

The synthesis of novel hexahydrodibenzo[*b,e*][1,4]diazepin-1-one derivatives

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DOI: <http://dx.doi.org/10.3998/ark.5550190.p009.195>

Abstract

11-Aroyl-2,3,4,5,10,11-hexahydrodibenzo[*b,e*][1,4]diazepin-1-ones are obtained by reaction of 3-(2-aminophenylamino)cyclohex-2-en-1-ones with arylglyoxal hydrates in 2-propanol. Also, several of their chemical properties (alkylation, acetylation, nitrosation) were investigated.

Keywords: Dibenzodiazepines, arylglyoxals, enamino ketones, acylation, nitrosation, alkylation

Introduction

Out of the class of tricyclic dibenzo[*b,e*][1,4]diazepines, the anxiolytic Clozapene,¹ the antidepressant Dibenzepine,² and also the drug Pirenzepine, which is used for ulcer treatment,³ are the most widely-applied in medicine. Today research into tricyclic 1,4-diazepines is connected with the modification of their structure furnishing, first of all, potential antipsychotic drugs.^{4,5} Functionalized diphenylamines containing amino and ester groups in *o*-positions of the phenyl rings serve as the initial compounds for the synthesis of dibenzo[*b,e*][1,4]diazepines.^{6,7} Also partially hydrogenated dibenzodiazepines obtained from 3-aminoenones of cyclohexene-1,3-dione and aldehydes were described in references 8-12. As we showed earlier,¹³ adducts of dimedone and aromatic aldehydes depending on the electronic properties of the substituent in the reaction with *o*-phenylenediamine (*o*-PDA) form either 11-arylhexasubstituteddibenzo[*b,e*][1,4]diazepin-1-ones (**1**, R = Ar) or decahydroacridinones (**2**, R = Ar). Diazepines **1** were also obtained via one-pot condensation¹³ by sequential addition of reagents, namely: by reflux of dimedone with *o*-PDA in 2-propanol in the presence of a catalytic amount of acetic acid for 40 minutes followed by the addition of aldehyde. We have reported the synthesis of two compounds of the 11-arylhexasubstituteddibenzo[*b,e*][1,4]diazepin-1-ones series (R = COAr), when arylglyoxals were used instead of benzaldehydes.¹³

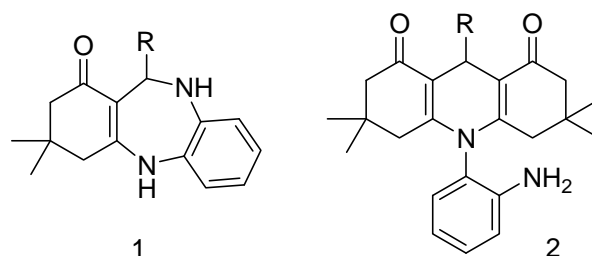


Figure 1. Structures obtained in reactions of adducts of dimedone and aldehydes with *o*-PDA.

An article devoted to the synthesis of 11-aryloxyhexahydrodibenzo[*b,e*][1,4]diazepin-1-ones based on enaminoketones of dimedone and 4,5-disubstituted *o*-phenylenediamines with arylglyoxals under microwave activation appeared later.¹⁴

The purpose of this paper was to research the class of hexahydrodibenzo[*b,e*][1,4]diazepin-1-ones by varying the structure of cyclohexane-1,3-diones, arylglyoxals and also to study the transformations of the compounds synthesized in reactions specific for secondary amines.

Results and Discussion

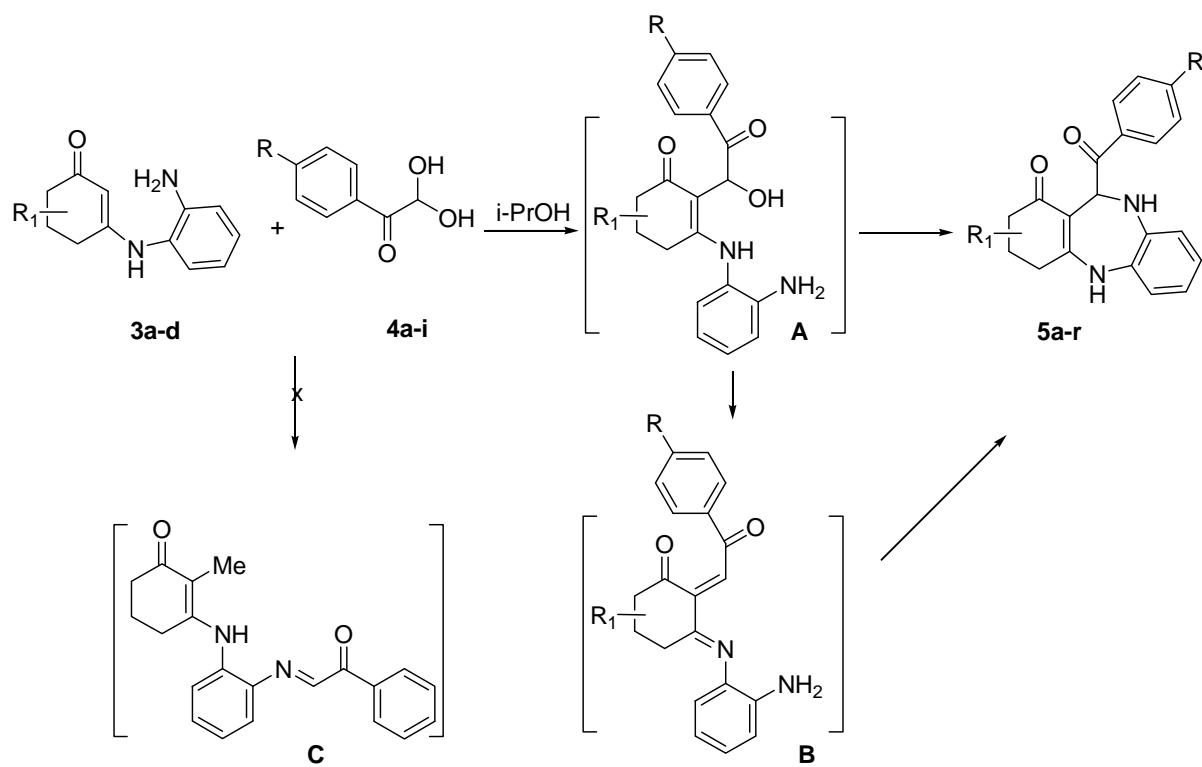
The method of sequential addition of the reagents used in our research led in most cases to the target structures **5** in low yields (<50%) contaminated by byproducts – 2-arylquinoxalines. Therefore intermediate enaminoketones **3a-d** were synthesized by us (the synthesis of compounds **3a,b** was described in references 15-17), which were then employed in a reaction with arylglyoxal hydrates **4a-i**.

Under these conditions the target products precipitated from the hot reaction mixture 10 to 25 minutes after addition of the arylglyoxal hydrate, giving good yields of 60-80% (enaminoketone **3d** being an exception, did not react with arylglyoxals). It can be noted, that compounds **5a-d** were obtained with lower yields compared to those dibenzodiazepinones which contain methyl groups in the cyclohexene fragment which can, probably, be explained by their higher solubility.

The composition and structure of diazepinones **5a-r** have been proved via elemental analysis, ¹H, ¹³C NMR spectroscopy and in some cases mass spectrometry data. The presence of molecular ion peaks of low intensity and also fragmentary ion signals corresponding to the masses of dibenzodiazepine (highest in intensity) and aroyl fragments was common for all mass spectra of hexahydrodibenzo[*b,e*][1,4]diazepin-1-ones **5a-d,f,g,k,o**. The presence of the other peaks is connected with further decomposition of subsequent fragments.

The signals of all proton-containing fragments are present in ¹H NMR spectra of compounds **5a-p**. Determining the NH-group signals was carried out via hydrogen–deuterium exchange. The signals at 6.0 ppm and 9.0 ppm belong to the imine and enamine protons accordingly. The methylene proton and iminogroup proton in diazepinones **5a-r** interact with each other which leads to a doublet in the spectra (*J* 5.0 Hz). In ¹³C NMR spectra of compounds **5e,f,h-j,m** all the

necessary carbon signals are present, and using the DEPT-135 procedure allows us to identify the signals of secondary and tertiary carbon atoms.



3a R₁ = H; **b** R₁ = 5,5-(CH₃)₂; **c** R₁ = 6,6-(CH₃)₂; **d** R₁ = 2-CH₃; **4a** R = H; **b** R = CH₃; **c** R = F; **d** R = Cl; **e** R = Br; **f** R = SCH₃; **g** R = NO₂; **h** R = C₆H₄; **i** R = cyclo-C₆H₁₁; **5a-d** R₁ = H; **a** R = H; **b** R = F; **c** R = Cl; **d** R = Br; **5e-o** R₁ = 3,3-(CH₃)₂; **e** R = H; **f** R = CH₃; **g** R = C₂H₅; **h** R = F; **i** R = Cl; **j** R = Br; **k** R = I; **l** R = NO₂; **m** R = SCH₃; **n** R = C₆H₄; **o** R = cyclo-C₆H₁₁; **5p,r** R₁ = 2,2-(CH₃)₂; **p** R = H; **r** R = Br.

Scheme 1. Synthesis of diazepines **5a-r**.

The formation of a seven membered ring probably includes the stage of intermediate **A** generation, which undergoes *endo*-tetragonal cyclization. Obtaining unsaturated ketones (intermediate **B**) followed by cyclization can be an alternative method. Lack of interaction in the case of enaminoketone **3d** can be explained by the impossibility of formation of such intermediates in these conditions. It should be also noted, that the possible intermediate azomethine **C** was not isolated in reactions of compounds **3d** with arylglyoxals as well.

Diazepinones **5e,h-j,l,n,o,r** are easily acetylated by reflux in acetic anhydride. In the ¹H NMR spectra of products **6a-g** we observed signals of acetyl group protons which experience noticeable upfield shifts due to the anisotropic influence of the *o*-phenylenediamine group. The singlet of H-11 with a downfield shift of 1.3 ppm indicates that the N-10 atom is attacked during acylation.

The structure of **6c** (3,3-dimethyl-10-acetyl-11-(*p*-chlorobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*]1,4]diazepin-1-one) was confirmed by an X-ray diffraction study.

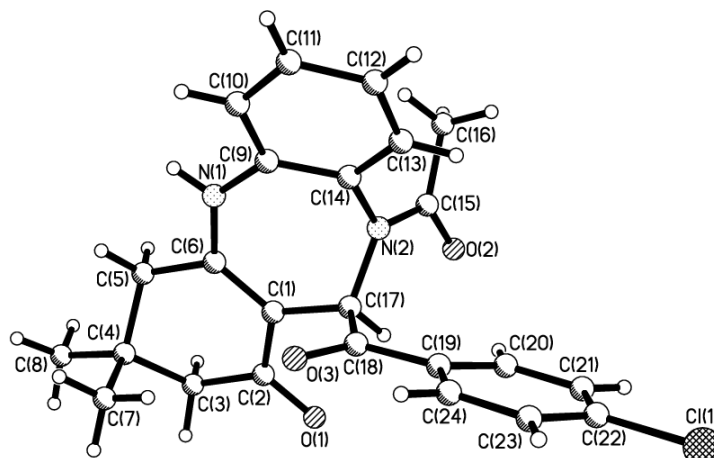


Figure 2. Molecular structure of **6c** according to the X-ray diffraction data.

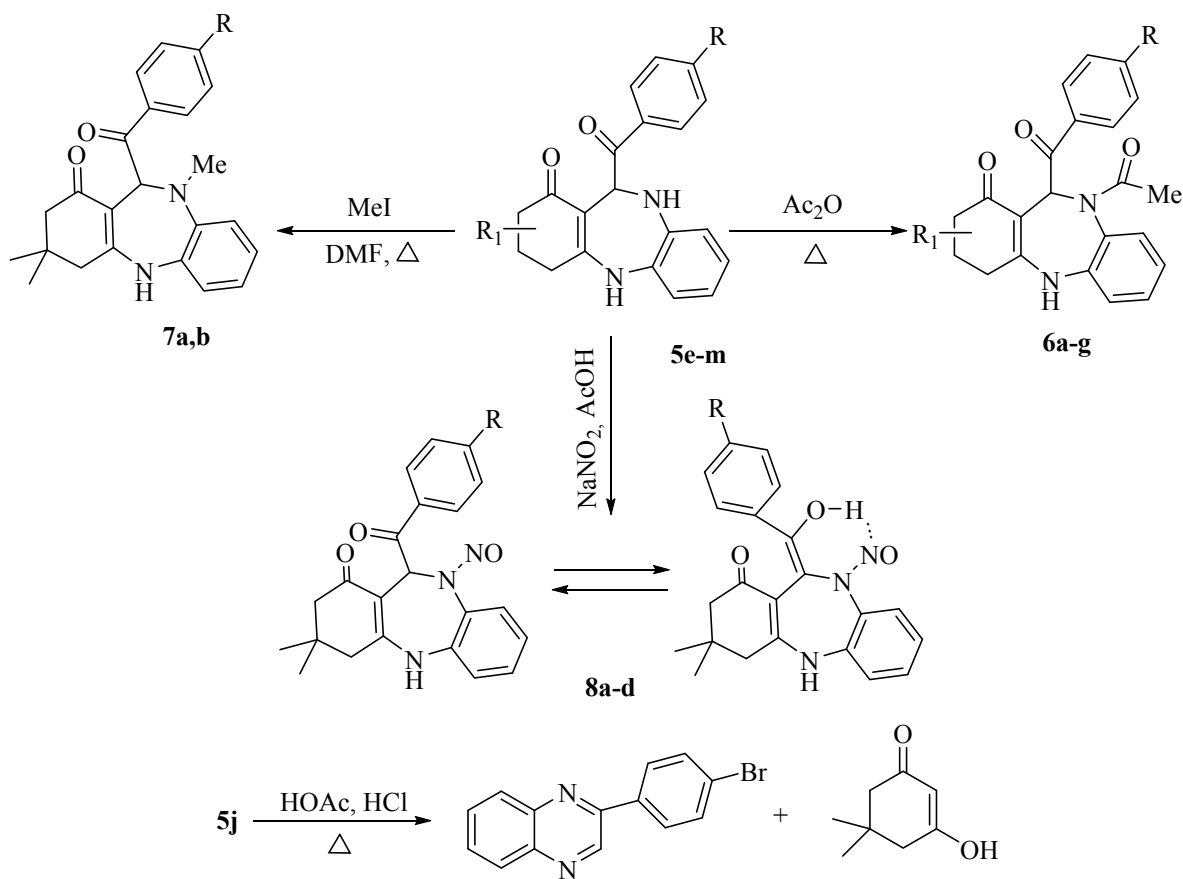
The dihydrodiazepine ring adopts a twist-boat conformation the (C(17)-C(1)-C(6)-N(1)-C(9) fragment is planar to within 0.02 Å, deviations of C(14) and N(2) atoms are 0.33 Å and 0.86 Å, respectively). The hexenone ring adopts a sofa conformation (deviation of the C(4) atom from the plane of the rest atoms is 0.68 Å, puckering parameters¹⁸ are: $S = 0.72$, $\theta = 39^\circ$, $\psi = 2^\circ$). The C(6)-C(1)-C(2)-O(1) unsaturated fragment is planar to within 0.02 Å and demonstrates essential π -conjugation between double bonds C(6)=C(1) (1.357(2) Å) and C(2)=O(1) (1.232(2) Å) – both are elongated as compared to the mean values (1.340 Å and 1.222 Å¹⁹, respectively). Length of the C(1)-C(2) bond 1.460(2) Å corresponds to the mean value for conjugated systems (1.464 Å).

N(1) atom has almost planar configuration (sum of the valence angles centered on N(1) is 358°). Values of torsion angles C(6)-N(1)-C(9)-C(10) 155.1(2)° and N(1)-C(6)-C(1)-C(2) 178.1(2)° allow conjugation between lone pair of N(1) and π -system of the C(9)...C(14) benzene ring, as well as unsaturated fragment of hexenone ring. However, N(1)-C(9) and N(1)-C(6) bonds (1.397(2) Å and 1.372(2) Å) are elongated as compare to mean values (1.353 Å and 1.339 Å, respectively) due to substantial repulsion between hydrogen atoms of amino group and neighboring rings (short contacts H(1)...H(10) 2.25 Å and H(1)...H(5A) 2.07 Å, sum of VdW radii is 2.32 Å²⁰).

Planar configuration of the N(2) atom is determined by sharing its lone pair within the π -system of the amide group N(2)-C(15)-O(2). At the time the conjugation of this lone pair with benzene ring C(9)...C(14) is hampered due to the non-coplanarity of the π -systems (the C(13)-C(14)-N(2)-C(15) torsion angle is 62.9(2)°). That is confirmed by the elongation of the N(2)-C(14) bond 1.423(2) Å as against mean value of 1.371 Å.¹⁹

In the crystal, molecules form chains along the [010] crystallographic direction due to the intermolecular hydrogen bonds N(1)–H(1)...O(2)' ($x, 1+y, z$; H...O' 2.12 Å, N–H...O' 173°).

Continuous mixing of diazepinones **5e,g** with methyl iodide in DMF in the presence of KOH leads to products **7a,b**. Alkylation also proceeds via the imino group in position 10. The products of alkylation were extracted with low yields (56-59%) which is, probably, due to their high solubility in reaction mixture. Reaction mixture control, which was carried out by TLC, confirmed the presence of the starting compounds. Nitrosation of diazepinones **5e,g,i,l** by potassium nitrite in acetic acid furnished *N*-nitroso derivatives **8a-d** which apparently exist as a mixture of the ketone and enol tautomeric forms. So the signal of the imine proton (N-10) does not appear in ^1H NMR spectra of the above mentioned products and aryl-substituent proton signals experience a downfield shift, pointing to the absence of the carbonyl group in the molecule. Molecular ion peaks are not registered in mass-spectra; however they can be witnessed in chromatography-mass spectra.



6a-f: $\text{R}_1 = 3,3\text{-(CH}_3\text{)}_2$, **a** $\text{R} = \text{H}$; **b** $\text{R} = \text{F}$; **c** $\text{R} = \text{Cl}$; **d** $\text{R} = \text{Br}$; **e** $\text{R} = \text{NO}_2$; **f** $\text{R} = \text{cyclo-C}_6\text{H}_{11}$; **6g:** $\text{R}_1 = 2,2\text{-(CH}_3\text{)}_2$, $\text{R} = \text{Br}$; **7a,b:** **a** $\text{R} = \text{H}$; **b** $\text{R} = \text{C}_2\text{H}_5$; **8a-d:** **a** $\text{R} = \text{H}$; **b** $\text{R} = \text{C}_2\text{H}_5$; **c** $\text{R} = \text{Br}$; **d** $\text{R} = \text{NO}_2$.

Scheme 2. Some chemical properties of compounds **5e-m**.

We investigated the stability of seven-membered cycle in the presence of acids and base. The heating of the compound **5j** in DMF in the presence of a 20% KOH solution didn't lead to the formation of any new products. At the same time the refluxing of the compound **5j** in acetic acid in the presence of conc. HCl, transforming into 2-(p-bromophenyl)quinoxaline (the product was determined via comparison of the literary data), while diketone **3b** was detected in the solution via TLC.

The presence of an additional carbonyl group in tricyclic structures **5** can make them convenient models for carrying out various heterocyclizations with nitrogen containing binucleophiles, however continuous reflux of compound **5e** with hydrazine hydrate or phenyl hydrazine in ethanol didn't furnish any novel products.

Conclusions

In summary, we report a general and efficient protocol for the preparation of various 11-aryl-hexahydrodibenzo[*b,e*][1,4]diazepin-1-one derivatives resulted from enaminketones of cyclohexane-1,3-dione and arylglyoxal hydrates. We find the seven membered ring in dibenzodiazepines **5** to be fairly stable, remaining unaltered in the reactions of acetylation, alkylation, and nitrosation, atom N-10 being the center of primary electrophilic attack.

Experimental Section

General. IR spectra were recorded by a diffuse reflectance measurement of samples dispersed in KBr powder with Agilent Technologies Cary 630 spectrometer. ¹H NMR spectra were measured by a Varian VX-Mercury 200 MHz spectrometer in DMSO-*d*₆ with chemical shift (δ) given in parts per million relative to TMS as internal standard. ¹³C NMR spectra were obtained with Bruker AM-400 (100 MHz) spectrometer. The chemical shift values are reported in parts per million relative to the standard chemical shift for DMSO-*d*₆. Mass-spectrometry was acquired on Hewlett-Packard LC/MSD 1100. Chromatography-mass-spectra were taken on Agilent 1100 Series SL instrument with diode matrix and selective detector Agilent LC/MSD SL. Elemental analysis was carried out on EA 3000 Eurovector. Melting points were determined on the Kofler table. The reaction monitoring was accomplished by thin-layer chromatography (TLC), performed on Silufol UV-254 plates in the following systems: PhMe – EtOAc, 1:1, CH₂Cl₂ – *i*-PrOH, 10:1.

3-((2-Aminophenyl)amino)-6,6-dimethylcyclohexen-2-en-1-one (3c). Yellow crystals; mp 259-260 °C (MeOH).

3-((2-Aminophenyl)amino)-2-methylcyclohexen-2-en-1-one (3d). Yellow crystals, mp 137-138 °C (MeOH).

General procedure for the synthesis of dibenzo[*b,e*][1,4]diazepin-1-ones 5a-p. A mixture of the appropriate enamines **3a-c** (1 mmol), arylglyoxals **4a-j** (1 mmol) in 10 ml of *i*-PrOH was heated at reflux with stirring until precipitation occurred from the hot solution (10-25 min), the precipitate was filtered off, the product was washed twice with benzene, and recrystallized.

11-Benzoyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5a). Yield 63%; (0.20 g), light yellow crystals, mp 205-206 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.68-1.93 (2H, m, 3-CH₂), 2.10-2.25 (2H, m, 4-CH₂), 2.59-2.72 (2H, m, 2-CH₂), 6.12 (1H, d, H-11, *J* 5.0 Hz), 6.24 (1H, d, 10-NH, *J* 5.0 Hz), 6.39-7.08 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.47-7.52 (3H, m, H-3,4,5, H Ar), 7.92 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.98 (1H, s, 5-NH). MS (EI) *m/z*: 318 (M⁺), 213 (100%). Anal. Calcd for C₂₀H₁₈N₂O₂: C, 75.45; H, 5.70; N, 8.80; Found: C, 75.51; H, 5.97; N, 8.75%.

11-(*p*-Fluorobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5b). Yield 60%; (0.20 g), light yellow crystals, mp 207-208 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.63-1.96 (2H, m, 3-CH₂), 2.09-2.25 (2H, m, 4-CH₂), 2.58-2.72 (2H, m, 2-CH₂), 6.11 (1H, d, H-11, *J* 5.0 Hz), 6.22 (1H, d, 10-NH, *J* 5.0 Hz), 6.41-7.08 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.31 (2H, t, H-3,5, H Ar, *J* 8.0 Hz), 8.08 (2H, t, H-2,6, H Ar, *J* 8.0 Hz), 9.00 (1H, s, 5-NH). MS (EI) *m/z*: 336 (M⁺), 213 (100%), Anal. Calcd for C₂₀H₁₇FN₂O₂: C, 71.42; H, 5.09; N, 8.33; Found: C, 71.52; H, 5.20; N, 8.37%.

11-(*p*-Chlorobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5c). Yield 65%; (0.23 g), light yellow crystals, mp 221-222 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.64-1.97 (2H, m, 3-CH₂), 2.09-2.26 (2H, m, 4-CH₂), 2.58-2.75 (2H, m, 2-CH₂), 6.10 (1H, d, H-11, *J* 5.0 Hz), 6.25 (1H, d, 10-NH, *J* 5.0 Hz), 6.40-7.06 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.55 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.92 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.00 (1H, s, 5-NH). MS (EI) *m/z*: 352 (M⁺), 213 (100%). Anal. Calcd for C₂₀H₁₇ClN₂O₂: C, 68.09; H, 4.86; N, 7.94; Found: C, 68.02; H, 4.67; N, 7.70%.

11-(*p*-Bromobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5d). Yield 60%; (0.24 g), light yellow crystals, mp 223-225 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.64-1.97 (2H, m, 3-CH₂), 2.09-2.25 (2H, m, 4-CH₂), 2.58-2.73 (2H, m, 2-CH₂), 6.09 (1H, d, H-11, *J* 5.0 Hz), 6.24 (1H, d, 10-NH, *J* 5.0 Hz), 6.41-7.10 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.66 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.84 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.99 (1H, s, 5-NH). MS (EI) *m/z*: 396 (M⁺), 213 (100%), 183 (10%). Anal. Calcd for C₂₀H₁₇BrN₂O₂: C, 60.47; H, 4.31; N, 7.05; Found: C, 60.32; H, 4.36; N, 7.10%.

Diazepinones **5e,l** were described in ref. 13.

3,3-Dimethyl-11-benzoyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5e). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 26.7 (CH₃), 28.5 (CH₃), 31.8 (C-3), 44.2 (C-4), 49.3 (C-2), 55.2 (C-11), 106.7 (C-11a), 119.3, 119.5, 120.3, 122.7, 128.3, 128.5, 130.6, 132.6, 136.4, 138.5, 155.6 (C Ar+C-4a), 192.4 (PhC=O), 196.9 (C=O).

3,3-Dimethyl-11-(*p*-methylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5f). Yield 75%; (0.27 g), light yellow crystals, mp 247-248 °C (from MeOH) (lit.¹⁴ mp 243-245 °C). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.92 (3H, s, CH₃), 1.07 (3H, s, CH₃), 2.12 (2H,

d, 4-CH₂, *J* 16.0 Hz), 2.21 (3H, s, C₆H₄CH₃), 2.56-2.63 (2H, m, 2-CH₂), 6.18 (1H, d, H-11, *J* 5.0 Hz), 6.24 (1H, d, 10-NH, *J* 5.0 Hz), 6.49-7.08 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.31 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.88 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.92 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 21.1 (CH₃), 26.8 (CH₃), 28.5 (CH₃), 31.8 (C-3), 44.2 (C-4), 49.3 (C-2), 55.1 (C-11), 106.8 (C-11a), 119.3, 119.4, 120.2, 122.7, 128.5, 129.0, 130.6, 133.7, 136.9, 142.8, 155.5 (C Ar+C-4a), 192.3 (ArC=O), 196.3 (C=O). DEPT-135 (100 MHz, DMSO-*d*₆): δ_C 21.1 (CH₃), 26.8 (CH₃), 28.5 (CH₃), 44.2 (C-4), 49.3 (C-2), 55.1 (C-11), 119.3, 119.4, 120.2, 122.7, 128.5, 129.0 (C Ar). MS (EI) *m/z*: 360 (M⁺), 241 (100%), 185 (15%). Anal. Calcd for C₂₃H₂₄N₂O₂: C, 76.64; H, 6.71; N, 7.77. Found: C 76.35; H 6.69; N 7.40%.

3,3-Dimethyl-11-(*p*-ethylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5g). Yield 69%; (0.25 g), light yellow crystals, mp 214-216 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_C 0.87 (3H, s, CH₃), 1.03 (3H, s, CH₃), 1.18 (3H, t, C₆H₄CH₂CH₃, *J* 8.0 Hz), 2.09 (2H, d, 4-CH₂, *J* 16.5 Hz), 2.52-2.57 (2H, m, 2-CH₂), 2.65 (2H, q, C₆H₄CH₂CH₃, *J* 8.2 Hz), 6.14 (1H, d, H-11, *J* 5.2 Hz), 6.22 (1H, d, 10-NH, *J* 5.2 Hz), 6.41-7.08 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.30 (2H, d, H-3,5, H Ar, *J* 8.0), 7.86 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.89 (1H, s, 5-NH). MS (EI) *m/z*: 374 (M⁺), 185 (100%), 241 (73%), 157 (37%), 133 (67%). Anal. Calcd for C₂₄H₂₆N₂O₂: C, 76.98; H, 7.00; N, 7.48; Found: C, 76.95; H, 7.03; N, 7.50%.

3,3-Dimethyl-11-(*p*-fluorobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5h). Yield 72%; (0.26 g), light yellow crystals, mp 241-242 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.91 (3H, s, CH₃), 1.07 (3H, s, CH₃), 2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.54-2.58 (2H, m, 2-CH₂), 6.18 (1H, d, H-11, *J* 5.0 Hz), 6.26 (1H, d, 10-NH, *J* 5.0 Hz), 6.49-7.09 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.34 (2H, dd, H-3,5, H Ar, *J* 8.0 Hz, *J*_{H-F} 7.9 Hz), 8.02 (2H, dd, H-2,6, H Ar, *J* 8.0 Hz, *J*_{H-F} 5.5 Hz), 8.96 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 26.7 (CH₃), 28.5 (CH₃), 31.8 (C-3), 44.1 (C-4), 49.3 (C-2), 55.2 (C-11), 106.5 (C-11a), 119.4, 119.5, 120.3, 122.8, 129.8, 130.6, 131.2, 132.9, 136.9, 141.1, 165.6 (C Ar+C-4a), 192.4 (ArC=O), 195.6 (C=O). Anal. Calcd for C₂₂H₂₁FN₂O₂: C, 72.51; H, 5.81; N, 7.69; Found: C, 72.31; H, 5.77; N, 7.55%.

3,3-Dimethyl-11-(*p*-chlorobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5i). Yield 74%; (0.28 g), light yellow crystals, mp 243-244 °C (from MeOH) (lit.¹⁴ mp 242-243 °C). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.87 (3H, s, CH₃), 1.03 (3H, s, CH₃), 2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.54-2.59 (2H, m, 2-CH₂), 6.11 (1H, d, H-11, *J* 5.0 Hz), 6.23 (1H, d, 10-NH, *J* 5.0 Hz), 6.46-7.02 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.55 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.93 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.94 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 26.6 (CH₃), 28.7(CH₃), 31.8 (C-3), 44.1 (C-4), 49.3 (C-2), 55.3 (C-11), 106.4 (C-11a), 119.4, 119.5, 120.3, 122.9, 128.6, 130.2, 130.6, 135.4, 136.8, 141.3, 155.6 (C Ar+C-4a), 192.4 (ArC=O), 198.0 (C=O). Anal. Calcd for C₂₂H₂₁ClN₂O₂: C, 69.38; H, 5.56; N, 7.36; Found: C, 69.31; H, 5.75; N, 7.45%.

3,3-Dimethyl-11-(*p*-bromobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5j). Yield 77%; (0.33 g), yellow crystals, mp 247-248 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.98 (3H, s, CH₃), 1.03 (3H, s, CH₃), 2.09 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.58-

2.62 (2H, m, 2-CH₂), 6.10 (1H, d, H-11, *J* 5.0 Hz), 6.25 (1H, d, 10-NH, *J* 5.0 Hz), 6.46-7.03 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.70 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.85 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.93 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 26.7 (CH₃), 28.4 (CH₃), 31.8 (C-3), 44.1 (C-4), 49.2 (C-2), 55.3 (C-11), 106.2 (C-11a), 119.4, 119.5, 120.3, 122.8, 130.3, 130.6, 131.5, 135.3, 136.8, 143.3, 155.6 (C Ar+C-4a), 192.4 (ArC=O), 196.2 (C=O). Anal. Calcd for C₂₂H₂₁BrN₂O₂: C, 62.13; H, 4.98; N, 6.59; Found: C, 62.10; H, 4.89; N, 6.55%.

3,3-Dimethyl-11-(*p*-iodobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5k). Yield 58%; (0.41 g), light yellow crystals, mp 216-218 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.87 (3H, s, CH₃), 1.03 (3H, s, CH₃), 2.09 (2H, d, 4-CH₂, *J* 16.2 Hz), 2.51-2.56 (2H, m, 2-CH₂), 6.08 (1H, d, H-11, *J* 5.4 Hz), 6.25 (1H, d, 10-NH, *J* 5.4 Hz), 6.41-7.08 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.67 (2H, d, H-3,5, H Ar, *J* 8.5 Hz), 7.87 (2H, d, H-2,6, H Ar, *J* 8.5 Hz), 8.93 (1H, s, 5-NH). MS (EI) *m/z*: 472 (M⁺), 241 (100%), 185 (28%), 157 (5%). Anal. Calcd for C₂₂H₂₁IN₂O₂: C, 55.94; H, 4.48; N, 5.93; Found: C, 55.91; H, 4.51; N, 5.90%.

3,3-Dimethyl-11-(*p*-nitrobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5l): see ref. 13.

3,3-Dimethyl-11-(*p*-methylthiobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5m). Yield 77%; (0.30 g), yellow crystals; mp 233-234 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.93 (3H, s, CH₃), 1.07 (3H, s, CH₃), 2.12 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.40 (3H, s, SCH₃), 2.57-2.64 (2H, m, 2-CH₂), 6.14 (1H, d, H-11, *J* 5.0 Hz), 6.25 (1H, d, 10-NH, *J* 5.0 Hz), 6.51-7.07 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.35 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.72 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.95 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 13.9 (CH₃), 26.8 (CH₃), 28.4 (CH₃), 31.8 (C-3), 44.2 (C-4), 49.3 (C-2), 54.9 (C-11), 106.7 (C-11a), 119.3, 119.4, 120.2, 122.7, 124.7, 128.9, 130.6, 132.3, 136.9, 144.7, 155.5 (C Ar+C-4a), 192.3 (ArC=O), 195.8 (C=O). Anal. Calcd for C₂₃H₂₄N₂O₂S: C, 70.38; H, 6.16; N, 7.14; Found: C, 70.35; H, 6.19; N, 7.10%.

3,3-Dimethyl-11-(1,1'-biphenyl-4-carbonyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5n). Yield 76%; (0.32 g), bright yellow crystals, mp 211-212 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.89 (3H, s, CH₃), 1.04 (3H, s, CH₃), 2.10 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.57-2.62 (2H, m, 2-CH₂), 6.19 (1H, d, H-11, *J* 5.0 Hz), 6.29 (1H, d, 10-NH, *J* 5.0 Hz), 6.50-7.10 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.40-8.05 (9H, m, H Ar), 8.93 (1H, s, 5-NH). Anal. Calcd for C₂₈H₂₆N₂O₂: C, 79.59; H, 6.20; N, 6.63; Found: C, 79.35; H, 6.10; N, 6.80%.

3,3-Dimethyl-11-(*p*-cyclohexylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (5o). Yield 71%; (0.30 g), yellow crystals; mp 216-218 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.88 (3H, s, CH₃), 1.02 (3H, s, CH₃), 1.26-1.40 (4H, m, 2CH₂), 1.64-1.80 (7H, m, 3CH₂+CH), 2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.50-2.57 (2H, m, 2-CH₂), 6.15 (1H, d, H-11, *J* 5.0 Hz), 6.24 (1H, d, 10-NH, *J* 5.0 Hz), 6.45-7.03 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.47 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.86 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.89 (1H, s, 5-NH). MS (EI) *m/z*: 428 (M⁺), 241 (100%), 187 (7%), 159 (6%), 148 (19%), 117 (10%). Anal. Calcd for C₂₈H₃₂N₂O₂: C, 78.47; H, 7.53; N, 6.54; Found: C, 78.32; H, 7.40; N, 6.70%.

2,2-Dimethyl-11-benzoyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (5p). Yield 75%; (0.26 g), yellow crystals; mp 237-238 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.72-1.79 (2H, m, 3-CH₂), 2.64-2.70 (2H, m, 4-CH₂), 6.09 (1H, d, H-11, *J* 5.0 Hz), 6.18 (1H, d, 10-NH, *J* 5.0 Hz), 6.42-6.98 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.43-7.57 (3H, m, H-3,4,5, H Ar), 7.82 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.78 (1H, s, 5-NH). Anal. Calcd for C₂₂H₂₂N₂O₂: C, 76.28; H, 6.40; N, 8.09; Found: C, 76.30; H, 6.25; N, 8.01%.

2,2-Dimethyl-11-(*p*-bromobenzoyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (5r). Yield 71%; (0.30 g), yellow crystals; mp 230-231 °C (from MeOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.90 (3H, s, CH₃), 1.02 (3H, s, CH₃), 1.65-1.75 (2H, m, 3-CH₂), 2.65-2.70 (2H, m, 4-CH₂), 6.03 (1H, d, H-11, *J* 5.0 Hz), 6.17 (1H, d, 10-NH, *J* 5.0 Hz), 6.45-7.01 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.73 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.83 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.89 (1H, s, 5-NH). Anal. Calcd for C₂₂H₂₁BrN₂O₂: C, 62.13; H, 4.98; N, 6.59; Found: C, 62.05; H, 4.79; N, 6.40%.

General procedure for the synthesis 10-acetyl-dibenzo[*b,e*][1,4]diazepin-1-one 6a-g. A mixture of the appropriate diazepine **5** (1 mmol) and 1 ml acetic anhydride (10 mmol) was heated at reflux (for 30 min.), then the mixture was poured into icy water, the resulting product was filtered off, washed with cold ethanol and recrystallized.

3,3-Dimethyl-10-acetyl-11-benzoyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (6a). Yield 78%; (0.30 g), light yellow crystals; mp 229-230 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.06 (3H, s, CH₃), 1.76 (3H, s, COCH₃), 2.15 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.52-2.60 (2H, m, 2-CH₂), 6.27-7.19 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.47-7.60 (4H, m, H-3,4,5, H Ar+H-11), 7.70 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.09 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₄N₂O₃: C, 74.21; H, 6.23; N, 7.21; Found: C, 74.15; H, 6.37; N, 7.30%.

3,3-Dimethyl-10-acetyl-11-(*p*-fluorobenzoyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (6b). Yield 72%; (0.29 g), light yellow crystals; mp 226-227 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.06 (3H, s, CH₃), 1.77 (3H, s, COCH₃), 2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.47-2.54 (2H, m, 2-CH₂), 6.35-7.19 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.47 (1H, s, H-11), 7.35 (2H, dd, H-3,5, H Ar, *J* 8.0 Hz, *J*_{H-F} 7.9), 7.77 (2H, dd, H-2,6, H Ar, *J* 8.0 Hz, *J*_{H-F} 5.5 Hz), 9.10 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₃FN₂O₃: C, 70.92; H, 5.70; N, 6.89; Found: C, 70.95; H, 5.55; N, 6.70%.

3,3-Dimethyl-10-acetyl-11-(*p*-chlorobenzoyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (6c). Yield 71%; (0.30 g), light yellow crystals; mp 249-250 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.06 (3H, s, CH₃), 1.77 (3H, s, COCH₃), 2.14 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.46-2.52 (2H, m, 2-CH₂), 6.36-7.18 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.45 (1H, s, H-11), 7.52 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.73 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.10 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₃ClN₂O₃: C, 68.16; H, 5.48; N, 6.62; Found: C, 68.26; H, 5.55; N, 6.71%.

3,3-Dimethyl-10-acetyl-11-(*p*-bromobenzoyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[*b,e*][1,4]diazepin-1-one (6d). Yield 75%; (0.35 g), light yellow crystals; mp 225-226 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.06 (3H, s, CH₃), 1.76 (3H, s, COCH₃),

2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.45-2.50 (2H, m, 2-CH₂), 6.36-7.18 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.45 (1H, s, H-11), 7.54 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.70 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.04 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₃BrN₂O₃: C, 61.68; H, 4.96; N, 5.99; Found: C, 61.66; H, 4.77; N, 5.79%.

3,3-Dimethyl-10-acetyl-11-(*p*-nitrobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-one (6e). Yield 75%; (0.32 g), yellow crystals; mp 230 °C (decomp.), (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.03 (3H, s, CH₃), 1.07 (3H, s, CH₃), 1.78 (3H, s, COCH₃), 2.16 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.46-2.52 (2H, m, 2-CH₂), 6.38-7.19 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.55 (1H, s, H-11), 7.88 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 8.34 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.18 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₃N₃O₅: C, 66.50; H, 5.35; N, 9.69; Found: C, 66.35; H, 5.10; N, 9.80%.

3,3-Dimethyl-10-acetyl-11-(*p*-cyclohexylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (6f). Yield 70%; (0.33 g), light yellow crystals; mp 152-153 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.06 (3H, s, CH₃), 1.27-1.39 (6H, m, 3CH₂), 1.67-1.78 (8H, m, 2CH₂+CH+COCH₃), 2.14 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.47-2.54 (2H, m, 2-CH₂), 6.31-7.18 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.33 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.46 (1H, s, H-11), 7.64 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.01 (1H, s, 5-NH). MS (EI) *m/z*: 370 (M⁺), 283 (100%), 241 (8%), 131 (5%), 105 (11%), 77 (12%). Anal. Calcd for C₃₀H₃₄N₂O₃: C, 76.57; H, 7.28; N, 5.95; Found: C, 76.43; H, 7.40; N, 5.79%.

2,2-Dimethyl-10-acetyl-11-(*p*-bromobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-one (6g). Yield 77%; (0.36 g), light yellow crystals; mp 239-240 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.97 (3H, s, CH₃), 1.00 (3H, s, CH₃), 1.68-1.78 (5H, m, 3-CH₂+COCH₃), 2.65-2.72 (2H, m, 4-CH₂), 6.35-7.18 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.45 (1H, s, H-11), 7.63 (2H, d, H-3,5, H Ar, *J* 8.0 Hz), 7.73 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 9.04 (1H, s, 5-NH). Anal. Calcd for C₂₄H₂₃BrN₂O₃: C, 61.68; H, 4.96; N, 5.99; Found: C, 61.55; H, 4.84; N, 5.72%.

General procedure for the synthesis 10-methyl-dibenzo[*b,e*][1,4]diazepin-1-ones 7a,b. A mixture of the appropriate diazepine **5** (1 mmol), KOH (1 mmol) and MeI (2 mmol) in 3 ml DMF was stirred for 6 h at 60 °C, then water was added dropwise into the mixture, the precipitate was filtered off and recrystallized.

3,3-Dimethyl-10-methyl-11-benzoyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (7a). Yield 56%; (0.32 g), yellow crystals; mp 202-204 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.91 (3H, s, CH₃), 1.05 (3H, s, CH₃), 2.11 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.50-2.56 (2H, m, 2-CH₂), 2.85 (3H, s, NCH₃), 6.13 (1H, s, H-11), 6.42-7.09 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.47 (2H, t, H-3,5, H Ar, *J* 8.0 Hz), 7.58 (1H, t, H-4, H Ar, *J* 8.0 Hz), 7.80 (2H, d, H-2,6, H Ar, *J* 8.0 Hz), 8.90 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 27.2 (CH₃), 28.4 (CH₃), 32.0 (C-3), 43.0 (N-CH₃), 43.9 (C-4), 49.4 (C-2), 64.0 (C-11), 106.2 (C-11a), 120.5, 120.6, 121.8, 123.1, 128.4, 128.5, 132.7, 134.6, 138.0, 138.6, 155.5 (C Ar+C-4a), 193.0 (ArC=O), 196.6 (C=O). Anal. Calcd for C₂₃H₂₄N₂O₂: C, 76.64; H, 6.71; N, 7.77; Found: C, 76.66; H, 6.69; N, 7.75%.

3,3-Dimethyl-10-methyl-11-(*p*-ethylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-one (7b). Yield 59%; (0.20 g), yellow crystals; mp 156-158 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 0.91 (3H, s, CH₃), 1.05 (3H, s, CH₃), 1.18 (3H, t, CH₃, *J* 7.6 Hz), 2.13 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.50-2.57 (2H, m, 2-CH₂), 2.65 (2H, d, C₆H₄CH₂CH₃, *J* 7.6 Hz), 2.85 (3H, s, NCH₃), 6.13 (1H, s, H-11), 6.43-7.10 (4H, m, H-6,7,8,9, *o*-C₆H₄), 7.31 (2H, d, H-3,5, H Ar, *J* 7.9 Hz), 7.76 (2H, d, H-2,6, H Ar, *J* 7.9 Hz), 8.90 (1H, s, 5-NH). Anal. Calcd for C₂₅H₂₈N₂O₂: C, 77.29; H, 7.26; N, 7.21; Found: C, 77.31; H, 7.23; N, 7.24%.

General procedure for the synthesis of 10-nitrosodibenzo[*b,e*][1,4]diazepin-1-ones 8a-c. A mixture of compound **5** (1.0 mmol), NaNO₂ (1.5 mmol) previously dissolved in 2 ml of water and 5 ml of acetic acid, was stirred at room temperature for 1.0 h. The resulting product was filtered off, washed with cold ethanol and recrystallized.

3,3-Dimethyl-10-nitroso-11-benzoyl-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepin-1-one (8a). Yield 64%; (0.24 g), yellow crystals; mp 219-220 °C (from EtOH). IR (KBr) ν_{max} (cm⁻¹): 3364 (NH), 3309 (NH), 1692 (C=O), 1600 (C=C), 1494 (N-N=O). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.02 (3H, s, CH₃), 1.07 (3H, s, CH₃), 2.20 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.58 (2H, d, 2-CH₂, *J* 16.0 Hz), 6.58-7.51 (8H, m, H-6,7,8,9, *o*-C₆H₄+H-2,3,5,6, H Ar), 7.62 (1H, t, H-4, H Ar, *J* 7.0 Hz), 8.11 (1H, s, OH), 9.48 (1H, s, 5-NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ_C 26.8 (CH₃), 29.1 (CH₃), 32.7 (C-3), 44.1 (C-4), 49.5 (C-2), 53.7 (C-11), 103.5 (C-11a), 121.2, 123.4, 126.1, 127.8, 129.6, 130.4, 134.3, 134.5, 134.7, 144.2, 156.2 (C Ar+C-4a), 192.2 (ArC=O), 193.8 (C=O). MS (EI) *m/z*: 345 ([M-NO]⁺), 105 (100%), 241 (33%), 77 (36%). MS (CI) *m/z*: 376 [M+H]⁺, 345 [M-NO]. Anal. Calcd for C₂₂H₂₁N₃O₃: C, 70.38; H, 5.64; N, 11.19; Found: C, 70.35; H, 5.67; N, 11.17%.

3,3-Dimethyl-10-nitroso-11-(*p*-ethylbenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-one (8b). Yield 87%; (0.35 g), yellow crystals; mp 193-195 °C (from EtOH). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.01 (3H, s, CH₃), 1.07 (3H, s, CH₃), 1.15 (3H, t, C₆H₄CH₃, *J* 7.6 Hz), 2.19 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.54-2.72 (4H, m, 2-CH₂+C₆H₄CH₂CH₃), 6.62-7.41 (8H, m, H-6,7,8,9, *o*-C₆H₄, H-3,4,5,6, H Ar), 8.09 (1H, s, H-12), 9.50 (1H, s, 5-NH). MS (EI) *m/z*: 373 ([M-NO]⁺), 241 (100%), 372 (11%), 288 (17%), 185 (18%), 155 (9%), 105 (25%). MS (CI) *m/z*: 404 [M+H]⁺, 373 [M-NO]. Anal. Calcd for C₂₄H₂₅N₃O₃: C, 71.44; H, 6.25; N, 10.41; Found: C, 71.41; H, 6.28; N, 10.38.

3,3-Dimethyl-10-nitroso-11-(*p*-bromobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*]-[1,4]diazepin-1-one (8c). Yield 74%; (0.34 g), pale yellow crystals; mp 216-218 °C (from EtOH). IR (KBr) ν_{max} (cm⁻¹): 3368 (NH), 3299 (NH), 1694 (C=O), 1600 (C=C), 1502 (N-N=O). ¹H NMR (200 MHz, DMSO-*d*₆): δ_H 1.01 (3H, s, CH₃), 1.06 (3H, s, CH₃), 2.20 (2H, d, 4-CH₂, *J* 16.0 Hz), 2.56-2.60 (2H, m, 2-CH₂), 6.68-7.74 (8H, m, H-6,7,8,9, *o*-C₆H₄, H-3,4,5,6, H Ar), 8.08 (1H, s, H-12), 9.50 (1H, s, 5-NH). MS (EI) *m/z*: 425 (7%), 241 (39%), 185 (100%), 157 (30%). Anal. Calcd for C₂₂H₂₀BrN₃O₃: C, 58.16; H, 4.44; N, 9.25; Found: C, 58.18; H, 4.46; N, 9.22%.

3,3-Dimethyl-10-nitroso-11-(*p*-nitrobenzoyl)-2,3,4,5,10,11-hexahydro-1*H*-dibenzo[*b,e*][1,4]-diazepin-1-one (8d). Yield 58%; (0.24 g), yellow crystals; mp 238-240 °C (from EtOH). IR

(KBr) ν_{\max} (cm^{-1}): 3311 (NH), 3238 (NH), 1703 (C=O), 1623 (C=C), 1535 (NO_2), 1500 (N=N=O), 1380 (NO_2). ^1H NMR (200 MHz, $\text{DMSO}-d_6$): δ_{H} 1.02 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.22 (2H, d, 4- CH_2 , J 16.0 Hz), 2.53-2.71 (2H, m, 2- CH_2), 6.66-7.38 (4H, m, H-6,7,8,9, o - C_6H_4), 7.55 (2H, d, H-3,5, H Ar, J 8.0 Hz), 8.16 (1H, s, H-12), 8.27 (2H, d, H-2,6, H Ar, J 8.0 Hz), 9.56 (1H, s, 5-NH). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} 26.7 (CH_3), 28.7 (CH_3), 32.3 (C-3), 43.7 (C-4), 49.1 (C-2), 55.8 (C-11), 102.7 (C-11a), 120.9, 123.3, 124.4, 125.9, 127.4, 128.9, 130.2, 133.9, 139.0, 144.3, 156.0 (C Ar+C-4a), 191.5 (ArC=O), 193.4 (C=O). MS (EI) m/z : 390 ($[\text{M}-\text{NO}]^+$), 241 (100%), 389 (39%), 150 (96%), 120 (50%). Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_4\text{O}_5$: C, 62.85; H, 4.80; N, 13.33; Found: C, 62.86; H, 4.77; N, 13.30%.

2-(*p*-Bromophenyl)quinoxaline. A mixture of compound **5j** (1.0 mmol), in 5 ml of acetic acid and 4-5 drops conc. HCl was heated at reflux (for 30 min.), then the mixture was poured into ice water, the resulting product was filtered off, washed with cold ethanol and recrystallized. Yield 70%; (0.20 g), beige crystals; mp 147-148 °C (from EtOH). (lit.²¹ mp 148-149 °C).

X-ray diffraction study: Crystals of **6c** ($\text{C}_{24}\text{H}_{23}\text{ClN}_2\text{O}_3$, $M_r = 422.89$) are orthorhombic, $Pna2_1$, $a = 36.672(2)$, $b = 7.6272(3)$, $c = 7.7162(3)$ Å, $V = 2158.3(2)$ Å³, $Z = 4$, $d_{\text{calc}} = 1.301$ g/sm³, $\mu(\text{MoK}_\alpha) = 0.205$ mm⁻¹, $F(000) = 888$. 13913 reflections (5977 independent, $R_{\text{int}} = 0.018$) were collected on an Xcalibur-3 diffractometer at room temperature (MoK_α radiation, CCD-detector, graphite monochromator, ω -scanning, $2\theta_{\text{max}} = 55^\circ$). The structure was solved by direct methods and refined against F^2 within anisotropic approximation for all non-hydrogen atoms by full-matrix least squares procedure as a racemic twin, the contributions of twin components were found to be equal ($\text{BASF} = 0.50(7)$). All H atoms were placed in idealized positions and constrained to ride on their parent atoms, with $U_{\text{iso}} = 1.2U_{\text{eq}}$ (except $U_{\text{iso}} = 1.5U_{\text{eq}}$ for methyl groups), except the donor H atom at N(1) that was refined isotropically. Final refinement was converged at $wR_2 = 0.114$ for all 5966 reflections, $R_1 = 0.047$ for 5132 reflections with $F > 4\sigma(F)$, $S = 1.03$. OLEX2 program package²¹ with SHELXS and SHELXL modules²² were used for structural data handling. Atom coordinates and crystallographic parameters have been deposited to the Cambridge Crystallographic Data Centre (CCDC **1025136**). These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

References

1. Hudepohl, N. S.; Nasrallah, H. A. *Handbook Clinic. Neurol.* **2012**, *106*, 657.
<http://dx.doi:10.1016/B978-0-444-52002-9.00039-5>
2. Macdonald, G. J.; Bartolomé, J. M. *Progress Med. Chemistry* **2010**, *49*, 37.
[http://dx.doi:10.1016/S0079-6468\(10\)49002-5](http://dx.doi:10.1016/S0079-6468(10)49002-5)
3. Shvayka, O. *Bases of synthesis of medicinal compounds and their intermediates*; 2th Eds., Nord-Computer: Donetsk, 2004, pp 448- 452.
4. Phillips, S. T.; Paulis, T.; Baron, B. M.; Siegel, B. W.; Seeman, P.; Van Tol H. M.; Guan, H.-C.; Smith, H. E. *J. Med. Chem.* 1994, *37*, 2686.
<http://dx.doi:10.1021/jm00043a008>

5. Capuano, B. *Molecules* **1999**, *4*, 329.
<http://dx.doi:10.3390/41100329>
6. Wang, X.-J.; Tian, Y.-L.; Zhang, Q.-Y.; Qi, J.-G.; Yin, D.-L. *Chin. Chem. Lett.* **2013**, *24*, 743.
<http://dx.doi:10.1016/j.cclet.2013.04.028>
7. Zhang, Q.-Y.; Wang, X.-J.; Tian, Y.-L.; Qi, J.-G.; Li, Ch.; Yin, D.-L. *Chin. Chem. Lett.* **2013**, *24*, 825.
<http://dx.doi:10.1016/j.cclet.2013.04.049>
8. Soriano-Garcia, M.; Cortes, E.; Toscano, R. A.; Arellano, M. R.; Martinez, R. *Acta Crystallogr.* **1987**, 1161.
<http://dx.doi:10.1107/S0108270187092679>
9. Blache, Y.; Hichour, M.; Di Blasi, G.; Chezal, J.-M.; Viols, H.; Chavignon, O.; Teulade, J.-C.; Chapat, J.-P. *Heterocycles* **1999**, *51*, 1003.
<http://dx.doi:10.3987/COM-98-8466>
10. Parmar N. J.; Barad, H. A.; Pansuriya, B. R.; Teraiya, S. B.; Gupta, V. K.; Kan, R. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 3816.
<http://dx.doi:10.1016/j.bmcl.2012.03.100>
11. Cortes, C. E.; Sanabria, A. M.; Mellado de Cortes, O. G. *J. Heterocycl. Chem.* **2002**, *39*, 55.
<http://dx.doi:10.1002/jhet.5570390107>
12. El Ashry, El-S. H.; Awad, L. F.; El Kilany, Y.; Ibrahim I. El-S., *Adv. Heterocyclic Chem.* **2009**, *98*, 1-141.
[http://dx.doi:10.1016/S0065-2725\(09\)09801-8](http://dx.doi:10.1016/S0065-2725(09)09801-8)
13. Kolos, N. N.; Yurchenko, E. N.; Orlov, V. D.; Shishkina, S. V.; Shishkin, O. V. *Chem. Heterocycl. Compd.* **2004**, *40*, 1798.
<http://dx.doi:10.1007/s10593-005-0098-3>
14. Jiang, B.; Li, Q.-Y.; Zhang, H.; Tu, S.-J.; Pindi, S.; Li, G. *Org. Lett.* **2012**, *14*, 700.
<http://dx.doi:10.1021/ol203166c>
15. Greenhill, J. V. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2207.
<http://dx.doi:10.1039/P19760002207>
16. Nardi, M.; Cozza, A.; Denimo, A.; Olivero, M.; Procopio A. *Synthesis* **2012**, *44*, 800.
<http://dx.doi:10.1055/s-0031-1289691>
17. Cortes, E. C.; Baños, M. A.; Mellado de Cortes, O. G. *J. Heterocycl. Chem.* **2004**, *41*, 277.
<http://dx.doi:10.1002/jhet.5570410221>
18. Zefirov, N. S.; Palyulin, V. A.; Dashevskaya, E. E. *J. Phys. Org. Chem.* **1990**, *3*, 147.
<http://dx.doi:10.1002/poc.610030304>
19. Burgi, H.-B.; Dunitz, J. D. *Structure correlation*, VCH, Weinheim, **1994**, *2*, 741.
20. Zefirov, Yu. V. *Crystallography* **1997**, *42*, 936.
21. Figueras J. *J. Org. Chem.* **1966**, *31*, 803.
22. Dolomanov, O.; Bourhis, L.; Gildea, R. *J. Appl. Cryst.* **2009**, *42*, 339.
<http://dx.doi:10.1107/S0021889808042726>
23. Sheldrick, G. M. *Acta Crystallogr.* **2008**, *64*, 112.

<http://dx.doi:10.1107/S0108767307043930>