterochloroform 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-AC505 and JEOL MS-SX 102A high-resolution mass spectrometer with accurate mass determination of the molecular ion and the principal fragment 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.

Compounds **I** and **II** were prepared following methods developed by us, with modifications [13,11].

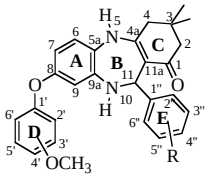
General Procedure for the Synthesis of the 3-{4-[(*o*- and *p*-Methoxy)phenyl]-1,2-phenylenediamine}-5,5-dimethyl-2-cyclohexenone III. A mixture of 1 x 10^{-2} mole of the 5,5-dimethyl-1,3-cyclohexanedione (Dimedone) and 4-[(*o*-; and *p*-methoxy)-phenoxy]-1,2-phenylendiamine II (1 x 10^{-2} mole) in 20 mL of benzene were heated at reflux for 24 hours, afforded compound III with a 72-78% yield.

General Procedure for the Synthesis of the 3,3-Dimethyl-2,3,4,5,10,11-Hexahydro-8-[(*o*-; and *p*-methoxy)-phenyl]-11-[(*o*-; and *p*-R)phenyl]-1*H*-dibenzo[*b*,*e*][1,4]-diazepin-1-ones IV, 1-12. A mixture of 1x10^{-3} mole of the cyclohexenone **III**; 1x10^{-3} mole of the (*o*-; and *p*-R)benzaldehyde, 0.5 mL of acetic acid glacial in 5.0 mL ethanol was heated at reflux for 3-4 hours. The reaction mixture was cooled to room temperature and evaporated at vacuum to yield a semisolid. The residual semisolid was purified by crystallization from hexane-ethyl acetate to yield compounds **IV**, **1**-**12**, in a 76-98%.

3,3-Dimethyl-8-[(*o*-methoxy)phenoxy]-11-[(*o*-methyl)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one

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	*o*-OCH_3	*o*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3	*p*-OCH_3
R	*o*-CH_3	*p*-CH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3	*o*-CH_3	*p*-CH_3	*o*-Cl	*p*-Cl	*o*-OCH_3	*p*-OCH_3
C-1	193.9	193.8	193.6	193.7	193.6	193.6	193.9	193.8	193.7	193.8	191.7	193.7
C-2	49.7	49.7	49.6	49.7	49.8	49.7	49.7	49.7	49.7	49.6	49.5	49.7
C-3	32.3	32.2	32.3	32.3	32.3	32.3	32.4	32.3	32.3	32.3	31.7	32.2
C-4	46.1	46.1	46.2	46.3	46.2	46.3	46.2	46.2	46.1	46.2	44.2	46.1
C-4a	153.9	153.7	154.6	154.0	156.8	158.1	155.3	155.4	155.4	155.5	156.5	155.4
C-5a	127.5	126.8	127.1	126.5	130.0	126.8	127.3	126.7	126.9	126.6	127.0	126.8
C-6	120.8	121.0	120.8	121.0	119.8	120.9	120.9	121.0	120.9	121.1	120.8	121.0
C-7	111.7	111.3	112.0	111.4	111.6	111.3	111.8	111.3	111.9	111.7	110.1	111.4
C-8	153.3	153.4	153.4	153.5	154.4	153.5	153.9	153.7	154.2	153.8	154.5	153.6
C-9	111.2	111.2	111.3	110.9	111.3	111.2	111.4	111.3	111.3	111.4	109.8	111.3
C-9a	141.2	140.6	138.6	138.2	139.6	138.6	135.2	135.9	133.6	132.2	130.8	136.0
C-11	55.3	57.8	56.0	57.6	53.9	57.5	55.4	57.8	56.1	57.6	52.6	57.6
C-11a	111.0	110.8	109.3	110.4	110.2	111.1	111.0	110.9	109.2	110.2	108.4	110.9
C-1'	153.3	153.7	145.9	153.4	153.2	153.0	154.0	154.1	154.8	154.4	155.0	154.1
C-2'	150.4	150.5	150.4	150.8	150.5	150.6	114.6	114.6	114.6	114.8	114.3	114.6
C-3'	131.1	129.6	129.6	124.3	129.9	128.2	119.4	119.6	119.5	119.7	119.0	119.6
C-4'	130.5	123.9	123.9	112.7	123.8	123.9	150.8	150.8	150.7	150.7	150.4	150.8
C-5'	125.2	120.8	127.6	121.0	120.9	120.8	119.4	119.4	119.5	119.7	119.0	119.6
C-6'	118.9	119.2	118.9	119.8	119.0	119.7	114.6	114.6	114.6	114.8	114.3	114.6
C-1"	146.1	135.9	133.6	145.6	146.3	145.9	141.1	140.6	139.8	142.3	140.0	138.7
C-2"	138.3	128.8	139.8	128.2	139.7	128.2	138.4	127.0	138.8	128.3	139.9	128.1
C-3"	129.7	127.0	129.6	128.5	128.0	113.5	130.6	128.9	129.6	128.5	127.0	113.4
C-4"	129.7	129.5	129.6	142.3	128.5	136.0	126.7	138.7	128.2	138.3	127.5	136.0
C-5"	112.5	127.0	128.2	128.5	124.2	113.5	125.2	128.9	126.2	128.5	126.5	113.4
C-6"	126.7	128.8	126.2	128.2	126.9	128.2	125.7	127.0	127.6	128.3	126.6	128.1
C-3(CH_3)	27.8	27.7	28.1	27.8	28.1	27.8	27.9	27.8	28.1	27.8	27.7	27.7
C-3(CH_3)	28.5	28.7	28.5	28.6	28.7	28.7	28.6	28.7	28.5	28.6	28.3	28.7
$C_{2'}$-OCH_3	55.8	55.8	55.8	55.9	55.8	55.8	-	-	-	-	-	-
$C_{2''}$-OCH_3	-	-	-	-	55.2	-	-	-	-	-	55.1	-
$C_{4'}$-OCH_3						-	55.6	55.6	55.6	55.6	54.9	55.5
$C_{4''}$-OCH_3	-	-	-	-	-	55.0	-	-	-	-	-	55.0
$C_{2''}$-CH_3	19.5	-	-	-	-	-	19.6	-	-	-	-	-
$C_{4''}$-CH_3	-	20.9	-	-	-	-	-	21.0	-	-	-	-

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

(1). This compound was obtained as a brown-reddish solid in a 90% yield; mp 108°; ir (chloroform): ν N-H 3415, C=O 1620, C-N 1371 and 1313, C-O 1261 and 1116 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.03 and 1.09 (s, 6H, C_3-CH_3); 2.15 (d, 1H, J=16.3 Hz, 2-Ha); 2.25 (d, 1H, J=16.3 Hz, 2-Hb); 2.45 (d, 1H, J=15.6 Hz, 4-Ha); 2.48 (s, 3H, $C_{2''}$-CH_3); 2.57 (d, 1H, J=15.6 Hz, 4-Hb); 3.72 (s, 3H, $C_{2'}$-OCH_3); 5.95 (d, 1H, J=2.5 Hz, 9-H); 6.10 (s, 1H, 11-H); 6.34 (dd, 1H, J=2.4, 8.5 Hz, 7-H); 6.49 (dd, 1H, J=1.4, 7.9 Hz, 6'-H); 6.64 (bs, 2H, N-H, deuterium oxide exchangeable); 6.76 (d, 1H, J=8.7 Hz, 6-H); 6.80 (dt, 1H, J=1.2; 7.4 Hz, 5'-H); 6.91 (dt, 1H, J=1.4, 7.1 Hz, 5''-H); 6.97 (dd, 1H, J=1.4, 7.9 Hz, 6''-H); 7.03 (dt, 1H, J=1.1, 6.5 Hz, 4'-H); 7.26 (dt, 1H, J=1.2, 6.4 Hz, 4''-H); 7.50 (dd, 1H, J=1.2, 8.0 Hz, 3'-H); 7.57 (dd, 1H, J=1.3, 7.3 Hz, 3''-H); ms: m/z 454 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_3$: C, 76.62; H, 6.65; N, 6.16. Found: C, 76.52; H, 6.72; N, 6.24.

3,3-Dimethyl-8-[(*o*-metoxy)phenoxy]-11-[(*p*-methyl)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (2). This compound was obtained as a brown-reddish solid in a 93% yield; mp 103°, ir (chloroform): ν N-H 3415; C=O 1619; C-N 1371 and 1319, C-O 1261 and 1116 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.03 and 1.08 (s, 6H, C_3-CH_3); 2.19 (s, $C_{4''}$-CH_3); 2.19 (d, 1H, J=16.2 Hz, 2-Ha); 2.28 (d, 1H, J=16.2 Hz, 2-Hb); 2.40 (d, 1H, J=15.8 Hz, 4-Ha); 2.55 (d, 1H, J=15.8 Hz, 4-Hb); 3.74 ($C_{2'}$-OCH_3); 5.86 (s, 1H, 11-H); 6.03 (d, 1H, J=2.5 Hz, 9-H); 6.31 (bs, 2H, N-H, deuterium oxide exchangeable); 6.35 (dd, 1H, J=2.5, 8.6 Hz, 7-H); 6.60 (dd, 1H, J=1.5, 7.9 Hz, 6'-H); 6.73 (d, 1H, J=8.6 Hz, 6-H); 6.80 (dt, 1H, J=1.5, 7.7 Hz, 5'-H); 6.90 and 6.92 (AA'BB", 4H, J=9.0 Hz, phenyl protons of "E" ring); 7.03 (dt, 1H, J=1.6, 7.7 Hz, 4'-H); 7.14 (dd, 1H, J=1.2, 7.8 Hz, 3'-H); ms: m/z 454 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_3$: C, 76.62; H, 6.65; N, 6.16. Found: C, 76.71; H, 6.56; N, 6.06.

3,3-Dimethyl-8-[(*o*-metoxy)phenoxy]-11-[(*o*-chloro)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (3). This compound was obtained as a brown-reddish solid in a 91% yield; mp 116°; ir (chloroform): ν N-H 3414, C=O 1619, C-N 1371 and 1309, C-O 1261 and 1115 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.11 and 1.14 (s, 6H, C_3-CH_3); 2.23 (d, 1H, J=16.2 Hz, 2-Ha); 2.31 (d, 1H, J=16.2 Hz, 2-Hb); 2.49 (d, 1H, J=15.8 Hz, 4-Ha); 2.61 (d, 1H, J=15.8 Hz, 4-Hb); 3.75 (s, 3H, $C_{2'}$-OCH_3); 6.10 (d, 1H, J=2.5 Hz, 9-H); 6.20 (s, 1H, 11-H); 6.34 (dd, 1H, J=2.5, 8.6 Hz, 7-H); 6.49 (dd, 1H, J=1.7, 7.9 Hz, 6'-H); 6.69 (d, 1H, J=8.8 Hz, 6-H); 6.79 (dt, 1H, J=1.6; 6.9 Hz, 5'-H); 6.92 (dd, 1H, J=1.4, 8.4 Hz, 6''-H); 7.01 (dt, 1H, J=1.5, 6.9 Hz, 5''-H); 7.02 (dt, 1H, J=1.4, 7.4 Hz, 4'-H); 7.26 (dt, 1H, J=1.2, 7.8 Hz, 4''-H); 7.31 (bs, 2H, N-H, deuterium oxide exchangeable); 7.33 (dd, 1H, J=1.4, 8.1 Hz, 3'-H); 7.39 (dd, 1H, J=1.6, 6.5 Hz, 3''-H); ms: m/z 474 (M^+); 476 $[M+2]^+$. *Anal*. Calcd. for $C_{28}H_{27}ClN_2O_3$: C, 70.80; H, 5.73; N, 5.90. Found: C, 70.89; H, 5.66; N, 5.81.

3,3-Dimethyl-8-[(*o*-metoxy)phenoxy]-11-[(*p*-chloro)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (4). This compound was obtained as an orange solid in a 90% yield; mp 114°, ir (chloroform): ν N-H 3414; C=O 1619; C-N 1370 and 1313, C-O 1263 and 1114 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.05 and 1.12 (s, 6H, C_3-CH_3); 2.20 (d, 1H, J=16.5 Hz, 2-Ha); 2.29 (d, 1H, J=16.5 Hz, 2-Hb); 2.42 (d, 1H, J=16.2 Hz, 4-Ha); 2.56 (d, 1H, J=16.2 Hz, 4-Hb); 3.74 ($C_{2'}$-OCH_3); 5.85 (s, 1H, 11-H); 6.01 (d, 1H, J=2.7 Hz, 9-H); 6.39 (dd, 1H, J=2.4, 8.5 Hz, 7-H); 6.63 (dd, 1H, J=1.5, 7.9 Hz, 6'-H); 6.69 (bs, 2H, N-H, deuterium oxide exchangeable); 6.70 (d, 1H, J=8.4 Hz, 6-H); 6.85 (dt, 1H, J=1.5, 7.7 Hz, 5'-H); 6.92 (dt, 1H, J=1.5, 7.7 Hz, 4'-H); 6.96 and 7.08 (AA'BB", 4H, J=8.5 Hz, phenyl protons of "E" ring); 7.03 (dd, 1H, J=1.5, 8.0 Hz, 3'-H); ms: m/z 474 (M^+); 476 $[M+2]^+$. *Anal*. Calcd. for $C_{28}H_{27}ClN_2O_3$: C, 70.80; H, 5.73; N, 5.90. Found: C, 70.71; H, 5.80; N, 5.96.

3,3-Dimethyl-8-[(*o*-metoxy)phenoxy]-11-[(*o*-methoxy)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (5). This compound was obtained as a brown-reddish solid in a 87% yield; mp 79°; ir (chloroform): ν N-H 3416, C=O 1620, C-N 1373 and 1320, C-O 1259 and 1116 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.12 and 1.14 (s, 6H, C_3-CH_3); 2.27 (d, 1H, J=16.5 Hz, 2-Ha); 2.32 (d, 1H, J=16.5 Hz, 2-Hb); 2.45 (d, 1H, J=15.6 Hz, 4-Ha); 2.59 (d, 1H, J=15.6 Hz, 4-Hb); 3.76 (s, 3H, $C_{2''}$-OCH_3); 3.79 (s, 3H, $C_{2'}$-OCH_3); 6.00 (d, 1H, J=2.7 Hz, 9-H); 6.14 (s, 1H, 11-H); 6.30 (dd, 1H, J=2.5, 8.5 Hz, 7-H); 6.45 (dd, 1H, J=1.5, 7.6 Hz, 6'-H); 6.66 (dd, 1H, J=1.4, 8.4 Hz, 6''-H); 6.67 (d, 1H, J=8.8 Hz, 6-H); 6.76 (dt, 1H, J=1.4; 7.0 Hz, 5''-H); 6.79 (dt, 1H, J=1.5, 6.9 Hz, 5'-H); 7.00 (dt, 1H, J=1.2, 7.4 Hz, 4''-H); 7.02 (dt, 1H, J=1.4, 7.5 Hz, 4'-H); 7.14 (dd, 1H, J=1.2, 8.1 Hz, 3'-H); 7.15 (dd, 1H, J=1.3, 7.0 Hz, 3''-H); 7.24 (bs, 2H, N-H, deuterium oxide exchangeable); ms: m/z 470 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95. Found: C, 74.12; H, 6.50; N, 5.87.

3,3-Dimethyl-8-[(*o*-metoxy)phenoxy]-11-[(*p*-methoxy)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (6). This compound was obtained as a brown-reddish solid in a 79% yield; mp 84°, ir (chloroform): ν N-H 3409; C=O 1616; C-N 1368 and 1318, C-O 1260 and 1111 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.06 and 1.12 (s, 6H, C_3-CH_3); 2.21 (d, 1H, J=16.2 Hz, H-2a); 2.30 (d, 1H, J=16.2 Hz, 2-Hb); 2.38 (d, 1H, J=15.9 Hz, 4-Ha); 2.55 (d, 1H, J=15.9 Hz, 4-Hb); 3.70 (s, 3H, $C_{4''}$-OCH_3); 3.72 (s, 3H, $C_{2'}$-OCH_3); 5.86 (s, 1H, 11-H); 6.04 (d, 1H, J=2.7 Hz, 9-H); 6.38 (dd, 1H, J=2.7, 8.7 Hz, 7-H); 6.62 and 6.95 (AA'BB', 4H, J=8.7 Hz, phenyl protons of "E" ring); 6.63 (dd, 1H, J=1.5, 7.9 Hz, 6'-H); 6.68 (d, 1H, J=8.4 Hz, 6-H); 6.82 (dt, 1H, J=1.5, 7.7 Hz,5'-H); 6.94 (dd, 1H, J=1.5, 8.1, 3'-H); 7.03 (dt, 1H, J=1.5, 7.8 Hz, 4'-H); 7.22 (bs, 2H, N-H, deuterium oxide exchangeable); ms: m/z 470 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95. Found: C, 74.10; H, 6.38; N, 6.02.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*o*-methyl)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (7). This compound was obtained as a brown-reddish solid in a 98% yield; mp 82°; ir (chloroform): ν N-H 3416, C=O 1620, C-N 1371 and 1318, C-O 1267 and 1116 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.07 and 1.13 (s, 6H, C_3-CH_3); 2.18 (d, 1H, J=16.2 Hz, 2-Ha); and 2.28 (d, 1H, J=16.3 Hz, 2-Hb); 2.48 (d, 1H, J=15.6 Hz, 4-Ha); 2.51 (s, 3H, $C_{2''}$-CH_3); 2.61 (d, 1H, J=15.6 Hz, 4-Hb); 3.77 (s, 3H, $C_{4'}$-OCH_3); 5.93 (d, 1H, J=2.4 Hz, 9-H); 6.10 (s, 1H, 11-H); 6.32 (dd, 1H, J=2.4, 8.7 Hz, 7-H); 6.63 (dd, 1H, J=1.8, 7.9 Hz, 6''-H); 6.63 and 6.76 (AA'BB', 4H, J=8.7 Hz, phenyl protons of "D" ring); 6.72 (bs, 2H, N-H, deuterium oxide exchangeable); 6.76 (d, 1H, J=8.8 Hz, 6-H); 6.82 (dt, 1H, J=1.3; 7.1 Hz, 5''-H); 6.98 (dt, 1H, J=1.2, 7.1 Hz, 4''-H); 7.07 (dd, 1H, J=1.2, 6.9 Hz, 3''-H); ms: m/z 454 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_3$: C, 76.62; H, 6.65; N, 6.16. Found: C, 76.68; H, 6.58; N, 6.07.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*p*-methyl)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (8). This compound was obtained as a brown-reddish solid in a 91% yield; mp 120°, ir (chloroform): ν N-H 3416; C=O 1619; C-N 1370 and 1319, C-O 1268 and 11132 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.05 and 1.11 (s, 6H, C_3-CH_3); 2.20 (d, 1H, J=16.2 Hz, 2-Ha); 2.22 (s, $C_{4''}$-CH_3); 2.29 (d, 1H, J=16.2 Hz,

2-Hb); 2.40 (d, 1H, J=15.9 Hz, 4-Ha); 2.55 (d, 1H, J=15.9 Hz, 4-Hb); 3.77 ($C_{4'}$-OCH_3); 5.86 (s, 1H, 11-H); 6.03 (d, 1H, J=2.4 Hz, 9-H); 6.32 (dd, 1H, J=2.4, 8.4 Hz, 7-H); 6.69 (d, 1H, J=8.7 Hz, 6-H); 6.70 and 6.78 (AA'BB', 4H, J=8.7 Hz, phenyl protons of "D" ring); 6.92 (s, 4H, J=9.0 Hz, phenyl protons of "E" ring); 9.96 (bs, 2H, N-H, deuterium oxide exchangeable); ms: m/z 454 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_3$: C, 76.62; H, 6.65; N, 6.16. Found: C, 76.72; H, 6.60; N, 6.26.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*o*-chloro)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (9). This compound was obtained as a brown-reddish solid in a 98% yield; mp 96°; ir (chloroform): ν N-H 3415, C=O 1620, C-N 1371 and 1320, C-O 1268 and 1116 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.12 and 1.15 (s, 6H, C_3-CH_3); 2.23 (d, 1H, J=16.2 Hz, 2-Ha); 2.32 (d, 1H, J=16.2 Hz, 2-Hb); 2.48 (d, 1H, J=15.6 Hz, 4-Ha); 2.61 (d, 1H, J=15.6 Hz, 4-Hb); 3.77 (s, 3H, $C_{4'}$-OCH_3); 6.09 (d, 1H, J=2.7 Hz, 9-H); 6.21 (s, 1H, 11-H); 6.29 (dd, 1H, J=2.5, 8.6 Hz, 7-H); 6.64 and 6.78 (AA'BB', 4H, J=8.7 Hz, phenyl protons of "D" ring); 6.67 (d, 1H, J= 8.7 Hz, 6-H); 6.73 (bs, 2H, N-H, deuterium oxide exchangeable); 6.67 (dd, 1H, J=1.8, 9.2 Hz, 6"-H); 6.91 (dt, 1H, J=1.2, 7.2 Hz, 5"-H); 7.04 (dt, 1H, J=1.5, 7.7 Hz, 4"-H); 7.28(dd, 1H, J=1.8, 8.5 Hz, 3"-H); ms: m/z 474 (M^+); 476 $[M+2]^+$. *Anal*. Calcd. for $C_{28}H_{27}ClN_2O_3$: C, 70.80; H, 5.73; N, 5.90. Found: C, 70.90; H, 5.82; N, 5.99.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*p*-chloro)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (10). This compound was obtained as an orange solid in a 82% yield; mp 133°, ir (chloroform): ν N-H 3415; C=O 1619; C-N 1370 and 1315, C-O 1268 and 1112 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.05 and 1.11 (s, 6H, C_3-CH_3); 2.21 (d, 1H, J=16.2 Hz, 2-Ha); 2.309 (d, 1H, J=16.2 Hz, 2-Hb); 2.42 (d, 1H, J=15.9 Hz, 4-Ha); 2.55 (d, 1H, J=15.9 Hz, 4-Hb); 3.77 ($C_{4'}$-OCH_3); 5.85 (s, 1H, 11-H); 6.00 (d, 1H, J=2.7 Hz, 9-H); 6.35 (dd, 1H, J=2.4, 8.6 Hz, 7-H); 6.70 and 6.81 (AA'BB", 4H, J=9.0 Hz, phenyl protons of "D" ring); 6.71 (d, 1H, J=8.1 Hz, 6-H); 6.85 (bs, 2H, N-H, deuterium oxide exchangeable); 6.95 and 7.09 (AA'BB", 4H, J=8.4 Hz, phenyl protons of "E" ring); ms: m/z 474 (M^+); 476 $[M+2]^+$. *Anal*. Calcd. for $C_{28}H_{27}ClN_2O_3$: C, 70.80; H, 5.73; N, 5.90. Found: C, 70.73; H, 5.63; N, 5.80.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*o*-methoxy)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (11). This compound was obtained as a yellow solid in a 76% yield; mp 196°; ir (chloroform): ν N-H 3416, C=O 1619, C-N 1372 and 1320, C-O 1265 and 1114 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.12 and 1.13 (s, 6H, C_3-CH_3); 2.11 (d, 1H, J=16.1 Hz, 2-Ha), and 2.20 (d, 1H, J=16.1 Hz, 2-Hb); 2.51 (d, 1H, J=15.9 Hz, 4-Ha); 2.61 (d, 1H, J=15.9 Hz, 4-Hb); 3.74 (s, 3H, $C_{2''}$-OCH_3); 3.83 (s, 3H, $C_{4'}$-OCH_3); 5.94 (s, 1H, 11-H); 6.0 (d, 1H, J=2.4 Hz, 9-H); 6.19 (dd, 1H, J=2.7, 7.4 Hz, 7-H); 6.61 and 6.81 (AA'BB", 4H, J=9.0 Hz, phenyl protons of "D" ring); 6.81 (dd, 1H, J=1.8, 9.3 Hz, 6"-H); 6.86 (dd, 1H, J=1.8, 7.8 Hz, 3"-H); 6.87 (dt, 1H, J=1.8; 7.3 Hz, 5"-H); 6.89 (d, 1H, J=8.1 Hz, 6-H); 7.09 (dt, 1H, J=1.8, 6.9 Hz, 4"-H); 8.80 (bs, 2H, N-H, deuterium oxide exchangeable); ms: m/z 470 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95. Found: C, 73.93; H, 6.33; N, 6.02.

3,3-Dimethyl-8-[(*p*-metoxy)phenoxy]-11-[(*p*-methoxy)phenyl]-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepin-1-one (12). This compound was obtained as a brown-reddish solid in a 78% yield; mp 128°, ir (chloroform): ν N-H 3416; C=O 1619; C-N 1371 and 1325, C-O 1265 and 1117 cm^{-1}; ^{1}H-nmr (deuterochloroform): δ 1.05 and 1.10 (s, 6H, C_3-CH_3); 2.20 (d, 1H, J=16.5 Hz, H-2a); 2.29 (d, 1H, J=16.5 Hz, 2-Hb); 2.38 (d, 1H, J=15.9 Hz, 4-Ha); 2.53 (d, 1H, J=15.9 Hz, 4-Hb); 3.69 (s, 3H, $C_{4''}$-OCH_3); 3.77 (s, 3H, $C_{4'}$-OCH_3); 5.85 (s, 1H, 11-H); 6.02 (d, 1H, J=2.7 Hz, 9-H); 6.33 (dd, 1H, J=2.4, 8.6 Hz, 7-H); 6.66 and 6.95 (AA'BB", 4H, J=8.4 Hz, phenyl protons of "E" ring); 6.69 (d, 1H, J= 8.7 Hz, 6-H); 6.69 and 6.79 (AA'BB', 4H, J=8.7 Hz, phenyl protons of "D" ring); 7.26 (bs, 2H, N-H, deuterium oxide exchangeable); ms: m/z 470 (M^+). *Anal*. Calcd. for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95. Found: C, 73.95; H, 6.36; N, 6.04.

Acknowledgement. This work was supported by UNAM-DGAPA project IN 225503. We wish to thank to J. Pérez for their assistance in the acquisition of the mass spectral data, H. Rios for the nmr determination; and M. Adaya for the ir determination.

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