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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis of 5-benzyl-4-aryl-octahydro-1*H*-benzo[*b*][1,5]diazepin-2-ones as potent antidepressant and antimicrobial agents

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Abstract The present study describes the chemical synthesis and pharmacological evaluation of a new series of 11 compounds of aryloctahydrobenzo[*b*][1,5]-diazepin-2-one in the forced-swimming test in mice. Three compounds (**3e**, **3f** and **3h**) exhibited impressive antidepressant activity, measured in terms of percentage decrease in immobility duration. The potent compounds did not show any neurotoxicity in the rotarod test, and the preliminary results are promising enough to warrant further studies around this scaffold. All the compounds were also screened for antimicrobial activity against *P. aeruginosa*, *E. coli*, *S. Aureus* and *B. subtilis* strains. Some of the compounds possessed marked antimicrobial activities comparable to that of reference drug, Ciprofloxacin.

Keywords Benzodiazepines · Forced swim test · Disc diffusion method · Antidepressant · Antibacterial activity

Introduction

Depression is one of the most prevalent psychopathologies and its therapy relies on classical antidepressant drugs such as monoamine oxidase inhibitors and drugs that inhibit the reuptake of catecholamines (Richelson, 1994). A common problem with the current antidepressant therapies is the several side effects (e.g. anti-cholinergic, gastrointestinal distress, anxiety, insomnia and sexual dysfunction) produced by these drugs besides their slow onset of action (Mendels, 1992). Clinical limitations and adverse effects of currently used antidepressants necessitate continuous development of novel, efficient and safe drugs for the treatment of depression.

Benzodiazepines were first introduced for the treatment of anxiety, then later on, they have been used as sedatives, anticonvulsants, antibacterial, antifungal and muscle relaxants (Shader and Greenblatt, 1993; Schutz and Benzodiazepines, 1982; Landquist, 1984; Failli *et al.*, 2006; Hadac *et al.*, 2006). Many benzodiazepine and their derivatives underwent extensive investigations aimed to assess their potential beneficial effects on human health. The recognition of key structural features within benzodiazepine family is crucial for the design and development of new analogues with improved activity and for the characterization of their mechanism of action and potential side effects. The different substituents in the benzodiazepine nucleus strongly influence the biological activity of the resulting derivatives. Therefore, considerable attention has been drawn to devise improved methods for the preparation of 1,5-benzodiazepinones.

A scrutiny of literature on pharmacological properties of 1,4-benzodiazepines emphasised that there was scanty information on the medicinal properties of the isomeric 1,5-benzodiazepine derivatives (Srinivas *et al.*, 2007; Saini *et al.*, 2008; Hekmatshoar *et al.*, 2009; Escobar *et al.*, 2009). Further, there is virtually no record of synthesis of any derivative of either 1,4- or 1,5-benzodiazepine bearing phenyl ring is saturated (Yadav *et al.*, 2004; Guzen *et al.*, 2006; Vaghei and Veisi, 2010; Polshettiwar and Varma, 2008; Madhav and Rajitha, 2008; Insuasty *et al.*, 2008).

These observations prompted us to undertake the synthesis of a series of 5-benzyl-4-aryloctahydrobenzo[*b*][1,5]diazepin-

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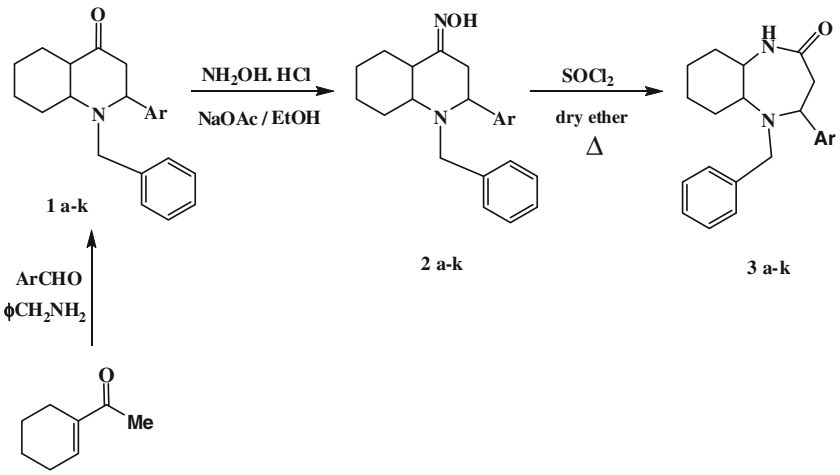
2-ones with a view to evaluate them for antidepressant and antimicrobial activities.

Results and discussion

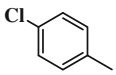
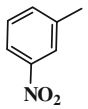
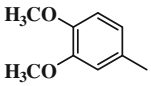
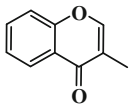
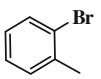
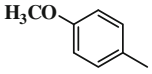
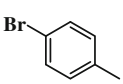
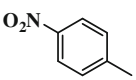
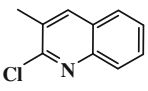
The general synthetic route to the core octahydro-1*H*–benzo[*b*][1,5] diazepin-2-one scaffold can be seen in Scheme 1. Reaction of the 1-benzyl-2-aryldecahydroquinolin-4-one **1a–k** with hydroxylamine hydrochloride provided the intermediate oximes **2a–k**, which served as an useful precursors for construction of the desired products. Selective Beckmann rearrangement of the oximes induced by thionyl chloride afforded the 5-benzyl-4-aryl-octahydro-1*H*-benzo[*b*][1,5]diazepin-2-ones **3a–k**. All the intermediates and final products were characterized by their analytical and spectroscopic data.

The newly synthesized compounds (**3a–k**) were screened for antidepressant activity *by* forced swim test (FST) (Porsolt *et al.*, 1977; Porsolt *et al.*, 1978) and antibacterial activity against four *bacterial* strains (*Pseudomonas aeruginosa* ATCC 9027, *Escherichia coli* ATCC 35218, *Staphylococcus aureus* ATCC 6538 and *Bacillus subtilis* ATCC 6631) by disc diffusion method (Smyth *et al.*, 1991; Reid Pelczar and Cohn, 1989) using MH medium (Mueller–Hinton medium). Clomipramine (the antidepressant drug) and Ciprofloxacin (the antibacterial drug) were used as reference standards.

All compounds **1a–k** (Babu *et al.*, 2012) were homogeneous on TLC and contained nitrogen. The presence of CO function was evident from an IR band at 1,722 cm^{-1}. In the ^{1}H NMR spectrum of **1a**, the one-proton doublet of doublet (J = 12.0 and 2.4) centered at δ 3.37 was ascribed to *N*-benzylic methine proton (H-2, N*CH*ϕ) based on its multiplicity pattern that arises due to its coupling interaction with the adjacent axial (H_a) and equatorial (H_e) protons of C-3, while the two-proton singlet at δ 3.71 was assigned to *N*-benzylic methylene protons. The upfield complex multiplet (12H) in the region δ 1.16–2.85 was associated with methylene and methine protons of the heterocyclic ring, and the aromatic protons (10H) resonated as complex multiplet in the region δ 7.25–7.74. The ^{13}C NMR spectrum of **1a** registered only seven signals for



Scheme 1 Beckmann rearrangement of oxime to 1,5-benzodiazepinone **3a–k**

3	Ar	3	Ar	3	Ar
a		e		i	
b		f		j	
c		g			
d		h		k	

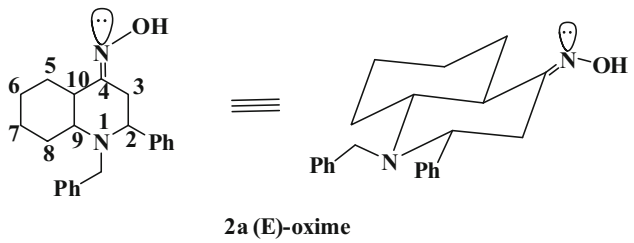
aliphatic carbons which were grouped into five methylene and two methine carbons based on DEPT-135 experiment. The far downfield signal at δ 198.28 substantiated the IR band at 1,722 cm^{-1} was assigned to oxo function of the six-membered ring. Thus, based on the spectroscopic data, compound **1a** was formulated as 1-benzyl-2-phenyldecahydroquinolin-4-one; its identity was further confirmed by HMBC experiment. The MS of **1a** with its molecular ion and base peaks at *m/z* 319 (10), 242 ($M^{+}_{-} - C_6H^{\bullet}_5$), along with diagnostic fragment ions 291 ($M^{+}_{-} - CO$), 292 [($M^{+}_{-} + H^{\bullet}$)–CO], further supported the structure assigned to **1a** based on NMR spectral data.

The presence of oxime in compounds **2a–k** was evident by an IR band at 3,419 cm^{-1}, (oxime hydroxyl) and 1,591 cm^{-1} (C=N stretching band) and by the absence of characteristic IR band (at 1,722 cm^{-1}) for the oxo function of its precursor **1a.** The ^{1}H NMR spectrum displayed, in addition to signals due to protons of *N*-benzylic methine (δ 3.12 dd) and *N*-benzylic methylene (δ 3.56, s), a downfield one-proton signal at δ 11.04 that exchanged with D_2O and disappeared on acetylation (Ac_2O/Py, room temperature) was assigned to oxime hydroxy. The ^{13}C NMR spectrum of **2a** displayed signals for nine aliphatic carbon atoms which were grouped into six methylene and three methine carbons based on DEPT experiment. The only one downfield carbon signal at δ 158.71 was assigned to *ipso* carbon (C=NOH) (Breitmaier and Voelter, 1987).

A comparison of the spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR) of **2a** with that of its precursor **1a** established the structure of the oxime beyond doubt. However, the oxime **2a** can exist in two isomeric forms *Z* and *E* differing in the spatial orientation of the oxime hydroxyl. A choice between the two isomeric forms, *Z* and *E*, was made based on the assumption that *Z*-isomer was subjected to $A^{1,3}$-type of interaction, and therefore was less stable than *E*-isomer in which no such interaction exists.

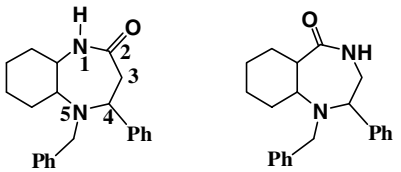
Further support for the assignment of *E*-configuration for the oxime **2a** is based on the generalization that oximation of a ketone results in an upfield shift in α-carbon atoms of the oxime; the magnitude of the shift is much larger in *syn* α-carbon atom than in *anti* α-carbon atom (Breitmaier and Voelter, 1987). A comparison of ^{13}C NMR spectral data of the oxime **2a** with that of its precursor **1a** (ketone) disclosed that the C-3 (C-α) of the former resonated at higher field (δ 34.58) than that of the latter (δ 49.35); a large upfield shift of 14.77 ppm in C-3 of **2a** proves that the oxime OH was *syn* to C-3 and hence, the configuration of the oxime **2a** was *E*. Based on the spectroscopic data and on the above generalisation, the oxime **2a** was formulated as *E*-1-benzyl-2-phenyloctahydroquinolin-4-one oxime (Fig. 1).

Compound **3a**, the product of Beckmann rearrangement contained nitrogen and its MS recorded molecular ion peak at *m/z* 334 (26) revealing the presence of two nitrogens atoms



2a (E)-oxime

Fig. 1 Chair form representation of *t*-decahydroqinoline oxime



3a (A) **3a (B)**

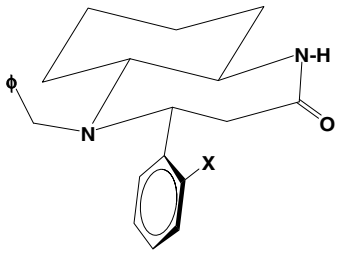


Fig. 2 Chair form representation of 1,5-benzodiazepinones

in it. The presence of lactam ring in **3a** was evident from IR bands at 3,316 cm^{-1} (NH stretch), 1,678 cm^{-1}(C=O of amide) and by the appearance of fragment ion at *m/z* 291 ($M^{+}_{-} -^{\bullet}$ NCO). This conclusion was also supported by its ^{1}H NMR spectrum which displayed in addition to signals due to protons of –NCHPh (δ 4.02, dd) and –NCH_2Ph (δ 3.62, s), a downfield sharp one-proton signal at δ 8.62 assignable to the proton of –NH–CO group. The downfield shift in signal due to *N*-benzylic methine proton (–NCHPh) (δ 4.02 dd) relative to that of its precursor **2a** (δ 3.12 dd) is noteworthy. The ^{13}C NMR spectrum of **3a** resembled that of its precursor **2a** (oxime) in all respects except for the presence of a downfield signal at δ 176.82 which was assigned to amide carbon. Thus, a comparison of spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR) of **3a** with that of its precursor **2a** (oxime) proved beyond doubt the formation of lactam ring in **3a** (Fig. 2).

It was well established that during Beckmann rearrangement, the group *anti* to oxime hydroxy is the one that migrates, although there are some exceptions. Since the structure of the oxime **2a** (the precursor of **3a**) has been established as *E*-oxime, the 4–10 bond of **2a** which is *anti* to oxime hydroxy is expected to migrate during Beckmann rearrangement to afford **3a (A)**.

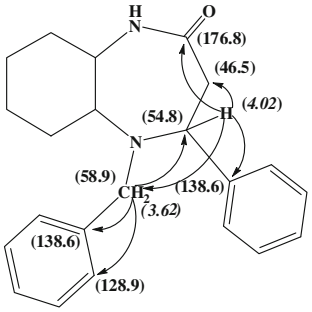


Fig. 3 Selected HMBC correlations for **3a**

A choice in favour of **3a (A)** has been arrived based on HMBC experiment. A scrutiny of HMBC spectrum of the product of Beckmann rearrangement **3a** (Fig. 3), revealed that the proton signal at 4.02 (H-3, dd) correlated with carbon signal at δ 176.8 (amide CO). An examination of reference structures for isomeric lactams **3a (A)** and **3a (B)** disclosed that such inverse three bond correlation between *N*-benzylic methine proton (–NCHϕ) (δ 4.02 dd) and carbonyl carbon of amide group (–CONH) (δ 176.8) was possible only in structure **3a (A)** but not in **3a (B).** Therefore, the product of Beckmann rearrangement **3a** was characterised as 5-benzyl-4-phenyloctahydro-1H-benzo[*b*][1,5]diazepin-2-(3*H*)-one.

In vitro antidepressant activity

The main objective of this study is to modulate the effect on CNS by varying the nature of the nuclear substituents of the aryl group at C-4. Table 1 shows the results of the primary screening of the synthesised compounds **3a–k** by FST. The majority of the synthesised compounds exhibited considerable antidepressant potential as evident from the reduction of duration of immobility values and high-percentage decrease in immobility duration (% DID) values.

Among 11 compounds tested, 8 compounds (**3d, 3e**, **3f, 3g, 3h, 3i, 3j** and **3k**) showed potent antidepressant activity; the dimethoxy compound (entry **3f**) was substantially more active than the unsubstituted compound **3a**, further the introduction of the *electron-withdrawing* groups Cl and NO_2 in 4 and 3, 4 positions **(3e, 3h, 3i)** and methoxyls in either 4 position (**3g**) or in 3 and 4 positions (**3f**) of C-4 and C-4 aryl group increased the activity significantly and substitution with a bulky chromone and quinoline groups (entry **3j** and **3k**) for aryl group at C-4 did result in a significant increase in activity.

In contrast, the introduction of electron-withdrawing groups in the *ortho* position (**3b, 3c**) gave compounds with lower potency than the unsubstituted compound **3a**. In particular, compound **3c (2–Br)** was ineffective while **3d (4–Br)** induced a marked reduction of the duration of immobility.

Table 1 Antidepressant activity of the compounds **3a–k**

Compounds **3a–k**	Duration of immobility in secs. (mean ± SEM)	% change from control[a]	Neurotoxicity coordination time in secs. (mean ± SEM)
a (Ph)	40.1 ± 3.06	−81.56	100.33 ± 1.80
b (2-Cl)	52.2 ± 1.93	−78.23	95.17 ± 2.52
c (2-Br)	69.3 ± 5.52	−71.10	91.33 ± 3.27
d (4-Br)	34.0 ± 3.53	−85.82	93.67 ± 2.98
e (4-Cl)	28.7 ± 2.51	−88.03	90.83 ± 2.34
f (3,4-OMe)	26.3 ± 3.71	−89.03	96.50 ± 2.67
g (4-OMe)	32.6 ± 4.67	−86.40	97.83 ± 2.26
h (4-NO_2)	25.3 ± 2.88	−89.44	93.50 ± 3.97
i (3-NO_2)	34.0 ± 3.42	−85.82	92.34 ± 3.09
j (3-chromonyl)	39.4 ± 2.39	−83.56	97.17 ± 2.36
k (2-chloro-quinolin-3-yl)	35.3 ± 3.53	−85.27	98.33 ± 2.93
Clomipramine	18.68 ± 2.25	−92.21	110.83 ± 1.49
Control	112.4 ± 2.88	–	

[a] Compounds were tested at 20 mg kg^{-1} dose level, ip

Although, methoxyl in 4-position can exert both electron-withdrawing inductive (−I) and electron-donating mesomeric effect (+M), in the absence of direct conjugation of 4-aryl group with heterocyclic ring, its −I effect dominates over +M effect, that is, it can be regarded as an electron-withdrawing group.

Evidently, the introduction of electron-withdrawing groups in 4- and 3-positions resulted in a significant increase in potency, although such groups are also sterically bulky. The decreased activity on introduction of electron-withdrawing groups into *ortho* position of C-4 aryl group may be attributed to steric hindrance felt by the *ortho*-substituent either by the adjacent methylene (C-3) or by the *N*-benzylic methylene group. Such steric hindrance which may operate in whatever conformation the aryl and N–CH_2Ph groups adopt, may force the C-4 aryl group out of its receptor-binding site. However, such steric hindrance is not felt by *meta* and *para* substituents of C-4 aryl group.

In vitro antibacterial activity

The data generated from antibacterial study (Table 2) revealed that the majority of the synthesized compounds **(3a–k)** showed variable inhibition activities against the tested strains and all of them showed moderate to good antibacterial activity as compared to that of the standard. Of all the compounds in series, **3b, 3c, 3d, 3f, 3g, 3h** and **3i** showed significant inhibition against Gram-negative

Table 2 In vitro antibacterial activity of the compounds, **3a–k**

Compounds	Zone of inhibition in mm at 10 μg/mL			
	Gram-negative bacteria		Gram-positive bacteria	
	P. aeruginosa ATCC 9027	*E. coli* ATCC 35218	*S. aureus* ATCC 6538	*B. subtilis* ATCC 6631
a (Ph)	6	5	9	6
b (2-Cl)	9	4	8	4
c (2-Br)	5	6	15	6
d (4-Br)	8	5	10	5
e (4-Cl)	4	3	10	3
f (3,4-OMe)	5	8	7	7
g (4-OMe)	7	5	12	3
h (4-NO_2)	9	4	15	6
i (3-NO_2)	7	4	10	3
j (3-chromonyl)	5	5	8	4
k (2-chloro- quinolin-3-yl)	6	6	13	6
Ciproflaxacin	12	9	18	9

Gram-positive bacterial strain—*S. aureus* (ATCC 6538). Gram-negative bacterial strain—*P. aeruginosa* (ATCC 9027)

strains, whereas **3a, 3c, 3h and 3k** registered significant activity against Gram-positive strains. Compounds **3c** and **3k** showed significant inhibitory activity against all bacterial strains in comparison to that of the standard.

Conclusions

In conclusion, readily available starting materials have been successfully utilised to develop synthetic pathways in devising compounds incorporating the 1,5-benzodiazepine nucleus with a substituted C-4 aryl moiety, and most of these compounds significantly reduced the duration of immobility at a very low dose of 20 mg/kg in FST, the potency of which was comparable to that of the standard drug such as clomipramine (20 mg/kg), ip underlying their antidepressant potential. Further, the most potent compounds **3e** and **3f** did not show any neurotoxicity in the rotarod test and the preliminary results are promising enough to warrant further detailed mechanistic and antidepressant studies on this scaffold. From the antimicrobial activity studies, it was concluded that among all 1,5-benzodiazepine derivatives, antibacterial activity increases with electron-withdrawing groups at *o*-substitution, whereas compounds **3c** and **3k** showed overall maximum activity against both the strains.

Experimental section

General

Melting points were determined in open capillary tubes and were uncorrected. The purity of the compounds was checked on silica gel-G plates (TLC) and visualised using iodine/UV lamp. IR spectra were recorded on a Schimadzu FT-IR spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded on a Bruker Avance 300 MHz NMR spectrometer in $CDCl_3$ using TMS as an internal standard. Elemental analyses were carried out with Elementer-Vario EL III elemental analyzer. Microanalyses (C and H) of new compounds agreed with the theoretical values within ±0.4 %.

Antidepressant assay

Behavioural despair or FST was proposed as a model to test antidepressant activity by Porsolt *et al.* It was suggested that mice or rats when forced to swim in restricted space from where they cannot escape are induced to a characteristic behaviour of immobility. This behaviour reflects a state of despair which can be reduced by several agents which are therapeutically effective in human depression. This behavioural despair test was employed to assess the antidepressant activity of newly synthesized compounds **3a–k**. Albino rats of 150–180 g in a group of six each were used and on the first day of the experiment (pretest session), rats were individually placed in a cylindrical recipient (Plexiglass cylinder) of dimensions (diameter 20 cm, height 40 cm) containing 30 cm of water at 25 ± 1 °C. The animals were left to swim for 15 min before being removed, dried and returned to their cages. The procedure was repeated 24 h later, in 5 min swim session (test session). The test compounds (20 mg/kg), and clomipramine (20 mg/kg) separately were administered as suspension in aqueous DMSO. During 5 min test session, the duration of immobility was recorded. Immobility time is the time spent by the rat floating in water without struggling, making only those moment necessary to keep the head above the water. The results of FST have been summarized in Table 1. % DID for test and standard drugs was calculated using following formula:

$$\% \text{ DID } = [A - B]/A * 100,$$

where A is the duration of immobility (s) in control group and B is the duration of immobility (s) in test group.

Antibacterial activity

The antibacterial activity was assessed by disc diffusion method. Compounds **3a–k** were evaluated in vitro *activity*

against Gram-positive strains: *S. aureus* and *B. subtilis;* Gram-negative strains: *P. aeruginosa and E. coli* at a concentration of 10 μg/mL in meat peptone agar medium. Ciprofloxacin (10 μg/mL) was used as a standard for antibacterial screening. For each biological activity test, two to three experiments were performed and the average zone of inhibition is reported in Table 2.

Neurotoxicity

Minimal motor impairment was measured in rats by the rotarod method. The rats were trained to stay on an accelerating rotarod rotating at 30 rpm over 120 s. The trained animals were injected intraperitoneally with the test compounds **3a**–**k** at doses of 100 mg/kg, 30 min prior to the test session. Neurotoxicity was indicated by the inability of the animal to maintain equilibrium on the rotating rod, and results are reported as duration for which the animal is able to balance on the moving rod (i.e. till the animal falls) is noted as coordination time (mean ± SEM).

Synthesis of (*t*) 1-benzyl-2-phenyloctahydroquinolin-4(1*H*)-one (**1a**–**k**) (Babu *et al.*, 2012)

To an ethanolic solution of 1-acetylcyclohexene (0.01 mol), benzylamine (0.01 mol), benzaldehyde (0.01 mol) and catalytic amount of piperidine were added and the reaction mixture was refluxed for 5 h. After the completion of the reaction (as monitored by TLC), the contents were concentrated, cooled and poured into crushed ice. The resulting mass was extracted with chloroform, washed with water, dried and concentrated *in vacuo*; crystallisation from aq. ethanol gave pure compound **1a**.

m.p. 165–167 °C; ^{1}H NMR (ppm, $CDCl_3$): δ 1.0–2.7 (m, 12H, 4 CH_2 and 2 CH, –COC$\underline{H}_2$), 3.5 (dd, 1H, $J = 8$ Hz, 1.5 Hz, –N–C$\underline{H}\phi$), 3.7 (s, 2H, –N–CH_2–Ph), 7.2–7.4 (m, 10H, Ar–H); ^{13}C NMR (ppm, $CDCl_3$): 25.6, 29.3 (–CO$\underline{C}H_2$), 49.5, 55.6 (–NCH-9), 61.5 (–N–$\underline{C}H\phi$), 65.7 (–N–$\underline{C}H_2\phi$), 125.6, 128.8, 139.5, 146.9, 198.2 ($\underline{C}$=O). DEPT-135 (ppm): δ 25.69 (↓), 28.62 (↓), 49.36 (↓), 55.50 (↑) (–NCH-9), 59.56 (↑) (N–CHϕ), 68.40 (↓) (–N–$CH_2\phi$), 125.67 (↑), 126.28 (↑), 129.56 (↑), 134.00 (↑), 139.14 (↑).

Typical procedure for the synthesis of 1-benzyl-2-aryldecahydroquinolin-4(1*H*)-one oximes (**2a**–**k**)

To an ethanolic solution of compounds **1a**–**k** (0.01 mol), an aqueous solution of hydroxylamine hydrochloride (0.05 mol) and crystalline sodium acetate (0.05 mol) was added and the reaction mixture was refluxed on a water-bath for 3 h and left overnight; the solid that separated was filtered, washed with water, dried and crystallised from aq. ethanol.

*1-Benzyl-2-phenyldecahydroquinolin-4(1H)-one oxime (**2a**)*

m.p. 124–126 °C; (aq. ethanol) yield: 68 %. IR (KBr, cm^{-1}): 3419 (OH str.), 1591 (–CN str.), 1519 (*NO* asym. str.), 1139 (–CN str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.20–2.46 (m, 12H, 5×$C\underline{H}_2$ and 2×$C\underline{H}$), 3.12 (dd, 1H, $J = 12.3$ and *2.1* Hz, –NC$\underline{H}\phi$), 3.56 (s, 2H, N$C\underline{H}_2\phi$), 7.11–7.42 (m, 10H, Ar$\underline{H}$), 11.04 (s, 1H, N–O$\underline{H}$). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 24.9, 28.4, 32.5, 41.7, 53.9, 65.4 (N$CH_2\phi$), 68.2 (N$CH\phi$), 125.6, 126.0, 127.3, 128.6, 136.4, 137.4, 158.7. DEPT-135: δ 22.21 (↓), 24.35 (↓), 26.72 (↓), 29.46 (↓), 34.58 (↓), 42.35 (↑), 55. 34 (↑), 65.95 (↓) (N$CH_2\phi$), 67.52 (↑) (N$CH\phi$), 127.76 (↑), 128.51 (↑), 129.02 (↑). Anal. Calcd for $C_{22}H_{26}N_2O$: C 79.00 %; H 7.84 %. Found: C 79.02 %; H 7.82 %.

*1-Benzyl-2-chlorophenyldecahydroquinolin-4(1H)-one oxime (**2b**)*

m.p. 142–143 °C; (aq. ethanol) yield: 71 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.20–2. 64 (m, 12H, 5×$C\underline{H}_2$ and 2×$C\underline{H}$), 3. 25 (dd, 1H, $J = 12.0$ and *2.4* Hz, –NC$\underline{H}\phi$), 3.58 (s, 2H, N$C\underline{H}_2\phi$), 7.23–7.72 (m, 9H, Ar$\underline{H}$), 11.14 (s, 1H, N–$O\underline{H}$). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 25.6, 26.0, 28.4, 33.4, 39.6, 53.6, 64.4 (N$CH_2\phi$), 67.2 (N$CH\phi$), 125.6, 126.0, 127.3, 128.6, 130.5, 137.4, 138.4, 162.4. Anal. Calcd for $C_{22}H_{25}ClN_2O$: C 71.63 %; H 6.83 %. Found: C 71.62 %; H 6.82 %.

*1-Benzyl-2-bromophenyldecahydroquinolin-4(1H)-one oxime (**2c**)*

m.p. 165–167 °C; (aq. ethanol) yield: 74 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.12–2.53 (m, 12H, 5×$C\underline{H}_2$ and 2×$C\underline{H}$), 3.31 (dd, 1H, $J = 12.3$ and *2.1* Hz, –NC$\underline{H}\phi$), 3.65 (s, 2H, N$C\underline{H}_2\phi$), 7.16–7.55 (m, 10H, Ar$\underline{H}$), 11.12 (s, 1H, N–$O\underline{H}$). ^{13}C NMR (ppm, $CDCl_3$): 23.2, 25.3, 27.3, 35.6, 40.2, 54.3, 65.3 (N$CH_2\phi$), 67.2 (N$CH\phi$), 125.4, 126.7, 127.5, 128.7, 136.9, 137.0, 162.5. Anal. Calcd for $C_{22}H_{25}BrN_2O$: C 63.93 %; H 6.10 %. Found: C 63.94 %; H 6.11 %.

*1-Benzyl-4-bromophenyldecahydroquinolin-4(1H)-one oxime (**2d**)*

m.p. 148–149 °C; (aq. ethanol) yield: 64 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.24–2.65 (m, 12H, 5×$C\underline{H}_2$ and 2×$C\underline{H}$), 3.26 (dd, 1H, $J = 12.6$ and *2.4* Hz, –NC$\underline{H}\phi$), 3.57 (s, 2H, N$C\underline{H}_2\phi$), 7.16–7.62 (m, 10H, Ar$\underline{H}$), 11.14 (s, 1H, N–$O\underline{H}$). ^{13}C NMR (ppm, $CDCl_3$): 23.6, 25.2, 29.2, 31.3, 40.5, 54.6, 65.1 (N$CH_2\phi$), 68.3 (N$CH\phi$), 124.6, 125.6, 127.4, 128.3, 135.7, 136.4, 159.8. Anal. Calcd for $C_{22}H_{25}BrN_2O$: C 63.93 %; H 6.10 %. Found: C 63.91 %; H 6.09 %.

*1-Benzyl-4-chlorophenyldecahydroquinolin-4(1H)-one oxime (**2e**)*

m.p. 134–135 °C; (aq. ethanol) yield: 70 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.16–2.65 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.26 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.60 (s, 2H, NC<u>H</u>$_2$ϕ), 7.20–7.55 (m, 9H, Ar<u>H</u>), 11.10 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.2, 23.7, 26.3, 34.5, 40.2, 54.5, 65.9 (NCH_2ϕ), 67.7 (N*C*Hϕ), 125.6, 126.5, 127.5, 128.7, 135.4, 137.2, 159.4. Anal. Calcd for $C_{22}H_{25}ClN_2O$: C 71.63 %; H 6.83 %. Found: C 71.64 %; H 6.81 %.

*1-Benzyl-3,4-dimethoxyphenyldecahydroquinolin-4(1H)-one oxime (**2f**)*

m.p. 150–151 °C; (aq. ethanol) yield: 73 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.22–2.16 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.32 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.55 (s, 2H, NC<u>H</u>$_2$ϕ), 7.18–7.62 (m, 8H, Ar<u>H</u>), 11.12 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.5, 24.6, 28.2, 31.6, 40.7, 54.2, 65.6 (NCH_2ϕ), 67.4 (NC<u>H</u>ϕ), 125.4, 126.5, 127.2, 128.5, 136.6, 138.2, 160.4. Anal. Calcd for $C_{24}H_{30}N_2O_3$: C 73.07 %; H 7.66 %. Found: C 73.05 %; H 7.67 %.

*1-Benzyl-4-methoxyphenyldecahydroquinolin-4(1H)-one oxime (**2g**)*

m.p. 169–170 °C; (aq. ethanol) yield: 65 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.22–2.55 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.20 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.56 (s, 2H, NC<u>H</u>$_2$ϕ), 7.20–7.76 (m, 9H, Ar<u>H</u>), 11.14 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 23.2, 25.1, 28.2, 31.8, 39.5, 53.5, 65.2 (NCH_2ϕ), 68.1 (NC<u>H</u>ϕ), 125.5, 126.5, 127.2, 128.5, 136.5, 137.3, 161.7. Anal. Calcd for $C_{23}H_{28}N_2O_2$: C 75.79 %; H 7.74 %. Found: C 75.80 %; H 7.75 %.

*1-Benzyl-4-nitrophenyldecahydroquinolin-4(1H)-one oxime (**2h**)*

m.p. 125–126 °C; (aq. ethanol) yield: 62 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.18–2.05 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.26 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.62 (s, 2H, NC<u>H</u>$_2$ϕ), 7.22–8.24 (m, 10H, Ar<u>H</u>), 11.24 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 25.6, 26.4, 28.9, 32.5, 40.7, 56.9, 65.4 (NCH_2ϕ), 67.2 (N*C*Hϕ), 125.6, 126.0, 127.3, 128.6, 136.4, 145.4, 146.3, 162.7. Anal. Calcd for $C_{22}H_{25}N_3O_3$: C 69.64 %; H 6.64 %. Found: C 69.65 %; H 6.63 %.

*1-Benzyl-3-nitrophenyldecahydroquinolin-4(1H)-one oxime (**2i**)*

m.p. 154–156 °C; (aq. ethanol) yield: 69 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.20–2.46 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.12 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.56 (s, 2H, NC<u>H</u>$_2$ϕ), 7.11–7.42 (m, 10H, Ar<u>H</u>), 11.04 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 24.9, 28.4, 32.5, 41.7, 53.9, 65.4 (NCH_2ϕ), 68.2 (N*C*Hϕ), 125.6, 126.0, 127.3, 128.6, 136.4, 137.4, 158.7. Anal. Calcd for $C_{22}H_{25}N_3O_3$: C 69.64 %; H 6.64 %. Found: C 69.63 %; H 6.62 %.

*1-Benzyl-4-(4-oxo-4H-chromen-3-yl)-decahydroquinolin-4(1H)-one oxime (**2j**)*

m.p. 147–148 °C; (aq. ethanol) yield: 74 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.21–2.56 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.22 (dd, 1H, J = *12.3* and *2.1* Hz, –NC<u>H</u>ϕ), 3.54 (s, 2H, NC<u>H</u>$_2$ϕ), 7.10–7.82 (m, 10H, Ar<u>H</u>), 11.12 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 25.5, 28.4, 34.2, 40.7, 54.3, 65.4 (NCH_2ϕ), 68.5 (N*C*Hϕ), 125.1, 126.3, 127.4, 128.5, 136.2, 137.4, 160.4. Anal. Calcd for $C_{25}H_{26}N_2O_3$: C 74.60 %; H 6.51 %. Found: C 74.62 %; H 6.52 %.

*1-Benzyl-4-(2-chloroquinolin-3-yl)decahydroquinolin-4(1H)-one oxime (**2k**)*

m.p. 141–142 °C; (aq. ethanol) yield: 71 %. ^{1}H NMR (ppm, $CDCl_3$): δ 1.23–2.56 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.22 (dd, 1H, J = *12.3* and *2.1* Hz, -NC<u>H</u>ϕ), 3.56 (s, 2H, NC<u>H</u>$_2$ϕ), 7.10–7.92 (m, 10H, Ar<u>H</u>), 11.14 (s, 1H, N–*O*H). ^{13}C NMR (ppm, $CDCl_3$): 22.6, 24.9, 28.4, 33.5, 40.7, 53.9, 65.4 (NCH_2ϕ), 68.2 (NC<u>H</u>ϕ), 125.6, 126.0, 127.3, 128.6, 136.4, 138.4, 159.2. Anal. Calcd for $C_{25}H_{29}N_3O$: C 77. 48 %; H 7.54 %. Found: C 77.50 %; H 7.53 %.

Typical procedure for the synthesis of 5-benzyl-4-aryloctahydro-1*H*-benzo[*b*][1,5] diazepin-2(3*H*)-ones (**3a**–**k**)

To a solution of decahydroquinoline-2-one oximes **2 a**–**k** (0.01 mol) in dry ether (25 mL) taken in a R.B. flask fitted with a double-surface condenser carrying a $CaCl_2$ guard tube, freshly distilled thionyl chloride (0.05 mol) was added and the reaction mixture was refluxed on a water-bath for 1 h. After completion of the reaction (TLC), the excess of ether and thionyl chloride were removed *in vacuo* and the residue was treated with water. The solid that separated was filtered, washed with water and dried; crystallisation from ethylacetate-petroleum ether (2:1) afforded compounds **3a**–**k**.

*5-Benzyl-4-phenyloctahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3a**)*

Yield: 77 %; m.p. 156–157 °C (ethyl acetate–petroleum ether). IR (KBr, cm^{-1}): 3316 (NH str.), 3160 (aromatic–CH str.), 1678 (CO), 1220–1070 (CN str.). ^{1}H NMR (ppm,

$CDCl_3$): δ 1.16–2.61 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.62 (s, 2H, NC$\underline{H}_2\phi$), 4.02 (dd, 1H, J = *12.6* and *1.8* Hz, NC$\underline{H}\phi$), 7.04–7.39 (m, 10H, Ar$\underline{H}$), 8.62 (s, 1H, –NHCO). ^{13}C NMR (ppm, $CDCl_3$): 22.5, 24.8, 25.4, 32.4, 46.5, 51.2, 54.8 (NCHϕ), 56.5, 58.9 ($NCH_2\phi$), 125.4, 126.4, 127.5, 128.9, 138.6, 176.8 (CO). DEPT-135: δ 23.45 (↓), 25.93 (↓), 27.51 (↓), 32.28 (↓), 44.71 (↓), 51.44 (↑), 53.81 (↑) (NC$\underline{H}\phi$), 56.73 (↑), 59.52 (↓) (N$\underline{C}H_2\phi$), 125.05 (↑), 127.45 (↑), 128.71(↑). MS (FAB$^+$, *m/z*, %): 334 ($M^{+\cdot}$). Anal. Calcd for $C_{22}H_{26}N_2O$: C 79.00 %; H 7.84 %. Found: C 79.03 %; H 7.83 %.

*5-Benzyl-4-(2-chlorophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3b**)*

m.p. 191–193 °C (ethyl acetate – pet. ether); yield: 62 %. IR (KBr, cm^{-1}): 3344 (NH str.), 1653 (NHCO). ^{1}H NMR (ppm, $CDCl_3$): δ 1.34–3.08 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 4.1 (dd, 1H, J = *12.0* and *2.4* Hz, NC$\underline{H}\phi$), 7.2–7.5 (m, 9H, Ar$\underline{H}$), 9.1 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.5, 27.6, 32.6, 45.2, 53.4 (NCHϕ), 56.8, 59.9 ($NCH_2\phi$), 123.4, 127.0, 128.4, 128.3, 138.0, 145.5, 146.4, 172.0 (CO). DEPT-135: δ 24.62 (↓), 25.46 (↓), 27.47 (↓), 32.93 (↓), 44.43 (↑), 51.43 (↑), 53.03 (↑) (NCHϕ), 56.72 (↑), 59.26 (↓) ($NCH_2\phi$), 123.53 (↑), 128.63 (↑), 127.63 (↑), 128.45 (↑).

*5-Benzyl-4-(2-bromophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3c**)*

m.p. 217–218 °C (ethyl acetate–petroleum ether); yield: 73 %. IR (KBr, cm^{-1}): 3371 (NH str.), 1649 (NHCO). ^{1}H NMR (ppm, $CDCl_3$): δ 1.1–3.2 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 4.1 (dd, 1H, J = *12.6* and *2.4* Hz, NC$\underline{H}\phi$), 7.2–7.6 (m, 9H, Ar$\underline{H}$), 9.3 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.5, 27.6, 32.6, 45.2, 50.4, 51.8 (NCHϕ), 56.9, 60.1($NCH_2\phi$), 123.4, 127.0, 128.4, 129.3, 132.0, 138.0, 139.5, 172.3 (CO). DEPT-135: δ 24.62 (↓), 25.36 (↓), 27.77 (↓), 32.45 (↓), 44.40 (↑), 49.33 (↑), 53.44 (↑) (NCHϕ), 59.26 (↓) ($NCH_2\phi$), 127.43 (↑), 128.20 (↑), 129.32 (↑), 132.75 (↑).

*5-Benzyl-4-(4-bromophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3d**)*

m.p. 181–182 °C, (ethyl acetate–petroleum ether), yield: 74 %. IR (KBr, cm^{-1}): 3374 (NH str.), 1642 (CO str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.15–3.16 (m, 12H, 5×C$\underline{H}_2$ and 2CH), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 4.2 (dd, 1H, J = *11.7* and *2.1* Hz, NC$\underline{H}\phi$), 7.16–7.92 (m, 9H, Ar$\underline{H}$), 9.2 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.8, 25.4, 27.3, 32.5, 45.8, 50.4, 51.3 (NCHϕ), 56.8, 59.2 (NCH_2 ϕ), 123.1, 127.8, 128.6, 129.2, 132.4, 138.3, 139.1, 172.2 (CO). DEPT-135: δ 24.72 (↓), 25.56 (↓), 27.37 (↓), 32.25 (↓), 44.20 (↑), 49.63 (↑), 54.34 (↑) (NCHϕ), 56.56 (↑), 59.56 (↓) (NCH_2 ϕ), 127.43 (↑), 128.30 (↑), 129.42 (↑), 132.75 (↑).

*5-Benzyl-4-(4-chlorophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3e**)*

Viscous paste; yield: 74 %. IR (KBr, cm^{-1}): 3344 (NH str.), 1671 (CO str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.3–3.1 (m, 12H, 5×C$\underline{H}_2$ and 2CH), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 4.3 (dd, 1H, J = *11.4* and *1.8* Hz, NC$\underline{H}\phi$), 7.28–7.64 (m, 9H, Ar$\underline{H}$), 9.2 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.6, 27.2, 32.6, 45.5, 51.3 (NCHϕ), 56.8, 59.4 ($NCH_2\phi$), 123.7, 127.1, 128.4, 128.8, 138.3, 145.4, 146.2, 172.6 (CO). DEPT-135: δ 24.64 (↓), 25. 36 (↓), 27.27 (↓), 32.44 (↓), 44.54 (↑), 51.35 (↑), 53.52 (↑) (NCHϕ), 56.32 (↓), 59.67 (↑) ($NCH_2\phi$), 123.30 (↑), 128.43 (↑), 127.63 (↑), 128.63 (↑).

*5-Benzyl-4-(3,4-dimethoxyphenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3f**)*

m.p. 145 °C (ethyl acetate–petroleum ether); yield: 76 %. IR (KBr, cm^{-1}): 3355 (–NH str.), 1656 (CO str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.2–2.9 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 3.9 (s, 6H, 2×OC$\underline{H}_3$), 4.1 (dd, 1H, J = *12.6* and *2.1* Hz, NC$\underline{H}\phi$), 6.74–7.47 (m, 8H, Ar$\underline{H}$), 9.1 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.8, 25.5, 27.1, 32.8, 45.3, 51.3, 52.2 (NCHϕ), 56.2 (OCH_3), 56.8, 59.4 ($NCH_2\phi$), 116.7, 120.4, 121.1, 127.1, 128.2, 131.3, 137.2, 147.2, 149.3, 172.7 (CO).

*5-Benzyl-4-(4-methoxyphenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3g**)*

m.p. 154 °C (ethyl acetate–petroleum ether); yield: 72 %. IR (KBr, cm^{-1}): 3347 (–NH str.), 1652 (CO str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.2–3.0 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 3.9 (s, 3H, 1×OC$\underline{H}_3$), 4.2(dd, 1H, J = *12.3* and *2.4* Hz, NC$\underline{H}\phi$), 6.82–7.45 (m, 7H, Ar$\underline{H}$), 9.0 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.4, 27.7, 31.4, 45.6, 53.2, 52.3 (NCHϕ), 55.2 (OCH_3), 56.5, 59.7 ($NCH_2\phi$), 115.7, 122.0, 124.1, 125.1, 126.2, 130.3, 135.3, 145.6, 149.3, 173.2 (CO).

*5-Benzyl-4-(4-nitrophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3h**)*

m.p. 201–202 °C (ethyl acetate–petroleum ether); yield:72 %. IR (KBr, cm^{-1}): 3342 (NH str.), 1654 (C=O str. in ring), 1564 (NO_2, asym. str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.2–3.1 (m, 12H, 5×C$\underline{H}_2$ and 2×C$\underline{H}$), 3.6 (s, 2H, NC$\underline{H}_2\phi$), 4.2 (dd, 1H, J = *12.0* and *2.1* Hz, NCHϕ), 7.3–8.2 (m, 9H, Ar$\underline{H}$), 9.1(s, 1H, NHCO). ^{13}C NMR (ppm,

$CDCl_3$): 24.6, 25.6, 27.6, 32.8, 44.3, 51.3, 54.2 (NCHϕ), 56.2, 59.3 (NCH_2ϕ), 123.4, 127.1, 128.2, 137.2, 145.2, 146.3, 172.1 (CO).

*5-Benzyl-4-(3-nitrophenyl)octahydro-1H-benzo[b][1,5]diazepin-2(3H)-one (**3i**)*

m.p. 141 °C (ethylacetate–petroleum ether); yield: 69 %. IR (KBr, cm^{-1}): 3326 (NH str.), 1665 (CO str.), 1586 (NO_2, asym. str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.3–2.6 (m, 12H, 5×C<u>H</u>$_2$ and 2×C<u>H</u>), 3.6 (s, 2H, NC<u>H</u>$_2$ϕ), 4.3 (dd, 1H, J = *11.7* and *2.1* Hz, NC<u>H</u>ϕ), 7.2–8.2 (m, 9H, Ar<u>H</u>), 9.2 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.0, 27.6, 32.1, 44.3, 51.3, 54.2 (NCHϕ), 56.8, 59.3 (NCH_2ϕ), 123.4, 127.1, 128.3, 137.2, 145.9, 146.6, 172.3 (CO).

*5-Benzyl-4-(4-oxo-4H-chromen-3-yl)octahydro-1H-benzo[b][1,5]diazepin-2-(3H)-one (**3j**)*

m.p. 138 °C; (ethyl acetate–petroleum ether), yield: 62 %. IR (KBr, cm^{-1}): 3349 (NH str.), 1645 (CO str.). ^{1}H NMR (ppm, $CDCl_3$): δ 1.1–3.4 (m, 12H, 5×C<u>H</u>$_2$ and 2CH), 3.6 (s, 2H, NC<u>H</u>$_2$ϕ), 4.1 (dd, 1H, J = *11.4* and *1.5* Hz, NC<u>H</u>ϕ), 6.8 (s, 1H, H-2′), 7.3–8.3 (m, 9H, Ar<u>H</u>), 9.2 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.3, 27.7, 32.5, 36.1, 46.6, 53.8 (NCHϕ), 56.1, 59.7 (NCH_2ϕ), 116.9, 123.8, 125.2, 127.3, 128.4, 135.2, 138.9, 150.2, 156.7, 174.3 (NHC=O), 179.3 (CO of chromone).

*5-Benzyl-4-(2-chloroquinolin-3-yl)octahydrobenzo[b][1,5]diazepin-2(3H)-one (**3k**)*

m.p. 162 °C; (ethyl acetate–petroleum ether), yield: 63 %. IR (KBr, cm^{-1}): 3324 (–NH str.), 1652 (C=O str. in ring). ^{1}H NMR (ppm, $CDCl_3$): δ 1.1–3.4 (m, 12H, 5×C<u>H</u>$_2$ and 2CH), 3.6(s, 2H, NC<u>H</u>$_2$ϕ), 4.1(dd, 1H, J = *11.1* and *1.5* Hz, NC<u>H</u>ϕ), 7.1–8.0 (m, 10H, Ar<u>H</u>), 9.1 (s, 1H, NHCO). ^{13}C NMR (ppm, $CDCl_3$): 24.6, 25.1, 27.8, 32.3, 36.7, 45.2, 51.7(NCHϕ), 56.4, 59.3 (NCH_2ϕ), 116.5, 125.2, 127.4, 128.5, 129.3, 135.4, 137.9, 138.1, 150.8, 157.0, 174.2 (C=O). DEPT-135: δ 24.35 (↓), 25.11 (↓), 27.96 (↓), 32.72 (↓), 36.76 (↓), 46.08 (↑), 53.42 (↑) (NCHϕ), 56.39 (↓) (NCH_2ϕ), 57.82 (↑), 116.72 (↑), 123.06 (↑), 125.20 (↑), 127.18 (↑), 128.54 (↑), 129.10 (↑), 135.71 (↑), 137.32 (↑), 150.84 (↑).

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