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Dihydroquinazolino[3,2-*a*][1,5]benzodiazepines: Synthesis and Computational Study of Reductive N-Heterocyclization of *N*-(2-Nitrobenzoyl)-1,5-benzodiazepin-2-ones

Regina Janciene,[a]* Gema Mikulskiene,[a] Tomas Javorskis,[a] Ausra Vektariene,[b] Gytis Vektaris,[b] and Lidija Kosychova[a]

[a]Vilnius University Institute of Biochemistry, Mokslininku 12, LT-08662 Vilnius, Lithuania
[b]Vilnius University Institute of Theoretical Physics and Astronomy, A. Gostauto 12, LT-01108 Vilnius, Lithuania
*E-mail: regina.janciene@bchi.vu.lt

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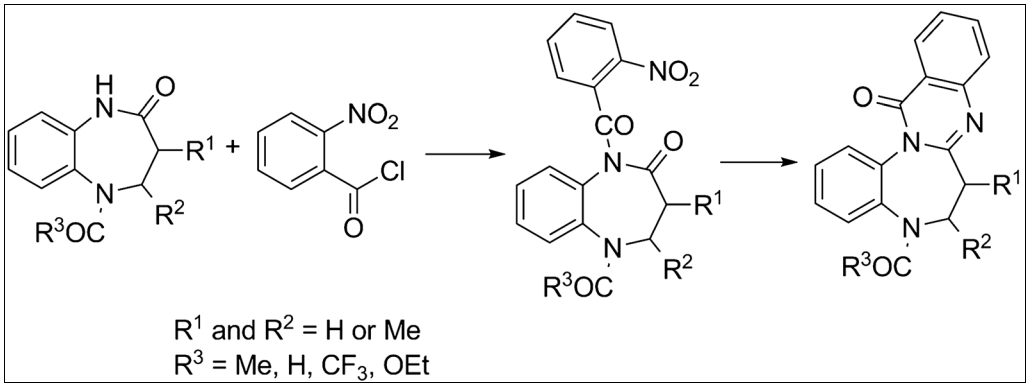

A number of 6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-ones were prepared utilizing the coupling of readily available 5-acyl-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-ones with 2-nitrobenzoyl chloride followed by a reductive N-heterocyclization. 3-Methylsubstituted 1-(2-nitrobenzoyl)-1,5-benzodiazepinone derivatives did not cyclize under the reductive N-heterocyclization conditions. The possible mechanism of this heterocyclization was discussed, and it was demonstrated that the hydroxylamine intermediate was the initiator of this reaction. To clarify the reasons of different reactivities of various 1,5-benzodiazepine derivatives, the quantum-chemical reactivity descriptors of the hydroxylamine intermediates were calculated and evaluated.

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INTRODUCTION

Quinazolinones and their derivatives are of great interest because of their pharmacological properties. The quinazolin-4-one moiety fused with a benzodiazepine ring system is a building block of naturally occurring alkaloids [1] such as asperlicins [2,3], sclerotigenin [4], and circumdatins [5,6], which are now known to have a wide range of useful biological properties. For instance, the asperlicin family has antagonist activity against cholecystokinin, sclerotigenin has insecticidal properties, and circumdatins have shown biological activity as inhibitors of the mammalian mitochondrial chain. These alkaloids incorporate quinazolino[3,2-*a*] or [3,2-*d*][1,4]benzodiazepine systems, and the main synthetic routes to these quinazolinone compounds are published in a broad range of scientific journals including those mentioned earlier.

Following our previous studies on the construction of polycyclic compounds containing different heterocyclic rings annelated to the basic 1,5-benzodiazepine bicyclic system ([1,3]thiazolo[3,2-*a*][1,5]benzodiazepines [7], [1,2,4]oxadiazolo[4,3-*a*][1,5]benzodiazepines [8], [1,4]diazepino[3,2,1-*hi*]pyrido[4,3,2-*cd*]indoles, and [1,4]diazepino[2,3-*g*]quinolines [9]), we planned the preparation of some quinazolino[1,5]benzodiazepines. Several examples of the synthesis of such combined heterocyclic rings, where the quinazoline nucleus is fused at different positions of the 1,5-benzodiazepine skeleton, have been reported [10,11]. It concerns the reaction of 2-carbethoxymethyl-4*H*-3,1-benzoxazin-4-one with primary aromatic amine (1,2-phenylenediamine) followed by thermal cyclization of the obtained product [10] or the reaction of 2-chloroquinoline-3-carboxaldehyde with 1,2-phenylenediamine [11].

To extend our study, we present herein the synthesis of novel dihydroquinazolino[3,2-*a*][1,5]benzodiazepine derivatives with possible biological activity [12,13]. The influence of the substituents of the heptatomic nucleus of *N*-(2-nitrobenzoyl)-1,5-benzodiazepin-2-ones on the course of the studied reductive N-heterocyclization was also investigated; the possible mechanism of this cyclization reaction was suggested and confirmed by means of quantum-chemical reactivity descriptors calculations.

RESULTS AND DISCUSSION

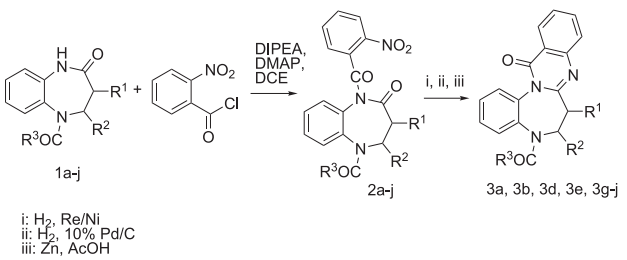
The cyclofunctionalization strategy of the 1,5-benzodiazepine system was realized by employing the overall sequence of acylation of tetrahydro-1,5-benzodiazepin-2-ones with 2-nitrobenzoyl chloride

followed by reductive N-heterocyclization of the obtained *N*-(2-nitrobenzoyl)amides (Scheme 1).

5-Acyl(acetyl, formyl, trifluoroacetyl, ethoxycarbonyl)-3-R^1-4-R^2-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-ones **1a–j** were used as starting compounds. Compounds **1a–c** were described by us in [14], **1d–f** in [15], and **1g** in [16]. Compounds **1h–j** were synthesized by acylation of the corresponding N5-unsubstituted 3-R^1-4-R^2-tetrahydro-1,5-benzodiazepinones with trifluoroacetic acid anhydride (**1h**) using the procedure described in [17] and by treatment with ethyl chloroformate (**1i** and **1j**).

As shown in Scheme 1, the benzoylation of 1,5-benzodiazepinones **1a–j** with freshly prepared 2-nitrobenzoyl chloride in the presence of 4-dimethylaminopyridine (DMAP) and *N*,*N*-diisopropylethylamine (DIPEA) in dry dichloroethane (DCE) at room temperature gave 2-nitrobenzoylamides **2a–j**. The yields of these products ranged from 41 to 70%. The generation of better yields by increasing the reaction temperature and the amount of catalyst and chloranhydride was unsuccessful. The monitoring of the crude reaction mixture by TLC indicated the incomplete conversion of **1a–j** to the corresponding nitro derivatives **2a–j** within 24 h. Some products were isolated after chromatographic purification. Furthermore, we can point out that in some cases after the purification of products **2b** and **2f** by chromatography, starting compounds **1b** and **1f** were isolated (21 and 18%, respectively). On the other hand, in [6], it is mentioned that aqueous work up of the reaction mixture resulted in partial hydrolysis of 1-nitrobenzoylamides of 1,4-benzodiazepines to the starting materials and 2-nitrobenzoic acid. As planned, the process of the reduction of nitro compounds **2a**, **2b**, **2d**, **2e**, and **2g–j** to the corresponding amines was accomplished by a simultaneous N-heterocyclization leading to dihydroquinazolino[3,2-*a*][1,5]benzodiazepinones **3a**, **3b**, **3d**, **3e**, and **3g–j**. The study of the reduction of nitroamides **2a–e** was commenced under mild catalytic conditions (i: H_2, Re/Ni; ii: H_2, 10% Pd/C) in methanol. It was observed that the reduction reaction conducted with H_2, 10% Pd/C afforded quinazolino[1,5]benzodiazepines **3a**, **3b**, **3d**, and **3e** with slightly higher yields (Table 1) than the experiments performed using H_2, Re/Ni. Although the use of catalytic hydrogenation conditions has become a common practice, in our study, the N-heterocyclization process was accompanied by the formation of by-products of unknown structure. Therefore, the isolation and purification of the main polycyclic products **3** were complicated. Then, we turned our attention towards the reductive cyclization of nitrobenzoylamides **2c** and **2f–j** employing zinc dust in glacial acetic acid [4]. TLC monitoring indicated that these reactions, in comparison with procedures i and ii, proceeded without the formation of by-products. Compounds **3g–j** were isolated in acceptable 68–57% yields.

Scheme 1



Compd 1, 2, 3	a	b	c	d	e	f	g	h	i	j
R^1	H	H	Me	H	H	Me	H	H	H	H
R^2	H	Me	H	H	Me	H	H	Me	H	Me
R^3	Me	Me	Me	H	H	H	CF_3	CF_3	OEt	OEt

The structures of all synthesized compounds were characterized by elemental analysis, IR, and ^{1}H and ^{13}C NMR spectral data presented in Table 1 and the Experimental section.

In the IR spectra of amides **2a–j**, typical asymmetric and symmetric absorption bands of nitro group at ~1530 and ~1346 cm^{-1} and carbonyl group absorption bands in the region of 1744–1663 cm^{-1} were observed. The absence of the nitro group and one of the carbonyl group absorption bands and the rise of the C=N linkage absorption band at ~1610 cm^{-1} in the IR spectra confirmed the structure of quinazolinones **3**.

For the analysis of NMR spectra, we used the arbitrary numbering of atoms as in Scheme 2 (**A** for compounds **2a–j** and **B** for compounds **3a**, **3b**, **3d**, **3e**, and **3g–j**).

^{1}H NMR spectra of starting compounds **1h–j** exhibited the singlet at 8.4–8.7 ppm attributed to NH group analogously to the spectral data of compounds **1a–g** published previously [15–18].

The formation of compounds **2a–j** was evidenced by the disappearance of NH singlet and the increase in the number of aromatic protons (8H) in ^{1}H NMR spectra. The most deshielded proton (at ~8.3 ppm) in the aromatic region of compounds **2a–j** was assigned to H-C3′ by means of HMBC spectra. The characteristic signals of ^{13}C NMR spectra for the three CO groups of molecules **2a–j** also confirmed the predictable structure. The values of the chemical shift of the resonances of CO-N1 group varied about 1.0 ppm among compounds **2a–j** in the range 166.5–167.5 ppm. The carbons of C2 and CO-N5 were affected by CH_3-C3, CH_3-C4, and N5-substituents; therefore, their resonances were found in wider regions of 169.0–173.5 and 154.5–170.5 ppm, respectively. The carbons of C2 and C4 of heterocyclic moiety of compounds **2a–j** were shielded at approximately 1.8 ppm, whereas C3 was deshielded at ~2 ppm, compared with the respective carbons of **1a–j**.

The formation of the compounds of structure **3** was confirmed by the appearance of resonance at ~153.4 ppm attributed to C=N group carbon and the absence of the signal of CO group in 2-position compared with the respective

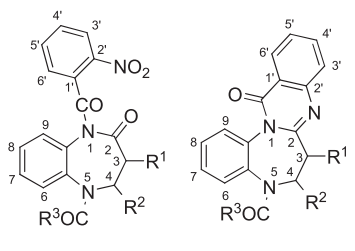
Table 1

Physicochemical properties of compounds **2a–j**, **3a**, **3b**, **3d**, **3e**, and **3g–j**.

				Elemental analysis %		
				Calcd./Found		
Compound	Yield (%)	mp (°C)	Molecular formula	C	H	N
2a	74	199–201	$C_{18}H_{15}N_3O_5$	61.19	4.28	11.89
				61.01	4.32	11.97
2b	70	205–207	$C_{19}H_{17}N_3O_5$	62.12	4.66	11.44
				62.00	4.79	11.65
2c	55	263–265	$C_{19}H_{17}N_3O_5$	62.12	4.66	11.44
				62.41	4.49	11.66
2d	61	202–204	$C_{17}H_{13}N_3O_5$	60.18	3.86	12.38
				60.44	3.77	12.13
2e	52	200–202	$C_{18}H_{15}N_3O_5$	61.19	4.28	11.89
				61.41	4.19	11.67
2f	41	224–226	$C_{18}H_{15}N_3O_5$	61.19	4.28	11.89
				60.94	4.36	11.99
2g	65	186–188	$C_{18}H_{12}F_3N_3O_5$	53.08	2.97	10.32
				53.31	2.86	10.50
2h	67	199–201	$C_{19}H_{14}F_3N_3O_5$	54.16	3.35	9.97
				54.32	3.27	10.03
2i	56	154–156	$C_{19}H_{17}N_3O_6$	59.53	4.47	10.96
				59.34	4.59	10.73
2j	55	169–171	$C_{20}H_{19}N_3O_6$	60.45	4.82	10.57
				60.67	4.67	10.74
3a	47 (i)	216–218	$C_{18}H_{15}N_3O_2$	70.81	4.95	13.76
	57 (ii)			70.50	4.81	13.98
3b	45 (i)	193–195	$C_{19}H_{17}N_3O_2$	71.46	5.37	13.16
	55 (ii)			71.18	5.31	13.39
3d	48 (i)	270–273	$C_{17}H_{13}N_3O_2$	70.09	4.50	14.42
	77 (ii)			70.37	4.58	14.15
3e	48 (i)	204–205	$C_{18}H_{15}N_3O_2$	70.81	4.95	13.76
	61 (ii)			70.56	4.84	13.51
3g	57 (iii)	236–239	$C_{18}H_{12}F_3N_3O_2$	60.17	3.37	11.69
				60.38	3.31	11.41
3h	42 (ii)	199–201	$C_{19}H_{14}F_3N_3O_2$	61.13	3.78	11.26
	65 (iii)			60.89	3.90	11.47
3i	62 (iii)	120–122	$C_{19}H_{17}N_3O_3$	68.05	5.11	12.53
				68.29	5.04	12.77
3j	68 (iii)	130–132	$C_{20}H_{19}N_3O_3$	68.75	5.48	12.03
				68.51	5.56	12.20

spectra of compounds **2a–j**. The resonances of CO-N1 group were shifted up-field at approximately 7 ppm and were observed in the range 160.1–160.8 ppm; the resonances of C1′ carbon were shifted up-field ~13.5 ppm and those of C2′ down-field ~2.3 ppm. The carbons of the C2 and C3 atoms of heterocyclic moiety of the compounds of structure **3** were shielded ~16.8 and ~1 ppm, respectively, whereas C4 was deshielded ~2.5 ppm compared with the corresponding atoms of compounds **2a–j**. In the case of compounds **3**, the most deshielded ArH (at ~8.3 ppm) in the aromatic region was assigned to H-C6′ in ^{1}H NMR spectra.

Scheme 2



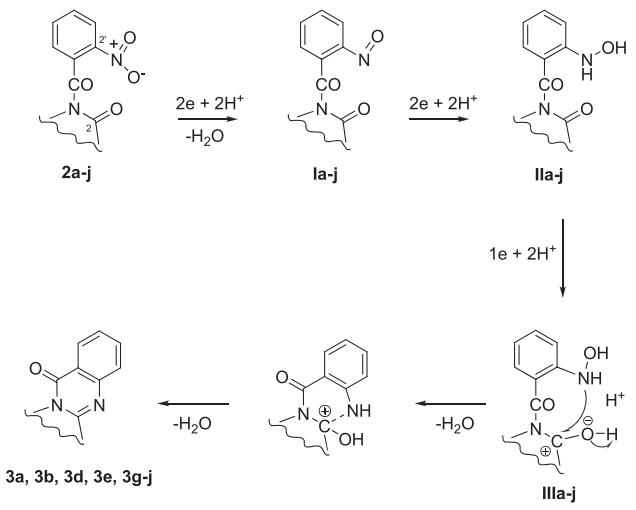
The specific splitting of resonances of carbon atoms (CF_3 at about 115.9 ppm, $\sim^1J_{C\text{-}F} = 288.6$ Hz and CO at about 156.3 ppm, $\sim^2J_{C\text{-}F} = 36.5$ Hz) of compounds **1h**, **2g**, **2h**, **3g**, and **3h** possessing $COCF_3$ group on 5-position was observed in ^{13}C NMR spectra.

The aforementioned procedures (i–iii) for the N-heterocyclization of 2-nitrobenzoylamides **2c** and **2f** were also explored. In all cases, the reduction of compounds **2c** and **2f** was not successful. Unchanged **2c** and **2f**

(~60%) and starting benzodiazepinones **1c** and **1f** (~25%) were isolated after chromatographic separation of the mixture of the reaction products. Thus, we can point out that the reaction of the reductive cyclization of compounds **2c** and **2f**, carrying the methyl substituent in 3-position of the diazepine nucleus, proceeded differently as compared with the other studied 1,5-benzodiazepin-2-one derivatives. To have more insight into the nature of the studied reductive cyclization process and to explain the unexpected reactivity pattern, the theoretical studies of the reactivity descriptors of 2-nitrobenzoylamides were carried out. It is worth mentioning that the mechanism of the reductive N-heterocyclization of benzodiazepines bearing nitrobenzoylamide moiety has not been established yet. A possible mechanism for this heterocyclization is proposed in Scheme 3.

We assumed that the studied reductive cyclization reaction starts in a similar way to the reduction reaction of aromatic nitro compounds to amines [19]. After the nitro group is activated by metal-mediated electrons and two hydrogen atoms, the elimination of water molecule occurs, leading to nitroso intermediates **Ia–j**, which after the reductive addition of two hydrogen atoms form hydroxylamine intermediates **IIa–j**. The formation of hydroxylamine intermediates **IIa–j** enables the nucleophilic attack of the N-C2′ atom on the C2 atom of the protonated carbonyl group. After the reductive addition of a hydrogen atom, intermediates **IIIa–j** possessing the weak interaction between the C2 and N-C2′ atoms are formed. The subsequent elimination of two water molecules afforded the CN double bond and final products **3a**, **3b**, **3d**, **3e**, and **3g–j**. The presented reaction mechanism (Scheme 3) demonstrates that the initiation of heterocyclization reaction becomes possible after intermediate **III** is formed. Thus, the insight into the electronic structure of intermediate **III** can be of great importance for the explanation of different reactivity patterns of nitrobenzoylamides **2a–j** in the reductive heterocyclization reaction. To confirm our assumptions, the theoretical investigation of intermediates **IIIa–j** was carried out by means of quantum-chemical reactivity descriptors calculations. The calculated reactivity descriptors: frontier orbital π electron population and Fukui functions for nucleophilic and electrophilic attack on the selected atoms allowed us to estimate the outcome of the studied reaction.

Scheme 3



The frontier orbital electron population on atoms provides a useful tool for the detailed characterization of donor–acceptor interactions that can strictly be used only to describe the reactivity of different atoms in the same molecule [20]. According to the frontier orbital electron reactivity theory, the majority of chemical reactions take place at the position and in the orientation where the overlap of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) of the respective reactants can reach a maximum [20–22].

The Fukui function is a local reactivity descriptor that indicates the best way to change the number of electrons in a molecule. Hence, it indicates the propensity of the electronic density to deform at a given position, that is, to accept or donate electrons [7,23–26]. With the aim of estimating the outcome of the reductive cyclization progress, we calculated the condensed Fukui function [23–25] for nucleophilic attack [f + (r)] and electrophilic attack [f − (r)], and the frontier orbital π electron population on the particular atoms C2 and N-C2′ of intermediates **IIIa–j** (Table 2).

The results of our computation reveal that the presence of substituents on the diazepine skeleton of intermediates **IIIa–j** influence the values of all calculated reactivity descriptors. HOMO and LUMO populations on particular atoms illustrate the most favorable sites for electrophilic or nucleophilic attack. A higher LUMO electron population on the C2 atom in intermediates **IIIa**, **IIIb**, **IIId**, **IIIe**, and **IIIg–j** (~0.41–0.51) as compared with the values of **IIIc** and **IIIf** (~0.1) and a comparatively high HOMO electron population on the N-C2′ atom support the idea that with the first clash between reacting atoms, an intrinsic molecular rearrangement should start in places of enhanced electron density, that is, between the N-C2′ and C2 atoms. This initial interaction could succeed the subsequent rearrangements to final products **3a**, **3b**, **3d**, **3e**, and **3g–j**. Meanwhile, the comparably small values of LUMO electron population on the C2 atom of **IIIc** and **IIIf** (0.095 and 0.104, respectively) are compatible with the experimental fact that cyclization of 3-methyl substituted compounds **2c** and **2f** does not take place. In the case when the intermolecular rearrangement of intermediates **IIIa**, **IIIb**, **IIId**, **IIIe**, and **IIIg–j** occurs, the Fukui function values for nucleophilic attack [f + (r)] on the C2 atom are from 0.39 to 0.57, and those for electrophilic attack [f − (r)] of the N-C2′ atom are from 0.30 to 0.48. Comparatively small values of [f + (r)] on the C2 atom of **IIIc** and **IIIf** (0.104 and 0.082,

Table 2

Calculated HOMO and LUMO electron populations and Fukui functions [f + (r)], [f − (r)] on N-C2′ and C2 atoms of **IIIa–j** intermediates.

				N-C2′		C2	
Intermediate	R^1	R^2	R^3	HOMO	[f − (r)]	LUMO	[f + (r)]
IIIa	H	H	Me	0.349	0.480	0.510	0.390
IIIb	H	Me	Me	0.292	0.414	0.444	0.566
IIIc	Me	H	Me	0.283	0.392	0.095	0.104
IIId	H	H	H	0.276	0.421	0.456	0.386
IIIe	H	Me	H	0.265	0.414	0.406	0.566
IIIf	Me	H	H	0.215	0.298	0.104	0.082
IIIg	H	H	CF_3	0.245	0.399	0.428	0.552
IIIh	H	Me	CF_3	0.261	0.401	0.416	0.524
IIIi	H	H	OEt	0.337	0.362	0.476	0.555
IIIj	H	Me	OEt	0.270	0.395	0.407	0.567

HOMO, highest occupied molecular orbital; LUMO, lowest unoccupied molecular orbital.

respectively) suggest rather the reduced reactivity of these intermediates.

Thus, our computational results reveal that the presence of substituents on 3-position on the diazepine skeleton causes changes in the electron population on the frontier molecular orbitals. The presence of the electron donating the 3-methyl substituent decreases the electrophilicity of the C2 atom and evokes resistance to further intramolecular rearrangements. The computational results are in agreement with experimental observations and support the proposed reaction mechanism.

In conclusion, a series of new 6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-ones was successfully synthesized using a metal-induced reductive N-heterocyclization of 1-(2-nitrobenzoyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-ones. It was established that the course of this heterocyclization depended on the presence of substituents in the heptatomic ring of the starting heterocycles. The possible mechanism of this heterocyclization was discussed, and it was demonstrated that the hydroxylamine intermediate was the initiator of this reaction. The suggested reaction mechanism was supported by means of quantum-chemical reactivity descriptors calculations and evaluation. The computational studies reported herein are a powerful tool for the interpretation of experimental results and for the design of synthetic pathways to novel fused heterocycles.

EXPERIMENTAL

Melting points were determined in open capillaries on a MEL-TEMP 1202D apparatus and are uncorrected. The IR spectra (potassium bromide) were taken on a Perkin Elmer Spectrum GX FT-IR spectrometer. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in deuteriochloroform on a Varian Unity Inova 300 spectrometer. The chemical shifts are referenced to tetramethylsilane [δ (^{1}H) = 0] and the solvent signal deuteriochloroform [δ (^{13}C) = 77.0 ppm]. The reactions were controlled by the TLC method and performed on a Merck precoated silica gel aluminum roll ($60F_{254}$) with chloroform–ethyl acetate–methanol (v/v, 14:7:1) as the eluent and was visualized with UV light. Dry column vacuum chromatography [27] was performed with silica gel Chemapol L 5/40 mesh. The first optimization of intermediate structures was carried out with AM1 method. Consequently, the AM1 geometry optimized structures were used as initial coordinates for optimization at the DFT level using the B3LYP functional and the 6-31G* basis sets using the program product [28]. The vibrational frequencies were computed for optimized intermediate structures and checked to present no imaginary vibrational frequency to ensure that they were local minima points on potential energy profile [29]. The calculation of local reactivity descriptors was implemented according to [20,23–25,30].

General procedure for the synthesis of 5-acyl-1-(2-nitrobenzoyl)-3-R^1-4-R^2-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-ones (2a–j). To a stirred solution of appropriate benzodiazepinones **1a–j** (5 mmol) in dry DCE (40–60 mL) containing DIPEA (1.05 mL, 6 mmol) and catalytic amount of DMAP, a solution of freshly prepared *o*-nitrobenzoylchloride (0.8 mL, 6 mmol) in dry DCE (6 mL) was added dropwise at room temperature. The reaction mixture was stirred at room temperature for 24 h. Then, the reaction mixture was diluted with 60 mL DCE and washed with 1*N* HCl, 5% $NaHCO_3$, and water. After drying and removal of the solvent in vacuum, the residues were subjected to purification to give **2a–j**. The solid residues were recrystallized from dichloromethane–diethyl ether mixture. The oily residues were firstly subjected to dry column vacuum chromatography (silicagel) using the benzene-DCE system for gradient elution and then recrystallized from dichloromethane–diethyl ether mixture. The yields, mp, and elemental analysis data are presented in Table 1.

5-Acetyl-1-(2-nitrobenzoyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (2a). IR: *v* CO 1742, 1684, 1663, $_{as}NO_2$ 1533, $_{s}NO_2$ 1357 cm^{-1}; ^{1}H NMR: δ 2.00 (s, 3H, $COCH_3$), 2.36 (dd, 1H, *J* = 3.9, 13.6 Hz, 3-CH_2), 2.56 (dt, 1H, *J* = 7.1, 13.7 Hz, 3-CH_2), 3.35 (dd, 1H, *J* = 6.9, 12.9 Hz, 4-CH_2), 4.87 (dt, 1H, *J* = 5.0, 13.4 Hz, 4-CH_2), 7.27–7.74 (m, 7H, ArH), 8.25 (dd, 1H, *J* = 0.8, 8.3 Hz, H-C3′); ^{13}C NMR: δ 22.59 ($CO\mathit{C}H_3$), 35.23 (C3), 45.04 (C4), 124.25 (CH), 126. 56 (CH), 129.14 (CH), 129.41 (CH), 129.51 (CH), 129.73 (CH), 130.17 (CH), 134.53

(C1′), 134.60 (CH), 135.18 (C9a), 135.81 (C5a), 144.50 (C2′), 167.52 (CO-N1), 170.50 (CO-N5), 170.80 ppm (C2).

5-Acetyl-4-methyl-1-(2-nitrobenzoyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (2b). IR: *v* CO 1743, 1686, 1666, $_{as}NO_2$ 1531, $_{s}NO_2$ 1355 cm^{-1}; ^1H NMR: δ 1.00 (d, 3H, $J = 6.4$ Hz, CH_3-C4), 1.83 (s, 3H, $COCH_3$), 2.07–2.24 (m, 2H, 3-CH_2), 5.00–5.13 (m, 1H, 4-CH), 7.17–7.67 (m, 7H, ArH), 8.13 (dd, 1H, $J = 1.1$, 8.3 Hz, H-C3′); ^{13}C NMR: δ 18.49 (CH_3-C4), 22.57 ($COCH_3$), 42.12 (C3), 51.27 (C4), 123.73 (CH), 125.93 (CH), 128.80 (CH), 128.96 (CH), 129.25 (CH), 129.39 (CH), 130.09 (CH), 133.36 (C9a or C5a), 134.17 (CH), 134.17 (C5a or C9a), 134.86 (C1′), 143.86 (C2′), 167.17 (CO-N1), 169.04 (C2), 170.07 ppm (CO-N5).

5-Acetyl-3-methyl-1-(2-nitrobenzoyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (2c). IR: *v* CO 1738, 1702, 1667, $_{as}NO_2$ 1523, $_{s}NO_2$ 1347 cm^{-1}; ^1H NMR: δ 0.98 (d, 3H, $J = 6.4$ Hz, CH_3-C3), 2.01 (s, 3H, $COCH_3$), 2.61–2.74 (m, 1H, 3-CH), 3.31 (dd, 1H, $J = 6.7$, 12.6 Hz, 4-CH_2), 4.50 (t, 1H, $J = 12.6$ Hz, 4-CH_2), 7.26–7.78 (m, 7H, ArH), 8.27 (dd, 1H, $J = 1.1$, 8.3 Hz, H-C3′); ^{13}C NMR: δ 12.15 (CH_3-C3), 22.63 ($COCH_3$), 37.80 (C3), 52.08 (C4), 124.30 (CH), 126.47 (CH), 128.81 (CH), 129.36 (CH), 129.56 (CH), 129.67 (CH), 130.10 (CH), 134.64 (CH), 134.74 (C1′), 134.81 (C9a or C5a), 136.56 (C5a or C9a), 144.37 (C2′), 167.72 (CO-N1), 170.31 (CO-N5), 173.50 ppm (C2).

5-(2-Nitrobenzoyl)-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carbaldehyde (2d). IR: *v* CO 1724, 1692, 1678, $_{as}NO_2$1526, $_{s}NO_2$ 1346 cm^{-1}; ^1H NMR: δ 2.60 (br, 2H, 3-CH_2), 3.56 (br, 1H, 4-CH_2), 4.46 (br, 1H, 4-CH_2), 7.29–7.80 (m, 7H, ArH), 8.26 (dd, 1H, $J = 1.1$, 8.2 Hz, H-C3′), 8.45 (s, (0.02)1H, COH), 8.48 (s, (0.98)1H, COH); ^{13}C NMR: δ 34.34 (C3), 43.85 (C4), 124.21 (CH), 126.66 (CH), 127.74 (CH), 129.06 (CH), 129.79 (CH), 129.88 (CH), 130.27 (CH), 133.75 (C9a or C5a), 133.92 (C5a or C9a), 134.42 (C1′), 134.63 (CH), 144.56 (C2′), 162.03 (CO-N5), 167.32 (CO-N1), 170.49 ppm (C2).

2-Methyl-5-(2-nitrobenzoyl)-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carbaldehyde (2e). IR: *v* CO 1725, 1704, 1663, $_{as}NO_2$ 1524, $_{s}NO_2$ 1346 cm^{-1}; ^1H NMR: δ 1.17 (d, 3H, $J = 6.4$ Hz, CH_3-C4), 2.35–2.50 (m, 2H, 3-CH_2), 4.99 (pd, 1H, $J = 5.9$, 12.0 Hz, 4-CH), 7.26–7.81 (m, 7H, ArH), 8.25 (dd, 1H, $J = 0.8$, 8.3 Hz, H-C3′), 8.36 (s, (0.96)1H, COH), 8.44 (s, (0.04)1H, COH); ^{13}C NMR: δ 18.75 (CH_3-C4), 41.93 (C3), 50.97 (C4), 124.20 (CH), 126.80 (CH), 129.35 (CH), 129.50 (2CH), 129.74 (CH), 129.93 (CH), 132.12 (C9a or C5a), 134.56 (C1′), 134.64 (CH), 135.07 (C5a or C9a), 144.41 (C2′), 161.33 (CO-N5), 167.49 (CO-N1), 170.10 ppm (C2).

3-Methyl-5-(2-nitrobenzoyl)-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carbaldehyde (2f). IR: *v* CO 1737, 1694, 1671, $_{as}NO_2$ 1530, $_{s}NO_2$ 1346 cm^{-1}; ^1H NMR: δ 1.01 (d, 3H, $J = 6.5$ Hz, CH_3-C3), 2.88 (tt, 1H, $J = 6.4$, 12.8 Hz, 3-CH), 3.43 (dd, 1H, $J = 5.8$, 12.7 Hz, 4-CH_2), 4.22 (t, 1H, $J = 13.1$ Hz, 4-CH_2), 7.27–7.78 (m, 7H, ArH), 8.26 (d, 1H, $J = 8.2$ Hz, H-C3′), 8.41 (s, (0.05)1H, COH), 8.45 (s, (0.95) 1H, COH); ^{13}C NMR: δ 12.33 (CH_3-C3), 36.77 (C3), 50.65 (C4), 124.24 (CH), 126.58 (CH), 127.43 (CH), 129.02 (CH), 129.69 (CH), 129.86 (CH), 130.16 (CH), 133.71 (C9a or C5a), 134.47 (C1′), 134.63 (CH), 134.73 (C5a or C9a), 144.41 (C2′), 161.77 (CO-N5), 167.50 (CO-N1), 173.17 ppm (C2).

1-(2-Nitrobenzoyl)-5-(trifluoroacetyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (2g). IR: *v* CO 1731, 1708, 1699, $_{as}NO_2$ 1530, $_{s}NO_2$ 1348 cm^{-1}; ^1H NMR: δ, 2.44 (ddd, 1H, $J = 1.2$, 5.1, 13.6 Hz, 3-CH_2), 2.64 (dt, 1H, $J = 7.2$, 13.6 Hz, 3-CH_2), 3.55 (dd, 1H, $J = 7.1$, 13.1 Hz, 4-CH_2), 4.80 (dt, 1H, $J = 5.1$, 13.4 Hz, 4-CH_2), 7.25–7.81 (m, 7H, ArH), 8.27 (dd, 1H, $J = 1.1$, 8.3 Hz, H-C3′); ^{13}C NMR: δ 34.65 (3C), 47.11 (C4), 115.91 ($^1J_{C\text{-}F} = 288.3$ Hz, CF_3), 124.23 (CH), 126.64 (CH), 128.92 (CH), 129.56 (CH), 129.83 (2CH), 130.53 (CH), 132.02 (C9a or C5a), 134.43 (C1′), 134.74 (CH), 135.02 (C5a or C9a), 144.40 (C2′), 156.17 ($^2J_{C\text{-}F} = 36.3$ Hz, CO-N5), 166.64 (CO-N1), 169.80 ppm (C2).

4-Methyl-1-(2-nitrobenzoyl)-5-(trifluoroacetyl)-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (2h). IR: *v* CO 1744, 1698, $_{as}NO_2$1524, $_{s}NO_2$ 1346 cm^{-1}; ^1H NMR: δ 1.20 (d, 3H, $J = 6.4$ Hz, CH_3-C4), 2.34 (ddd, 2H, $J = 8.8$, 13.4, 25.6 Hz, 3-CH_2), 5.06–5.18 (m, 1H, 4-CH), 7.24–7.83 (m, 7H, ArH), 8.27 (dd, 1H, $J = 1.1$, 8.3 Hz, H-C3′); ^{13}C NMR: δ 18.01 (CH_3-C4), 41.98 (C3), 54.24 (C4), 115.93 ($^1J_{C\text{-}F} = 288.7$ Hz, CF_3), 124.22 (CH), 126.64 (CH), 129.34 (CH), 129.43 (CH), 129.76 (CH), 129.94 (C9a or C5a), 130.27 (CH), 130.55 (CH), 134.51 (C1′), 134.73 (CH), 135.30 (C5a or C9a), 144.36 (C2′), 156.17 ($^2J_{C\text{-}F} = 36.3$ Hz, CO-N5), 166.70 (CO-N1), 169.49 ppm (C2).

Ethyl 5-(2-nitrobenzoyl)-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carboxylate (2i). IR: *v* CO 1723, 1703, 1663, $_{as}NO_2$ 1529, $_{s}NO_2$ 1347 cm^{-1}; ^1H NMR: δ 1.23 (br, 3H, OCH_2CH_3), 2.39 (br, 1H, 3-CH_2), 2.56 (br, 1H, 3-CH_2), 3.55 (br, 1H, 4-CH_2), 4.23 (br q, 2H, $J = 6.4$ Hz, OCH_2CH_3), 4.54 (br, 1H, 4-CH_2), 7.28–7.75 (m, 7H, ArH), 8.25 (dd, 1H, $J = 0.7$, 8.2 Hz, H-C3′); ^{13}C NMR: δ 14.50 (OCH_2CH_3), 35.41 (C3), 46.93 (C4), 62.32 (OCH_2CH_3), 124.20 (CH), 126.60 (CH), 128.21 (CH), 128.84 (CH), 129.47 (CH), 129.54 (2CH), 129.54 (C9a or C5a), 134.43 (CH), 134.66 (C1′), 134.86 (C5a or C9a), 144.59 (C2′), 155.13 (CO-N5), 167.02 (CO-N1), 171.18 ppm (C2).

Ethyl 2-methyl-5-(2-nitrobenzoyl)-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carboxylate (2j). IR: *v* CO 1731, 1703, $_{as}NO_2$ 1527, $_{s}NO_2$ 1347 cm^{-1}; ^1H NMR: δ 1.14 (d, 3H, $J = 6.4$ Hz, CH_3-C4), 1.18 (br t, 3H, OCH_2CH_3), 2.16–2.35 (m, 2H, 3-CH_2), 4.19 (br q, 2H, $J = 6.8$ Hz, OCH_2CH_3), 4.90 (br, 1H, 4-CH), 7.26–7.75 (m, 7H, ArH), 8.24 (d, 1H, $J = 8.3$ Hz, H-C3′); ^{13}C NMR: δ 14.52 (OCH_2CH_3), 19.10 (CH_3-C4), 42.58 (C3), 53.55 (C4), 62.10 (OCH_2CH_3), 124.20 (CH), 126.50 (CH), 128.41 (CH), 128.61 (CH), 129.17 (CH), 129.51 (CH), 129.51 (C9a or C5a), 130.79 (CH), 132.66 (C5a or C9a), 134.46 (CH), 134.90 (C1′), 144.51 (C2′), 154.54 (CO-N5), 167.20 (CO-N1), 170.76 ppm (C2).

General procedure for the synthesis of 5-acyl-3-R^1-4-R^2-6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-ones (3a, 3b, 3d, 3e, and 3g–i).

i. In a hydrogenation apparatus equipped with a magnetic stirrer, the Re/Ni catalyst was added to a solution of appropriate nitrobenzoylamides **2a–e** (2.5 mmol) in methanol (150–200 mL), and the mixture was hydrogenated at room temperature and atmospheric pressure. After the reduction was complete, as observed by TLC monitoring, the catalyst was filtered off. The filtrate was concentrated to dryness in vacuum. In case when the residue obtained is a solid, it was crystallized from methyl *tert*-butyl ether. The oily residues were subjected to dry column vacuum chromatography (silicagel) using the DCE-ethyl acetate system for gradient elution. Thus, compounds **3a**, **3b**, **3d**, and **3e** were obtained.

ii. An analogous catalytic hydrogenation procedure was performed for appropriate nitrobenzoylamides **2a–h**

(2.5 mmol) using 10% palladium on carbon catalyst (10% of the weight of the starting **2a–h**). Compounds **3a**, **3b**, **3d**, **3e**, and **3h** were obtained.

iii. To a solution of appropriate nitrobenzoylamides **2c**, **2f–j** (2.5 mmol) in glacial acetic acid (20–30 mL), Zn dust (1.63 g, 25 mmol) was added, and the reaction mixture was stirred at room temperature for 2–3 h. After the reduction was complete, as observed by TLC monitoring, the reaction mixture was filtered. The filtrate was concentrated to dryness in vacuum. The residue was dissolved in dichloromethane, and the solution was washed with 5% $NaHCO_3$ and water, dried, and evaporated to dryness in vacuum. Compounds **3g–j** were worked-up analogously to procedure i.

The reduction of compounds **2c** and **2f** in all cases (i, ii, and iii) did not occur. Unchanged **2c** and **2f** (61%, ii and 57%, iii, respectively) and benzodiazepinones **1c** and **1f** (19%, ii and 26%, iii, respectively) were isolated after chromatographic separation of the reaction mixture. Mixed samples with authentic compounds did not show depression of the melting point.

The yields, mp, and elemental analysis data of compounds **3a**, **3b**, **3d**, **3e**, and **3g-j** are presented in Table 1.

5-Acetyl-6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-one (3a). IR: *v* CO 1694, 1663, CN 1610 cm^{-1}; ^1H NMR: δ 1.85 (s, 3H, $COCH_3$), 2.74 (dt, 1H, *J* = 6.5, 13.6 Hz, 3-CH_2), 2.99 (dd, 1H, *J* = 4.5, 13.9 Hz, 3-CH_2), 3.47 (dd, 1H, *J* = 6.4, 12.7 Hz, 4-CH_2), 4.92 (dt, 1H, *J* = 5.2, 13.2 Hz, 4-CH_2), 7.32–7.81 (m, 7H, ArH), 8.28 (d, 1H, *J* = 7.8 Hz, H-C6′); ^{13}C NMR: δ 22.77 ($CO\mathit{C}H_3$), 34.04 (C3), 47.53 (C4), 120.92 (C1′), 127.14 (CH), 127.18 (CH), 127.25 (CH), 129.09 (CH), 129.11 (CH), 129.15 (CH), 130.08 (CH), 133.99 (C9a), 134.97 (CH), 135.43 (C5a), 146.68 (C2′), 153.91 (C2), 160.68 (CO-N1), 170.42 ppm (CO-N5).

5-Acetyl-6-methyl-6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-one (3b). IR: *v* CO 1690, 1655, CN 1610 cm^{-1}; ^1H NMR: δ 1.12 (d, 3H, *J* = 6.3 Hz, CH_3-C4), 1.72 (s, 3H, $COCH_3$), 2.31 (dd, 1H, *J* = 12.5, 13.6 Hz, 3-CH_2), 2.89 (dd, 1H, *J* = 5.0, 13.7 Hz, 3-CH_2), 5.11–5.23 (m, 1H, 4-CH), 7.19–7.73 (m, 7H, ArH), 8.22 (dd, 1H, *J* = 1.1, 8.0 Hz, H-C6′); ^{13}C NMR: δ 18.49 ($\mathit{C}H_3$-C4), 22.96 ($CO\mathit{C}H_3$), 41.32 (C3), 54.00 (C4), 120.83 (C1′), 127.10 (2CH), 127.20 (CH), 128.95 (CH), 129.06 (CH), 129.62 (CH), 130.37 (CH), 133.47 (C9a or C5a), 134.23 (C5a or C9a), 134.88 (CH), 146.87 (C2′), 153.50 (C2), 160.73 (CO-N1), 169.68 ppm (CO-N5).

13-Oxo-7,13-dihydroquinazolino[3,2-*a*][1,5]benzodiazepine-5(6*H*)-carbaldehyde (3d). IR: *v* CO 1699, 1668, CN 1610 cm^{-1}; ^1H NMR: δ 2.95 (dt, 1H, *J* = 5.8, 13.9 Hz, 3-CH_2), 3.10–3.18 (m, 1H, 3-CH_2), 3.58–3.66 (m, 1H, 4-CH_2), 4.68 (dt, 1H, *J* = 4.9, 13.4 Hz, 4-CH_2), 7.28–7.84 (m, 7H, ArH), 8.31 (ddd, 1H, *J* = 0.5, 1.1, 8.0 Hz, H-C6′), 8.32 (br q, 1H, *J* = 0.9 Hz, COH); ^{13}C NMR: δ 33.29 (C3), 46.48 (C4), 120.98(C1′), 127.06 (CH), 127.36 (CH), 127.45 (CH), 128.10 (CH), 128.87 (CH), 129.43 (CH), 130.28 (CH), 133.09 (C9a or C5a), 133.46 (C5a or C9a), 135.12 (CH), 146.53 (C2′), 153.63 (C2), 160.79 (CO-N1), 162.19 ppm (CO-N5).

6-Methyl-13-oxo-7,13-dihydroquinazolino[3,2-*a*][1,5]benzodiazepine-5(6*H*)-carbaldehyde (3e). IR: *v* CO 1679, 1668, CN 1610 cm^{-1}; ^1H NMR: δ 1.25 (d, (0.95)3H, *J* = 6.4 Hz, CH_3-C4), 1.33 (d, (0.05)3H, *J* = 6.4 Hz, CH_3-C4), 2.61 (dd, 1H, *J* = 12.6, 13.8 Hz, 3-CH_2), 3.04 (ddd, 1H, *J* = 1.0, 4.6, 13.7 Hz, 3-CH_2), 5.07 (tt, 1H, *J* = 6.0, 12.0 Hz, 4-CH), 7.24–7.82 (m, 7H, ArH), 8.21 (br t, 1H, COH), 8.32 (dd, 1H, *J* = 0.9, 7.9 Hz, H-C6′); ^{13}C NMR: δ 18.50 ($\mathit{C}H_3$-C4), 41.00 (C3), 53.49 (C4), 120.97 (C1′), 127.21 (CH), 127.27 (2CH), 129.01 (CH), 129.21 (CH), 129.39 (CH), 129.89 (CH), 131.88 (C9a or C5a), 133.87 (C5a or C9a), 134.98 (CH), 146.80 (C2′), 153.05 (C2), 160.80 (CO-N1), 161.49 ppm (CO-N5).

5-(Trifluoroacetyl)-6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-one (3g). IR: *v* CO 1698, CN 1614 cm^{-1}; ^1H NMR: δ 2.82 (dt, 1H, *J* = 6.7, 13.5 Hz, 3-CH_2), 3.08 (dd, 1H, *J* = 5.0, 14.0 Hz, 3-CH_2), 3.66 (dd, 1H, *J* = 6.6, 12.7 Hz, 4-CH_2), 4.89 (dt, 1H, *J* = 5.2, 13.0 Hz, 4-CH_2), 7.36–7.84 (m, 7H, ArH), 8.29 (ddd, 1H, *J* = 0.5, 1.5, 8.0 Hz, H-C6′); ^{13}C NMR: δ 33.42 (C3), 49.34 (C4), 115.94 ($^1J_{C\text{-}F}$ = 288.5 Hz, CF_3), 120.95 (C1′), 127.29 (CH), 127.36 (2CH), 128.87 (CH), 128.96 (CH), 129.65 (CH), 130.20 (CH), 131.61 (C9a or C5a), 134.10 (C5a or C9a), 134.94 (CH), 146.73 (C2′), 152.55(C2), 156.83 ($^2J_{C\text{-}F}$ = 37.0 Hz, CO-N5), 160.14 ppm (C2).

6-Methyl-5-(trifluoroacetyl)-6,7-dihydroquinazolino[3,2-*a*][1,5]benzodiazepin-13(5*H*)-one (3h). IR: *v* CO 1690, CN 1612 cm^{-1}; ^1H NMR: δ 1.29 (d, 3H, *J* = 6.4 Hz, CH_3-C4), 2.46 (dd, 1H, *J* = 12.4, 13.8 Hz, 3-CH_2), 3.02 (dd, 1H, *J* = 5.0, 13.8 Hz, 3-CH_2), 5.13–5.25 (m, 1H, 4-CH), 7.32–7.82 (m, 7H, ArH), 8.31 (dd, 1H, *J* = 1.0, 8.0 Hz, H-C6′); ^{13}C NMR: δ 17.77 ($\mathit{C}H_3$-C4), 40.84 (C3), 56.54 (C4), 115.79 ($^1J_{C\text{-}F}$ = 288.7 Hz, CF_3), 120.97 (C1′), 127.33 (CH), 127.40 (2CH), 128.92 (CH), 129.22 (CH), 129.62 (C9a or C5a), 130.25 (2CH), 134.40 (C5a or C9a), 134.98 (CH), 146.78 (C2′), 152.46 (C2), 156.23 ($^2J_{C\text{-}F}$ = 36.4 Hz, CO-N5), 160.17 ppm (C2).

Ethyl 13-oxo-7,13-dihydroquinazolino[3,2-*a*][1,5]benzodiazepine-5(6*H*)-carboxylate (3i). IR: *v* CO 1705, 1663, CN 1612 cm^{-1}; ^1H NMR: δ 1.13 (br s, (0.7)3H, $OCH_2C\mathit{H}_3$), 1.91 (br s, (0.3)3H, $OCH_2C\mathit{H}_3$), 2.79 (dt, 1H, *J* = 6.4, 13.7 Hz, 3-CH_2), 3.01 (dd, 1H, *J* = 4.3, 13.9 Hz, 3-CH_2), 3.69 (dd, 1H, *J* = 6.2, 11.8 Hz, 4-CH_2), 4.00 (br, (0.3)2H, $OC\mathit{H}_2CH_3$), 4.15 (qd, 1H, *J* = 7.2, 10.3 Hz, 4-CH_2), 4.62 (br, (0.7)2H, $OC\mathit{H}_2CH_3$), 7.40–7.83 (m, 7H, ArH), 8.33 (dd, 1H, *J* = 1.5, 8.0 Hz, H-C6′); ^{13}C NMR: δ 14.32 ($OCH_2\mathit{C}H_3$), 34.34 (C3), 49.48 (C4), 62.13 ($O\mathit{C}H_2CH_3$), 121.20 (C1′), 127.03 (CH), 127.10 (CH), 127.30 (CH), 127.82 (CH), 128.41 (CH), 129.46 (2CH), 133.26 (C9a or C5a), 134.34 (C5a or C9a), 134.72 (CH), 146.94 (C2′), 154.16 (C2), 155.19 (CO-N5), 160.63 ppm (CO-N1).

Ethyl 6-methyl-13-oxo-7,13-dihydroquinazolino[3,2-*a*][1,5]benzodiazepine-5(6*H*)-carboxylate (3j). IR: *v* CO 1697, CN 1610 cm^{-1}; ^1H NMR: δ 1.05 (br t, 3H, $OCH_2C\mathit{H}_3$), 1.22 (d, 3H, *J* = 6.3 Hz, CH_3-C4), 2.41 (t, 1H, *J* = 13.0 Hz, 3-CH_2), 2.95 (dd, 1H, *J* = 4.9, 13.7 Hz, 3-CH_2), 3.87–4.13 (br m, 2H, $OC\mathit{H}_2CH_3$), 4.95 (tt, 1H, *J* = 6.3, 12.4 Hz, 4-CH), 7.02–7.79 (m, 7H, ArH), 8.29 (dd, 1H, *J* = 1.4, 8.0 Hz, H-C6′); ^{13}C NMR: δ 14.25 ($OCH_2\mathit{C}H_3$), 18.67 ($\mathit{C}H_3$-C4), 41.55 (C3), 56.03 (C4), 61.83 ($O\mathit{C}H_2CH_3$), 121.20 (C1′), 126.92 (CH), 127.10 (CH), 127.17 (CH), 127.88 (CH), 128.22 (CH), 128.99 (CH), 130.77 (CH), 132.36 (C9a or C5a), 133.60 (C5a or C9a), 134.63 (CH), 146.89 (C2′), 153.84 (C2), 154.50 (CO-N5), 160.57 ppm (CO-N1).

4-Methyl-5-trifluoroacetyl-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one (1h). This compound was obtained according to procedure [17] from 4-methyl-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one [14] (3.6 g, 20 mmol) and trifluoroacetic acid anhydride (4.2 mL, 30 mmol) in dry dichloromethane (50 mL). Isolation and crystallization from ethyl acetate–diethyl ether mixture gave 3.9 g (72%) of **1h**; mp: 195–198°C; IR: *v* CO 1675, 1698, NH 3170 cm^{-1}; ^1H NMR: δ

1.27 (d, 3H, $J = 6.4$ Hz, CH_3-C4), 2.33–2.51 (m, 2H, 3-CH_2), 5.21–5.33 (m, 1H, 4-CH), 7.18–7.50 (m, 4H, ArH), 8.69 (s, 1H, NH); ^{13}C NMR: δ 18.41 (CH_3-C4), 39.86 (C3), 56.69 (C4), 115.84 ($^1J_{C\text{-}F} = 288.9$ Hz, CF_3), 123.01 (C9), 126.20 (C7), 128.31 (C5a), 130.59 (C6), 130.75 (C8), 136.57 (C9a), 156.30 ($^2J_{C\text{-}F} = 36.3$ Hz, CO-N5), 172.19 ppm (C2). *Anal.* Calcd. for $C_{12}H_{11}F_3N_2O_2$: C, 52.94; H, 4.07; N, 10.29. Found: C, 52.77; H, 4.21; N, 10.51.

Ethyl 4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carboxylate (1i). To a stirred solution of 1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one [14] (3.2 g, 20 mmol) and triethylamine (2.8 mL, 20 mmol) in dry THF (100 mL), a solution of ethyl chloroformate (2.1 mL, 22 mmol) in dry THF (10 mL) was added dropwise at room temperature. The reaction mixture was refluxed for 8 h with stirring. After quenching, the formed precipitate was filtered off and the filtrate concentrated to dryness. The residue was dissolved in chloroform, the solution was washed with 1*N* HCl, 5% $NaHCO_3$, and water, and dried, and the solvent was removed in vacuum. The solid residue was crystallized from ethyl acetate to give 3.1 g (69%) of **1i**; mp: 120–122°C; IR: *v* CO 1704, 1657, NH 3203 cm^{-1}; ^{1}H NMR: δ 1.18 (br, 3H, OCH_2CH_3), 2.63 (t, 2H, $J = 6.7$ Hz, 3-CH_2), 4.12 (br, 4H, 4-CH_2 + OCH_2CH_3), 7.05–7.29 (m, 4H, ArH), 8.38 (br, 1H, NH). ^{13}C NMR: δ 14.43 (OCH_2CH_3), 33.59 (C3), 48.12 (C4), 62.11 (OCH_2CH_3), 122.28 (C9), 125.50 (C7), 127.97 (C8), 129.97 (C6), 132.58 (C5a), 134.75 (C9a), 154.99 (CO-N5), 173.11 ppm (C2). *Anal.* Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.24; H, 6.17; N, 11.81.

Ethyl 2-methyl-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-1-carboxylate (1j). Compound **1j** was obtained according to the procedure described for **1i** from 4-methyl-1,3,4,5-tetrahydro-2*H*-1,5-benzodiazepin-2-one [14] (3.6 g, 20 mmol). Crystallization from ethyl acetate–diethyl ether mixture gave 3.35 g (71%) of **1j**; mp: 193–196°C; IR: *v* CO 1703, 1667, NH 3176 cm^{-1}; ^{1}H NMR: δ 1.09 (br, (0.7)3H, OCH_2CH_3), 1.21 (d, 3H, $J = 6.3$ Hz, CH_3-C4), 1.31 (br, (0.3)3H, OCH_2CH_3), 2.28–2.44 (m, 2H, 3-CH_2), 3.98 (br, (0.3)2H, OCH_2CH_3), 4.14 (br m, (0.7)2H, OCH_2CH_3), 5.03 (br, 1H, 4-CH), 7.08–7.34 (m, 4H, ArH), 8.49 (br, (0.3)1H, NH), 8.72 (br, (0.7)1H, NH); ^{13}C NMR: δ 14.14 and 14.43 (OCH_2CH_3), 19.56 and 20.12 (CH_3-C4), 40.42 (C3), 56.00 (C4), 61.74 and 62.01 (OCH_2CH_3), 122.61 (C9), 125.65 and 125.99 (C7), 128.34 (C8), 130.92 (C5a), 131.40 (C6), 135.82 (C9a), 154.51 (CO-N5), 173.16 ppm (C2). *Anal.* Calcd. for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 63.06; H, 6.49; N, 11.02.

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