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Three-component synthesis of 2-imino-1,4-benzoxazines

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This paper is dedicated to the memory of Bertha Maqueda

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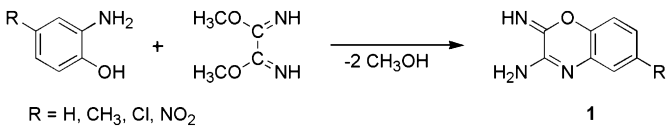
ABSTRACT

A series of 2-imino-1,4-benzoxazines (**8a**–**e**) were prepared by the one-pot, three-component, condensation of salicylaldehyde (**4**), various *ortho*-aminophenols (**5**), and 2,6-dimethylphenylisonitrile (**6**). The structures of four of the crystalline benzoxazine derivatives (**8b**–**e**) were unambiguously established by X-ray analysis.

1. Introduction

In 1964, Weidinger and Kranz reported the first and to date the only synthesis of 2-imino-3-amino-1,4-benzoxazines (**1**) by the condensation of various *ortho*-aminophenols with oxalyl bis-methylimidate under acidic conditions (Scheme 1).[1] In contrast, several routes to the related 3-oxo-2*H*-1,4-benzoxazine **2a** (Fig. 1), which sometimes are used as precursors of biologically active compounds, have been reported.[2] For example, these compounds and derivatives thereof can be prepared from *ortho*-aminophenols and 1,2-dibromoethane[3] or ethyl 2-bromopropionate.[4,5]



Scheme 1. Synthesis of imino-1,4-benzoxazines.

Multicomponent reactions have become of considerable importance in synthetic organic chemistry.[6] The Passerini three-component reaction (P-3CR), and the Ugi three- and four-component reactions (U-3CR, and U-4CR) are of particular importance, and an isocyanide derivative is a component common to all three of these coupling processes. Thus, these reactions have become known as isocyanide-based multicomponent reactions (IMCR).[6] Indeed,

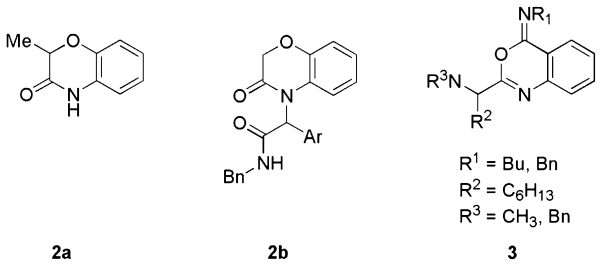


Figure 1.

Table 1
Selected ^{1}H, ^{13}C NMR (ppm), and IR (cm^{-1}) data for compounds **8a**–**e**

Compounds	^{1}H NMR (ppm) (H-6)	^{13}C NMR (ppm) C-7	^{13}C NMR (ppm) C-14	IR (C=N) (cm^{-1})	Yield[a] (%) two-steps	Yield[b] (%) one-pot
8a	9.19	1156.9	134.0	1659, 1610	33	78
8b	9.16	154.7	129.9	1670, 1590	45	93
8c	9.18	153.5	129.0	1665, 1618	47	90
8d	9.29	151.9	135.7	1666, 1611	43	45
8e	9.17	152.2	140.4	1660, 1618	41	83

[a] Isolated yield.
[b] Yields were determined by ^{1}H NMR.

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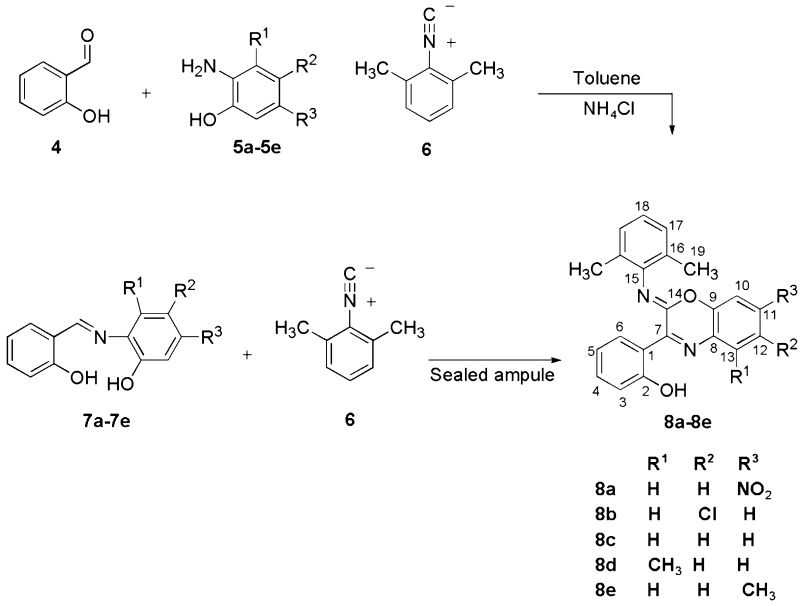


Scheme 2. Preparation of 2-imino-1,4-benzoxazines.

a recent synthesis of 3,4-dihydro-3-oxo-2*H*-1,4-benzoxazine (**2b**) is based on an U-4CR process,[7] and a one-pot, multicomponent route to 4-imino-4*H*-3,1-benzoxazines **3** has also been described.[8]

It occurred to us that 2-imino-1,4-benzoxazine derivatives might be accessible via a multicomponent process involving an arylisocyanide, an *ortho*-aminophenol, and a salicylaldehyde. This article describes our initial results in this area.

2. Results and discussion

An anhydrous toluene solution of an equimolar mixture of salicylaldehyde (**4**) and the *ortho*-aminophenol (**5a**) containing ammonium chloride (1.2 equiv) was briefly (0.5 h) stirred at room temperature and then an equivalent of 2,6-dimethylphenylisonitrile (**6**) was added. Heating at reflux temperature was required for a reasonable reaction rate to be observed, and the yield of the crystalline product **8a** (Table 1) was significantly better in the presence of ammonium chloride. In the same way, the imino-benzoxazines **8b–e** were produced, all except the sterically hindered compound **8d** being obtained in good yield. The benzoxazine derivatives could also be obtained by first preparing the putative Schiff base intermediates **7a–e** ex situ,[9] followed by addition of the isonitrile **6**, but the reactions had to be conducted under more vigorous conditions (120 °C, sealed tube), Scheme 2. In addition,

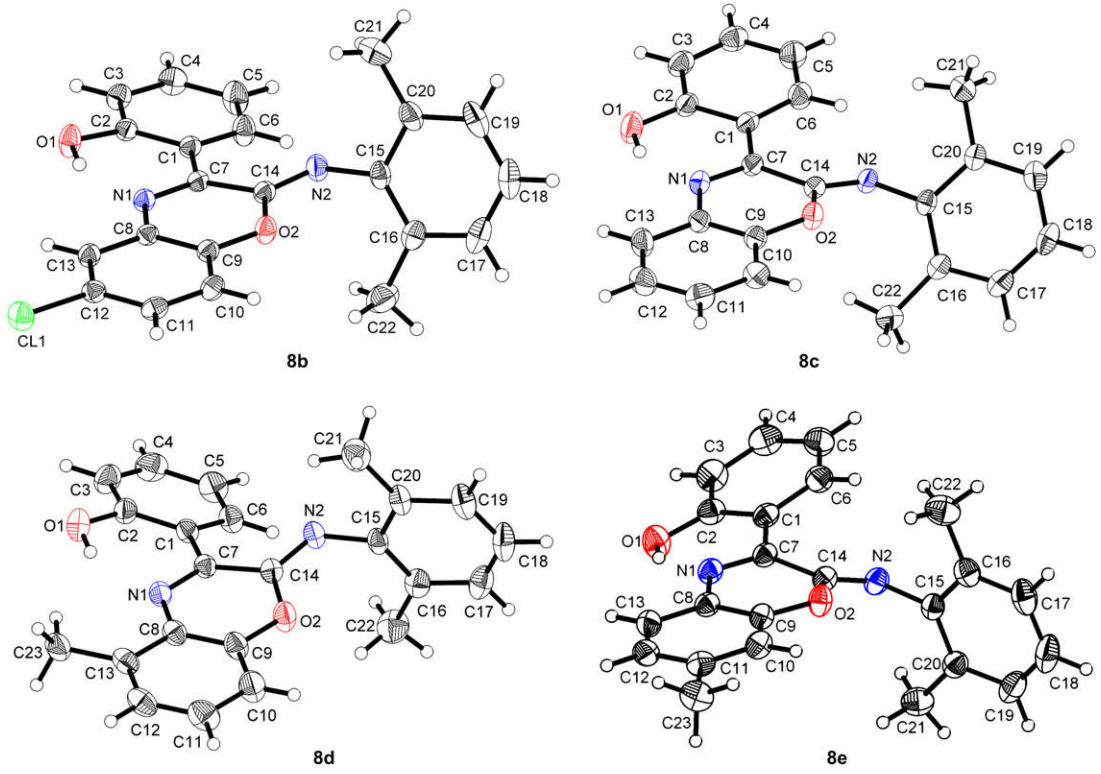


Figure 2. X-ray molecular structures of compounds **8b**, **8c**, **8d**, and **8e**. Ellipsoids are drawn at 35% probability level.

Table 2
Crystallographic data for compounds **8b–e**

Compounds	**8b**	**8c**	**8d**	**8e**
Crystal data				
Formula	$C_{22}H_{17}Cl\ N_2O_2$	$C_{22}H_{18}N_2O_2$	$C_{23}H_{20}N_2O_2$	$C_{23}H_{20}\ N_2O_2$
Crystal size	0.50×0.50×0.45	0.55×0.30×0.30	0.30×0.10×0.10	0.50×0.45×0.17
FW (g mol^{-1})	376.84	342.38	356.43	356.43
Space group	$P2_1/a$	$P2_1/c$	$P2_1/n$	$P2_1/c$
Cell parameters				
a (Å)	14.8591(4)	7.2055(2)	13.4609(4)	15.0887(13)
b (Å)	7.4213(3)	9.2170(3)	7.4313(2)	5.822(3)
c (Å)	16.9179(5)	26.1763(8)	18.9330(6)	22.020(3)
α (°)	90.00	90.00	90.00	90.00
β (°)	101.759(2)	93.110(2)	101.1460	109.481(8)
γ (°)	90.00	90.00	90.00	90.00
V (Å^3)	1826.45(10)	1735.89(9)	1858.18(9)	1823.6(8)
Z	4	4	4	4
δ_{calcd} (Mg m^{-3})	1.370	1.310	1.274	1.298
Data collection				
Limit of θ	2.46–54.92	6.44–54.90	3.42–55.30	4.02–55.38
Total reflections	7035	8085	18,568	7598
Unique reflections	4103	3381	4268	4039
Refinement				
R/R_w (F)[a]	0.0499/0.1305	0.0710/0.1782	0.0608/0.1473	0.0459/0.1197
R/R_w (F^2) (all data)	0.0827/0.1524	0.1293/0.2098	0.1539/0.1945	0.0680/0.1378
Goodness-of-fit	1.058	1.056	1.020	1.044
Number of variables	250	235	246	249
$\Delta\rho_{min}$ (e Å^{-3})	−0.305	−0.243	−0.291	−0.165
$\Delta\rho_{max}$ (e Å^{-3})	0.220	0.266	0.284	0.167

T=293 K, $\lambda_{MoK\alpha}$=0.7173 radiation.
[a] $R=\sum(||F_o|-|F_c||)/\sum|F_o|$, $R_o w=[\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2]^{1/2}$.

the product yields were considerably lower (See Table 1) than for the three-component, ammonium chloride, presumably acid catalyzed[10] process.

The ^{1}H and ^{13}C NMR spectra of the products provide strong support for the benzoxazine structure (see Table 1 for selected NMR spectroscopic data.). Thus, all of the compounds showed a low field signal at δ 9.16–9.29 attributable to H-6, which is deshielded by the isonitrile derived imine nitrogen atom. These signals are shifted downfield by ca. 1.7 δ with respect to the corresponding signals for the precursor Schiff bases.[9a, 11a] It should be noted that the ^{1}H NMR signals for the aromatic rings were assigned based on their COSY spectra. The ^{13}C spectra showed signals corresponding to the oxazine carbons, at δ 151.9–156.9 for C-7, and at δ 129.0–140.4 for C-14. The assignment of the quaternary carbon atoms was determined from an analysis of long-range correlations using the HMBC technique. For example, C-7 in **8c** shows a long-range correlation with H-6 and H-3 and, C-14, which resonates at δ 129.0 correlates with H-10. In addition, C-9 exhibits a correlation with H-13 and H-12. The HMBC spectra thus allowed assignment of all of the quaternary carbons of the benzoxazines.

Crystals suitable for X-ray diffraction were obtained for all of the benzoxazines except **8a**. These were produced by slow evaporation of concentrated solutions thereof from various solvent systems [**8b** (chloroform–hexane); **8c** (hexane); **8d**, **8e** (acetone–hexane)]. The crystal structures for these compounds are shown in Figure 2, and the details of the crystal data and summary of the collection parameters are given in Table 2. The compounds crystallized in monoclinic space groups, $P2_1/a$, $P2_1/c$, $P2_1/n$, and $P2_1/c$ for **8b**, **8c**, **8d**, and **8e**, respectively.

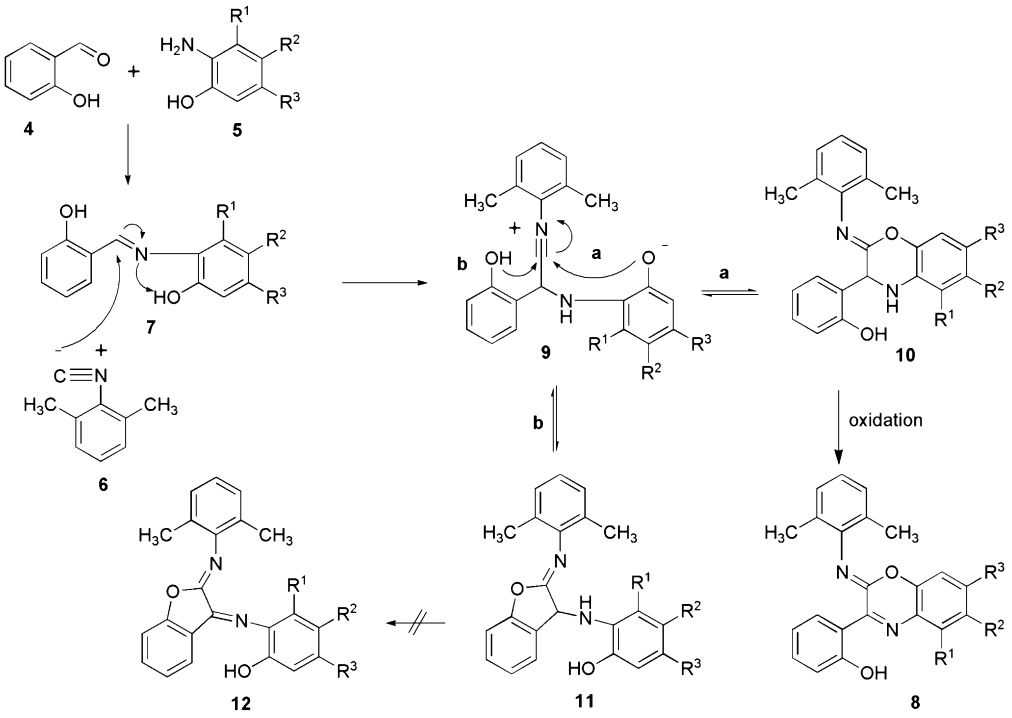
The X-ray analysis unambiguously established the structure of the benzoxazines **8b–e** (Fig. 2). The data shows that the bond distances for C(7)–N(1) and C(14)–N(2) range from 1.251(2) to 1.312(3) Å, in agreement with the values reported for a C–N double bond.[12] Moreover, the C(7)–N(1) distance in benzoxazines **8c** and **8e** [1.300(3) and 1.294(2) Å] are shorter than for the corresponding imine precursors **7c** and **7e** [1.317(6) and 1.323(6) Å],[11] which is the evidence for a stronger C(7)–N(1) bond in these benzoxazines. In contrast, these distances are very similar in the benzoxazine **8b** [1.304(2) Å] and the imine **7b** [1.303(2) Å].[13] The oxazine rings defined by the N(1)–C(7)–C(14)–O(2)–C(9)–C(8) fragment are nearly planar in all compounds, as evidenced by observation of the N(1)–C(7)–C(14), C(14)–O(2)–C(9), and C(7)–N(1)–C(8) bond angles, whose values are very close to 120° (Table 3).

It is of considerable importance that the crystal structures of benzoxazines **8b–e** show two intramolecular interactions (D–H⋯A), between O(1)–H(1)⋯N(1) and C(6)–H(6)⋯N(2), with distances ranging from 1.79 to 1.87 Å (A⋯H) and 2.512 to 2.578 Å (D⋯A) for O(1)–H(1)⋯N(1), while the C(6)–H(6)⋯N(2) distances are from 2.21 to 2.42 Å (A⋯H) and 2.857 to 2.936 Å (D⋯A). This proximity is fully consistent with the strong deshielding of H-6 found in the ^{1}H NMR spectra of the benzoxazine derivatives.

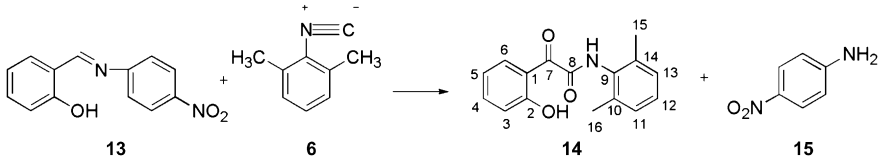
A possible reaction sequence that accounts for the formation of the 2-imino-1,4-benzoxazines is depicted in Scheme 3. Initial condensation of salicylaldehyde **4** with an aminophenol **5** gives the

Table 3
Selected bond lengths (Å) and angles (°) for **8b–e**

Compounds	**8b**	**8c**	**8d**	**8e**
Bond distances (Å)				
C(1)–C(7)	1.474(2)	1.475(4)	1.491(3)	1.465(2)
C(7)–C(14)	1.500(2)	1.506(4)	1.490(4)	1.490(2)
C(7)–N(1)	1.304(2)	1.300(3)	1.312 (3)	1.294(2)
C(8)–N(1)	1.391(2)	1.391(3)	1.396(4)	1.385(2)
C(9)–O(2)	1.3779(19)	1.387(3)	1.393(3)	1.377(2)
C(14)–N(2)	1.255(2)	1.258(3)	1.257(3)	1.251(2)
C(14)–O(2)	1.376(2)	1.382(3)	1.371(3)	1.3694(19)
Bond angles (°)				
N(1)–C(7)–C(1)	117.35(15)	117.4(2)	118.1(2)	118.51(14)
N(1)–C(7)–C(14)	119.96(15)	119.5(2)	120.0(2)	120.36(15)
N(2)–C(14)–O(2)	119.82(16)	119.9(2)	120.2(2)	120.58(14)
N(2)–C(14)–C(7)	123.15(16)	123.9(2)	123.2(3)	123.24(15)
O(2)–C(14)–C(7)	117.00(14)	116.2(2)	116.6(2)	116.12(14)
C(14)–O(2)–C(9)	121.19(13)	120.4(2)	120.2(2)	119.62(13)
C(7)–N(1)–C(8)	120.86(14)	121.6(2)	120.58(18)	120.25(13)



Scheme 3. Mechanism proposed for the formation of benzoxazines.



Scheme 4. Synthesis of 2-oxoacetamide.

Schiff base **7**, which reacts with the isonitrile **6** to give the nitrilium intermediate **9**. Nucleophilic attack by the oxygen of the *ortho*-aminophenol on the electrophilic isonitrile derived carbon atom gives 2-imino-3,4-dihydrobenzoxazine **10**, which on subsequent oxidation[14] provides the 2-imino-benzoxazine, **8** (path **a**). The alternative cyclization, which would involve the salicylaldehyde hydroxyl moiety and subsequent oxidation leading to formation of the imino-1-benzofuran **12**, was not observed (Scheme 3, path **b**). It is possible that the putative NH precursor of **12** is in equilibrium with **9**, and that the formation of **10** and the final product **8** is thermodynamic sink driving the reaction exclusively to the observed benzoxazines.

To cast light on the importance of the hydroxyl group of the *ortho*-aminophenols in the formation of the benzoxazines, the Schiff base **13** was prepared and reacted with isonitrile **6** (Scheme 4). The only product isolated, after column chromatographic purification, was the 2-oxoacetamide derivative **14** (37% yield), the formation of which is precedented.[15] Thus the presence of the hydroxyl group of the *ortho*-aminophenol is a requirement for the generation of the benzoxazines **8**a–**e**, and this is a limitation of the synthesis described herein.

Additionally, the X-ray diffraction study of **14** allowed its structural determination. The bond distances for C(7)–O(2), C(8)–O(3), and C(8)–N(1) are 1.229(3), 1.243(3), and 1.324(3) Å, respectively. Compound **14** crystallized in the monoclinic space group $P2_1/c$ with two molecules in the asymmetric unit (Fig. 3).

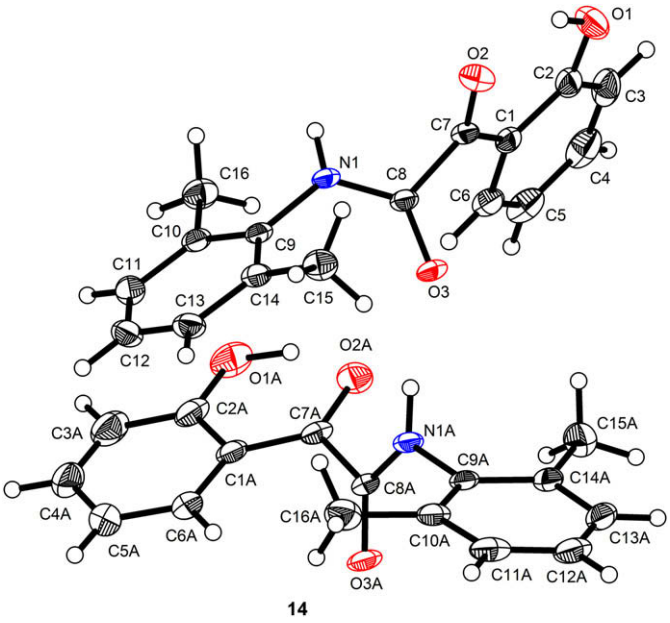


Figure 3. X-ray molecular structure of 2-oxoacetamide **14**. Ellipsoids are drawn at 35% probability level.

3. Conclusions

In summary, a one-pot synthesis of five new 2-imino-1,4-benzoxazines was achieved by a multicomponent process involving salicylaldehyde, an *ortho*-aminophenol, and 2,6-dimethylphenylisonitrile, in the presence of a stoichiometric amount of ammonium chloride. The *ortho* hydroxyl group in the aminophenol is essential for the formation of the benzoxazine ring system.

4. Experimental

4.1. General information

All reagents were purchased from Aldrich. Toluene was routinely dried (sodium/benzophenone).[16] All reactions requiring anhydrous conditions were performed under a nitrogen atmosphere. Melting points were recorded using an Electrothermal 9200 melting point apparatus. Infrared spectra were measured on a FTIR Perkin–Elmer GX spectrophotometer using KBr pellets. Mass spectra were obtained on a Hewlett–Packard 5989A spectrometer. The high resolution mass spectra (HRMS) were taken on Agilent Technologies, model 1100 coupled MSD-TOF spectrometer with APCI as ionization source. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker avance DPX 300, Jeol GX 270, Jeol Eclipse +400, and Bruker AMX 500 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to $Si(CH_3)_4$ for ^{1}H and ^{13}C. NMR experiments were carried out in deuterochloroform ($CDCl_3$). Coupling constants (J) are reported in hertz (Hz), peak multiplicity is indicated as follows: s: singlet, d: doublet, m: multiplet, br s: broad singlet for proton spectra.

4.2. X-ray crystallography

Single crystal X-ray diffraction studies were realized on a KAPPA CCD diffractometer. Solution and refinement: direct methods SHELXS-86[17] and SIR-2004[18] for structure solution and the SHELXL-97[19] software package for refinement and data output. For compounds **8b**–**e** and **14** full crystallographic data were submitted as CIF files with the Cambridge Crystallographic Data Center, CCDC Nos. 718286 for **8b**, 718287 for **8c**, 718285 for **8d**, 718284 for **8e**, and 718283 for **14**.

4.3. General procedure for the preparation of benzoxazines

4.3.1. Method A

2,6-Dimethylphenylisonitrile **6** (2.00 mmol) and Schiff bases **7a**–**e** (1.00 mmol) in 2 ml of dry toluene were placed in a sealed ampule and heated for 16–24 h at 120 °C under a nitrogen atmosphere. The solvent was removed under vacuum and the product was purified by column chromatography on silica gel using hexane as the eluant.

4.3.2. Method B

Salicylaldehyde **4** (1.00 mmol) was added to a solution of the amines **5a**–**e** (1.00 mmol) in 15 ml of dry toluene followed by ammonium chloride (1.20 mmol) and the mixture was stirred for 30 min at room temperature. Finally, 2,6-dimethylphenylisonitrile **6** (1.20 mmol) was added, the mixture was refluxed for 72 h. The reaction course was followed by TLC. The reaction mixture was cooled to room temperature and evaporated to dryness. The crude product was purified by column chromatography on silica gel using hexane as the eluant.

*4.3.3. 2-(2-(2,6-Dimethylphenylimino)-7-nitro-2H-benzo[b][1,4]oxazin-3-yl)phenol (**8a**)*

Compound **8a** was obtained from 0.25 g (2.00 mmol) of 2-amino-5-nitrophenol, 0.32 g (2.00 mmol) of salicylaldehyde, 0.13 g (2.40 mmol) of ammonium chloride, and 0.27 g (2.00 mmol) of 2,6-dimethylphenylisonitrile. The product **8a** was obtained as an orange solid, 78% yield, mp 215–217 °C. IR ν_{max} (KBr) 3433 (OH), 3103, 1659 (C=N), 1610, 1530, 1341, 1236, 770 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 13.38 (1H, br s, OH), 9.19 (1H, dd, J=8.3, 1.5 Hz, H-6), 8.12 (1H, dd, J=8.7, 2.3 Hz, H-12), 7.87 (1H, d, J=2.3 Hz, H-10), 7.75 (1H, d, J=8.7 Hz, H-13), 7.51 (1H, ddd, J=8.5, 7.0, 1.5 Hz, H-4), 7.17–7.05 (4H, m, H-3, H-17, H-18), 6.98 (1H, ddd, J=8.3, 7.0, 1.0 Hz, H-5), 2.17 (6H, s, H-19). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.3 (C-2), 156.9 (C-7), 147.8 (C-11), 145.8 (C-9), 143.0 (C-8), 138.9 (C-15), 135.7 (C-4), 134.0 (C-14), 133.4 (C-6), 128.5 (C-17), 127.9 (C-13), 126.9 (C-16), 124.9 (C-18), 120.3 (C-12), 119.6 (C-5), 118.9 (C-3), 117.0 (C-1), 111.8 (C-10), 19.0 (C-19). MS (20 eV) m/z: 388 ([M+1]$^+$, 9), 387 ([M]$^+$, 35), 372 (65), 267 (100), 256 (95), 210 (19), 182 (40), 43 (11). HRMS: $C_{22}H_{18}N_3O_4$, [M$^+$+H]$^+$ calcd 388.1292, found 388.1290, error 0.4707.

*4.3.4. 2-(2-(2,6-Dimethylphenylimino)-6-chloro-2H-benzo[b][1,4]oxazin-3-yl)phenol (**8b**)*

Compound **8b** was obtained from 0.25 g (1.74 mmol) of 2-amino-4-chlorophenol, 0.12 g (1.74 mmol) of salicylaldehyde, 0.11 g (2.08 mmol) of ammonium chloride, and 0.27 g (2.08 mmol) of 2,6-dimethylphenylisonitrile. The product was obtained as an orange solid (0.54 g), 93% yield, mp 185–187 °C. IR ν_{max} (KBr) 3365 (OH), 2918, 1670 (C=N), 1590, 1443, 1235, 770 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.30 (1H, br s, OH), 9.16 (1H, dd, J=8.3, 1.5 Hz, H-6), 7.59 (1H, d, J=2.4 Hz, H-13), 7.43 (1H, ddd, J=8.3, 7.2, 1.5 Hz, H-4), 7.25 (1H, dd, 8.6, 2.4 Hz, H-11), 7.12 (2H, d, J=7.7 Hz, H-17), 7.09–7.06 (2H, m, H-3, H-18), 6.96–6.91 (2H, m, H-5, H-10), 2.16 (6H, s, H-19). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.1 (C-2), 154.7 (C-7), 144.3 (C-9), 143.1 (C-8), 139.8 (C-15), 134.3 (C-4), 132.8 (C-6), 130.0 (C-11), 129.9 (C-14), 129.8 (C-12), 128.0 (C-17), 126.9 (C-16), 126.8 (C-13), 124.2 (C-18), 118.9 (C-10), 118.5 (C-3), 117.1 (C-1), 116.7 (C-5), 18.7 (C-19). MS m/z: 378 ([M+2]$^+$, 9), 377 ([M+1]$^+$, 6), 376 ([M]$^+$, 23), 361 (65), 258 (25), 256 (63), 245 (100), 217 (29), 133 (12). HRMS: $C_{22}H_{18}ClN_2O_2$ [M$^+$+H]$^+$, calcd 377.1051, found 377.1055, error 0.9754.

*4.3.5. 2-(2-(2,6-Dimethylphenylimino)-2H-benzo[b][1,4]oxazin-3-yl)phenol (**8c**)*

Compound **8c** was obtained from 0.25 g (2.00 mmol) of 2-aminophenol, 0.22 g (2.00 mmol) of salicylaldehyde, 0.13 g (2.40 mmol) of ammonium chloride, and 0.32 g (2.40 mmol) of 2,6-dimethylphenylisonitrile. The product was obtained as a yellow solid, 90% yield, mp 124–125 °C. IR ν_{max} (KBr) 3361 (OH), 2971, 1665 (C=N), 1618, 1464, 1228, 754 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 13.58 (1H, br s, OH), 9.18 (1H, dd, J=8.3, 1.7 Hz, H-6), 7.56 (1H, dd, J=7.8, 1.7 Hz, H-13), 7.39 (1H, ddd, J=8.3, 7.1, 1.7 Hz, H-4), 7.26 (1H, ddd, J=8.1, 7.4, 1.7 Hz, H-11), 7.19 (1H, ddd, J=8.1, 7.4, 1.7 Hz, H-12), 7.10 (1H, d, J=7.7 Hz, H-17), 7.05 (1H, dd, J=8.3, 1.3 Hz, H-3), 6.99 (1H, t, J=7.7 Hz, H-18), 6.94–6.89 (2H, m, H-5, H-10), 2.15 (6H, s, H-19). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.8 (C-2), 153.4 (C-7), 145.5 (C-9), 143.2 (C-15), 140.1 (C-8), 133.6 (C-4), 132.5 (C-6), 130.1 (C-11), 129.0 (C-14), 127.8 (C-17), 127.1 (C-13), 126.9 (C-16), 124.7 (C-12), 123.8 (C-18), 118.6 (C-5), 118.1 (C-3), 117.2 (C-1), 115.4 (C-10), 18.5 (C-19). MS m/z: 343 ([M+1]$^+$, 6), 342 ([M]$^+$, 24), 327 (32), 222 (83), 211 (100), 183 (27), 133 (16). HRMS: $C_{22}H_{19}N_2O_2$ [M$^+$+H]$^+$, calcd 343.1441, found 343.1445, error 1.1526.

*4.3.6. 2-(2-(2,6-Dimethylphenylimino)-5-methyl-2H-benzo[b][1,4]oxazin-3-yl)phenol (**8d**)*

Compound **8d** was obtained from 0.30 g (2.40 mmol) of 2-amino-3-methylphenol, 0.29 g (2.40 mmol) of salicylaldehyde, 0.16 g (2.90 mmol) of ammonium chloride, and 0.32 g (2.40 mmol) of 2,6-dimethylphenylisonitrile. The product was obtained as a yellow solid (0.38 g), 45% yield, mp 153–154 °C. IR ν_{max} (KBr) 3435 (OH), 2950, 2918, 1666 (C=N), 1611, 1474, 1242, 745 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 13.93 (1H, br s, OH), 9.29 (1H, dd, J=8.3, 1.7 Hz,

H-6), 7.41 (1H, ddd, *J*=8.3, 7.1, 1.7 Hz, H-4), 7.15 (1H, t, *J*=7.8 Hz, H-11), 7.10 (2H, d, *J*=7.5 Hz, H-17), 7.08–7.05 (2H, m, H-3, H-10), 6.99 (1H, t, *J*=7.5 Hz, H-18), 6.92 (1H, ddd, *J*=8.3, 7.1, 1.3 Hz, H-5), 6.77 (1H, d, *J*=8.2 Hz, H-12), 2.58 (3H, s, H-20), 2.15 (6H, s, H-19). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.1 (C-2), 151.9 (C-7), 145.8 (C-9), 143.4 (C-15), 140.1 (C-8), 135.7 (C-14), 133.6 (C-4), 132.5 (C-6), 129.6 (C-11), 127.8 (C-17), 127.7 (C-13), 126.9 (C-16), 125.9 (C-10), 123.7 (C-18), 118.6 (C-5), 118.0 (C-3), 117.2 (C-1), 113.2 (C-12), 18.6 (C-19), 17.4 (C-20). MS *m*/*z*: 357 ($[M+1]^+$, 6), 356 ($[M]^+$, 22), 341 (17), 236 (100), 225 (98), 197 (14). HRMS: $C_{23}H_{21}N_2O_2$ $[M^+ + H]^+$, calcd 357.1598, found 357.1596, error 0.4327.

4.3.7. 2-(2-(2,6-Dimethylphenylimino)-7-methyl-2H-benzo[b][1,4]oxazin-3-yl)phenol (**8e**)

Compound **8e** was obtained from 0.25 g (2.00 mmol) of 2-amino-5-methylphenol, 0.25 g (2.00 mmol) of salicylaldehyde, 0.13 g (2.40 mmol) of ammonium chloride, and 0.32 g (2.40 mmol) of 2,6-dimethylphenylisonitrile. The product was obtained as a yellow solid, 83% yield, mp 154–156 °C. IR ν_{max} (KBr) 3353 (OH), 2917, 1660 (C=N), 1618, 1442, 1106, 754 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 13.57 (1H, br s, OH), 9.17 (1H, dd, *J*=8.3, 1.7 Hz, H-6), 7.44 (1H, d, *J*=8.1 Hz, H-13), 7.38 (1H, ddd, *J*=8.3, 7.1, 1.7 Hz, H-4), 7.10 (2H, d, *J*=7.6 Hz, H-17), 7.04 (1H, dd, *J*=8.3, 1.3 Hz, H-3), 7.01–6.98 (2H, m, H-10, H-18), 6.90 (1H, ddd, *J*=8.3, 7.1, 1.3 Hz, H-5), 6.76–6.75 (1H, m, H-12), 2.31 (3H, s, H-20), 2.14 (6H, s, H-19). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.6 (C-2), 152.3 (C-7), 145.3 (C-9), 143.4 (C-15), 141.3 (C-11), 140.4 (C-8, C-14), 133.3 (C-4), 132.4 (C-6), 127.8 (C-17), 126.9 (C-16), 126.7 (C-13), 125.6 (C-18), 123.7 (C-10), 118.5 (C-5), 118.1 (C-3), 117.4 (C-1), 115.7 (C-12), 21.4 (C-20), 18.5 (C-19). MS *m*/*z*: 357 ($[M+1]^+$, 5), 356 ($[M]^+$, 20), 341 (22), 270 (16), 259 (14), 236 (100), 225 (84), 197 (17). HRMS: $C_{23}H_{21}N_2O_2$ $[M^+ + H]^+$, calcd 357.1598, found 357.1597, error 0.1527.

4.3.8. N-(2,6-Dimethylphenyl)-2-(2-hydroxyphenyl)-2-oxoacetamide (**14**)

Compound **14**, obtained from 0.26 g (1.07 mmol) of Schiff base **13** and 0.28 g (2.14 mmol) of 2,6-dimethylphenylisonitrile, in dry toluene, was placed in a sealed ampule and heated for 16 h at 120 °C under nitrogen atmosphere. The solvent was removed under vacuum. Purification by column chromatography and recrystallization using hexane–ethyl acetate (98:2) afforded a yellow solid (0.107 g), 37% yield, mp 145–147 °C. IR ν_{max} (KBr) 3190 (OH), 1657 (C=O), 1629 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 11.84 (1H, s, OH), 8.66 (1H, dd, *J*=8.2, 1.5 Hz, H-6), 8.47 (1H, br s, NH), 7.60 (1H, ddd, *J*=8.5, 7.0, 1.5 Hz, H-4), 7.23–7.14 (2H, m, H-11, H-12), 7.06 (1H, d, *J*=8.5 Hz, H-3), 6.98 (1H, t, *J*=7.4 Hz, H-5), 2.31 (6H, s, H–Me). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 190.6 (C-7), 164.4 (C-8), 160.8 (C-2), 138.9 (C-4), 135.5 (C-9), 134.2 (C-6), 132.4 (C-10), 128.9 (C-11), 128.5 (C-12), 120.1 (C-5), 119.0 (C-3), 118.0 (C-1), 18.9 (C–Me). HRMS: $C_{16}H_{16}NO_3$ $[M^+ + H]^+$, calcd 270.1124, found 270.1119, error 2.1101.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.04.080.

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