Synthesis of 1,5-Benzodiazepine Derivatives Containing 1,2,3-Triazole Moiety via 1,3-Dipolar Cycloaddition Reaction

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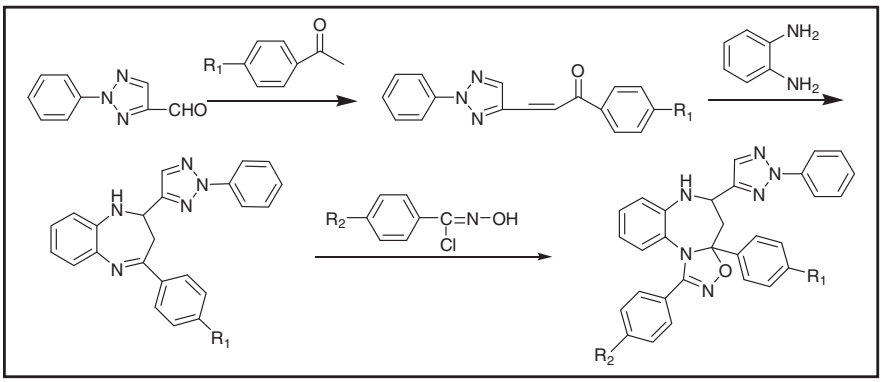

A series of 1,5-benzodiazepine derivatives were synthesized by the reaction of 1,5-benzodiazepine containing 1,2,3-triazole moiety with benzohydroximinoyl chlorides at room temperature. The structural identities of these novel compounds were confirmed on the basis of IR, ^{1}H NMR, mass spectral and elemental analysis data, and by X-ray crystallographic analysis of a typical example of the new class of 1,5-benzodiazepine analogs.

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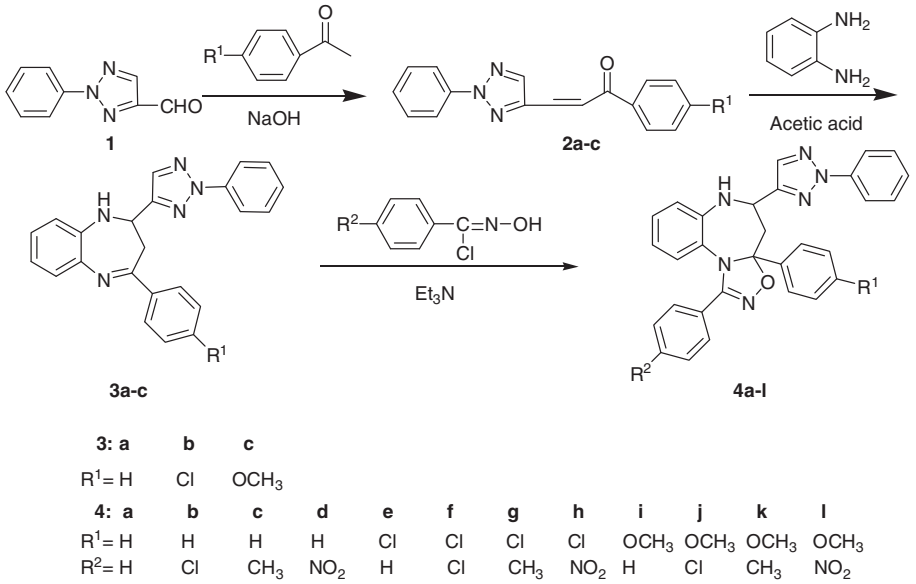
INTRODUCTION

Design and construction of privileged structures are important strategy in medicinal chemistry. The 1,5-benzodiazepine is commonly used as anxiolytic and anticonvulsive drugs, and its derivatives have attracted considerable attention to synthetic and medicinal chemists because of their broad spectrum of biological activities such as allosteric inhibitor [1], antioxidants [2], anti-inflammatory [3], and native gamma-aminobutyric acid ($GABA_A$) receptor [4] activities. In recent years, 1,5-benzodiazepines also serve as key intermediates for the synthesis of fused ring compounds such as triazolo-, oxadiazolo-, oxazino- or furano-benzodiazepines [5–7], and the resulting tricyclic 1,5-benzodiazepine derivatives have shown clinical interest as drugs [8–10]. For example, clozapine, olanzapine, and quetiapine are used to treat schizophrenia, and clonazepam, diazepam, lorazepam, nitrazepam, and oxazepam are used as antianxiety drugs. In addition, the 1,2,3-triazole constitute an important class of biologically active compounds showing remarkable therapeutic and pharmacological properties such as antibacterial [11], anti-HIV [12], antimicrobial [13] agents, and β_3-adrenergic receptor agonist [14] activities. Meanwhile, 1,2,4-oxadiazole is also a major five-membered heterocyclic ring, which serves as the core component of many substances that display a wide range of biological activities including apoptosis inducers and potential anticancer [15], anti-HIV [16], and selective cathepsin inhibitors [17] activities. Taking into consideration the important biological activity of azole derivatives as well as the combination principles for drug design, we herein report the synthesis of new 1,5-benzodiazepine derivatives containing 1,2,3-triazole and 1,2,4-oxadiazole moieties via 1,3-dipolar cycloaddition reaction. The synthetic route is shown in Scheme 1.

RESULT AND DISCUSSION

A series of novel benzodiazepine derivatives containing a 1,2,3-triazole moiety was synthesized using 2-phenyl-4-formyl-2*H*-1,2,3-triazole **1** as a starting material. Then, intermediate compounds α,β-unsaturated ketone **2a–c** via the Claisen–Schmidt condensation reaction between 2-phenyl-4-formyl-2*H*-1,2,3-triazole **1** and 1-arylethanones. After that, the benzodiazepine derivatives **3a–c** were synthesized by reacting equimolar quantities of α,β-unsaturated ketone **2a–c** with benzene-1,2-diamine in ethanol using acetic acid as catalyst. Finally, the compounds **3a–c** underwent 1,3-dipolar cycloadditions with various benzohydroximinoyl chlorides in the presence of Et_3N leading to the formation of cycloadducts **4a–l**. Various techniques, including IR, ^{1}H NMR, mass spectral and elemental analysis,

Scheme 1. Synthesis route for titled compounds.



3:	a	b	c
R^1=	H	Cl	OCH_3

4:	a	b	c	d	e	f	g	h	i	j	k	l
R^1=	H	H	H	H	Cl	Cl	Cl	Cl	OCH_3	OCH_3	OCH_3	OCH_3
R^2=	H	Cl	CH_3	NO_2	H	Cl	CH_3	NO_2	H	Cl	CH_3	NO_2

and X-ray crystallographic, were utilized to confirm the structural identities of the final products.

In IR spectra, the synthesized final compounds show a strong stretching vibration at 1607–1581 cm^{-1} because of the presence of C═N. For the titled compounds, the presence of the multiplet at δ 8.18–6.55 ppm is attributed to the Ar—H, N—H, and triazol-H. Also, the ^1H NMR spectrum revealed a distinct doubled doublet at δ 4.41–4.30 ppm and multiplet at δ 3.02–2.83 ppm for **4a–l**, which could be attributed to the characteristic peak of dihydrobenzodiazepine moiety as ABX pattern. In MS spectra, molecular ions peaks of all target compounds were attained from EI to MS.

We propose a conceivable intramolecular 1,3-diploar cycloaddition mechanism. In the presence of Et_3N, the nitrile oxide generated *in situ* and C═N double bond in the benzodiazepine ring forms a cyclic transition state, and the σ-bonds of C—N and C—O were formed simultaneously to obtain the 1,2,4-oxadiazole ring, the central diazepine ring of the cycloadduct adopts a boat-like conformation.

To establish the exact structure of the cycloadducts, compounds **4b** was crystallized, and their atomic coordinates was obtained by X-ray analysis. The crystal data and structure refinement are shown in Table 1. Selected bond lengths and angles are listed in Table 2. CCDC–814232 for **4b** contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC) via e-mail: deposit@ccdc.cam.ac.uk.

The crystal structure of the compound **4b** is shown in Fig. 1, and a perspective view of the crystal packing in the unit cell is tabulated in Fig. 2. The oxadiazoline ring, resulting from the 1,3-cycloaddition reaction, adopts an envelope conformation, only with maximum deviation of −0.1752 Å for atom C(11) for the plane defined by N(1)—C(11)—O(1)—N(2)—C(18), which is nearly coplanar

Table 1

Crystal data and structure refinement for compound **4b**.

Empirical formula	$C_{30}H_{23}ClN_6O$	γ (°)	90
Formula weight	518.99	V (Å^3)	2662.4(8)
Temperature	296 K	Z	4
Wavelength	0.71073 A	*D*c (mg/m^3)	1.295
Crystal system	Monoclinic	F(000)	1080
Space group	*P*21/n	θ range (°)	2.2–27.6
a, Å	10.1738(18)	μ(mm^{-1})	0.178
b, Å	18.785(3)	Reflections collected	23,934
c, Å	14.190(3)	Data/restraints/ parameters	6166/0/347
α (°)	90	Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0498$, $wR_2 = 0.1582$
β (°)	100.969(4)	*R* indices (all data)	$R_1 = 0.0857$, $wR_2 = 0.1364$

Table 2

Selected bond lengths (Å) and angles (°) of compound **4b**.

N(2)—C(18)	1.286(3)	C(18)—N(2)—O(1)	106.51(14)
N(2)—O(1)	1.431(2)	N(2)—O(1)—C(11)	105.48(12)
N(1)—C(11)	1.467(2)	O(1)—C(11)—N(1)	101.64(13)
O(1)—C(11)	1.456(2)	C(18)—N(1)—C(11)	103.31(13)
N(4)—C(7)	1.330(3)	C(12)—N(3)—C(9)	115.97(16)
N(6)—C(8)	1.324(2)	C(13)—N(1)—C(11)	121.57(13)
N(3)—C(9)	1.471(3)	N(4)—N(5)—N(6)	115.20(15)
C(9)—C(10)	1.529(3)	C(9)—C(10)—C(11)	112.03(16)

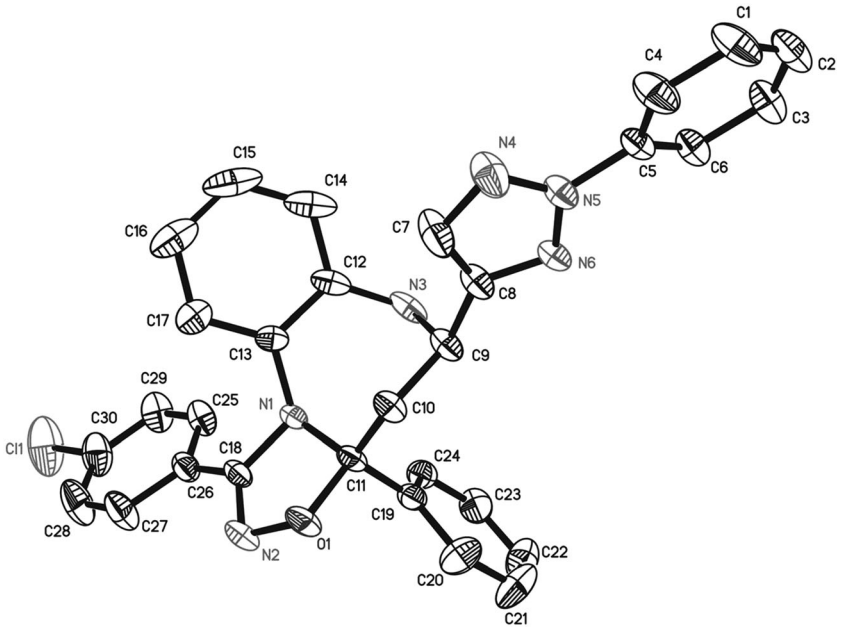


Figure 1. Molecular structure of **4b**.

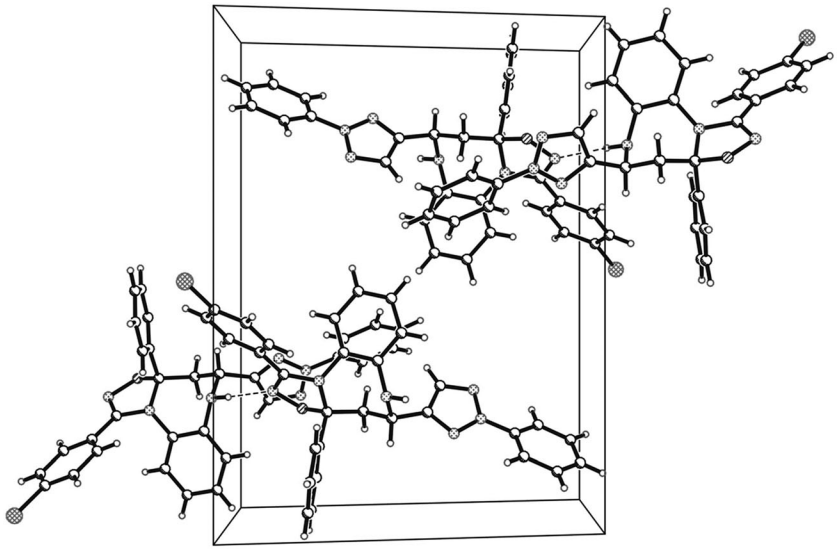


Figure 2. Packing of molecules in a unit cell of **4b**.

due to existing a mean deviation of 0.1160 Å. The seven-membered diazepine ring as the center is characterized by the endocyclic torsion angles (enumerated clockwise and starting with N(3)—C(9)—C(10)—C(11)): 46.6(2)°, −72.5(2)°, −2.8(2)°, 55.9(2)°, −3.9(3)°, −74.3(2)°, 45.3(2)°. N(1), C(11), C(9), and N(3) are almost coplanar, whereas C(10), C(12), and C(13) are below the plane. So, the seven-membered ring adopts a boat-like conformation. In addition, the phenyl ring (C(19)—C(24)) forms dihedral angles of 75.8° and 81.5° with the oxadiazoline ring and the 1,2,3-triazole ring. In crystal structure, there is no classic hydrogen bonds; thus, the structure is supported by weak intermolecular hydrogen bond of N—H. . .N as N(3)—H (13). . .N(2) (Fig. 2) with symmetry code $1/2+x$, $3/2-y$, $1/2+z$.

CONCLUSION

In summary, we have synthesized a series of 1,5-benzodiazepine derivatives **4a–l** bearing 1,2,3-triazole moiety via 1,3-dipolar cycloaddition reaction. The structural identities of these compounds were confirmed by X-ray analysis of compound **4b** as typical examples of the new 1,5-benzodiazepine analog class.

EXPERIMENTAL

Reactions were monitored by TLC. Melting points were determined by a Mettler FP-5 melting point apparatus and were uncorrected. Elemental analyses were conducted on a Perkin-Elmer 2400 elemental analyzer. The IR data was recorded on potassium bromide pellets by a Bruker Equinox 55 FTIR spectrophotometer. The ^{1}H NMR data was recorded on a Bruker NMR spectrophotometer (400 MHz) using TMS as an internal reference and $CDCl_3$ as solvent. Multiplicities are indicated as the following: s, singlet; m, multiplet; dd, doubled doublet. Coupling constants (J values) where noted are quoted in Hertz. Mass spectra were preformed on an Agilent 5975 apparatus (EI, 70 eV). X-ray diffraction data were collected on a Bruker Smart Apex Duo diffractometer. Compounds **1** [18] and **2** [19] were synthesized according to the reported literature.

General procedure for the synthesis of 3a–c. The chalcone **2** (10 mmol) and benzene-1,2-diamine (12.5 mmol) were dissolved in anhydrous ethanol (30 mL) and dry benzene (10 mL). The reaction mixture was heated under reflux for 5 h in the presence of acetic acid (1.0 mL) under stirring. After reaction, the mixture was evaporated off, and the residue was purified by silica gel column chromatography with ethylacetate: petroleum ether (V:V = 1:8) as eluent.

2-(2-Phenyl-1,2,3-triazol-4-yl)-4-phenyl-1,5-benzodiazepine (3a). Yellow solid, yield 67%; mp 178–179°C; ^{1}H NMR: δ 8.03–6.84 (m, 16H, Ar—H, N═C—H, and N—H), 5.52–5.49 (dd, 1H, H_{2x}, J_{ax} = 4.3 Hz, J_{bx} = 8.4 Hz), 3.35–3.30 (dd, 1H, H_{3a}, J_{ax} = 4.3 Hz, J_{ab} = 13.2 Hz), 3.18–3.13 (dd, 1H, H_{3b}, J_{bx} = 8.4 Hz, J_{ab} = 13.2 Hz) ppm; IR (KBr): ν 3389, 2993, 2785, 1644 cm^{-1}; MS: *m/z* 365 (M^+, 17); *Anal*. Calcd for $C_{23}H_{19}N_5$: C, 75.59; H, 5.24; N, 19.16; Found: C, 75.55; H, 5.28; N, 19.18.

4-(4-Chlorophenyl)-2-(2-phenyl-1,2,3-triazol-4-yl)-1,5-benzodiazepine (3b). Yellow solid, yield 65%; mp 192–193°C; ^{1}H NMR: δ 8.00–6.86 (m,15H, Ar—H, N═C—H, and N—H), 5.55–5.52 (dd, 1H, H_{2x}, J_{ax} = 4.6 Hz, J_{bx} = 8.6 Hz), 3.37–3.32 (dd, 1H, H_{3a}, J_{ax} = 4.6 Hz, J_{ab} = 13.2 Hz), 3.20–3.14 (dd, 1H, H_{3b}, J_{bx} = 8.6 Hz, J_{ab} = 13.2 Hz) ppm; IR (KBr): ν 3418, 3052, 2893, 1612 cm^{-1}; MS: *m/z* 402 [(M^++2), 7], 400 (M^+, 21); *Anal*. Calcd for $C_{23}H_{18}ClN_5$: C, 69.08; H, 4.54; N, 17.51; Found: C, 69.02; H, 4.56; N, 17.52.

4-(4-Methoxyphenyl)-2-(2-phenyl-1,2,3-triazol-4-yl)-1,5-benzodiazepine (3c). Yellow solid, yield 58%; mp 200–201°C; ^{1}H NMR: δ 8.04–6.93 (m, 15H, Ar—H, N═C—H, and N—H), 5.61–5.58 (dd, 1H, H_{2x}, J_{ax} = 4.8 Hz, J_{bx} = 8.9 Hz), 3.43–3.37 (dd, 1H, H_{3a}, J_{ax} = 4.8 Hz, J_{ab} = 13.2 Hz), 3.23–3.16 (dd, 1H, H_{3b}, J_{bx} = 8.9 Hz, J_{ab} = 13.2 Hz), 3.85 (s, 3H, —OCH_3) ppm; IR (KBr): ν 3432, 3002, 2884, 1627 cm^{-1}; MS: *m/z* 395 (M^+, 41); *Anal.* Calcd for $C_{24}H_{21}N_5O$: C, 72.89; H, 5.35; N, 17.71; Found: C, 72.84; H, 5.37; N, 17.67.

General procedure for the synthesis of 4a–l. The reaction mixture of compounds **3** (1.0 mmol) and benzohydroximinoyl chlorides (1.5 mmol) were stirred in CH_2Cl_2 (20 mL), and the solution of Et_3N (0.5 mL) in CH_2Cl_2 (8 mL) was added dropwise under stirring. The mixture was kept under stirring for 2 days at room temperature. The triethylamine hydrochloride was filtered after the completion of the reaction. The solution was evaporated off, and the residue was purified by silica gel column chromatography with ethylacetate: petroleum ether (V:V = 1:8 to 1:10) as eluent.

1,3a-Diphenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo [5,4-d][1,5]benzodiazepine (4a). Yellow solid, yield 35%; mp 184–186°C; ^{1}H NMR: δ 8.03–6.63 (m, 21H, Ar—H, N—H, and N═C—H), 4.35–4.31 (dd, 1H, H_{5x}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz), 2.99–2.86 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3298, 2983, 2890, 1594 cm^{-1}; MS: *m/z* 484 (M^+, 4); *Anal*. Calcd for $C_{30}H_{24}N_6O$: C, 74.36; H, 4.99; N, 17.34; Found: C, 74.33; H, 5.01; N, 17.36.

1-(4-Chlorophenyl)-3a-phenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4b). Yellow solid, yield 31%; mp 219–220°C; ^{1}H NMR: δ 8.02–6.60 (m, 20H, Ar—H, N—H, and N═C—H), 4.35–4.31 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 2.98–2.85 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3250, 2936, 2867, 1584 cm^{-1}; MS: *m/z* 521 [(M^++2), 2], 519 (M^+, 6); *Anal*. Calcd for $C_{30}H_{23}ClN_6O$: C, 69.43; H, 4.47; N, 16.19; Found: C, 69.41; H, 4.48; N, 16.20.

1-(4-Methylphenyl)-3a-phenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4c). Yellow solid, yield 37%; mp 179–180°C; ^{1}H NMR: δ 8.02–6.64 (m, 20H, Ar—H, N—H, and N═C—H), 4.34–4.30 (dd, 1H, H_{5x}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz), 2.98–2.84 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz), 2.34 (s, 3H, —CH_3) ppm; IR (KBr): ν 3290, 2985, 2880, 1602 cm^{-1}; MS: *m/z* 498 (M^+, 4); *Anal*. Calcd for $C_{31}H_{26}N_6O$: C, 74.68; H, 5.26; N, 16.86; Found: C, 74.66; H, 5.27; N, 16.87.

1-(4-Nitrophenyl)-3a-phenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4d). Yellow solid, yield 32%; mp 216–217°C; ^{1}H NMR: δ 8.18–6.55 (m, 20H, Ar—H, N—H, and N═C—H), 4.40–4.36 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 3.01–2.87 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3298, 2983, 2890, 1594 cm^{-1}; MS: *m/z* 529 (M^+, 4); *Anal*. Calcd for $C_{30}H_{23}N_7O_3$: C, 68.04; H, 4.38; N, 18.52; Found: C, 68.03; H, 4.40; N, 18.50.

3a-(4-Chlorophenyl)-1-phenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4e). Yellow solid, yield 34%; mp 186–187°C; ^{1}H NMR: δ 8.06–6.68 (m, 20H, Ar—H, N—H, and N═C—H), 4.34–4.30 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 2.98–2.84 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3247, 2980, 2884, 1583 cm^{-1}; MS: *m/z* 521 [(M^++2), 1], 519 (M^+, 3); *Anal*. Calcd for $C_{30}H_{23}ClN_6O$: C, 69.43; H, 4.47; N, 16.19; Found: C, 69.42; H, 4.49; N, 16.22.

1,3a-Bis-(4-chlorophenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4f). Yellow solid, yield 30%; mp 208–210°C; ^{1}H NMR: δ 8.06–6.65 (m, 19H, Ar—H, N—H, and N═C—H), 4.35–4.31 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 2.97–2.83 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3256, 2924, 2855, 1598 cm^{-1}; MS: *m/z* 557 [(M^++4), 1], 555 [(M^++2), 6], 553 (M^+, 9); *Anal*. Calcd for $C_{30}H_{22}Cl_2N_6O$: C, 65.11; H, 4.01; N, 15.19; Found: C, 65.09; H, 4.02; N, 15.21.

3a-(4-Chlorophenyl)-1-(4-methylphenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4g). Yellow solid, yield 32%; mp 194–195°C; ^{1}H NMR: δ 8.03–6.65 (m, 19H, Ar—H, N—H, and N═C—H), 4.34–4.30 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 4.0 Hz), 2.96–2.82 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 4.0 Hz, J_{ab} = 14.0 Hz), 2.34 (s, 3H, —CH_3) ppm; IR (KBr): ν 3268, 2979, 2894, 1585 cm^{-1}; MS: *m/z* 535 [(M^++2), 2], 533 (M^+, 6); *Anal*. Calcd for $C_{31}H_{25}ClN_6O$: C, 69.85; H, 4.73; N, 15.77; Found: C, 69.84; H, 4.75; N, 15,74.

3a-(4-Chlorophenyl)-1-(4-nitrophenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5] benzodiazepine (4h). Yellow solid, yield 30%; mp 195–197°C; ^{1}H NMR: δ 8.17–6.56 (m, 19H, Ar—H, N—H, and N═C—H), 4.39–4.35 (dd, 1H, H_{5x}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz), 3.02–2.88 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3231, 2934, 2859, 1591 cm^{-1}; MS: *m/z* 566 [(M^++2), 1], 564 (M^+, 3); *Anal*. Calcd for $C_{30}H_{22}ClN_7O_3$: C, 63.89; H, 3.93; N, 17.38; Found: C, 63.87; H, 3.94; N, 17.36.

3a-(4-Methoxyphenyl)-1-phenyl-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5]benzodiazepine (4i). Yellow solid, yield 38%; mp 89–91°C; ^{1}H NMR: δ 8.05–6.63 (m, 20H, Ar—H, N—H, and N═C—H), 4.38–4.34 (dd, 1H, H_{5x}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz), 3.80 (s, 3H, —OCH_3), 2.99–2.86 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.1 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3301,2993, 2895, 1588 cm^{-1}; MS: *m/z* 514 (M^+, 4); *Anal*. Calcd for $C_{31}H_{26}N_6O_2$: C, 72.36; H, 5.09; N, 16.33; Found: C, 72.34; H, 5.11; N, 16.29.

1-(4-Chlorophenyl)-3a-(4-methoxyphenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrohydro-[1,2,4]oxadiazolo[5,4-d][1,5] benzodiazepine (4j). Yellow solid, yield 33%; mp 97–98°C; ^{1}H NMR: δ 8.04–6.61 (m, 19H, Ar—H, N—H, and N═C—H), 4.37–4.33 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 3.80 (s, 3H, —OCH_3), 2.97–2.83 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3303, 2977, 2854, 1581 cm^{-1}; MS: *m/z* 551 [(M^++2), 3], 549 (M^+, 9); *Anal*. Calcd for $C_{31}H_{25}ClN_6O_2$: C, 67.82; H, 4.59; N, 15.31; Found: C, 67.80; H, 4.60; N, 15.33.

3a-(4-Methoxyphenyl)-1-(4-methylphenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5] benzodiazepine (4k). Yellow solid; yield 42%; mp 97–99°C; ^{1}H NMR: δ 8.05–6.60 (m, 19H, Ar—H, N—H, and N═C—H), 4.38–4.34 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 3.80 (s, 3H, —OCH_3), 2.98–2.84 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz), 2.33 (s, 3H, —CH_3) ppm; IR (KBr): ν 3310, 2976, 2898, 1589 cm^{-1}; MS: *m/z* 528 (M^+, 4); *Anal*. Calcd for $C_{32}H_{28}N_6O_2$: C, 72.71; H, 5.34; N, 15.90; Found: C, 72.69; H, 5.35; N, 15.88.

3a-(4-Methoxyphenyl)-1-(4-nitrophenyl)-5-(2-phenyl-1,2,3-triazol-4-yl)-3a,4,5,6-tetrahydro-[1,2,4]oxadiazolo[5,4-d][1,5] benzodiazepine (4l). Yellow solid, yield 35%; mp 181–183°C; ^{1}H NMR: δ 8.17–6.55 (m, 19H, Ar—H, N—H, and N═C—H), 4.41–4.37 (dd, 1H, H_{5x}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz), 3.81 (s, 3H, —OCH_3), 3.02–2.88 (m, 2H, H_{4a}, H_{4b}, J_{ax} = 12.0 Hz, J_{bx} = 3.9 Hz, J_{ab} = 14.0 Hz) ppm; IR (KBr): ν 3223, 2996, 2902, 1607 cm^{-1}; MS: *m/z* 559 (M^+, 6); *Anal*. Calcd for $C_{31}H_{25}N_7O_4$: C, 66.54; H, 4.50; N, 17.52; Found: C, 66.52; H, 4.51; N, 17.53.

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