Ultrasound-Promoted Catalyst-Free Synthesis of 2,2′-(1,4-Phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] Derivatives

by **Davood Azarifar*** and **Davood Sheikh**

Department of Chemistry, Bu-Ali Sina University, Zip Code 65178, Hamedan, Iran
(phone/fax: +98-811-8257407; e-mail: azarifar@basu.ac.ir)

A convenient approach to 2,2′-(1,4-phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] derivatives **4** was explored employing the one-pot condensation of anthranilic acids (=2-aminobenzoic acids) **1** with terephthalaldehyde (=benzene-1,4-dicarboxaldehyde; **2**) under ultrasound-irradiation conditions (*Scheme 1*). The reactions proceeded smoothly in the presence of excess Ac_2O in the absence of any other catalyst and solvent to afford the respective products in high yields.

Introduction. – Amongst heterocyclic compounds, 4*H*-3,1-benzoxazin-4-one scaffolds [1] are considered as important and valuable compounds for the synthesis of natural products [2] and synthetic compounds such as quinazolin-4(3*H*)-ones, 1,4-benzodiazepine-2,5-diones, and indoxyls [3], and also as linking units in polymer chemistry [4]. The 4*H*-3,1-benzoxazin-4-ones have been frequently utilized as suitable skeletons for designing a wide range of biologically active products including antimycobacterials [5], antifungals [6], antielastases [7], and potential drugs for treatments of heart diseases [8] and diabetes [9]. Some of these compounds have been known as neuroprotectants [10], inhibitors of nitric oxide syntheses (NOS), and as potential drugs for treating neurodegenerative, inflammatory, autoimmune, and cardiovascular disorders [11]. These compounds are also considered as key intermediates in synthetic organic chemistry [12].

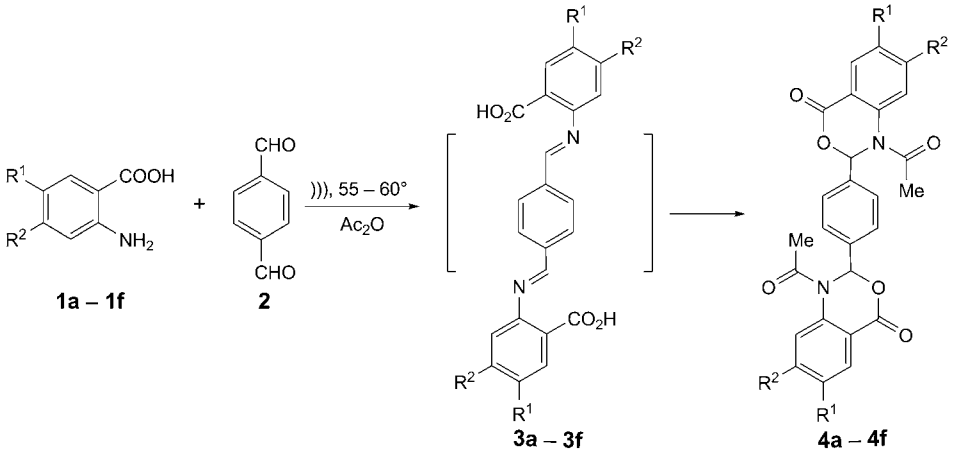
As evident from the literature, only few reports on the synthesis of *N*-substituted 1,2-dihydro-4*H*-3,1-benzoxazin-4-ones have been published so far [13]. Recently, a solid-phase synthesis of 4*H*-3,1-benzoxazine-4-ones under the mediation of silica-bound benzyl chloride has been reported [14]. As outlined before, the development of new approaches for the synthesis of these compounds appears as an important field of research interest owing to their biological and synthetic importance.

On the other hand, application of ultrasound in the so-called 'sonochemistry' has received enormous interest as a versatile and challenging technique in organic synthesis [15]. It is known that the ultrasonic-irradiation technique can not only enhance the reaction rates, but can also have a profound effect on the yields of various organic reactions [16]. The phenomenon called 'acoustic cavitations' is responsible for the beneficial effects of ultrasound on chemical reactions. Namely, the molecules of the liquid are separated during the rarefaction cycle of the wave, generating bubbles that undergo subsequent implosive collapse in a liquid, which produces unusual chemical and physical environments. These rapid and violent implosions of the bubbles generate

localized 'hot spots' with a transient temperature of roughly 5000 K, pressure of *ca.* 1000 atm, and heating and cooling rates above 10 billion K/s per second [17]. Such localized hot spots can be considered as microreactors in which the energy of sound is transformed into a useful chemical form.

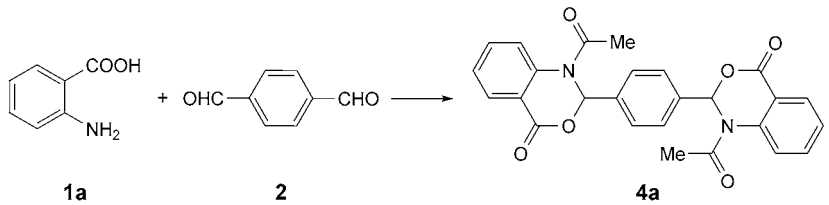
Results and Discussion. – In continuation of our efforts to explore new and more robust methods for the one-pot synthesis of various heterocyclic compounds including 4*H*-3,1-benzoxazin-4-one derivatives and also considering the merits of ultrasound-irradiation as a versatile and useful technique in the synthesis of these compounds [18], we report herein a convenient approach to some hitherto unknown 2,2′-(1,4-phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] derivatives by an ultrasound-promoted condensation of anthranilic acids (=2-aminobenzoic acids) **1a**–**1f** with terephthalaldehyde (=benzene-1,4-dicarboxaldehyde; **2**) in the presence of Ac_2O (*Scheme 1*). All the reactions proceeded smoothly in the absence of any acid or base catalysts to furnish the expected products **4a**–**4f** in moderate to high yields.

Scheme 1. *Condensation of Anthranilic Acids* **1a**–**1f** *with Terephthalaldehyde* **2**. For R^1 and R^2, see *Table 2*.



To establish the reaction conditions, we initially examined the condensation of anthranilic acid (**1a**) with **2** as the model reaction. The effects of solvent and conditions on the rate and yield of the reaction was studied in MeOH, MeCN, DMF, AcOEt, Et_2O, $CHCl_3$, CCl_4, and hexane as well as under solvent-free condition (excess Ac_2O) both under ultrasonication and conventional conditions at various temperatures (*Table 1*). The best results in terms of yield (85%) and reaction time (55 min) were obtained when the reaction was performed under ultrasound-irradiation conditions at 55–60° in the presence of excess Ac_2O without any other solvent. However, as shown in *Table 1*, the yields of the reaction obtained in the solvents MeOH (68%), AcOEt (76%), and hexane (77%), were comparable with that obtained under solvent-free condition (85%).

Table 1. *Screening of the Solvent and Conditions on the Synthesis of 2,2′-(1,4-Phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one]* (**4a**)[a])



1a **2** **4a**

Solvent, temperature [°]	Method	Time [min]	Yield[b]) [%]
Ac_2O (exc.), 35–40	ultrasound	60	75
Ac_2O (exc.), 55–60	ultrasound	55	85
Ac_2O (exc.), 65–70	ultrasound	50	80
MeOH, 55–60	ultrasound	60	68
MeCN, 55–60	ultrasound	65	75
AcOEt, 55–60	ultrasound	60	76
$CHCl_3$, 55–60	ultrasound	65	75
CCl_4, 55–60	ultrasound	70	69
Et_2O, 55–60	ultrasound	70	65
hexane, 55–60	ultrasound	65	77
Ac_2O (exc.), r.t.	thermal	60	70
Ac_2O (exc.), 60	thermal	60	68
Ac_2O (exc.), 100	thermal	60	66
Ac_2O (exc.), 138–140	thermal	60	65
MeOH, r.t.	thermal	60	60
MeCN, r.t.	thermal	60	64
AcOEt, r.t.	thermal	60	65
DMF, r.t.	thermal	60	68
$CHCl_3$, r.t.	thermal	60	60
Et_2O, r.t.	thermal	60	60
CCl_4, r.t.	thermal	60	62
hexane, r.t.	thermal	60	63

[a]) Conditions: anthranilic acid (**1a**; 0.274 g, 2 mmol), terephthalaldehyde (**2**; 0.134 g, 1 mmol), Ac_2O (10 ml), and solvent (5 ml). [b]) Yield of isolated product.

This achievement encouraged us to extend the scope of the reaction to various substituted anthranilic acids **1a**–**1f** under the optimized conditions (ultrasonication at 55–60° in excess Ac_2O). The experimental results are summarized in *Table 2*. This method proved to be unsuitable for the synthesis of 2,2′-(1,2-phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] derivatives of type **7** from phthalaldehyde (= benzene-1,2-dicarboxyaldehyde; **5**) with anthranilic acids **1a**–**1f** under the same optimized conditions. This can be attributed to the sterical hindrance between two (4*H*)-3,1-benzoxazin-4-one units when compactly located in *ortho* positions at the linking benzene moiety. However, the corresponding mono 1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one derivatives **8a**–**8f** were produced instead in quite good yields (*Table 3*). This implies that the cyclization of only one of two imino groups formed in the intermediates **6a**–**6f** has occurred, as shown in *Scheme 2*.

Table 2. *Ultrasound-Promoted Synthesis of 2,2′-(1,4-Phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] Derivatives* **4a**–**4f**[a])

Product	R^1	R^2	Time [min]	Yield[b]) [%]
4a	H	H	55	85
4b	MeO	MeO	45	75
4c	H	CO_2H	65	70
4d	OH[c])	H	50	75
4e	Br	H	55	78
4f	Cl	H	65	74

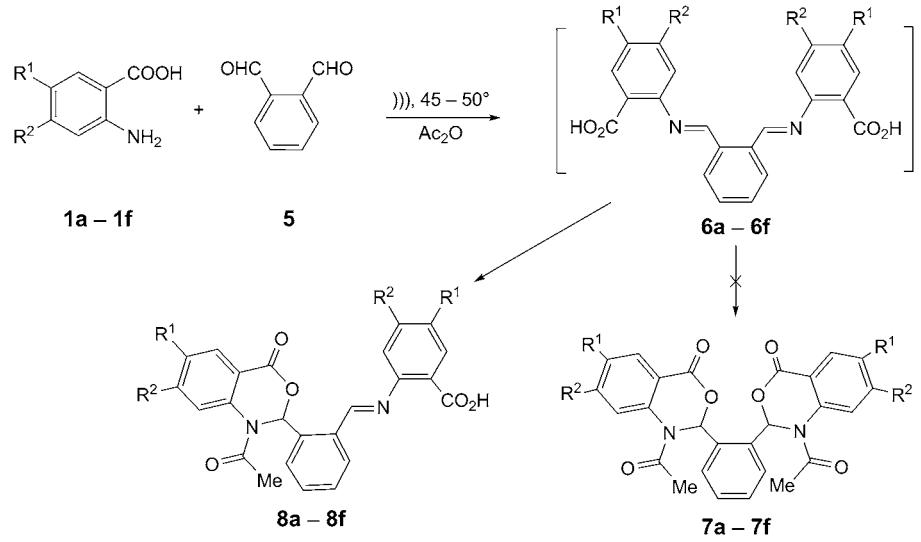
[a]) Conditions: anthranilic acid **1** (2 mmol), terephthalaldehyde (**2**; 0.14 g, 1 mmol), Ac_2O (10 ml), and ultrasonication at 55–60°. [b]) Yield of isolated product. [c]) OH Groups were acetylated in the product.

Table 3. *Ultrasound-Promoted Condensation of Anthranilic Acids* **1a**–**1f** *with Phthalaldehyde* (**5**)[a])

Product	R^1	R^2	Time [min]	Yield[b]) [%]
8a	H	H	50	60
8b	MeO	MeO	60	65
8c	H	CO_2H	90	58
8d	OH[c])	H	60	68
8e	Br	H	45	65
8f	Cl	H	70	65

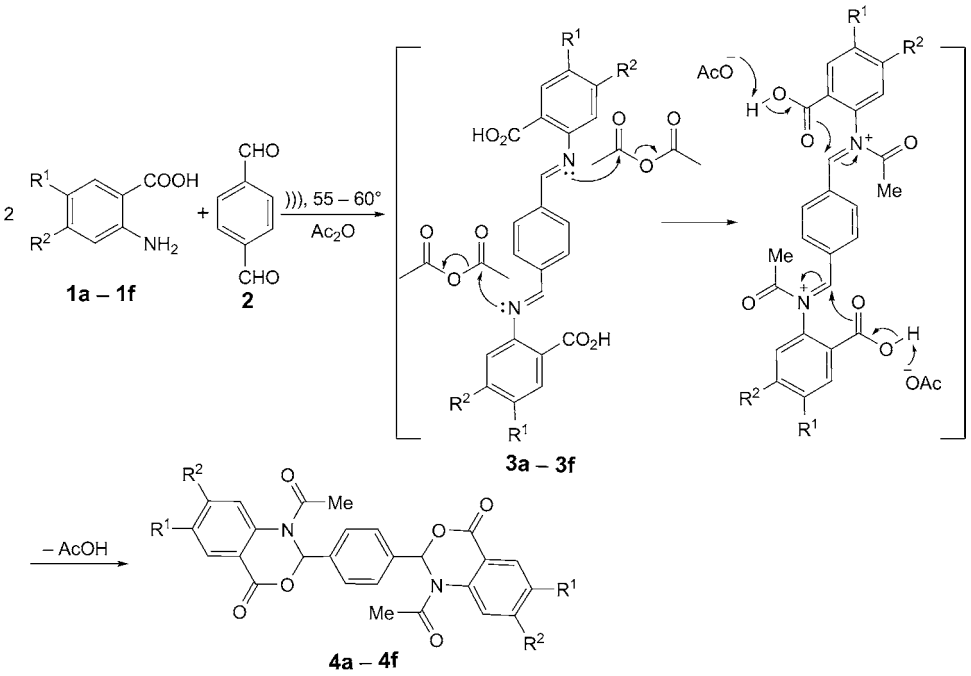
[a]) Conditions: anthranilic acid **1** (2 mmol), phthalaldehyde **5** (0.14 g, 1 mmol), Ac_2O (10 ml), and ultrasonication at 55–60°. [b]) Yield of isolated product. [c]) OH Groups were acetylated in the products.

Scheme 2. *Condensation of Anthranilic Acids* **1a**–**1f** *with Phthalaldehyde* **5**. For R^1 and R^2, see *Table 3*.



A likely mechanism to explain the formation of the products **4a**–**4f** is depicted in *Scheme 3*. It seems reasonable to assume that the first step may involve the condensation of anthranilic acid **1a**–**1f** with terephthalaldehyde (**2**) to produce the corresponding diimino intermediates **3a**–**3f**. This intermediate **3** undergoes subsequent acetylation at both imino groups with Ac_2O under ultrasound irradiation followed by cyclization to afford the products **4a**–**4f**.

Scheme 3. *Mechanism for the Condensation of Terephthalaldehyde* **2** *with Anthranilic Acids* **1a**–**1f**



To substantiate this mechanism, the imino derivative **3a** ($R^1 = R^2 = H$) was prepared as a stable compound in a separate experiment from the reaction of anthranilic acid (**1a**) with **2** in MeOH with conventionally stirring at room temperature and characterized by its spectroscopic (IR, ^{1}H-NMR, and ^{13}C-NMR) analysis. Treatment of the isolated diimino derivative **3a** with Ac_2O under ultrasound irradiation resulted solely in the expected product **4a** in almost the same yield (*ca.* 85%) as previously obtained by the direct one-pot reaction.

Conclusions. – The present protocol offers a simple and versatile one-pot procedure for a solvent- and catalyst-free synthesis of 2,2′-(1,4-phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one] derivatives **4** from the condensation of anthranilic acids with terephthalaldehyde in the presence of excess Ac_2O. The reactions proceeded smoothly under ultrasound-irradiation conditions in relatively short reaction times to furnish the products **4** in high yields.

The authors wish to thank the research council of the Bu-Ali Sina University for financial support to carry out this research.

Experimental Part

General. Chemicals used in this work were purchased from *Aldrich* and *Merck* and used without purification. Ultrasonication was performed in a *Transsoni-660/H* ultrasound cleaner with a frequency of 35 KHz and an output power of 70 W. The reactions were performed in open vessels. M.p.: *SMPI* apparatus. IR Spectra: *Shimadzu-435-U-04* FT spectrophotometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-DRX-400-Avance* instrument at 400 and 100 MHz, resp.; in (D_6)DMSO or $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS: *Finnigan-MAT-8430* spectrometer; at 70 eV; im *m*/*z*. Elemental analyses for C, H, and N: *Perkin–Elmer-2400* analyzer.

Conventional Synthesis of Diimino Derivatives **3a** *and* **6a**. A mixture of anthranilic acid (**1a**; 0.274 g, 2 mmol) and terephthalaldehyde or phthalaldehyde (**2** or **5**, resp.; 0.134 g, 1 mmol) in MeOH (10 ml) was stirred for *ca.* 1 h at r.t. (TLC monitoring). After completion of the reaction, the resulting mixture was concentrated, and the remaining yellow and red solid materials were crystallized from MeOH: pure **3a** or **6a** in 90 and 85% yield, resp.

2,2′-[1,4-Phenylenebis(methylidynenitrilo)]bis[benzoic Acid] (**3a**): Yellow solid. M.p. 308–310°. IR (KBr): 3350–2540, 1715, 1260, 900. ^{1}H-NMR (400 MHz, (D_6)DMSO): 6.39–8.12 (*m*, 12 arom. H); 8.48 (*s*, 2 CH=N); 10.08 (*s*, 2 CO_2H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 128.1; 128.7; 129.9; 130.2; 130.3; 130.5; 131.6; 134.2; 164.1; 170.1. EI-MS: 372 (M^+). Anal. calc. for $C_{22}H_{16}N_2O_4$ (372.38): C 70.96, H 4.30, N 7.52; found: C 70.87, H 4.23, N 7.58.

2,2′-[1,2-Phenylenebis(methylidynenitrilo)]bis[benzoic Acid] (**6a**): Red solid. M.p. 225–227°. IR (KBr): 3410–2430, 1710, 1255, 875. ^{1}H-NMR (400 MHz, (D_6)DMSO): 6.73–8.18 (*m*, 12 arom. H); 8.53 (*s*, 2 CH=N); 11.74 (*s*, 2 CO_2H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 119.8; 120.0; 128.2; 128.7; 130.0; 130.3; 130.4; 130.6; 131.7; 163.9; 193.4. EI-MS: 372 (M^+). Anal. calc. for $C_{22}H_{16}N_2O_4$: C 70.96, H 4.30, N 7.52; found: C 70.83, H 4.18, N 7.58.

Ultrasound-Promoted Condensation of Terephthalaldehyde (**2**) *or Phthalaldehyde* (**5**) *with Anthranilic Acids* (**1**). A flask containing anthranilic acid **1a**–**1f** (2 mmol) and terephthalaldehyde (**2**; 1 mmol) was placed in a water bath and stirred for 1–2 min. Then, Ac_2O (10 ml) was added followed by sonication at 55–60° for an appropriate time (*Table 2*) until the reaction was completed (TLC (hexane/AcOEt 2:1) monitoring). The mixture was then treated with ice/H_2O and filtered to leave solid products which were purified by prep. TLC (20 × 20 cm plates coated with *60-HF-254* SiO_2, hexane/AcOEt 2:1). The separated products were first exposed to air for a few minutes and then dried in an oven at 100°. For further purification, the products **4a**–**4f** were crystallized from EtOH.

The reactions with phthalaldehyde (**5**) were conducted exactly under the same conditions to give the products **8a**–**8f**.

*2,2′-(1,4-Phenylene)bis[1-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one]* (**4a**): White solid. M.p. 234–236°. IR (KBr): 3079, 2995, 1735, 1689, 1605, 1485. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.39 (*s*, 2 Me); 7.27 (*s*, 2 CH); 7.60–7.75 (*m*, 12 arom. H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 22.9; 70.3; 119.4; 125.6; 126.7; 126.9; 129.5; 135.4; 137.7; 139.1; 161.8; 170.6. EI-MS: 456 (M^+). Anal. calc. for $C_{26}H_{20}N_2O_6$: C 68.42, H 4.38, N 6.14; found: C 68.27, H 4.27, N 6.15.

*2,2′-(1,4-Phenylene)bis[*1*-acetyl-1,2-dihydro-6,7-dimethoxy-4*H*-3,1-benzoxazin-4-one]* (**4b**): Yellow solid. M.p. 239–241°. IR (KBr): 3056, 2930, 1720, 1680, 1285, 1150. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.26 (*s*, 2 Me); 3.92 (*s*, 2 MeO); 3.99 (*s*, 2 MeO); 6.91(*s*, 2 CH); 7.52 (*s*, 2 arom. H); 7.92 (*s*, 4 arom. H); 8.09 (*s*, 2 arom. H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 22.5; 55.6; 56.3; 83.0; 108.3; 109.9; 111.0; 126.5; 133.8; 137.3; 147.0; 154.1; 160.9; 170.4. EI- MS: 576 (M^+). Anal. calc. for $C_{30}H_{28}N_2O_{10}$: C 62.50, H 4.86, N 4.86; found: C 62.36, H 4.76, N 4.95.

*2,2′-(1,4-Phenylene)bis[1-acetyl-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazine-7-carboxylic Acid]* (**4c**): White solid. M.p. 280–282°. IR (KBr): 3033–2420, 17724, 1691, 1267, 1185. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.77 (*s*, 2 Me); 7.24–8.88 (*m*, 2 CH, 10 arom. H); 10.16 (*s*, 2 CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 23.6; 86.9; 125.7; 126.3; 126.5; 126.9; 127.7; 127.9; 128.0; 128.9; 164.3; 165.8; 168.4. EI-MS: 544 (M^+). Anal. calc. for $C_{28}H_{20}N_2O_{10}$: C 61.76, H 3.67, N 5.14; found: C 61.65, H 3.60, N 5.21.

*2,2′-(1,4-Phenylene)bis[1-acetyl-6-(acetyloxy)-1,2-dihydro-4*H*-3,1-benzoxazin-4-one]* (**4d**): Pale brown solid. M.p. 220–222°. IR (KBr): 3066, 2994, 1721, 1705, 1676, 1236, 1135. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.42 (*s*, 2 Me); 2.51 (*s*, 2 AcO); 7.25–7.89 (*m*, 2 CH, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.1; 25.0; 91.6; 118.5; 120.0; 126.6; 127.1; 128.0; 130.1; 132.1; 180.9; 183.9; 185.9. EI-MS: 572 (M^+). Anal. calc. for $C_{30}H_{24}N_2O_{10}$: C 62.93, H 4.19, N 4.89; found: C 62.86, H 4.15, N 4.97.

*2,2′-(1,4-Phenylene)bis[1-acetyl-6-bromo-1,2-dihydro-4*H*-3,1-benzoxazin-4-one]* (**4e**): Yellow solid. M.p. 236–238°. IR (KBr): 3096, 2991, 1733, 1694, 1310, 1120, 1045. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.13 (*s*, 2 Me); 6.89 (*s*, 2 CH); 7.72–8.41 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 25.5; 73.1; 114.4; 119.1; 122.5; 133.5; 136.9; 140.4; 144.9; 146.3; 168.6; 169.1. EI-MS: 612 (M^+), 614 ($[M+2]^+$), 616 ($[M+4]^+$). Anal. calc. for $C_{26}H_{18}Br_2N_2O_6$ (613.8): C 50.83, H 2.93, N 4.56; found: C 50.74, H 2.84, N 4.68.

*2,2′-(1,4-Phenylene)bis[1-acetyl-6-chloro-1,2-dihydro-4*H*-3,1-benzoxazin-4-one]* (**4f**): Pale yellow solid. M.p. 210–212°. IR (KBr): 3089, 2993, 1713, 1681, 1290, 1190, 1091. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.418 (*s*, 2 Me); 7.25–7.89 (*m*, 2 CH, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 22.63; 92.83; 126.76; 127.0; 128.0; 128.1; 128.2; 129.5; 129.9; 175.2; 186.0. EI-MS: 524 (M^+), 526 ($[M+2]^+$), 528 ($[M+4]^+$). Anal. calc. for $C_{26}H_{18}Cl_2N_2O_6$ (524.9): C 59.43, H 3.42, N 5.33; found: C 59.30, H 3.34, N 5.38.

*2-{{[2-(1-Acetyl-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazin-2-yl)phenyl]methylidene}amino}benzoic Acid* (**8a**): Yellow solid. M.p. 213–215°. IR (KBr): 3385–2449, 1715, 1705, 1690, 1654, 1275. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.29 (*s*, Me); 7.12–8.17 (*m*, CH–N, 12 arom. H); 8.76 (*s*, CH=N); 10.92 (*s*, CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 23.0; 94.1; 115.6; 116.3; 124.1; 124.2; 124.4; 124.9; 126.5; 126.8; 128.2; 128.8; 128.9; 130.1; 130.8; 131.0; 133.2; 135.2; 141.2; 153.9; 160.1; 166.5; 169.4; 170.2. EI-MS: 414 (M^+). Anal. calc. for $C_{24}H_{18}N_2O_5$: C 69.56, H 4.34, N 6.76; found: C 69.48, H 4.26, N, 6.86.

*2-{{[2-(1-Acetyl-1,4-dihydro-6,7-dimethoxy-4-oxo-2*H*-3,1-benzoxazin-2-yl)phenyl]methylidene}amino}-4,5-dimethoxybenzoic Acid* (**8b**): Pale yellow solid. M.p. 226–228°. IR (KBr): 3435–2356, 1722, 1711, 1694, 1647, 1261. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.27 (*s*, Me); 3.46 (*s*, 2 MeO); 3.53 (*s*, 2 MeO); 7.27–7.92 (*m*, CH–N, 8 arom. H); 8.83 (*s*, CH=N); 10.87 (*s*, CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 30.9; 66.1; 66.4; 86.2; 119.5; 121.1; 122.3; 125.8; 126.3; 126.6; 126.9; 127.7; 127.9; 128.0; 129.1; 129.7; 131.6; 133.7; 151.3; 160.4; 175.8; 179.2; 182.5. EI-MS: 534 (M^+). Anal. calc. for $C_{28}H_{26}N_2O_9$: C 62.92, H 4.86, N 5.24; found: C 62.83, H 4.80, N 5.32.

*2-{{[2-(1-Acetyl-7-carboxy-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazin-2-yl)phenyl]methylidene}amino}-benzene-1,4-dicarboxylic Acid* (**8c**): Yellow solid. M.p. 259–261°. IR (KBr): 3369–2380, 1731, 1718, 1688, 1623, 1283. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.90 (*s*, Me); 7.27–7.90 (*m*, CH–N, 10 arom. H); 8.87 (*s*, CH=N); 10.30 (*s*, 3 CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 22.7; 84.2; 119.4; 119.5; 121.2; 122.6; 122.7; 125.6; 125,7; 126.4; 126.5; 126.9; 127.7; 127.9; 128.8; 128.9; 131.5; 132.7; 133.7; 151.6; 151.7; 164.2; 168.3; 187.3; 187.4; 187.9. EI-MS: 502 (M^+). Anal. calc. for $C_{26}H_{18}N_2O_9$: C 62.15, H 3.58, N 5.57; found: C 62.07, H 3.52, N 5.67.

*2-{{[2-[1-Acetyl-6-(acetyloxy)-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazin-2-yl]phenyl}methylidene}amino}-5-(acetyloxy)benzoic Acid* (**8d**): Brown solid. M.p. 216–218°. IR (KBr): 3420–2453, 1735, 1722, 1718, 1701, 1690, 1640, 1310. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.10 (*s*, Me); 2.28 (*s*, 2 MeCOO); 7.15–7.38 (*m*, CH–N, 10 arom. H); 8.58 (*s*, CH=N); 10.85 (*s*, CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 24.7; 83.9; 119.5; 119.6; 122.4; 122.6; 122.7; 125.7; 125.8; 125.9; 126.5; 126.6; 126.7; 127.7; 127.9; 128.0; 129.0; 129.1; 131.6; 133.7; 151.5; 187.7; 187.9; 191.8; 193.6; 195.4. EI-MS: 530 (M^+). Anal. calc. for $C_{28}H_{22}N_2O_9$: C 63.39, H 4.15, N 5.28; found: C 63.31, H 4.07, N 5.38.

*2-{{[1-(1-Acetyl-6-bromo-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazin-2-yl)phenyl]methylidene}amino}-5-chlorobenzoic Acid* (**8e**): Yellow solid. M.p. 201–203°. IR (KBr): 3456–2487, 1723, 1708, 1694, 1637, 1294, 1065. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.51 (*s*, Me); 6.85–8.16 (*m*, CH–N, 10 arom. H); 8.72 (*s*, CH=N); 11.04 (*s*, CO_2H). ^{13}C-NMR (100 MHz, $CDCl_3$): 20.1; 80.7; 118.4; 120.5; 121.8; 122.2; 122.7; 124.2; 125,4; 126.1; 126.8; 127.3; 127.8; 128.5; 128.7; 130.6; 131.8; 132.4; 133.9; 150.2; 152.9; 165.6; 169.7; 184.6; 186.1; 187.3. EI-MS: 570 (M^+), 572 ($[M+2]^+$), 574 ($[M+4]^+$). Anal. calc. for $C_{24}H_{16}Br_2N_2O_5$ (571.8): C 50.35, H 2.79, N 4.89; found: C 50.32, H 2.74, N 4.86.

*2-{{[2-(1-Acetyl-6-chloro-1,4-dihydro-4-oxo-2*H*-3,1-benzoxazin-2-yl)phenyl]methylidene}amino}-5-chlorobenzoic Acid* (**8f**): Red solid. M.p. 220–222°. IR (KBr): 3450–2500, 1729, 1679, 1583, 1506, 1100, 700. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.04 (*s*, Me); 7.28–7.93 (*m*, CH–N, 10 arom. H); 8.46 (*s*, CH=N); 14.05 (*s*, CO_2H). ^{13}C-NMR (100 MHz, (D_6)DMSO): 25.6; 83.6; 120.2; 123.5; 123.7; 125.3; 127.2; 128.1;

128.7; 129.1; 129.6; 129.9; 130.4; 131.0; 131.6; 131.9; 132.1; 132.3; 132.9; 140.1; 143.0; 161.9; 167.6; 168.3; 170.2. EI-MS: 482 (M^+), 484 ($[M+2]^+$), 486 ($[M+4]^+$). Anal. calc. for $C_{24}H_{16}Cl_2N_2O_5$ (482.9): C 59.63, H 3.31, N 5.79; found: C 59.51, H 3.24, N 5.83.

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Received December 1, 2011