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Facile synthesis of 1,3,6-oxadiazepines from 2,2′-(1,2-ethanediyldiimino)bisphenols

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Abstract—A useful sequence of reactions for the syntheses of a variety of heterocyclic systems including an oxadiazepine ring is described. The key step involves the condensation of substituted 2,2′-(1,2-ethanediyldiimino)bisphenols with ethanedial to provide stereoselectively the 6a,7a-trans-6,6a,7a,8,15,16-hexahydro[1,4]benzoxazine[4′,3′:6,7][1,3,6]oxadiazepino[2,3-*c*][1,4]-benzoxazine-6,8-diol framework, as established by X-ray diffraction analyses.

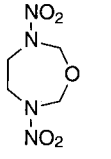
1. Introduction

α-Dicarbonyl compounds are valuable synthons for the preparation of heterocyclic molecules because of their high reactivity towards nucleophiles.[1–4]

Thus, many polyfunctionalized compounds having amino, hydroxyl and thiol groups react with α-dicarbonyl compounds to give a variety of bicyclic,[5] tricyclic,[6–9] tetracyclic[10] and cage[11] compounds, often with high stereoselectivity.

Polyheterocyclic seven-membered rings of the 1,3,6-oxadiazepine type containing one methylene group between the oxygen and the two nitrogen atoms have been described so far only sporadically in the literature.[12] The first studies reported are related to the preparation of 1,5-dinitro-3-oxa-1,5-diazacycloheptane[13–15] (**1**) by the reversible reaction of formaldehyde with nitroamines[13,14]. In 1957, Daeniker[16] reported the synthesis of the oxadiazepine **2** while investigating the chemotherapeutic use of a series of heterocycles and the synthesis was patented in view of the fact that the ethylene bis-phthalazinium chloride precursor possesses bacteriostatic activity.[17] Intramolecular Mannich reactions of 2-alkylaminomethylbenzimidazoles led to the preparation of compounds **3a**–**3d**,[18] and the intermediate oxadiazepines **4a**–**4d** were characterized during a study of the thermal ring contraction of oxygenated pyrazines.[19] The related 4,5-dihydro-1,3,6-oxadiazepine-2-thione **5** has been detected as a metabolite of manganous ethylenebis-(dithiocarbamate), a common fungicide used for controlling crop diseases.[20] An alternative method described in the literature for the synthesis of the saturated heterocycles (**6**) involves condensation of bis(chloromethyl)ether with aliphatic amines.[21] The related 4,5-benz[*d*][1,3,6]oxadiazepines (**7**) have been obtained by photolysis of quinoxaline *N*-oxides.[22–24]

Our interest in the reactions of *o*-aminophenols with various dicarbonyl compounds is focused on the highly



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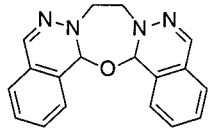

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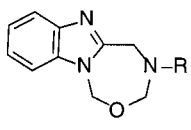
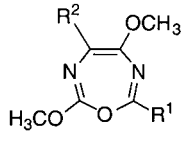


3a R=Me
3b R=Et
3c R=n-Pr
3d R=n-Bu



4a $R^1 = R^2 = Me$
4b $R^1 = CH_2=C(CH_2CH_2OTHP)$, $R^2 = H$
4c $R^1 = CH_2Ph$, $R^2 = H$
4d $R^1 = CH_2CHMe_2$, $R^2 = H$

Keywords: condensations; aminoalcohols; diazepines; X-ray crystal structures.

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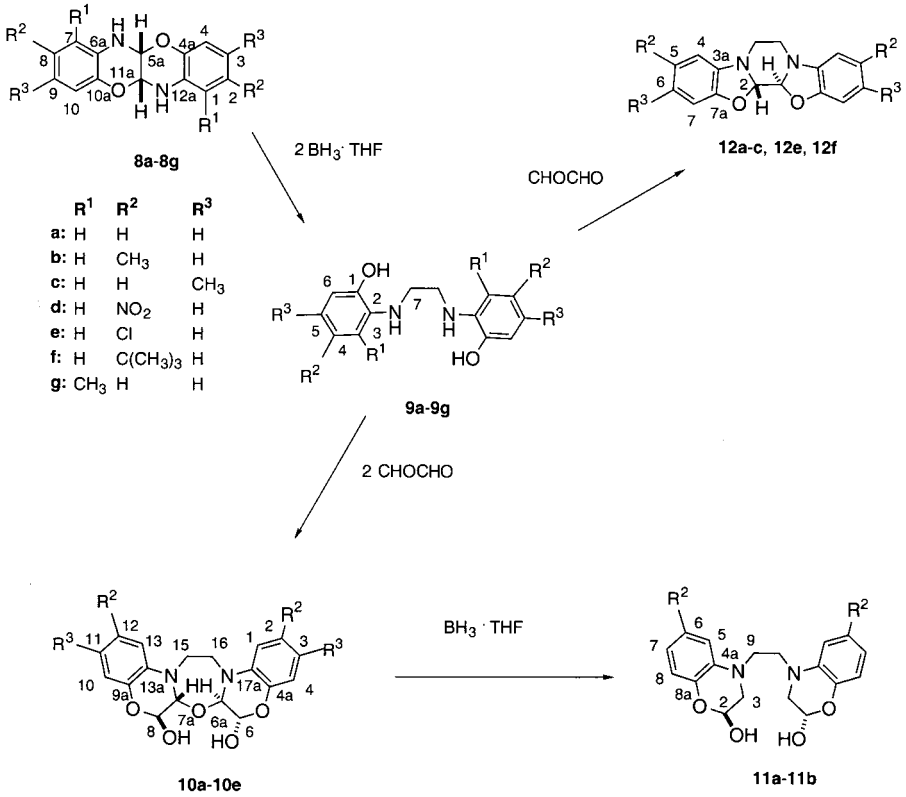
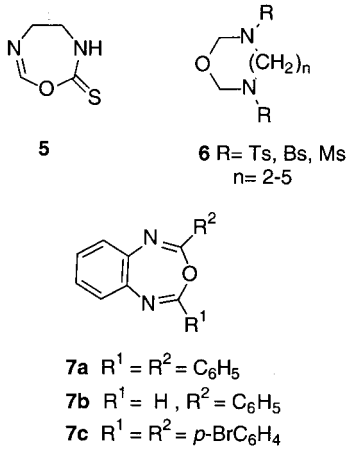


Scheme 1. Preparation of benzoxazino-benzoxazines (**8**), oxadiazepines (**10**) and bisoxazolidines (**12**).



stereoselective preparation of different heterocyclic systems.[5,8,9,25] In the present contribution a useful method for the synthesis of 1,3,6-oxadiazepines is presented with 2,2′-(1,2-ethanediyldiimino)bisphenols and glyoxal as starting materials. An interesting feature of the reaction is the stereoselective transformation of glyoxal. Moreover, 1,3,6-oxadiazepine derivatives are structurally related to known pharmacologically active molecules and the method of synthesis described in here should provide an easy route to the preparation of analogous molecules.

2. Results and discussion

The reactions between 1 equiv. of various *o*-aminophenol derivatives and glyoxal were carried out in benzene or mixtures of benzene–ethanol at reflux for 5–12 h to give the *cis*-benzoxazino–benzoxazines **8a**–**8g** in yields of 43–86% (Scheme 1). The structures of **8a**–**8g** were established by two-dimensional NMR experiments and compared with the data described for analogous compounds.[5,26–28] The ^{13}C NMR spectra of **8a**–**8g** showed only one half of the total number of expected carbons consistent with a structure of C_2 symmetry. Further evidence for the formation of these bicycles is the characteristic shift of the methine carbon at about 76 ppm. In the ^1H NMR spectra the signals for these methine protons are located between 5.17 and 5.66 ppm. In all cases the mass spectra showed peaks both for the molecular ion and the ion corresponding to half of the molecule.[29]

Reduction of the benzoxazino–benzoxazines **8a**–**8g** with 2 equiv. of BH_3–THF gave the corresponding 2,2′-(1,2-ethanediyldiimino)bisphenols **9a**–**9g**. Thereby, it is worth noting that the analogous *N*-hydroxyalkylethylenediamines possess antimycobacterial activity.[30] Furthermore, metal complexes of such bisphenols are useful models for the simulation of enzymatic systems.[31]

Although the syntheses of several bisphenols[32–36] have already been reported, their spectroscopic characterization has not been described previously. The ^1H NMR spectra of **9a**–**9g** show a characteristic singlet for the CH_2N group between 3.16 and 3.38 ppm. The mass spectra display peaks for the M^+ and half of the molecule which in the case of **9a**, **9c**, **9e**, **9g** correspond to the base peak. The X-ray structure of **9g** (Fig. 1) was determined and normal bond distances and angles are observed. The C–O bond length is 1.374 (3) Å, the $N–C_{arom}$ bond (N1–C2

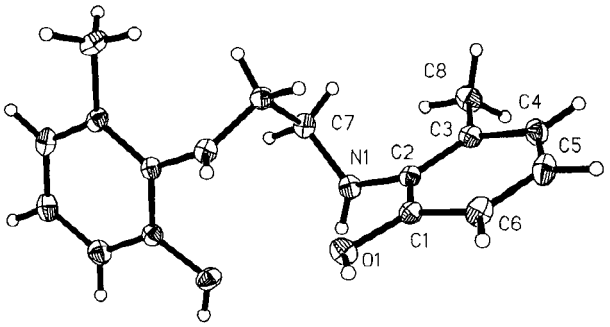


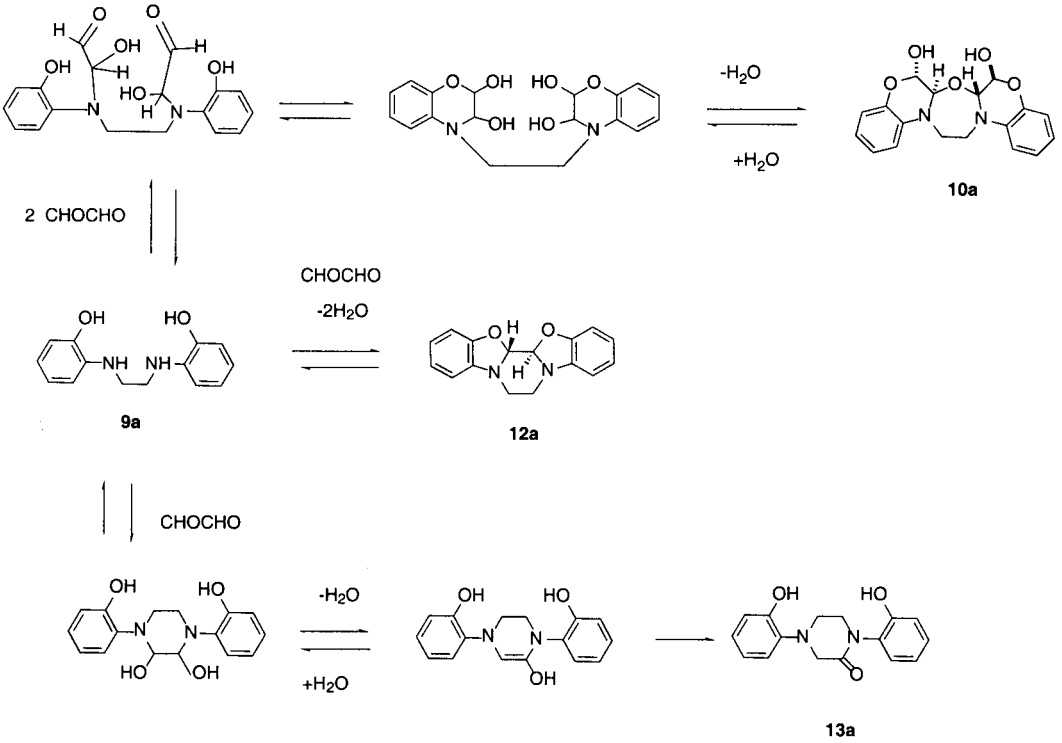
Figure 1. ORTEP drawing of compound **9g** showing atomic labeling and thermal ellipsoids at the 25% probability level. The symmetry transformation to generate the unlabeled atoms is A: $-x+1$, y, $-z+1/2$

1.433(3) Å) is shorter than the N–C_{aliph} bond (N1–C7, 1.468(3) Å). The orientation of the nitrogen atoms is *gauche* with the N1–C7–C7′–N1′ torsion angle being −64°. The torsion angle between the aromatic ring and the N-methylene groups (C1–C2–N1–C7) is 108° and that of the O1–C1–C2–N1 fragment is 6°.

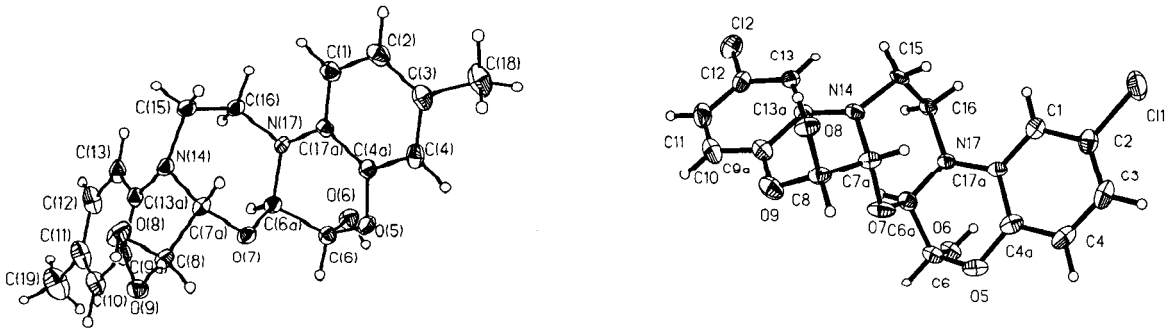
Based on the strategy described in a prior work for the synthesis of chiral piperazines,[25] and knowing that the course of the condensations with α-dicarbonyl derivatives is extremely sensitive to the reaction conditions, the condensation reactions of compounds **9a**–**9g** with glyoxal were carried out first with 2 equiv. of this reagent in ethanol–ethyl acetate (9:1). Thereby, the 1,3,6-oxadiazepines **10a**–**10e** were obtained in yields of 24–38%. It can be proposed that the reaction of **9a**–**9e** with glyoxal leads first to a tetrahydroxylated intermediate similar to the one described by Alcaide[37] and Chassonnery[38] that undergoes a highly stereoselective ring closure to provide the 1,3,6-oxadiazepine derivatives **10a**–**10e** (Scheme 2). It is worth mentioning that the modest yields are due to the fact that a mixture of products containing bisoxazolidines **12**, oxadiazepines **10** and traces of piperazinones **13** is formed which was separated by fractional crystallization.

In what follows the NMR and mass spectrometric data of compound **10a** will be discussed representatively for compounds **10a**–**10e**. The ^{1}H NMR spectrum of **10a** in DMSO-d_6 shows a doublet at 7.01 ppm (J=5.4 Hz) for the hydroxyl groups, a doublet at 5.31 ppm (J=5.8 Hz) for H-6 and H-8, a singlet at 4.19 ppm for H-6a and H-7a, as well as an AA′BB′ system at 3.23 and 4.14 for the H-15,16 hydrogens. Concerning the stereochemistry at carbons C-6 and C-8, the observation that the signals for these protons do not show coupling with H-6a and H-7a, respectively, allows one to deduce a *gauche* conformation according to the Karplus equation.[39] The COSY spectrum shows correlation between the hydroxyl protons and the H-6 and H-8 hydrogens.

The aromatic part of the ^{13}C NMR spectrum of **10a** was assigned by comparison with the starting materials and by use of two-dimensional experiments. The quaternary carbon C-4a (141.5 ppm) correlated with H-6 in a COLOC experiment. The mass spectrum of **10a** shows a peak for the molecular ion at m/z=342, and peaks corresponding to the loss of fragments with m/z=18. For compound **10a** there exist two possible structures, one possessing a plane of symmetry where all substituents are located on the same side of the molecule (all *cis*) and another one with a C_2 axis where the substituents are on opposite sides. Molecular modelling shows that the *trans*-substituted heterocycle is favored over the *cis*-substitued one by steric reasons. In order to confirm this statement, an X-ray crystallographic study was undertaken, whereby it was unambiguously established



Scheme 2. Reaction Scheme for the formation of **10**, **12** and **13**.



10c **10e**

Figure 2. ORTEP drawing of compounds **10c** and **10e** showing atomic labeling and thermal ellipsoids at the 25% probability level. Compound **10c** crystallized with a molecule of EtOH.

that the benzoxazinol moieties are joined in a *trans* configuration. The X-ray structures of **10c** and **10e** (Fig. 2) show that the seven-membered rings adopt the most stable *twist-chair* (TC) conformation.[40] The N14-C7a and N17-C6a bond distances are 1.428(5) and 1.425(5) Å for **10c** and 1.421(6) and 1.417(6) Å for **10e** which are shorter than the mean Csp^3–Nsp^3 distances (1.469(14) Å).[41] The six-membered rings adopt half-chair conformations with the oxygen atoms in *pseudoaxial* (*anti*) and the hydrogens in *pseudoequatorial* positions (*gauche*). The corresponding C–O distances are within the expected values.[41] The *pseudoaxial* hydroxyl groups at C-6 and C-8 have C–O distances of 1.397(5) and 1.400(5) Å for **10c** and 1.396(6) and 1.403(6) Å for **10e**. The O9–C8 and O5–C6 distances are 1.413(5)/1.411(5) Å and 1.428(7)/1.404(7) for **10c** and **10e**, respectively.

Reduction of **10a** and **10b** with BH_3THF gives the corresponding benzoxazinols **11a** and **11b** in yields of 48 and 73%, respectively. The ^{1}H NMR spectrum of **11a** shows a doublet at 5.28 ppm (J=4.8 Hz) for H-2, the diastereotopic protons at position 3 give rise to signals at 3.12 and 3.38 ppm and the broad signal at 3.45 ppm was assigned to the methylene group at C-9. In the ^{13}C NMR spectra of **11a** two distinct signals are observed for both C-9 (47.5 and 47.4 ppm) and C-3 (52.5 and 52.4 ppm). Again in the mass spectrum both the molecular ion at m/z=328 and an ion at m/z=164 corresponding to half of the molecule are present.

As expected, the formation of bisoxazolidines (**12b**–**12c**, **12e** and **12f**) was preferred when the reaction between bisphenols **9b**, **9c**, **9e** and **9f** and glyoxal was carried out in a 1:1 molar ratio in benzene:ethanol (9:1). The structures of these compounds were established by NMR spectroscopy in comparison with similar derivatives.[25] The formation of these compounds could be evidenced by the signal around 93 ppm for C-2. In solution, these bisoxazolidine type derivatives are in equilibrium with the starting materials (Scheme 2) thus precluding their purification by chromatographic procedures.

3. Conclusion

A series of five new 1,3,6-oxadiazepines have been prepared from 2,2′-(1,2-ethanediyldiimino)bisphenols and glyoxal as starting materials. The sequence of reactions described in this report is useful for the preparation of a variety of heterocyclic systems with potential bioactivity like bisoxazolidines, piperazines, oxadiazepines and benzoxazinols. The preparation of the 1,3,6-oxadiazepine provides the 6a,7a-*trans*-substituted seven-membered ring, as demonstrated by X-ray crystallography.

4. Experimental

NMR spectra were recorded on Jeol GLX 270, Jeol Eclipse+400 and Bruker Avance DPX spectrometers. Special techniques (APT, COSY, HMQC, HMBC, COLOC) were used to assign the spectra. Chemical shifts are stated in ppm with reference to TMS. IR spectra have been recorded on a Perkin–Elmer 16F-PC FT-IR spectrophotometer with KBr pellets. Mass spectra were obtained on a HP 5989A spectrometer using electron impact ionization (EI). Elemental analyses were carried out by Oneida Research Services, Whitesboro, N.Y. 13492. HRMS were determined on a Jeol 102A spectrometer at the Instituto de Química, UNAM.

X-Ray diffraction studies of monocrystals were performed on an Enraf–Nonius CAD4 diffractometer ($\lambda_{MoK\alpha}$= 0.71069 Å). A selected crystal was set upon a diffractometer, unit cell dimensions with estimated standard deviations were obtained from least-squares refinements of the setting angles of 25 well centered reflections. Three standard reflections were monitored periodically; they showed no change during data collection. Corrections were made for Lorentz and polarization effects. Absorption correction was not necessary. The structures of **9g**, **10c** and **10e** were determined by direct methods. Computations for all structures were performed with SHELXL (Sheldrick, 1993).[42] Atomic form factors for neutral C, N, O and H were taken from Ref. 43. Hydrogen atoms were calculated. Anisotropic temperature factors were introduced for all non-hydrogen atoms. Least-squares refinements were carried out by minimizing $\Sigma w(|F_o|-|F_c|)^2$, where F_o and F_c are the observed and calculated structure factors. Weights were used. Models reached convergence with $R=\Sigma(\||F_o|-|F_c|\|)/\Sigma|F_o|$ and $R_w=\Sigma w(\||F_o|-|F_c|\|)^2/\Sigma w(F_o)^2]^{1/2}$. Criteria for a

satisfactory complete analysis were the ratios of rms shifts to standard deviation being less than 0.1 and no significant features in the final difference Fourier map.

Crystal data for ***9g****:* $C_{16}H_{20}N_2O_2$, M=272.34 g/mol, monoclinic, space group C2/c, with a=25.137 (5) Å, b=6.053 (1) Å, c=9.617 (2) Å, β=103.88 (3)°, V=1420.5 (5) Å^3, Z=4, d_{calc}=1.273 g cm^{-3}, μ=0.085 cm^{-1}. A total of 1585 reflections were collected, from which 1552 were unique (R_{int} 0.02), 960 reflections were considered observed, $F>4\sigma(F)$, 91 parameters, final R=0.061, R_w=0.188. Weighting scheme $w^{-1}=\sigma^2F_o^2+(0.1150\ P)^2+1.3815\ P$ where $P=(F_o^2+2F_c^2)/3$.

Crystal data for ***10c****:* $C_{20}H_{22}N_2O_5$ C_2H_5OH, M=416.46 g/mol, monoclinic, space group $P2_1/a$, with a=12.928 (1) Å, b=8.363 (1) Å, c=19.319 (1) Å, β=91.706 (1)°, V=2087.8 (3) Å^3, Z=4, d_{calc}=1.325 g cm^{-3}, μ=0.097 cm^{-1}. A total of 1782 reflections were collected, from which 1700 were considered observed (R_{int} 0.032) $F>4\sigma(F)$, 271 parameters, final R=0.049, R_w=0.133. Weighting scheme: $w^{-1}=\sigma^2F_o^2+(0.0744\ P)^2+1.7055\ P$ where $P=(F_o^2+2F_c^2)/3$.

Crystal data for ***10e****:* $C_{18}H_{16}Cl_2N_2O_5$, M=411.23 g/mol, trigonal, space group P3, with a=15.066 (2) Å, b=15.066 (2) Å, c=6.8860 (10) Å, $\alpha=\beta$=90.0°, γ=120.0°, V=1353.6 (3) Å^3, Z=3, d_{calc}=1.513 g cm^{-3}, μ=0.393 mm^{-1}. A total of 3008 reflections were collected, from which 1934 were unique (R_{int} 0.044), 1316 reflections were considered observed, $F>4\sigma(F)$, 244 parameters, final R=0.041, R_w=0.105. Weighting scheme: $w^{-1}=\sigma^2F_o^2+(0.0618\ P)^2+0.1600\ P$ where $P=(F_o^2+2F_c^2)/3$.

4.1. General procedure for the preparation of benzoxazino–benzoxazines (8)

To a solution of the appropriate *o*-aminophenol (1.0 mmol) in benzene was added dropwise 40% aqueous glyoxal (0.5 mmol) and the solution was kept under reflux for 5 h using a Dean Stark trap. The solvent was evaporated *in vacuum* and the solid washed with ether and recrystallized from an appropriate solvent.

4.1.1. *cis*-5a,6,11a,12-Tetrahydro [1,4] benzoxazino [3,2-*b*][1,4]benzoxazine (8a). Mp 202–204°C lit[27] 231°C.

4.1.2. *cis*-5a,6,11a,12-Tetrahydro-2,8-dimethyl-[1,4]benzoxazino[3,2-*b*][1,4]benzoxazine (8b). Glyoxal (2.4 g, 16.3 mmol) was added to 2-amino-4-methylphenol (4.0 g, 32.5 mmol) in 50 mL of a mixture of benzene-ethanol (9:1) to give 3.4 g (78%) of **8b** which was recrystallized from acetone, mp 236–237°C. IR (KBr) 3374, 3304, 1618, 1604, 1506, 1310, 1288, 1258, 1216, 1140, 1126, 936, 848, 796 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.18 (2H, d, J=4.0 Hz, NH-6,12), 6.51 (2H, d, J=8.0 Hz, H-4,10), 6.48 (2H, s, H-1,7), 6.39 (2H, d, J=8.0 Hz, H-3,9), 5.17 (2H, d, J=4.0 Hz, H-5a, 11a), 2.14 (6H, s, CH_3-2,8); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.6 (C-4a), 130.5 and 130.3 (C-2, C-12a,), 119.5 (C-3), 116.2 (C-4), 115.1 (C-1), 75.8 (C-5a), 21.0 (CH_3); MS (EI, 70 eV) m/z (%): 268 (M$^+$, 76), 269 (M$^+$+1, 14), 147 (88), 146 (63), 134 (M$^+$/2, 100), 122 (33), 118 (32), 107 (21), 91 (29), 77 (47), 65 (26); *Anal. calcd for* $C_{16}H_{16}N_2O_2$: C, 71.64; H, 5.97; N, 10.45; *Found*: C, 71.72; H, 6.08; N, 10.35.

4.1.3. *cis*-5a,6,11a,12-Tetrahydro-3,9-dimethyl-[1,4]benzoxazino[3,2-*b*][1,4]benzoxazine (8c). Glyoxal (1.2 g, 8.1 mmol) was added to 2-amino-5-methylphenol (2.0 g, 16.3 mmol) in 35 mL benzene to yield 1.8 g (83%) of **8c** which was recrystallized from acetone, mp 231–232°C. IR (KBr) 3376, 3030, 2964, 2920, 2854, 1598, 1518, 1488, 1448, 1420, 1292, 1266, 1232, 1142, 1128 1010, 980, 874, 858, 800, 786, 756, 578 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.12 (2H, d, J=4.0 Hz, NH-6,12), 6.56 (4H, AB, J=7.7 Hz, H-1,7, H-2,8), 6.46 (2H, s, H-4,10), 5.20 (2H, d, J=4.0 Hz, H-5a,11a), 2.12 (6H, s, CH_3-3,9); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 142.2 (C-4a), 128.4 and 128.3 (C-3 and C-12a), 122.5 (C-2), 117.3 (C-4), 114.9 (C-1), 76.3 (C-5a), 21.1 (CH_3); MS (EI, 70 eV) m/z (%): 268 (M$^+$, 66), 269 (M$^+$+1, 11), 148 (10), 147 (87), 146 (82), 134 (M$^+$/2, 100), 118 (25), 91 (23), 77 (34), 65 (18); *Anal. calcd for* $C_{16}H_{16}N_2O_2$: C, 71.64; H, 5.97; N, 10.44. *Found*: C, 71.62; H, 6.17; N, 10.33.

4.1.4. *cis*-5a,6,11a,12-Tetrahydro-2,8-dinitro-[1,4]benzoxazino[3,2-*b*][1,4]benzoxazine (8d). Glyoxal (1.3 , 8.1 mmol) was added to 2-amino-4-nitrophenol (2.5 g, 16.2 mmol) in 30 mL benzene and refluxed for 10 h to yield 2.3 g (86%) of **8d** which was recrystallized from acetone, mp 241–242°C. IR (KBr) 3420, 1522, 1518, 1514, 1340, 1322, 1268, 1248, 1226, 1150, 968 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 8.13 (2H, d, J=4.3 Hz, NH-6,12), 7.65 (2H, d, J=2.7 Hz, H-1,7), 7.58 (2H, dd, J=8.6, 2.7 Hz, H-3,9), 6.91 (2H, d, J=8.6 Hz, H-4,10), 5.66 (2H, d, J=4.4 Hz, H-5a,11a); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 148.3 (C-4a), 142.5 (C-2), 131.0 (C-12a), 117.3 (C-4), 116.2 (C-3), 109.9 (C-1), 76.0 (C-5a); MS (EI, 70eV) m/z (%) 330 (M$^+$, 3), 98 (6), 73 (15), 60 (16), 55 (21), 45 (27), 44 (100); *HRMS calcd for* $C_{14}H_{10}N_4O_6$: 330.0600. *Found*: 330.0587. Error −4.1 ppm.

4.1.5. *cis*-5a,6,11a,12-Tetrahydro-2,8-dichloro[1,4]benzoxazino[3,2-*b*][1,4]benzoxazine (8e). Glyoxal (1.1 g, 7.0 mmol) was added to 2-amino-4-chlorophenol (2.0 g, 14.0 mmol) in 30 mL benzene and refluxed for 8 h to yield 1.64 g (76%) of **8e**, recrystallized from acetone, mp 202–203°C. IR (KBr) 3376, 1606, 1496, 1304, 1270, 1244, 1208, 1150, 1120, 898, 844, 808 $^{-1}$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.63 (2H, d, J=3.2 Hz, NH-6,12), 6.72 (2H, d, J=2.0 Hz, H-1,7), 6.68 (2H, d, J=8.4 Hz, H-4,10), 6.62 (2H, dd, J=8.4, 2.0 Hz, H-3,9), 5.31 (2H, d, J=4.0 Hz, H-5a,11a). ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 140.9 (C-4a), 132.4 (C-12a), 125.8 (C-2), 118.9 (C-3), 118.3 (C-4), 114.2 (C-1), 75.6 (C-5a); MS (EI, 70 eV) m/z (%): 308 (M$^+$, 56), 309 (M$^+$+1, 10), 310 (M$^+$+2, 37), 311 (M$^+$+3, 6), 312 (M$^+$+4, 6), 167 (77), 166 (52), 154 (M$^+$/2, 100), 156 (40), 155 (39), 142 (29), 138 (28), 78 (16), 77 (19), 63 (29); *Anal. calcd for* $C_{14}H_{10}N_2O_2Cl_2$: C, 54.40; H, 3.23; N, 9.06; Cl, 22.92; *Found*: C, 54.00; H, 3.28; N, 8.87; Cl, 22.86.

4.1.6. *cis*-5a,6,11a,12-Tetrahydro-2,8-di*tert*-butyl[1,4]benzoxazino[3,2-*b*][1,4]benzoxazine (8f). Glyoxal (0.4 g, 3.03 mmol) was added to 2-amino-4-*tert*butylphenol (1.0 g, 6.06 mmol) in 50 mL of a mixture of benzene:

ethanol (9:1) and refluxed for 12 h to yield 0.46 g (43%) of **8f**, recrystallized from methanol, mp 223–224°C (dec). IR (KBr) 3420, 3370, 2950, 1522, 1498, 1342, 1310, 1288, 1264, 1220, 1156, 1132, 1104 cm^{-1}; ^1H NMR (270 MHz, DMSO-d_6) δ 7.17 (2H, d, J=4.0 Hz, NH-6,12), 6.70 (2H, d, J=2.0 Hz, H-1,7), 6.62 (2H, dd, J=8.4, 2.0 Hz, H-3,9), 6.54 (2H, d, J=8.4 Hz, H-4,10), 5.20 (2H, d, J=4.0 Hz, H-5a,11a), 1.22 (18H, s, C(CH_3)$_3$); ^{13}C NMR (67.8 MHz, DMSO-d_6) δ 144.3 (C-2), 139.6 (C-4a), 129.9 (C-12a), 115.9 (C-3,4), 111.8 (C-1), 75.9 (C-5a), 34.4 (C-CH_3)$_3$), 32.0 (CH_3); MS (EI, 70 eV) m/z (%): 352 (M^+, 100), 353 (M^++1, 25), 189 (59), 188 (47), 176 (M^+/2, 27), 162 (26), 105 (6), 91 (9), 77 (10), 65 (5); *HRMS calcd for* $C_{22}H_{28}N_2O_2$: 352.2151. *Found*: 352.2162. Error +3.2 ppm.

4.1.7. *cis*-5a,6,11a,12-Tetrahydro-1,7-dimethyl-[1,4]benzoxazino-[3,2-*b*][1,4]benzoxazine (8g). Glyoxal (0.6 g, 4.1 mmol) was added to 2-amino-*m*-cresol (1.0 g, 8 mmol) in 15 mL benzene to yield 800 mg (74%) of **8g**, mp 243°C. IR (KBr) 3422, 1524, 1484, 1238, 1162, 768 cm^{-1};^1H NMR (270 MHz, DMSO-d_6) δ 6.81 (2H, d, J=4.0 Hz, NH-6,12), 6.63 (2H, dd, J=4.8, 4.0 Hz, H-3,9), 6.53 (2H, d, J=4.0 Hz, H-2,8 and H-4,10), 5.23 (2H, d, J=4.0 Hz, H-5a,11a), 2.12 (6H, s, CH_3-1,7); ^{13}C NMR (67.8 MHz, DMSO-d_6) δ 141.5 (C-4a), 128.6 (C-12a), 123.3 (C-3), 122.7 (C-1), 118.7 (C-2), 114.5 (C-4), 75.5 (C-5a), 17.5 (CH_3); MS (EI, 70 eV) m/z (%): 268 (M^+, 89), 269 (M^++1, 16), 147 (92), 134 (M^+/2, 100), 122 (34), 118 (29), 91 (27), 77 (33); *Anal. calcd for*: $C_{16}H_{16}N_2O_2$: C, 71.64; H, 5.97; N, 10.44; *Found*: C, 71.66; H, 6.17; N, 10.41.

4.2. General procedure for the preparation of 2,2′-(1,2-ethanediyldiimino)bisphenols (9)

To a solution of the appropriate benzoxazino–benzoxazine (1.0 mmol) in 50 mL THF, 2.0 mmol of BH_3–THF was added and the solution was refluxed for 5 h. The excess borane was destroyed with a few drops of 10% NaOH, the solution was dried over Na_2SO_4 and the solvent evaporated under vacuum. The solid was washed with acetone and recrystallized as described below.

4.2.1. 2,2′-(1,2-Ethanediyldiimino)bisphenol[30,32,35] (9a). To a solution of **8a** (4.3 g, 17.9 mmol) in 50 mL THF, 17.9 mL (35.8 mmol) BH_3–THF was added. The product was recrystallized from ethanol–chloroform to yield 4.1 g (94%) of **9a**, mp 236–237 °C [Lit[30] 228–232°C, Lit[32] 225–227°C, Lit[35] 214–217°C dec]. IR (KBr) 3308, 1510, 1446, 1110, 742 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.18 (2H, s, NH), 6.65 (2H, d, J=7.6 Hz, H-6,6′), 6.63 (2H, dd, J=8.0, 7.3 Hz, H-4,4′), 6.53 (2H, d, J=7.0 Hz, H-3,3′), 6.40 (2H, ddd, J=7.6, 7.3, 1.1 Hz, H-5,5′), 4.70 (2H, s, OH), 3.27 (4H, s, $(CH_2)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.6 (C-1), 137.9 (C-2), 120.2 (C-4), 116.2 (C-5), 113.9 (C-6), 110.2 (C-3), 42.7 (CH_2); MS (EI, 70 eV) m/z (%): 244 (M^+, 24), 245 (M^++1, 5), 123 (87), 122 (M^+/2, 100), 120 (16), 95 (28), 94 (15), 77 (29), 65 (16).

4.2.2. 2,2′-(1,2-Ethanediyldiimino)-4,4′-dimethylbisphenol[34] (9b). To a solution of **8b** (3.7 g, 13.8 mmol) in 50 mL THF, 13.5 mL (27.6 mmol) of BH_3–THF was added. After work-up the solid was washed with acetone to give 3.5 g (93%) of **9b**, that was recrystallized from acetone, mp 238–240°C. IR (KBr) 3304, 3048, 2920, 2850, 1596, 1524, 1420, 1302, 1278, 1250, 1230, 1208, 1124, 860, 810 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (2H, s, NH), 6.51 (2H, d, J=8.0 Hz, H-6,6′), 6.36 (2H, s, H-3,3′), 6.19 (2H, d, J=8.0 Hz, H-5,5′), 4.72 (2H, s, OH), 3.33 (4H, s, $(CH_2)_2$), 2.13 (6H, s, CH_3-4,4′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.7 (C-1), 138.0 (C-2), 128.9 (C-4), 116.7 (C-5), 114.1 (C-6), 111.4 (C-3), 43.0 (CH_2). 21.8 (CH_3); MS (EI, 70 eV) m/z (%) 272 (M^+, 21), 273 (M^++1, 5), 138 (95), 137 (100), 136 (M^+/2, 94), 134 (23), 109 (49), 91 (27), 77 (24), 65 (16); *Anal. calcd for* $C_{16}H_{20}N_2O_2$: C, 70.59; H, 7.35; N, 10.29*; Found*: C, 70.55; H, 7.50; N, 10.19.

4.2.3. 2,2′-(1,2-Ethanediyldiimino)-5,5′-dimethylbisphenol (9c). To a solution of **8c** (2.7 g, 10.1 mmol) in 50 mL THF, 10.1 mL (20.14 mmol) of BH_3–THF was added, 3 h reflux. After work-up 2.16 g (79%) of **9c** were obtained that was recrystallized from acetone, mp 246–248°C (dec). IR (KBr) 3302, 3040, 2918, 2860, 1522, 1506, 1498, 1422, 1216, 1208, 1122, 798, 796 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.10 (2H, s, NH), 6.48 (2H, s, H-6,6′), 6.43 (2H, d, J=10.0 Hz, H-3,3′) and 6.42 (2H, J=10 Hz, H-4,4′), 4.54 (2H, br, OH), 3.21 (4H, s, $(CH_2)_2$), 2.01 (6H, s, CH_3-5,5′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.6 (C-1), 135.5 (C-2), 124.9 (C-5), 120.3 (C-4), 115.0 (C-6), 110.3 (C-3), 43.1 (CH_2), 20.8 (CH_3); MS (EI, 70 eV) m/z (%) 272 (M^+, 16), 273 (M^++1, 3), 137 (92), 136 (M^+/2, 100), 134 (20), 109 (33), 91 (24), 77 (23), 65 (16); *Anal. calcd for* $C_{16}H_{20}N_2O_2$: C, 70.59; H, 7.35; N, 10.29; *Found*: C, 70.52; H, 7.41; N,10.28.

4.2.4. 2,2′-(1,2-Ethanediyldiimino)-4,4′-dinitrobisphenol (9d). To a solution of **8d** (1.94 g, 5.9 mmol) in 50 mL THF, 5.9 mL (11.7 mmol) of BH_3–THF was added, 3 h reflux. After work-up 1.5 g (77%) of **9d** were obtained that was recrystallized from acetone, mp 220–222°C (dec). IR (KBr) 3386, 3228, 2920, 1530, 1502, 1472, 1458, 1344, 1224, 744 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.01 (2H, br, NH), 7.43 (2H, dd, J=8.4, 2.6 Hz, H-5,5′), 7.30 (2H, d, J=2.6 Hz, H-3,3′), 6.78 (2H, d, J=8.4 Hz, H-6,6′), 5.63 (2H, br, OH), 3.38 (4H, s, $(CH_2)_2$); ^{13}C NMR (67.9 MHz, DMSO-d_6) δ 151.5 (C-1), 141.2 (C-4), 138.3 (C-2), 113.5 (C-5), 112.7 (C-6), 103.3 (C-3), 41.8 (CH_2); MS (EI, 70 eV) m/z % 334 (M^+, 1), 330 (3), 289 (8), 168 (12), 165 (20), 123 (16), 122 (100), 121 (25), 120 (16), 108 (11), 95 (20), 77 (20), 65 (21), 63 (13), 53 (32), 52 (22), 51 (21); *HRMS calcd for* $C_{14}H_{14}N_4O_6$: 334.0913. *Found*: 334.0908. Error −1.5 ppm.

4.2.5. 2,2′-(1,2-Ethanediyldiimino)-4,4′-dichlorobisphenol[34] (9e). To a solution of **8e** (1.0 g, 3.25 mmol) in 50 mL THF, 3.24 mL (6.5 mmol) of BH_3–THF was added. After work-up the product was washed with ethanol/hexane to yield 1.0 g (99%) of **9e** that was recrystallized from acetone, mp 205–207°C (dec). IR (KBr) 3301, 3040, 3020, 2918, 2850, 1616, 1612, 1596, 1522, 1508, 1498, 1472, 1458, 1436, 1420, 1298, 1290, 1256, 1216, 1208, 1158, 1122, 860, 798, 734, 688, 668 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 9.54 (2H, s, NH), 6.60 (2H, d, J=8.4 Hz, H-6,6′), 6.51 (2H, d, J=1.8 Hz, H-3,3′), 6.38 (2H, dd, J=8.4 Hz, 1.8, H-5,5′), 3.67 (2H, brs, OH), 3.24 (4H, s, $(CH_2)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.4

(C-1), 139.3 (C-2), 124.0 (C-4), 114.9 (C-6), 114.4 (C-3), 109.2 (C-5), 41.9 (CH_2); MS (EI, 70 eV) *m/z* (%) 312 (M^+, 30), 313 (M^++1, 8), 314 (M^++2, 20), 315 (M^++3, 5), 316 (M^++4, 4), 159 (27), 158 (40), 157 (78), 156 (M^+/2, 100), 129 (25), 93 (18); *Anal. calcd for* $C_{14}H_{14}N_2O_2Cl_2$: C, 53.70; H, 4.47; N, 8.95; Cl, 22.69; *Found*: C, 53.6; H, 4.47; N, 8.81.

4.2.6. 2,2′-(1,2-Ethanediyldiimino)-4,4′-*tert*-butylbisphenol[36] (9f). To a solution of **8f** (1.0 g, 2.84 mmol) in 50 mL THF, 2.8 mL (5.68 mmol) of BH_3–THF was added, 4 h reflux, 0.72 g (68%) yield that was recrystallized from ethanol, mp 180–182°C [Lit[36] mp 195°C]. IR (KBr) 3368, 3332, 3220, 3068, 2962, 2906, 1598, 1524, 1500, 1464, 1414, 1362, 1278, 1264, 1192, 1132 cm^{-1}; ^1H NMR (270 MHz, DMSO-d_6) δ 9.04 (2H, s, NH), 6.57 (2H, d, *J*=1.0 Hz, H-3,3′), 6.56 (2H, d, *J*=8.0 Hz, H-6,6′), 6.42 (2H, dd, *J*=8.0, 1.0 Hz, H-5,5′), 4.91 (2H, br, OH), 3.31 (4H, s, $(CH_2)_2$), 1.21 (18H, s, $C(CH_3)_3$-4,4′); ^{13}C NMR (67.9 MHz, DMSO-d_6) δ 142.6 and 142.3 (C-1 and C-4), 137.0 (C-2), 113.4 (C-6), 112.9 (C-5), 108.0 (C-3), 43.0 (CH_2). 34.4 ($C(CH_3)_3$), 32.1 ($C(CH_3)_3$); MS (EI, 70 eV) *m/z* (%) 356 (M^+, 29), 357 (M^++1, 9), 179 (100), 164 (20), 162 (12), 148 (8), 133 (8), 122 (9), 57 (18). *HRMS calcd for* $C_{22}H_{32}N_2O_2$: 356.2464. *Found*: 356.2460. Error −1.1 ppm.

4.2.7. 2,2′-(1,2-Ethanediyldiimino)-3,3′-dimethylbisphenol (9g). To a solution of **8g** (1.0 g, 3.73 mmol) in 50 mL THF, 3.73 mL (7.46 mmol) of BH_3–THF was added, 530 mg (52%) yield that was recrystallized from acetone, mp 170–173°C (dec). IR (KBr) 3330, 3050, 2982, 2940, 2850, 2674, 1586, 1482, 1454, 1352, 1338, 1270, 1240, 1186, 1108, 1014, 946, 932, 788, 778, 772, 748, 738, 662 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 6.77 (2H, dd, *J*=8.0, 7.7 Hz, H-5,5′), 6.65 (2H, d, *J*=8.0 Hz, H-6,6′), 6.61 (2H, d, *J*=7.7 Hz, H-4,4′), 3.16 (4H, s, $(CH_2)_2$), 2.31 (6H, s, CH_3-3,3′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.6 (C-1), 135.8 (C-2), 129.9 (C-3), 122.1 (C-5), 121.4 (C-4), 113.3 (C-6), 48.3 (CH_2), 18.6 (CH_3); MS (EI, 70 eV,) *m/z* (%) 272 (M^+, 22), 273 (M^++1, 15), 137 (79), 136 (100), 109 (24), 91 (15), 77 (16), 65 (10); *HRMS calcd for* $C_{16}H_{20}N_2O_2$: 272.1525. *Found*: 272.1527. Error −0.9 ppm.

4.3. General procedure for the preparation of 6,6a,7a,8,15,16-hexahydro[1,4]benzoxazino[4′,3′:6,7][1,3,6]-oxadiazepino[2,3-*c*][1,4]benzoxazine-6,8-diol (10)

To a solution of 2,2′-(1,2-ethanediyldiimino)bisphenol (1.0 mmol) in 25 mL of EtOH–ethyl acetate (9:1) 2.0 mmol of 40% aqueous glyoxal was added dropwise and the solution was refluxed for 5 h. The solution was concentrated, the precipitate washed with EtOH and the product recrystallized from ethanol.

4.3.1. 6,6a,7a,8,15,16-Hexahydro[1,4]benzoxazino[4′,3′:6,7][1,3,6]oxadiazepino[2,3-*c*][1,4]benzoxazine-6,8-diol (10a). Glyoxal (0.59 g, 4.1 mmol) was added to **9a** (0.5 g, 2.04 mmol) to yield 0.26 g (38%) of **10a** that was recrystallized from EtOH, mp 201°C. IR (KBr) 3252, 1506, 1350, 1238, 1216, 1058, 1042, 1010, 742 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.01 (2H, d, *J*=5.4 Hz, OH), 6.94 (2H, d, *J*=7.7 Hz, H-1,13), 6.87 (2H, t, *J*=7.7 Hz, H-2,12), 6.80 (2H, d, *J*=7.3 Hz, H-4,10), 6.70 (2H, dd, *J*=7.7, 7.3 Hz, H-3,11), 5.31 (2H, d, *J*=5.8 Hz, H-6,8), 4.19 (2H, s, H-6a,7a), 4.14 (2H, AA′BB′, H-15,16) 3.23 (2H, AA′BB′, H-15′,16′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.5 (C-4a), 130.4 (C-13a), 122.0 (C-2), 119.0 (C-3), 117.1 (C-4), 111.4 (C-1), 89.0 (C-6), 82.3 (C-6a), 46.8 (C-15); MS (EI, 70eV) *m/z* (%) 342 (M^+, 27), 343 (M^++1, 6), 324 (M^+-H_2O, 5), 284 (19), 266 (42), 221 (23), 175 (3), 147 (18), 121 (6), 119 (100), 93 (15), 91 (28), 65 (34); *Anal. calcd for* $C_{18}H_{18}N_2O_5$: C, 63.16; H, 5.29; N, 8.18; *Found*: C, 62.85; H, 5.26; N, 8.11.

4.3.2. 6,6a,7a,8,15,16-Hexahydro-2,12-dimethyl-[1,4]benzoxazino[4′,3′:6,7][1,3,6]-oxadiazepino[2,3-*c*][1,4]benzoxazine-6,8-diol (10b). Glyoxal (1.1 g, 9.55 mmol) was added to **9b** (1.3 g, 4.78 mmol) to yield 660 mg (36 %) of **10b** that was recrystallized from EtOH, mp 210–212°C. IR (KBr) 3334, 2918, 2360, 1616, 1514, 1466, 1346, 1276, 1254, 1216, 1200, 1096, 1052, 1042, 998, 668 cm^{-1};^1H NMR (400 MHz, DMSO-d_6) δ 6.89 (2H, d, *J*=5.5 Hz, OH-6,8), 6.75 (2H, s, H-1,13), 6.64 (2H, d, *J*=8.0 Hz, H-4,12), 6.48 (2H, d, *J*=8 Hz, H-3,11), 5.23 (2H, d, *J*=5.5 Hz, H-6,8), 4.15 (2H, s, H-6a,7a), 4.11 (2H, AA′BB′, H-15,16), 3.20 (2H, AA′BB′, H-15′,16′), 2.23 (6H, s, CH_3-2,12); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.3 (C-4a), 130.7 (C-13a), 130.1 (C-2), 119.2 (C-2), 116.7 (C-4), 111.9 (C-1), 88.9 (C-6), 82.3 (C-6a), 46.7 (C-15), 21.3 (CH_3-2,12); MS (EI, 70 eV) *m/z* (%) 371 (M^++1, 9), 370 (M^+, 40), 323 (14), 312 (34), 294 (20), 249 (40), 176 (21), 160 (22), 148 (30), 134,(98), 133 (100), 77 (64), 65 (30); *Anal. calcd for* $C_{20}H_{22}N_2O_5.H_2O$: C, 61.85; H, 6.18; N, 7.21; *Found*: C, 61.87; H, 6.18; N, 7.06.

4.3.3. 6,6a,7a,8,15,16-Hexahydro-3,11-dimethyl-[1,4]benzoxazino[4′,3′:6,7][1,3,6]oxadiazepino[2,3-*c*][1,4]benzoxazine-6,8-diol (10c). Glyoxal (0.85 g, 5.88 mmol) was added to **9c**. (0.8 g, 2.94 mmol), 260 mg (24%) of **10c** were obtained, mp 178–179°C, that was recystallized from ethanol. IR (KBr) 3416, 1514, 1286, 1244, 1184, 1062, 996, 878, cm^{-1}; ^1H NMR (270 MHz,DMSO-d_6) δ 6.94 (2H, d, *J*=5.5 Hz, OH-6,8), 6.81 (2H, d, *J*=8.2 Hz, H-1,13), 6.67 (2H, d, *J*=8.2 Hz, H-2,12), 6.62 (2H, s. H-4,10), 5.27 (2H, d, *J*=5.5 Hz, H-6,8), 4.15 (2H, s, H-6a,7a), 4.07 (2H, AA′BB′,H-15,16), 3.20 (2H, AA′BB′, H-15′,16′), 2.14 (6H, s, CH_3-3,11); ^{13}C NMR (67.9 MHz, DMSO-d_6) δ 141.5 (C-4a), 128.1 and 127.9 (C-3 and C-13a), 122.3 (C-2), 117.7 (C-4), 111.3 (C-1), 89.3 (C-6), 82.4 (C-6a), 46.71 (C-15), 20.7 (CH_3-3); MS (EI, 70 eV) *m/z* (%) 370 (M^+, 19), 371 (M^++1, 4), 312 (22), 295 (11), 294 (26), 249 (24), 176 (11), 161 (14), 160 (12), 148 (14), 147 (11), 134 (50), 133 (100), 132 (22), 107 (13), 106 (12), 79 (15), 78 (20), 77 (25), 65 (12), 43 (22). *HRMS calcd for* $C_{20}H_{22}N_2O_5$: 370.1529. *Found*: 370.1531. Error −0.6 ppm.

4.3.4. 6,6a,7a,8,15,16-Hexahydro-2,12-dinitro-[1,4]benzoxazino[4′,3′:6,7][1,3,6]-oxadiazepino[2,3-*c*][1,4]benzoxazine-6,8-diol (10d). Glyoxal (0.54, 3.7 mmol) was added to **9d** (0.62 g, 1.85 mmol). After work-up 300 mg (37%) of **10d** were obtained, mp 211–213°C. IR (KBr) 3412, 1518, 1344, 1316, 1272, 1246, 1228, 1056, 994 cm^1; ^1H NMR (400 MHz, DMSO-d_6) δ 7.78 (2H, d, *J*=2.5 Hz, H-1,13), 7.68 (2H, dd, *J*=8.6, 2.5 Hz, H-3,11), 7.55 (2H, d, *J*=5.7 Hz, OH), 7.03 (2H, d, *J*=8.6 Hz, H-4,10), 5.46 (2H, d, *J*=5.7 Hz, H-6,8), 4.36 (2H, s, H-6a,7a), 4.34 (2H, AA′BB′, H-15,16), 3.41 (2H, AA′BB′,

H-15′,16′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.4 (C-4a), 142.5 (C-2), 130.9 (C-13a), 117.4 (C-4), 115.5 (C-3), 106.6 (C-1), 89.64 (C-6), 81.8 (C-6a), 47.0 (C-15); MS (EI, 70eV, DIP) *m/z* (%) 414 (M^+-H_2O, 0.4), 385 (2), 356 (26), 207(27), 192 (19), 178 (11), 165 (20), 164 (47), 134 (14), 73 (11), 70(21), 61 (25), 45 (39), 44 (52), 43 (100); *Anal. calcd for* $C_{18}H_{16}N_4O_9$: C, 50.00; H, 3.70; N, 12.96; *Found*: C, 49.93; H, 4.08; N, 12.17.

4.3.5. 6,6a,7a,8,15,16-Hexahydro-2,12-dichloro-[1,4]benzoxazino[4′,3′:6,7][1,3,6] oxadiazepino [2,3-*c*][1,4]benzoxazine-6,8-diol (10e). Glyoxal (0.78 g, 5.4 mmol) was added to **9e** (0.85 g, 2.72 mmol), 36% (400 mg) yield of **10e,** mp 219–222 °C (dec). IR (KBr) 3288, 1676, 1604, 1502, 1354, 1214, 1206, 1096, 1052, 1040, 1000, 836, 804 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.40 (2H, brs, OH), 7.03 (2H, d, *J*=2.2 Hz, H-1,13), 6.79 (2H, d, *J*=8.5 Hz, H-4,10), 6.71 (2H, dd, *J*=8.5, 2.2 Hz, H-3,11), 5.31 (2H, d, *J*=1.3 Hz, H-6,8), 4.22 (2H, d, *J*=1.3 Hz, H-6a,7a), 4.16 (2H, AA′BB′,H-15,16), 3.23 (2H, AA′BB′, H-15′,16′); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 140.6 (C-4a), 132.2 (C-13a), 126.2 (C-2), 118.7 (C-3,4), 111.5 (C-1), 89.2 (C-6), 82.4 (C-6a), 47.3 (C-15); MS (EI, 70 eV, DIP) *m/z* (%) 412 (M^++1), 352 (35), 334 (27), 289 (33), 153 (100), 77 (17); *Anal. calcd for* $C_{18}H_{16}N_2O_5Cl_2$: C, 52.58; H, 3.89; N, 6.81; *Found*: C, 52.46; H, 3.91; N, 7.06.

4.4. General procedure for the preparation of 4,4′-(1,2-ethanediyl)-bis(3,4)dihydro-2H-benzo[1,4]-oxazin-2-ol (11)

To a solution of the appropriate oxadiazepine (1.0 mmol) in 20 mL of THF, 1.46 mmol of BH_3–THF was added dropwise and the reaction was kept under reflux for 2 h. After cooling to room temperature, a few drops of 10% NaOH were added, the solution was dried over Na_2SO_4 and the solvent was evaporated under vacuum. The solid residue was washed with ethanol.

4.4.1. 4,4′-(1,2-Ethanediyl-bis(3,4)dihydro-2H-benzo[1,4]-oxazin-2-ol (11a). Prepared from **10a** (0.25 g, 0.73 mmol) and 0.73 mL (1.46 mmol) of BH_3–THF. The solid residue was washed with ethanol to yield 122 mg (48%) of **11a**, mp 120–121°C. IR (KBr) 3446, 3216, 2918, 2850, 1606, 1504, 1470, 1458, 1358, 1282, 1238, 1200, 1170, 1110, 1048, 932, 816, 806, 740 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.12 (2H, d, *J*=2.6 Hz, OH), 7,10 (2H, d, *J*=2.6 Hz, OH), 6.74 (2H, ddd, *J*=8.0, 7.6, 1.5 Hz, H-6,6′), 6.68 (2H, dd, *J*=8.0, 1.5 Hz, H-5,5′), 6.67 (2H, dd, *J*=7.6, 1.5 Hz, H-8,8′), 6.53 (2H, ddd, *J*=7.6, 1.5 Hz, H-7,7′), 5.28 (2H, d, *J*=4.8 Hz, H-2,2′), 3.45 (4H, brs, $(CH_2)_2$), 3.38 (2H, d, *J*=11.5 Hz, H-3a,3a′), 3.12 (2H, dt, *J*=11.5, 4.8 Hz, H-3b,3b′); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.3 (C-8a), 134.7 (C-4a), 121.8 (C-6), 117.3 (C-7), 116.7 (C-8), 111.6 (C-5), 89.8 (C-2), 52.5 and 52.4 (C-3) 47.5 and 47.4 (C-9); MS (EI, 70 eV, DIP) *m/z* (%) 328 (M^+, 26), 329 (M^++1, 5), 165 (11), 164 (M^+/2, 100), 134 (70), 106 (22), 93 (11), 77 (14), 65 (23). *HRMS calcd for* $C_{18}H_{20}N_2O_4$: 328.1423. *Found*: 328.142. Error −0.6 ppm

4.4.2. 4,4′-(1,2)-Ethanediyl-bis(3,4)dihydro-2H-benzo[1,4]-oxazin-6-methyl-2-ol (11b). Prepared from oxadiazepine **10b** (0.31 g, 0.84 mmol) and 0.84 mL (1.7 mmol) of BH_3–THF. After work-up 220 mg (73%) of **11b** were obtained, mp 187–188°C. IR (KBr) 3336, 3032, 2916, 2852, 1610, 1516, 1458, 1438, 1368, 1354, 1312, 1278, 1208, 1190, 1102, 1054, 1038, 930, 796 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.05(2H, br, OH), 6.55 (2H, d, *J*=7.9 Hz, H-8,8′), 6.48 (2H, s, H-5,5′), 6.32 (2H, d, *J*=7.9 Hz, H-7,7′), 5.21 (2H, t, *J*=2.5 Hz, H-2,2′), 3.43 (4H, s, $(CH_2)_2$), 3.11 (4H, br, H-3a,3b,3a′,3b′), 2.13 (6H, s, Me); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 140.4 (C-8a), 134.7 (C-4a), 130.7 (C-6), 118.0 (C-7), 116.8 (C-8), 112.6 (C-5), 90.1 (C-2), 52.9 (C-3) 47.6 (C-9). 21.7 (CH_3); MS (EI, 70 eV, DIP) *m/z* (%) 356 (M^++1, 38), 179 (12), 178 (M^+/2, 100), 148 (52), 91 (10), 79 (12), 77 (16). *Anal. calcd for* $C_{20}H_{24}N_2O_4$: C, 67.41; H, 6.74; N,7.86; *Found*: C, 67.18; H, 6.72; N, 7.79.

4.5. General procedure for the preparation of *N,N′*-ethylene-2,2′-bisbenzoxazolidines (12)

To a solution of the appropriate bisphenol (1.0 mmol) 1.0 mmol of 40% aqueous glyoxal was added dropwise and the solution was refluxed for 24 h using a Dean Stark trap. The solvent was evaporated under vacuum and the residue washed with acetone. Attempts to recrystallize the products by column chromatography or crystallization caused extensive hydrolysis and recovery of the starting materials.

4.5.1. *N,N′*-Ethylene-2,2′-bisbenzoxazolidine (12a). It was prepared as reported.[25]

4.5.2. *N,N′*-Ethylene-5,5′-dimethyl-2,2′-bisbenzoxazolidine (12b). Glyoxal (0.16 g, 1.10 mmol) was added to **9b** (0.3 g, 1.10 mmol) in 25 mL toluene:ethanol (9:1) and the solution was refluxed 4 h. After work-up 150 mg (47%) of **12b** were obtained, mp 168–170°C. IR (KBr) 2918, 2854, 1612, 1508, 1496, 1472, 1464, 1442, 1370, 1352, 1336, 1276, 1262, 1218, 1180, 982 cm^{-1}; ^{1}H NMR (DMSO-d_6, 270 MHz) δ 6.60 (2H, d, *J*=7.9 Hz, H-7,7′), 6.47 (2H, s, H-4,4′), 6.37 (2H, d, *J*=7.9 Hz, H-6,6′), 5.39 (2H, s, H-2,2′), 3.67 and 3.16 (4H, AA′BB′, H-8a,8a′,8b,8b′), 2.17 (6H, s, CH_3); ^{13}C NMR (DMSO-d_6, 67.9 MHz) δ 147.9 (C-7a), 138.2 (C-3a), 131.6 (C-5), 119.0 (C-6), 108.1 (C-7), 107.9 (C-4), 93.6 (C-2), 42.0 (C-8), 21.5 (CH_3); MS (EI, 70 eV, DIP) *m/z* (%) 294 (M^+, 45), 295 (M^++1, 9), 161 (25), 133 (100), 132 (20), 91 (5), 78 (18) 77 (14), 65 (10).

4.5.3. *N,N′*-Ethylene-6,6′dimethyl-2,2′-bisbenzoxazolidine (12c). Glyoxal (0.26 g, 1.83 mmol) was added to **9c** (0.5 g, 1.83 mmol) in benzene–ethanol (9:1), 4 h reflux. The residue washed with hexane: ethyl acetate to yield 220 mg (41%) of **12c**, mp 172–173 °C. IR (KBr) 2918, 2850, 1506, 1494, 1472 cm^{-1};^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.62 (2H, d, *J*=7.8 Hz, H-5,5′), 6.61 (2H, brs, H-7,7′), 6.37 (2H, d, *J*=7.8 Hz, H-4,4′), 5.44 (2H, s H-2,2′), 3.50 and 3.32 (4H, AA′BB′, H-8a,8b,8a′,8b′). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 150.5 (C-7a), 135.9 (C-3a), 129.9 (C-6), 122.2 (C-5), 110.3 (C-7), 106.5 (C-4), 94.2 (C-2), 43.0 (C-8), 21.5 (CH_3); MS (EI, 70 eV, DIP) *m/z* (%) 294 (M^+, 32), 295 (M^++1, 7), 161 (17), 134 (12), 133 (100), 132 (20), 106 (9), 78 (21), 77 (15).

4.5.4. *N,N′*-Ethylene-5,5′dichloro-2,2′-bisbenzoxazolidine (12e). Glyoxal (0.25 ml, 2.24 mmol) was added to **9e**

(0.7 g, 2.24 mmol) in ethyl acetate. The residue was washed with ethyl acetate to yield 489 mg (62%) of **12e**, mp 205–206°C. IR (KBr) 2922, 2360, 1486, 1254, 1236, 1184 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 6.75 (2H, d, J=1.8 Hz, H-4,4′), 6.71 (2H, d, J=8.0 Hz, H-7,7′), 6.56 (2H, dd, J=8.0, 1.8 Hz, H-6,6′), 5.61 (2H, s H-2,2′), 3.79 and 3.21 (2H each, AA′BB′, H-8a,8b,8a′,8b′). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 148.9 (C-7a), 139.6 (C-3a), 126.5 (C-5), 117.8 (C-6), 109.1 (C-7), 106.7 (C-4), 93.8 (C-2), 40.2 (C-8); MS (EI, 70eV, DIP) m/z (%)338 (M^++4, 2) 337 (M^++3, 3), 336(M^++2, 14), 335 (M^++1, 4), 334 (M^+, 21), 181 (20), 155 (32), 153 (100), 125 (14), 63 (25). *HRMS* 334.0276. *Calcd for* $C_{16}H_{12}Cl_2N_2O_2$. *Found*: 334.0280. Error +1.3 ppm.

4.5.5. *N,N′*-Ethylene-5,5′-ditertbutyl-2,2′-bisbenzoxazolidine (12f). Glyoxal (0.24 g, 1.68 mmol) was added to **9f** (0.6 g, 1.68 mmol) in benzene:ethanol (9:1), 4 h reflux. The residue was washed with hexane: ethyl acetate to yield 200 mg (32%) of **12f**, mp 204–205°C. IR (KBr) 2958, 2918, 2850, 1636, 1622, 1616, 1604, 1540, 1522, 1500, 1474, 1466, 1458, 1436, 1354, 1290, 1268, 1248, 1218, 1192, 1144, 1050, 816 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 6.71 (2H, s, H-4,4′), 6.62 (2H, d, J=8.0 Hz, H-7,7′), 6.55 (2H, d, J=8.0 Hz, H-6,6′), 5.42 (2H, s, H-2,2′), 3.68 and 3.26 (2H each, AA′BB′, H-8a,8b,8a′8b′), 1.23 (18H, s, $C(CH_3)_3$). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 147.7 (C-7a), 145.4 (C-5), 137.9 (C-3a), 115.1 (C-6), 107.4 (C-7), 104.6 (C-4), 93.8 (C-2), 42.1 (C-8), 34.8 ($C(CH_3)_3$), 32.0 ($C(CH_3)_3$); MS (EI, 70eV, DIP) m/z (%) 379 (M^++1, 9), 378 (M^+, 33), 203 (M, 22), 175 (M, 23), 161 (14), 160 (100), 132 (18), 41 (12). *HRMS* 378.2307. *Calcd for* $C_{24}H_{30}N_2O_2$ *Found*: 378.2319. Error +3.1 ppm.

5. Supporting information available

Tables of atomic coordinates, thermal parameters, bond lengths and angles and observed and calculated structure factors have been deposited at the Cambridge Crystallographic Data Center.

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