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A convenient synthesis of 3,4-dihydro-1,4-benzoxazin-2-ones

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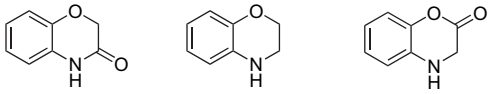
ABSTRACT

3,4-Dihydro-1,4-benzoxazin-2-one was prepared for the first time by catalytic hydrogenation of 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one. A simple and efficient synthesis of 4-benzyl- and 4-alkyl-3,4-dihydro-1,4-benzoxazin-2-one derivatives from ethyl 2-(2-hydroxyphenylamino)acetate and aldehydes is described. Some considerations regarding the reactivity of 3,4-dihydro-1,4-benzoxazin-2-ones are given.

1. Introduction

In contrast to the 2*H*-1,4-benzoxazin-3(4*H*)-one (**1**) and 3,4-dihydro-2*H*-1,4-benzoxazine (**2**) scaffolds, which have been intensively studied[1] and are present as structural subunits of many naturally occurring[2] and synthetic[3] bioactive compounds, derivatives of 3,4-dihydro-1,4-benzoxazin-2-one (**3**) are much less well known. While the majority of the described derivatives of **3** bear 3-alkyl[4–6] or 3-alkylidene[7,8] side chains, less information is available in the literature about the 3-unsubstituted derivatives. Moreover, a synthesis of the parent 3,4-dihydro-1,4-benzoxazin-2-one (**3**) has, to our knowledge, not yet been described.



1 **2** **3**

In the course of our synthetic work directed towards discovery of new potential antibacterial drugs, we required various *N*-substituted 3,4-dihydro-1,4-benzoxazin-2-one derivatives, which could be used as starting compounds for further functionalization. We report here the synthesis of hitherto unknown 4-benzyl- and 4-alkyl-3,4-dihydro-1,4-benzoxazin-2-ones **12**–**21** and the first successful synthesis of the parent 3,4-dihydro-1,4-benzoxazin-2-one (**3**).

2. Results and discussion

Our initial plan for the preparation of 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one derivatives was first to develop a suitable synthesis of 3,4-dihydro-1,4-benzoxazin-2-one (**3**) and then functionalize it by N-alkylation using appropriate benzyl halides as alkylating agents. In our first attempt to prepare **3** by analogy to the synthesis of 2*H*-1,4-benzoxazin-3(4*H*)-one derivatives from 2-aminophenols and chloroacetyl chloride,[9–13] 2-nitrophenol (**4**) and chloroacetyl chloride (**5**) were reacted in the presence of triethylamine to give the expected 2-nitrophenyl 2-chloroacetate (**6**) in almost quantitative yield (Scheme 1). In the next step, the nitro group was reduced to the amine by catalytic hydrogenation, using palladium on charcoal as catalyst. This was expected to induce a spontaneous ring closure to give the lactone **3**. However, analysis of the reaction product revealed that this did not happen and, using ethanol as a solvent, only 2-aminophenol (**7a**) was isolated, which demonstrated that the ester moiety in **6** was susceptible to alcoholysis. For this reason, we decided to use an inert solvent such as tetrahydrofuran, but again failed to obtain the desired product **3**. Instead, 2-chloro-*N*-(2-hydroxyphenyl)-acetamide (**8**) was unexpectedly obtained, indicating that, following reduction of the nitro group, oxygen to nitrogen rearrangement took place. Such rearrangements are common with acylated 2-aminophenols and lead to a reversible equilibrium in which the more stable isomer predominates (Scheme 2). According to the theory of LeRosen and Smith[14,15] for predicting the composition of an equilibrium mixture of *N*- and *O*-acylated phenols on the basis of the principle of minimum charge concentration, the predominance of the acetamide **8** in the reaction mixture can be explained by the possibility of delocalization of the lone pair of electrons on the nitrogen, leading to better equalization of charge over the molecule.

Since attempted cyclization of 2-nitrophenol with chloroacetyl chloride did not result in the desired product **3**, we were forced to choose a different reaction pathway. This time 2-aminophenol (**7a**) and ethyl 2-bromoacetate (**9**) were reacted in the presence of potassium fluoride and the *N*-alkylated product **10a** was obtained (Scheme 3). We anticipated that compound **10a** would be easily converted to lactone **3**, either by conventionally heating the

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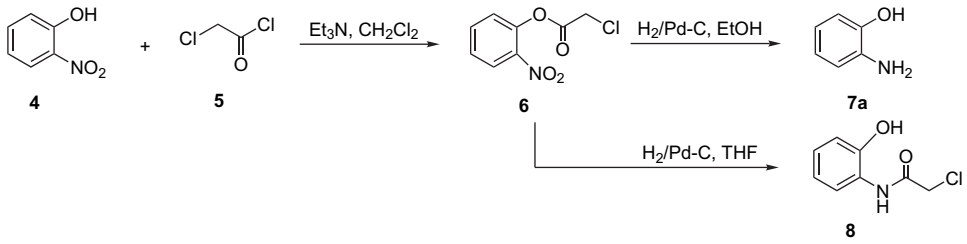
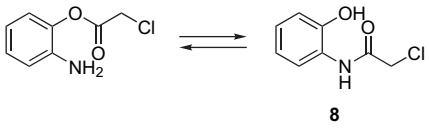
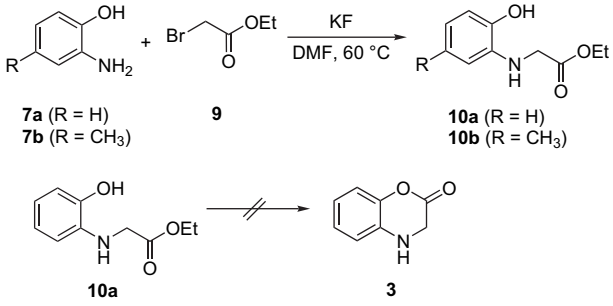


Scheme 1.



Scheme 2.



Scheme 3.

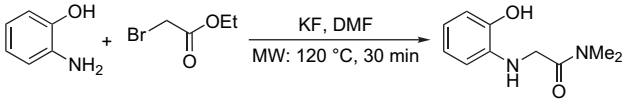
reaction mixture or by applying microwave radiation. Despite several attempts in which the solvent, temperature, acid or base catalyst and reaction time were varied, the target 3,4-dihydro-1,4-benzoxazin-2-one (**3**) could not be obtained (Table 1). This was surprising, since the isomeric 2*H*-1,4-benzoxazin-3(4*H*)-one (**1**) is easily formed by cyclization of in situ formed ethyl 2-(2-aminophenoxy)acetate.[16]

In an attempt to obtain 3,4-dihydro-1,4-benzoxazin-2-one (**3**) in a one pot reaction by heating 2-aminophenol (**7a**) and ethyl 2-bromoacetate (**9**) in the presence of potassium fluoride in a microwave reactor at 120 °C for 30 min, instead of the expected benzoxazinone **3**, 2-(2-hydroxyphenylamino)-*N*,*N*-dimethylacetamide (**11**) was obtained in moderate yield (Scheme 4). The occurrence of dimethylamine, which in the reaction mixture acts as a nucleophile to form the amide **11**, can be explained by partial decomposition of DMF on intense heating.[17] Compound **3** could also not be obtained when under same conditions DMF was replaced by *N*-methylpyrrolidone as solvent.

Table 1
Reaction conditions applied for the attempted synthesis of **3** by cyclization of **10a**

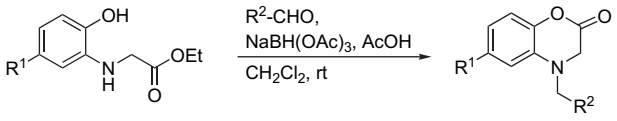
Reagent, solvent	*T* [°C]	*t*
KF, DMF	60	24 h
KF, DMF	120, MW[a]	30 min
K_2CO_3, $BnEt_3N^+Cl^-$, DMF	120, MW	25 min
—, DMF	100, MW	20 min
$NaHCO_3$, DMF	120, MW	20 min
$NaHCO_3$, DMF	70	24 h
NaOEt, EtOH	60	5 h
NaH, DMF	rt[b]	24 h
p-TosOH, toluene	120, MW	20 min
p-TosOH, 1,4-dioxane	150, MW	30 min

[a] Microwave irradiation.
[b] Room temperature.



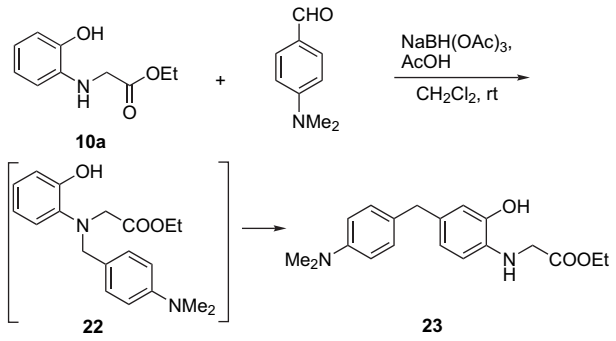
Scheme 4.

Searching for an explanation for the unsuccessful attempts to cyclize **10a** to 3,4-dihydro-2*H*-1,4-benzoxazin-2-one (**3**), we came across the suggestion of Freedman and Frost[18] that the formation of the morpholine-2-one ring from the corresponding *N*-substituted 2-aminophenols is spontaneous when the nitrogen is tertiary, but not when it is secondary. Although the presence or absence of an *N*-alkyl group appears to be the dominant factor, steric and electronic effects of the substituents in the α-position of the amino group also control the ring closure.[19,20] Thus, it became clear that, for successful preparation of *N*-substituted 3,4-dihydro-1,4-benzoxazin-2-one derivatives, the order of the initially envisaged synthetic steps should be reversed. The secondary amino group of ethyl 2-(2-hydroxyphenylamino)acetate (**10a**) was first benzylated and the obtained *N*-benzyl derivatives cyclized to 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one derivatives **12**–**17**. The N-benzylation step was performed by reductive amination of benzaldehyde derivatives with **10a**, using sodium triacetoxyborohydride[21] as a reducing agent (Scheme 5). After attachment of a benzyl group, spontaneous ring closure took place and lactones **12**–**17** were isolated as the sole products. As an exception, in the reaction of **10a** with 4-(dimethylamino)benzaldehyde, product **23** was obtained in 55% yield, probably as a result of Hofmann–Martius rearrangement[22–24] of intermediary formed ethyl 2-((4-(dimethylamino)benzyl)-(2-hydroxy-phenyl)amino)acetate (**22**) (Scheme 6).



R^1	R^2	Product	Yield (%)
H	C_6H_5	**12**	65
H	C_6H_4-4-CN	**13**	41
H	C_6H_4-4-COOH	**14**	15
H	C_6H_4-4-OMe	**15**	61
H	C_6H_4-4-OH	**16**	40
H	C_6H_4-3-OH	**17**	30
CH_3	C_6H_5	**18**	55
H	$CH_2C_6H_5$	**19**	70
H	CH_3	**20**	37
H	$(CH_2)_7CH_3$	**21**	62

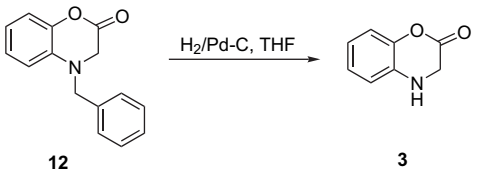
Scheme 5.



Scheme 6.

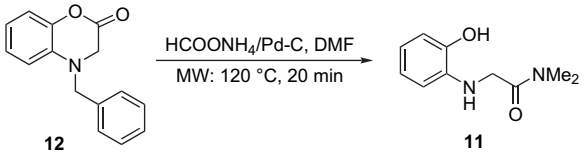
To broaden the scope of the method, we also performed reductive amination of **10a** with some aliphatic aldehydes, which, after spontaneous ring closure, afforded 4-alkyl-3,4-dihydro-1,4-benzoxazin-2-one derivatives **19**–**21**. Further, we tried to extend the scope of our synthesis with the preparation of 3,4-dihydro-1,4-benzoxazin-2-one derivatives bearing different substituents in the aromatic ring. Unfortunately, successful preparation of analogues of **10a**, using the method depicted in Scheme 3 was found to be strongly dependant on the position and electronic properties of substituents in the aromatic ring. 4-Chloro-, 5-ethoxycarbonyl-, 4-methyl- and 4-nitro-2-aminophenol were reacted with ethyl 2-bromoacetate (**9**) in the presence of potassium fluoride in *N*,*N*-dimethylformamide, but only 2-amino-4-methyl-phenol gave the expected product **10b**, which was successfully transformed to the 3,4-dihydro-1,4-benzoxazin-2-one derivative **18**. In all other cases O-alkylation and subsequent cyclization to the corresponding 3,4-dihydro-2*H*-1,4-benzoxazine-3-one derivatives took place.[25] However, this does not preclude the application of our method to the synthesis of 3,4-dihydro-1,4-benzoxazin-2-ones substituted in the aromatic ring from analogues of **10** accessible in a different way.

Encouraged by the successful preparation of 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-ones **12**–**18**, we presumed that **3** could be obtained from **12** by hydrogenolytic cleavage of the benzyl group. Indeed, 3,4-dihydro-2*H*-1,4-benzoxazin-2-one (**3**) was obtained for the first time by catalytic hydrogenation of **12** using palladium on charcoal as a catalyst (Scheme 7).



Scheme 7.

In an attempt to remove the benzyl group from **12** using ammonium formate as a hydrogen transfer agent in the presence of Pd/C as catalyst, and when the reaction was carried out in *N*,*N*-dimethylformamide or *N*-methylpyrrolidone in a microwave reactor, **3** was not formed; instead product **11** was obtained in DMF (Scheme 8). This reaction illustrates well the reactivity of the parent 3,4-dihydro-1,4-benzoxazin-2-one ring. Although debenzylation occurred, the dimethylamine formed in situ acted as a nucleophile and opened the lactone ring of **3**. It should thus be pointed out that 3,4-dihydro-1,4-benzoxazin-2-one (**3**) is unstable in the presence of nucleophiles and undergoes ring opening.



Scheme 8.

3. Conclusion

In conclusion, the first synthesis of 3,4-dihydro-1,4-benzoxazin-2-one (**3**) was accomplished by catalytic hydrogenation of 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one (**12**). The latter was formed by spontaneous lactonization of ethyl *N*-benzyl 2-(2-hydroxyphenyl-amino)acetate, itself obtained by reductive amination of benzaldehyde with ethyl 2-(2-hydroxyphenylamino)-acetate (**10a**). Using the same synthetic strategy, a series of 4-alkyl- and 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-ones were prepared. These results contribute to the chemistry of 3,4-dihydro-1,4-benzoxazin-2-ones, which, in comparison with isomeric 2*H*-1,4-benzoxazin-3(4*H*)-ones, have been much less explored.

4. Experimental

4.1. General

Chemicals obtained from Aldrich Chemical Co. and Merck were used without further purification. Analytical TLC was performed on Merck silica gel (60 F_{254}) plates (0.25 mm) and components visualized with ultraviolet light. Column chromatography was carried out on silica gel (particle size 240–400 mesh). Microwave assisted reactions were performed using a CEM Discover microwave reactor (CEM Corporation, USA). Melting points were determined on a Reichert hot stage microscope and are uncorrected. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX_{300} spectrometer in $CDCl_3$ or DMSO-d_6 solution, with TMS as the internal standard, at 300 MHz or 75 MHz, respectively. IR spectra were obtained on a Perkin–Elmer FTIR System Spectrum BX spectrometer. Microanalyses were performed on a Perkin–Elmer C, H, N analyzer 240C. Mass spectra were obtained using a VG Analytical Autospec Q mass spectrometer. All reported yields are those of the purified products.

4.2. 2-Nitrophenyl 2-chloroacetate (6)

Chloroacetyl chloride (**5**) (1.04 mL, 13.0 mmol) was added dropwise to a stirred solution of 2-nitrophenol (**4**) (1.39 g, 10.0 mmol) and triethylamine (2.1 mL, 15.0 mmol) in anhydrous dichloromethane (10 mL), cooled on ice bath. The reaction mixture was stirred for 5 h and allowed to reach room temperature. Dichloromethane (30 mL) was added and the organic phase was washed successively with water (2×15 mL), saturated aqueous $NaHCO_3$ (2×15 mL) and brine (2×15 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was crystallized from EtOAc/petroleum ether to afford **6** as white crystals (1.94 g, 90%), mp 62–63 °C (lit.[26] 62–62.5 °C); R_f=0.27 (EtOAc/petroleum ether=1:4). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 4.79 (s, 2H, CH_2), 7.53 (dd, 1H, $J_{5,6}$=8.1 Hz, $J_{4,6}$=1.2 Hz, 6-H), 7.60 (ddd, 1H, ^3J=8.1 Hz, ^4J=1.2 Hz, 4/5-H), 7.85 (ddd, 1H, ^3J=8.1 Hz, ^4J=1.2 Hz, 4/5-H), 8.19 (dd, 1H, $J_{3,4}$=8.1 Hz, $J_{3,5}$=1.2 Hz, 3-H). MS (EI) *m*/*z* (%): 217 ([M+2]$^+$, 10), 215 (M$^+$, 38), 188 (20), 169 (31), 139 (100), 122 (34), 109 (23), 106 (17), 92 (25), 77 (75), 63 (21).

4.3. 2-Chloro-*N*-(2-hydroxyphenyl)acetamide (8)

To a solution of compound **6** (200 mg, 0.93 mmol) and triethylamine (0.155 mL, 1.11 mmol) in anhydrous tetrahydrofuran (10 mL), 10% Pd–C (20 mg) was added. The reaction mixture was

stirred under a hydrogen atmosphere for 1 h. The catalyst was then filtered off and the solvent removed under reduced pressure. The residue was dissolved in EtOAc (30 mL) and washed with water (3×10 mL) and brine (2×10 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was separated by flash column chromatography using EtOAc/petroleum ether (1:2) as eluent, giving a brown-white solid (32 mg, 19%), mp 120–125 °C (lit.[27] 137–138 °C); R_f=0.49 (EtOAc/petroleum ether=1:1). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 4.38 (s, 2H, CH_2), 6.78 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.2 Hz, 4/5-H), 6.89 (dd, 1H, $J_{3,4}$=7.8 Hz, $J_{3,5}$=1.2 Hz, 3-H), 6.96 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.2 Hz, 4/5-H), 7.88 (d, 1H, J=7.8 Hz, 6-H), 9.41 (br s, 1H, NH), 9.92 (s, 1H, OH). MS (EI) m/z (%): 187 ([M+2]$^+$, 9), 185 (M$^+$, 27), 136 (16), 109 (100), 80 (41).

4.4. General procedure for the preparation of ethyl 2-(2-hydroxyphenylamino)acetates 10a and 10b

To a stirred suspension of 2-aminophenol **7a** (1.09 g, 10.0 mmol) or **7b** (1.23 g, 10.0 mmol) and potassium fluoride (1.45 g, 25.0 mmol) in dry *N*,*N*-dimethylformamide (50 mL), ethyl 2-bromoacetate (1.67 g, 10.0 mmol) was added. The resulting mixture was stirred at 60 °C for 6 h and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc (60 mL) and washed with saturated aqueous $NaHCO_3$ (2×15 mL), water (2×15 mL) and brine (2×15 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure.

4.4.1. Ethyl 2-(2-hydroxyphenylamino)acetate (*10a*)

Yield: 90%; brown crystals; mp 90–94 °C; R_f=0.65 (EtOAc/petroleum ether=1:1); IR (KBr) 3342, 1722, 1614, 1531, 1455, 1438, 1382, 1354, 1327, 1223, 1157, 1086, 1055, 1029, 894, 850, 826, 812, 738 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.20 (t, 3H, J=7.2 Hz, CH_2CH_3), 3.90 (d, 2H, J=6.0 Hz, CH_2CO), 4.13 (q, 2H, J=7.2 Hz, CH_2CH_3), 4.99 (t, 1H, J=6.0 Hz, NH), 6.36 (dd, 1H, $J_{3,4}$=7.8 Hz, $J_{3,5}$=1.5 Hz, 3-H), 6.46 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 4/5-H), 6.61 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 4/5-H), 6.68 (dd, 1H, $J_{6,5}$=7.8 Hz, $J_{6,4}$=1.5 Hz, 6-H), 9.29 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.02 (CH_3CH_2), 44.82 ($NHCH_2CO$), 60.26 (CH_3CH_2), 109.77 (Ar–C), 113.49 (Ar–C), 116.42 (Ar–C), 119.52 (Ar–C), 136.54 (1/2-C), 144.06 (1/2-C), 171.22 (C=O). MS (EI) m/z (%): 195 (M$^+$, 33), 122 (100), 94 (14), 77 (13), 65 (9). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.18; found C, 61.57; H, 6.74; N, 7.15.

4.4.2. Ethyl 2-(2-hydroxy-5-methylphenylamino)-acetate (*10b*)

Yield: 55%; brown crystals; mp 114–118 °C; R_f=0.59 (EtOAc/petroleum ether=1:1); IR (KBr) 3398, 3033, 2985, 2870, 2344, 2361, 1820, 1714, 1607, 1531, 1443, 1374, 1318, 1258, 1100, 1019, 866, 838, 812, 795, 606 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.20 (t, 3H, J=7.2 Hz, CH_2CH_3), 2.12 (s, 3H, $ArCH_3$), 3.88 (d, 2H, J=6.0 Hz, CH_2CO), 4.13 (q, 2H, J=7.2 Hz, CH_2CH_3), 4.92 (t, 1H, J=6.0 Hz, NH), 6.19 (s, 1H, 6-H), 6.24 (d, 1H, J=7.8 Hz, 4-H), 6.55 (d, 1H, J=7.8 Hz, 3-H), 9.03 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.02 (CH_3CH_2), 20.75 (Ar–CH_3), 44.86 ($NHCH_2CO$), 60.25 (CH_3CH_2), 110.71 (Ar–C), 113.35 (Ar–C), 116.58 (Ar–C), 127.91 (Ar–C), 136.32 (1/2-C), 141.84 (1/2-C), 171.23 (C=O). MS (EI) m/z (%): 209 (M$^+$, 43), 136 (100), 109 (28), 94 (5), 91 (19), 77 (11), 65 (7). Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69; found C, 63.32; H, 7.36; N, 6.77.

4.5. 2-(2-Hydroxyphenylamino)-*N*,*N*-dimethylacetamide (11)

4.5.1. Synthesis from 2-aminophenol (*7*) and ethyl 2-bromoacetate (*9*)

A suspension of 2-aminophenol (**7**) (500 mg, 4.58 mmol), potassium fluoride (666 mg, 11.46 mmol) and ethyl 2-bromoacetate (**9**) (0.512 mL, 4.58 mmol) in anhydrous *N*,*N*-dimethylformamide (4 mL) in a sealed 10 mL process vial was placed in a microwave reactor and heated at 120 °C for 30 min. The reaction mixture was cooled to room temperature and adjusted with 1 M NaOH to pH 10. The mixture was poured into ice/water (20 g) and stood in a refrigerator overnight. The precipitate was filtered off and washed with ether, yielding 227 mg (26%) of grey solid, mp 183–187 °C, R_f=0.42 (EtOAc/petroleum ether=4:1); IR (KBr) 3411, 3245, 2925, 2852, 2362, 1611, 1527, 1474, 1452, 1419, 1382, 1334, 1247, 1205, 1151, 1127, 1088, 1045, 995, 908, 830, 771, 732, 630, 593, 520, 486 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.90 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 3.85 (d, 2H, J=4.5 Hz, CH_2), 5.08 (t, 1H, J=4.5 Hz, NH), 6.43 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.2 Hz, 4/5-H), 6.50 (dd, 1H, $J_{3,4}$=7.8 Hz, $J_{3,5}$=1.2 Hz, 3-H), 6.61–6.69 (m, 2H, 5-H, 6-H), 9.28 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 34.93 (CH_3), 35.27 (CH_3), 44.43 (CH_2), 110.25 (Ar–C), 113.15 (Ar–C), 115.93 (Ar–C), 119.53 (Ar–C), 136.71 (1/2-C), 143.91 (1/2-C), 168.83 (C=O). MS (EI) m/z (%): 194 (M$^+$, 80), 149 (28), 122 (100), 95 (20), 77 (16), 72 (9), 65 (8). Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.84; H, 7.27; N, 14.42; found C, 61.81; H, 7.27; N, 14.33.

4.5.2. Synthesis from 4-benzyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (*12*)

A 10 mL process vial was charged with a solution of 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one (**12**) (100 mg, 0.418 mmol) in anhydrous *N*,*N*-dimethylformamide (1.5 mL), ammonium formate (132 mg, 2.09 mmol) and 10% Pd–C (20 mg). The vial was sealed, placed in a microwave reactor and heated at 120 °C for 20 min. The solvent was removed under reduced pressure and the residue dissolved in EtOAc (30 mL). The organic phase was washed with water (2×10 mL) and brine (2×10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Compound **11** was isolated from the residue by flash column chromatography using EtOAc/petroleum ether (6:1) as eluant, giving 19 mg (23%) of a grey solid. Spectroscopic data were identical to those described above.

4.6. General procedure for the preparation of *N*-alkyl/benzyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-ones 12–21 and ethyl 2-(4-(4-(dimethylamino)benzyl)-2-hydroxy-phenylamino)-acetate (23)

To a solution of ethyl 2-(2-hydroxyphenylamino)acetate (**10a**) (488 mg, 2.5 mmol) or ethyl 2-(2-hydroxy-5-methylphenylamino)-acetate (**10b**) (523 mg, 2.5 mmol) and the corresponding aldehyde (3.0 mmol for **12**–**18**, **23**; 3.5 mmol for **19**–**21**) in dichloromethane (15 mL), glacial acetic acid [0.21 mL (3.75 mmol) for **12**–**18**, **23**;0.43 mL (7.5 mmol) for **19**–**21**] was added and the mixture stirred for 30 min on ice bath. Sodium triacetoxyborohydride [795 mg (3.75 mmol) for **12**–**18**, **23**; 1.06 g (5 mmol) for **19**–**21**] was added in portions. The reaction mixture was stirred overnight and diluted with dichloromethane (15 mL) and the organic phase was washed with saturated aqueous $NaHCO_3$ (2×10 mL), water (2×10 mL) and brine (2×10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using EtOAc/petroleum ether or dichloromethane/methanol as eluant, yielding pure products **12**–**18** and **23**.

4.6.1. 4-Benzyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (*12*)

Yield: 65%; colourless oil; R_f=0.50 (EtOAc/petroleum ether=1:2); IR (NaCl-film) 3525, 3388, 3063, 3030, 2813, 2624, 2362, 2336, 1774, 1696, 1611, 1584, 1502, 1453, 1393, 1339, 1291, 1213, 1162, 1147, 1113, 1026, 1052, 990, 919, 835, 744, 699 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 4.00 (s, 2H, CH_2CO), 4.46 (s, 2H, $CH_2C_6H_5$), 6.82 (ddd, 1H, ^3J=8.1 Hz, ^4J=1.2 Hz, 6/7-H), 6.90 (dd, 1H, $J_{5,6}$=8.1 Hz, $J_{5,7}$=1.2 Hz, 5-H), 7.00–7.08 (m, 2H, 6/7-H, 8-H), 7.30–7.37 (m, 5H, C_6H_5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.65 (CH_2), 53.29 (CH_2), 113.08 (Ar–C), 116.83 (Ar–C), 119.86 (Ar–C), 125.13 (Ar–C),

127.63 (2′,6′/3′,5′-C), 127.74 (Ar–C), 128.78 (2′,6′/3′,5′-C), 134.64 (Ar–C), 135.48 (Ar–C), 141.55 (Ar–C), 164.75 (C=O). MS (EI) *m*/*z* (%): 239 (M^+, 95), 211 (42), 180 (10), 120 (48), 91 (100), 65 (30). HRMS for $C_{15}H_{13}NO_2$: calculated 239.0946; found 239.0951. Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85; found C, 74.73; H, 5.26; N, 5.94.

4.6.2. 4-(2-Oxo-2,3-dihydro-1,4-benzoxazin-4-ylmethyl)-benzonitrile (**13**)

Yield: 41%; red/brown crystals; mp 126–131 °C; R_f=0.43 (EtOAc/petroleum ether=1:2); IR (KBr) 2222, 1774, 1607, 1502, 1459, 1416, 1367, 1327, 1290, 1202, 1149, 1042, 998, 952, 919, 838, 821, 754, 676 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 4.10 (s, 2H, CH_2CO), 4.57 (s, 2H, CH_2N), 6.76 (dd, 1H, $J_{5',6'}$=7.8 Hz, $J_{5',7'}$=1.5 Hz, 5′-H), 6.82 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 6′/7′-H), 6.99 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 6′/7′-H), 7.08 (dd, 1H, $J_{7',8'}$=7.8 Hz, $J_{6',8'}$=1.5 Hz, 8′-H), 7.56 (d, 2H, *J*=8.4 Hz, 2-H, 6-H), 7.83 (d, 2H, *J*=8.4 Hz, 3-H, 5-H). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 51.03 (CH_2), 53.02 (CH_2), 110.94, 114.09, 117.32, 119.63, 120.22, 125.90, 129.19 (2′,6′-C), 133.36 (3′,5′-C), 135.20, 142.03, 143.84, 165.57 (C=O). MS (EI) *m*/*z* (%): 264 (M^+, 71), 236 (33), 120 (100), 116 (37), 93 (17), 89 (14), 65 (24). Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60; found C, 72.53; H, 4.85; N, 10.38.

4.6.3. 4-(2-Oxo-2,3-dihydro-1,4-benzoxazin-4-ylmethyl)-benzoic acid (**14**)

Yield: 15%; yellow crystals; mp 245–250 °C; R_f=0.28 (dichloromethane/methanol/AcOH=20:1:0.5); IR (KBr) 3480, 2840, 1951, 1766, 1671, 1610, 1577, 1497, 1465, 1450, 1424, 1359, 1323, 1293, 1211, 1146, 1042, 1018, 957, 918, 868, 796, 759, 676, 759, 702, 676, 604, 553, 489 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 4.07 (s, 2H, CH_2CO), 4.54 (s, 2H, CH_2N), 6.80–6.85 (m, 2H, 5′-H, 6′/7′-H), 7.01 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 6′/7′-H), 7.08 (dd, 1H, $J_{7',8'}$=7.8 Hz, $J_{6',8'}$=1.5 Hz, 8′-H), 7.48 (d, 2H, *J*=8.4 Hz, 2-H, 6-H), 7.92 (d, 2H, *J*=8.4 Hz, 3-H, 5-H), 12.90 (br s, 1H, COOH). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 49.93 (CH_2), 52.15 (CH_2), 113.21 (Ar–C), 116.28 (Ar–C), 119.16 (Ar–C), 124.91 (Ar–C), 127.45 (Ar–C), 129.51 (Ar–C), 129.68 (Ar–C), 134.48 (Ar–C), 141.06 (Ar–C), 141.97 (Ar–C), 164.67 (C=O), 166.95 (C=O). MS (ESI) *m*/*z* (%): 283 (M^+, 20), 282 (100), 237 (8), 235 (21), 233 (28), 231 (16), 212 (11), 135 (6), 113 (6). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94; found C, 67.60; H, 4.75; N, 4.81.

4.6.4. 4-(4-Methoxybenzyl)-3,4-dihydro-2H-1,4-benzoxazin-2-one (**15**)

Yield: 61%; red/brown crystals; mp 245–250 °C; R_f=0.40 (EtOAc/petroleum ether=1:4); IR (KBr) 1779, 1614, 1513, 1459, 1377, 1247, 1030, 916, 835, 818, 755, 672, 598, 554, 512, 472 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 3.74 (s, 3H, CH_3), 3.92 (s, 2H, CH_2CO), 4.37 (s, 2H, CH_2N), 6.84 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.6 Hz, 7-H), 6.92 (d, 2H, *J*=8.5 Hz, 3′-H, 5′-H), 6.96 (dd, 1H, $J_{5,6}$=7.8 Hz, $J_{6,7}$=1.6 Hz, 5-H), 7.01–7.08 (m, 2H, 6-H, 8-H), 7.29 (d, 2H, *J*=8.5 Hz, 2′-H, 6′-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.34 (CH_2), 52.72 (CH_2), 55.46 (CH_3), 113.11 (Ar–C), 114.23 (3′,5′-C), 116.85 (Ar–C), 119.87 (Ar–C), 125.13 (Ar–C), 127.26 (Ar–C), 129.10 (2′,6′-C), 134.82 (Ar–C), 141.68 (Ar–C), 159.21 (4′-C), 164.91 (C=O). MS (EI) *m*/*z* (%): 269 (M^+, 80), 162 (14), 149 (11), 135 (16), 121 (100), 106 (9), 91 (30), 77 (35), 65 (26). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20; found C, 71.71; H, 5.85; N, 5.15.

4.6.5. 4-(4-Hydroxybenzyl)-3,4-dihydro-2H-1,4-benzoxazin-2-one (**16**)

Yield: 40%; white solid; mp 113–118 °C; R_f=0.29 (dichloromethane/methanol=50:1); IR (KBr) 3408, 2361, 1747, 1636, 1614, 1595, 1518, 1499, 1459, 1451, 1368, 1354, 1327, 1289, 1272, 1200, 1170, 1144, 1106, 1043, 1022, 960, 922, 821, 790, 735, 676, 650, 602, 564, 553, 518, 494, 569 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.76 (s, 2H, CH_2CO), 4.31 (s, 2H, CH_2N), 5.18 (br s, 1H, OH), 6.84 (d, 2H, *J*=8.7 Hz, 3′-H, 5′-H), 6.85 (ddd, 1H, ^3J=7.5 Hz, ^4J=1.2 Hz, 6/7-H), 6.90 (d, 1H, *J*=7.5 Hz, 5-H), 7.05–7.11 (m, 2H, 6/7-H, 8-H), 7.20 (d, 2H, *J*=8.7 Hz, 2′-H, 6′-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.40 (CH_2), 52.84 (CH_2), 113.23 (Ar–C), 115.79 (3′,5′-C), 116.99 (Ar–C), 120.03 (Ar–C), 125.31 (Ar–C), 127.27 (Ar–C), 129.37 (2′,6′-C), 134.86 (Ar–C), 141.73 (Ar–C), 155.48 (4′-C), 165.43 (C=O). MS (EI) *m*/*z* (%): 255 (M^+, 43), 162 (14), 149 (62), 121 (28), 107 (100), 77 (12), 65 (7). Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49; found C, 70.26; H, 5.04; N, 5.41.

4.6.6. 4-(3-Hydroxybenzyl)-3,4-dihydro-2H-1,4-benzoxazin-2-one (**17**)

Yield: 30%; red oil; R_f=0.34 (dichloromethane/methanol=50:1); IR (NaCl-film) 3392, 3071, 2849, 2254, 1770, 1683, 1614, 1504, 1456, 1344, 1293, 1218, 1157, 1113, 1054, 1028, 1000, 916, 879, 835, 782, 747, 696 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 2H, CH_2CO), 4.34 (s, 2H, CH_2N), 5.55 (br s, 1H, OH), 6.78–6.91 (m, 5H, $5H_{Ar}$), 7.04–7.10 (m, 2H, $2H_{Ar}$), 7.24 (m, 1H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 49.69 (CH_2), 53.10 (CH_2), 113.17 (Ar–C), 114.51 (Ar–C), 114.90 (Ar–C), 116.85 (Ar–C), 119.67 (Ar–C), 119.87 (Ar–C), 125.34 (Ar–C), 130.06 (Ar–C), 134.53 (Ar–C), 137.31 (Ar–C), 141.40 (Ar–C), 156.27 (3′-C), 165.56 (C=O). MS (EI) *m*/*z* (%): 255 (M^+, 46), 227 (7), 134 (5), 120 (48), 108 (35), 107 (100), 94 (8), 84 (25), 77 (23), 65 (18). HRMS for $C_{15}H_{13}NO_3$: calculated 255.0895; found 255.0889.

4.6.7. 4-Benzyl-6-methyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (**18**)

Yield: 67%; colourless crystals; mp 93–96 °C; R_f=0.42 (EtOAc/petroleum ether=1:4); IR (KBr) 3850, 3500, 3067, 2917, 2860, 2803, 2358, 2338, 1960, 1764, 1608, 1506, 1454, 1506, 1454, 1370, 1287, 1208, 1146, 1078, 1031, 920, 816, 807, 761, 730, 703, 640, 570, 483 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 2.20 (s, 3H, CH_3), 3.91 (s, 2H, CH_2CO), 4.44 (s, 2H, $CH_2C_6H_5$), 6.63 (dd, 1H, ^3J=7.8 Hz, ^4J=1.2 Hz, 7-H), 6.77 (d, 1H, ^4J=1.2 Hz, 5-H), 6.95 (d, 1H, ^3J=7.8 Hz, 8-H), 7.29–7.37 (m, 5H, C_6H_5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.27 (CH_3), 49.62 (CH_2), 53.33 (CH_2), 113.64 (Ar–C), 116.68 (Ar–C), 120.48 (Ar–C), 127.83 (2′,6′/3′,5′-C), 127.86 (Ar–C), 128.89 (2′,6′/3′,5′-C), 134.51 (Ar–C), 134.99 (Ar–C), 135.63 (Ar–C), 139.73 (Ar–C), 164.94 (C=O). MS (EI) *m*/*z* (%): 253 (M^+, 60), 225 (22), 134 (96), 107 (8), 91 (100), 77 (15), 69 (9), 65 (18). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53; found C, 75.78; H, 6.01; N, 5.53.

4.6.8. 4-Phenethyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (**19**)

Yield: 70%; pink-white crystals; mp 85–88 °C; R_f=0.57 (EtOAc/petroleum ether=1:2); IR (KBr) 3398, 3074, 3025, 2961, 2358, 1768, 1611, 1506, 1466, 1347, 1294, 1229, 1208, 1143, 1083, 1052, 1012, 999, 918, 751, 701, 670, 566, 501, 470 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 2.87 (t, 2H, *J*=6.0 Hz, $CH_2CH_2C_6H_5$), 3.38 (t, 2H, *J*=6.0 Hz, $CH_2CH_2C_6H_5$), 4.06 (s, 2H, CH_2CO), 6.81 (dd, 1H, ^3J=8.1 Hz, ^4J=1.5 Hz, 6/7-H), 7.00 (ddd, 1H, $^3J \approx 8.1$ Hz, ^4J=1.5 Hz, 5/8-H), 7.05 (dd, 1H, ^3J=8.1 Hz, ^4J=1.5 Hz, 5/8-H), 7.10 (ddd, 1H, $^3J \approx 8.1$ Hz, ^4J=1.5 Hz, 6/7-H), 7.20–7.33 (m, 5H, C_6H_5). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 31.71 (CH_2Ph), 50.15 (CH_2), 51.13 (CH_2), 112.44 (Ar–C), 117.11 (Ar–C), 119.41 (Ar–C), 125.26 (Ar–C), 126.67 (Ar–C), 128.56 (2′,6′/3′,5′-C), 128.75 (2′,6′/3′,5′-C), 133.80 (Ar–C), 138.50 (Ar–C), 141.58 (Ar–C), 164.40 (C=O). MS (EI) *m*/*z* (%): 253 (M^+, 23), 162 (100), 134 (27), 107 (6), 91 (8), 77 (18), 65 (10). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53; found C, 75.71; H, 6.01; N, 5.47.

4.6.9. 4-Ethyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (**20**)

Yield: 37%; orange hygroscopic oil; R_f=0.34 (EtOAc/petroleum ether=1:4); IR (NaCl-film) 3523, 3318, 3070, 3045, 2976, 2876, 2815, 2628, 2344, 2330, 2021, 1770, 1694, 1611, 1584, 1504, 1470, 1461, 1394, 1379, 1340, 1292, 1205, 1127, 1100, 1042, 1021, 919, 746 cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz) δ 1.10 (t, 3H, *J*=6.9 Hz, CH_2CH_3), 3.32 (q, 2H, *J*=6.9 Hz, CH_2CH_3), 3.95 (s, 2H, CH_2CO), 6.80 (ddd, 1H, $^3J \approx 7.8$ Hz, ^4J=1.5 Hz, 6/7-H), 6.92 (dd, 1H, ^3J=7.8 Hz,

^4J=1.5 Hz, 5/8-H), 7.04 (dd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 5/8-H), 7.07 (ddd, 1H, $^3J\approx$7.8 Hz, ^4J=1.5 Hz, 6/7-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.10 (CH_3), 38.14 (CH_2), 49.09 (CH_2), 114.68 (Ar–C), 117.80 (Ar–C), 124.72 (Ar–C), 125.19 (4a/8a-C), 125.81 (Ar–C), 140.35 (4a/8a-C), 165.00 (C=O). MS (EI) *m*/*z* (%): 177 (M^+, 18), 163 (43), 148 (100), 135 (73), 122 (10), 120 (25), 106 (12), 97 (8), 91 (30), 79 (27), 77 (34), 65(18). HRMS for $C_{10}H_{11}NO_2$: calculated 177.0790; found 177.0791. Anal. Calcd for $C_{10}H_{11}NO_2\cdot 0.125H_2O$: C, 66.93; H, 6.32; N, 7.81; found C, 67.00; H, 6.46; N, 7.80.

*4.6.10. 4-Nonyl-3,4-dihydro-2H-1,4-benzoxazin-2-one (**21**)*

Yield: 62%; orange hygroscopic oil; R_f=0.74 (EtOAc/petroleum ether=1:4); IR (NaCl-film) 3309, 3045, 3070, 2952, 2925, 2853, 2361, 2343, 1778, 1697, 1612, 1503, 1462, 1340, 1290, 1206, 1162, 1128, 1043, 919, 834, 743 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.86 (t, 3H, J=6.6 Hz, CH_2CH_3), 1.25–1.31 (m, 12H, 6×CH_2), 1.51–1.56 (m, 2H, NCH_2CH_2), 3.21 (t, 2H, J=7.8 Hz, NCH_2CH_2), 3.96 (s, 2H, CH_2CO), 6.79 (ddd, 1H, $^3J\approx$8.0 Hz, ^4J=1.5 Hz, 6/7-H), 6.89 (dd, 1H, ^3J=8.1 Hz, ^4J=1.5 Hz, 5/8-H), 7.03 (dd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz, 5/8-H), 7.06 (ddd, 1H, $^3J\approx$8.0 Hz, ^4J=1.5 Hz, 6/7-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.07 (CH_3), 22.62 (CH_2), 26.73 (CH_2), 26.85 (CH_2), 29.17 (CH_2), 29.22 (CH_2), 29.40 (CH_2), 31.80 (CH_2), 43.14 (CH_2), 49.44 (NCH_2CO), 114.84 (Ar–C), 117.83 (Ar–C), 124.69 (Ar–C), 125.46 (4a/8a-C), 125.75 (Ar–C), 140.35 (4a/8a-C), 165.11 (C=O). MS (EI) *m*/*z* (%): 275 (M^+, 61), 247 (34), 191 (14), 177 (12), 162 (100), 148 (11), 134 (69), 120 (22), 55 (19). HRMS for $C_{17}H_{25}NO_2$: calculated 275.1885; found 275.1892. Anal. Calcd for $C_{17}H_{25}NO_2\cdot 0.25H_2O$: C, 72.95; H, 9.18; N, 5.00; found C, 72.88; H, 9.38; N, 4.78.

*4.6.11. Ethyl 2-(4-(4-(dimethylamino)benzyl)-2-hydroxyphenylamino)acetate (**23**)*

Yield: 55%; yellow crystals; mp 103–109 °C; R_f=0.25 (dichloromethane/methanol=20:1); IR (KBr) 3454, 1740, 1618, 1533, 1516, 1473, 1435, 1373, 1350, 1333, 1298, 1280, 1249, 1210, 1155, 1144, 1045, 1025, 960, 933, 910, 862, 811, 798, 616, 518 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.19 (t, 3H, J=7.2 Hz, CH_2CH_3), 2.83 (s, 6H, $N(CH_3)_2$), 3.61 (s, 2H, $ArCH_2Ar$), 3.86 (d, 2H, J=6.0 Hz, CH_2CO), 4.12 (q, 2H, J=7.2 Hz, CH_2CH_3), 4.82 (t, 1H, J=6.0 Hz, NH), 6.27 (d, 1H, J=8.1 Hz, 6-H), 6.46 (d, 1H, J=8.1 Hz, 5-H), 6.47 (s, 1H, 3-H), 6.64 (d, 2H, J=8.7 Hz, 3′-H, 5′-H), 6.97 (d, 2H, J=8.7 Hz, 2′-H, 6′-H), 9.16 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 75 MHz)[28] δ 14.00 (CH_3), 39.59, 44.98, 60.16, 109.60, 112.55 (3′-C, 5′-C), 113.97, 119.28, 128.94 (2′-C, 6′-C), 129.72, 130.25, 134.44, 143.98, 148.67, 171.23 (C=O). MS (EI) *m*/*z* (%): 328 (M^+, 80), 282 (14), 255 (100), 240 (6), 134 (24), 127 (12), 121 (8). HRMS for $C_{19}H_{25}N_2O_3$: calculated 329.1865; found 329.1870. Anal. Calcd for $C_{19}H_{24}N_2O_3\cdot 0.1H_2O$: C, 69.11; H, 7.39; N, 8.48; found C, 68.97; H, 7.33; N, 8.40.

4.7. 3,4-Dihydro-2*H*-1,4-benzoxazin-2-one (3)

4-Benzyl-3,4-dihydro-1,4-benzoxazin-2-one (**12**) (500 mg, 2.09 mmol) was dissolved in dry THF (8 mL), 10% Pd/C (100 mg) was added and the reaction mixture was stirred under a hydrogen atmosphere for 1 h. The catalyst was filtered off, solvent was removed under reduced pressure and the crude product was purified by flash column chromatography using EtOAc/hexane (1:2) as eluant, giving 156 mg (50%) of white crystals, mp 79–83 °C; R_f=0.27 (EtOAc/hexane=1:2); IR (KBr) 3458, 1901, 1760, 1636, 1616, 1593, 1503, 1434, 1336, 1300, 1266, 1242, 1184, 1112, 1061, 938, 918, 748, 691, 605, 552, 522, 470 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.96 (d, 2H, J=2.1 Hz, CH_2), 6.22 (br s, 1H, NH), 6.73 (ddd, 1H, ^3J=7.8 Hz, ^4J=1.2 Hz, 6/7-H), 6.84 (dd, 1H, $J_{5,6}$=7.8 Hz, $J_{5,7}$=1.2 Hz, 5-H), 6.94–6.99 (m, 2H, 8-H, 6/7-H). ^{13}C NMR (DMSO-d_6, 75 MHz) δ 45.23 (CH_2), 115.72 (5-C), 117.13 (8-C), 119.42 (7-C), 125.68 (6-C), 135.29 (8a-C), 141.61 (4a-C), 166.04 (C=O). MS (EI) *m*/*z* (%): 149 (M^+, 70), 122 (8), 121 (45), 120 (100), 93 (12), 91 (5), 69 (7), 65 (15), 63 (5), 52 (6). HRMS for $C_8H_7NO_2$: calculated 149.0477; found 149.0480. Anal. Calcd for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39; found C, 64.63; H, 4.53; N, 9.15.

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