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An Efficient and Facile Ultrasonic-Accelerated One-Pot Synthesis of *N*-Acetyl-2-aryl-1, 2-dihydro-(4*H*)-3,1-benzoxazin-4-ones

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ABSTRACT: *An application of ultrasonic irradiation in the one-pot synthesis of N-acetyl-2-aryl-1,2-dihydro-(4H)-3,1-benzoxazin-4-ones from the condensation reaction between aromatic aldehydes and anthranilic acid in the presence of excess amount of acetic anhydride has been explored. The reactions proceed smoothly under mild and solvent-free conditions at room temperature in the absence of any catalyst to afford the products in good to excellent yields.* © 2011 Wiley Periodicals, Inc. Heteroatom Chem 22:106–113, 2011; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20663

INTRODUCTION

As evident from the literature [1–7], application of ultrasound in the so-called "sonochemistry" has received enormous interests since it offers a versatile and challenging technique in organic synthesis [8]. Nowadays, ultrasonic irradiation technique has been employed not only to decrease reaction times but also to improve yields in a large variety of organic synthesis [1–7]. The phenomenon responsible for the beneficial effects of ultrasound on chemical reactions is based on acoustic cavitation. 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°C, and pressures of about 1000 atm, and heating and cooling rates are above 10 billion degree centigrades per second [2]. Such localized hot spots can be considered as microreactors in which the energy of sound is transformed into a useful chemical form.

On the other hand, one-pot multicomponent reactions have proven to be more advantageous over conventional linear-type synthesis [9–10], since the multistep reactions usually suffer from complex isolation procedures and produce a significant amount of waste products. Moreover, one-pot processes provide rapid and efficient approach to organic transformations including diverse synthesis of polyfunctionalized heterocycles [11]. Among the important heterocyclic compounds, 4*H*-3,1-benzoxazin-4-ones are known as important class of compounds [12], having significant biological activities as potent inactivators of chymotrypsin [13–15], inhibitors of human leukocyte elastase [16,17], and HSV-1 protease [18]. These compounds occur in nature [19,20] and have also been used as linking units in polymer chemistry [21] and as key intermediates in organic synthesis [12]. These compounds are also valuable starting materials in the synthesis of various heterocycles such as 2,3-disubstituted quinazolin-4(3*H*)-one [22–29]. In contrast to the parent 4*H*-3,1-benzoxazin-4-one, only very few routes have ever been reported on the synthesis of *N*-substituted-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-ones [30–32]. A

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method was previously reported on the synthesis of *N*-acetyl-1,2-dihydro-4*H*-3,1-benzoxazin-4-one employing the reaction of N-acylated anthranilic acids with paraformaldehyde in refluxing AcOH [33]. Recently, silica-bound benzoyl chloride mediated solid phase synthesis of 4*H*-3,1-benzoxazin-4-ones has been reported [34].

4*H*-3,1-Benzoxazin-4-ones are useful synthons in the synthesis of important heterocyclic compounds such as 1,4-bezodiazepin-2,5-dione and indoxyls [30,33,35]. The chemistry of benzoxazin-4-one is anticipated to play a vital role in the coming years in the synthesis of medicinal and natural products [12]. However, most of these reported methods suffer from certain drawbacks such as longer reaction times, low yields, and use of severe reaction conditions. To avoid such drawbacks, still there is a great demand for the development of milder and environmentally benign approaches to these heterocycles.

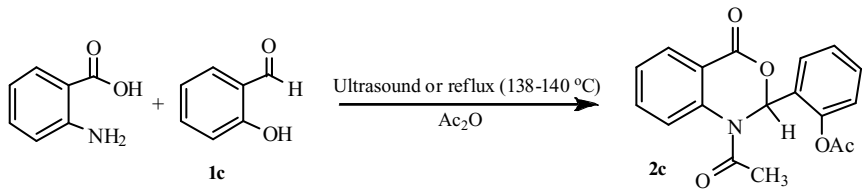
The objective of the present work is to explore the use of ultrasonic irradiation technique in the one-pot synthesis of *N*-acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one under mild and green conditions.

RESULTS AND DISCUSSION

As part of our ongoing research on the application of ultrasonic irradiation technique as a clean and useful protocol in organic synthesis [36] and also regarding the lack of sufficient reports on the synthesis of substituted 1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one [31,32], we were encouraged, in this report, to study the hitherto unreported useful application of ultrasound in the synthesis of *N*-acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one. We preliminarily examined the condensation reaction of 2-hydroxybenzaldehyde **1c** as the test compound with anthranilic acid in the presence of acetic anhydride under sonication and catalyst-free conditions.

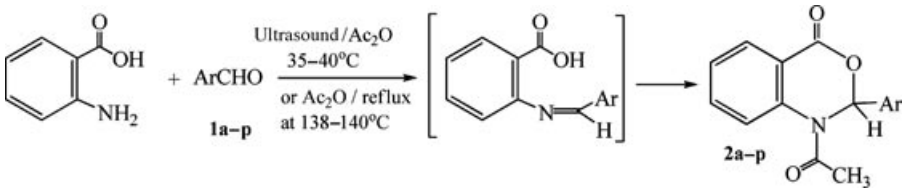
To achieve suitable reaction conditions in terms of reaction time, temperature, and yield, various solvents and reaction conditions were investigated and the results are summarized in Table 1. Effects of solvent and temperature (only for thermal condition)

TABLE 1 Effect of Reaction Conditions[a]



Entry	*Conditions*	*Method*	*Time (min)*	*Yield[b] (%)*
1	Ac_2O (exc.)/35–40°C	Ultrasound	18	98
2	MeOH/35–40°C	Ultrasound	45	45
3	MeCN/35–40°C	Ultrasound	58	48
4	EtOAc/35–40°C	Ultrasound	50	55
5	$CHCl_3$/35–40°C	Ultrasound	65	58
6	CCl_4/35–40°C	Ultrasound	55	60
7	Et_2O/35–40°C	Ultrasound	60	48
8	*n*-Hexane/35–40°C	Ultrasound	45	65
9	Ac_2O(exc.)/rt	Thermal	180	40
10	Ac_2O (exc.)/60°C	Thermal	150	45
11	Ac_2O (exc.)/100°C	Thermal	120	55
12	Ac_2O (exc.)/138–140°C	Thermal	90	63
13	MeOH/reflux	Thermal	120	35
14	MeCN/reflux	Thermal	130	45
15	EtOAc/reflux	Thermal	180	50
16	DMF/reflux	Thermal	105	55
17	$CHCl_3$/reflux	Thermal	150	58
18	Et_2O/reflux	Thermal	180	60
19	CCl_4/reflux	Thermal	165	62
20	*n*-hexane/reflux	Thermal	180	50

[a]Anthranilic acid (1 mmol), acetic anhydride (5 mL, 53 mmol), 2-hydroxybenzaldehyde (1 mmol), solvent (5 mL).
[b]Isolated yields.



SCHEME 1 Synthesis of *N*-acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one **2a–p**.

on the reaction was studied using different solvents such as MeOH, EtOAc, MeCN, DMF, $CHCl_3$, Et_2O, CCl_4, and *n*-hexane. As seen in Table 1, the reaction worked out best under sonication conditions in the absence of any solvent but excess amount of acetic anhydride at ambient temperature (35–40°C) to provide the highest possible yield (98%, entry 1) in 18 min compared with the yield obtained under optimum thermal condition (reflux, solvent-free) in 90 min (63%, entry 12). Apparently, increasing the temperature under solvent-free thermal conditions showed an improving effect on the yield as well as the reaction rate (entries 9–12).

To develop the scope of the reaction, we were encouraged to extend this reaction to a variety of aromatic aldehydes **1a–p** carrying different substituents under the determined optimum conditions (sonication, solvent-free, at 35–40°C or reflux) (Scheme 1). All the reactions proceeded smoothly to provide the corresponding products **2a–p** in satisfactory yields, and the results are summarized in Table 2. Also, the experimental results in Table 2 clearly indicate that under ultrasonic irradiation all the reactions proceed in shorter reaction times (7–30 min) and higher yields (90–98%) when compared with the reaction times (1–6 h) and yields (55–75%) obtained under reflux conditions.

This reaction seems to proceed through the intermediacy of a corresponding imine derivative (**A**) of the anthranilic acid in reaction with aromatic aldehyde **1**, which undergoes subsequent cyclization to the product **2** in the presence of Ac_2O (Scheme 2). To approve this mechanism, the imine (**A**) was obtained in a separate experiment as a stable compound from the reaction of anthranilic acid with benzaldehyde as a test compound in MeOH (92%) or Ac_2O (95%). This imine was then separately treated with Ac_2O both under sonication at 35–40°C and reflux conditions, which resulted in the respective product **2a** in 90% and 75% yields, respectively.

In summary, we have explored the application of ultrasonic irradiation technique as a rapid and reliable protocol in the synthesis of *N*-acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one from the one-pot reaction of aromatic aldehydes with anthranilic acid in the presence of acetic anhydride at room temperature. The reactions proceeded under solvent-free condition to provide the products in shorter reaction times and higher yields than those obtained under the conventional reflux condition.

EXPERIMENTAL

Material and Instruments

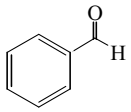
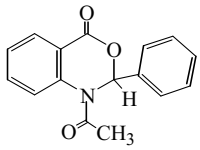
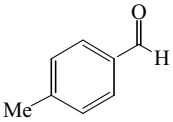
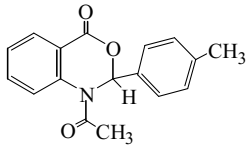
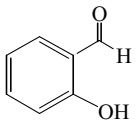
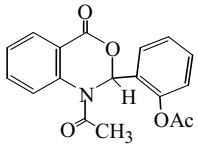
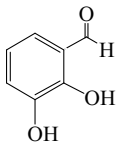
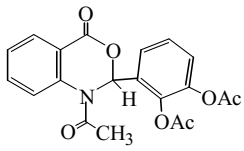
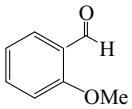
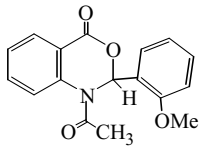
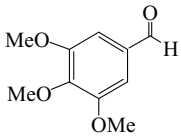
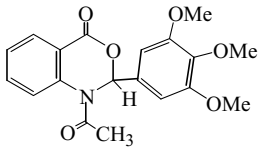
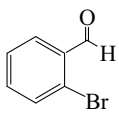
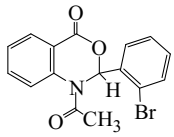
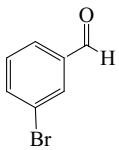
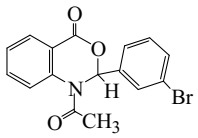
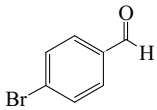
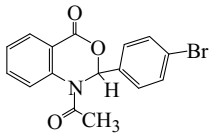
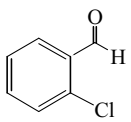
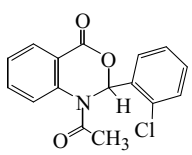
Chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and Merck (Hohenbrunn, Germany) and used without purification. IR spectra were recorded on a Perkin Elmer GX FT IR spectrometer from KBr pellets. ^1H and ^{13}C NMR spectra were measured for samples in $CDCl_3$ with a JEOL FX 90Q instrument at 90 and 22.5 MHz, respectively, using Me_4Si as an internal standard. Mass spectra were recorded with a spectrometer Finnigan-MAT 8430 operating at an ionization potential of 70 ev. Melting points were measured on a SMPI apparatus. Elemental analyses for C, H, and N atoms were performed using a Perkin–Elmer 2400 series analyzer. 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.

*Typical Procedure for the Synthesis of N-Acetyl-2-aryl-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (**2**)*

A mixture of aldehyde **1** (1 mmol), anthranilic acid (1 mmol), and acetic anhydride (5 mL, 53 mmol) in a flask was placed in a water bath and sonicated at 35–40°C (or refluxed without sonication) for an appropriate time (Table 2) until the reaction was completed as monitored by TLC (*n*-hexane/EtOAc; 2:1) analysis. The reaction mixture was then treated with iced water and filtered to leave a solid product, which was crystallized from ethanol to yield pure product. All the products were characterized by their physical and spectral data (IR, MS, ^1H NMR,^{13}C NMR) and elemental analysis.

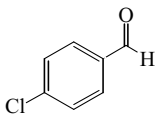
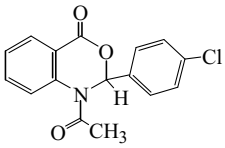
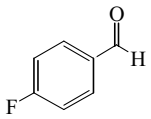
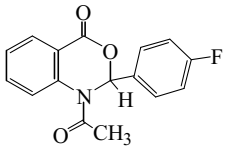
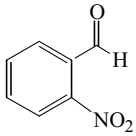
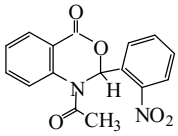
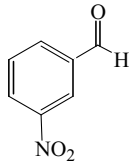
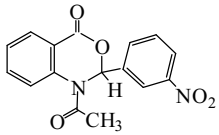
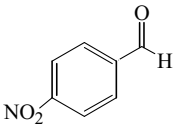
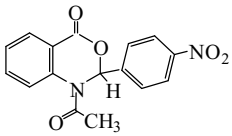
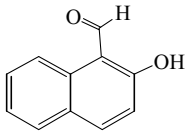
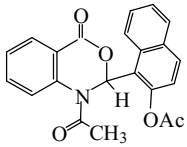
*N-Acetyl-1,2-dihydro-2-(phenyl)-(4H)-3,1-benzoxazin-4-one (**2a**).* Pale yellow solid; mp = 122–124°C; IR (KBr), *v*: 3050, 2996, 1729, 1682, 1607,

TABLE 2 Ultrasonic-Accelerated Synthesis of *N*-Acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one **2a–p**[a]

			Conditions			
			Sonication		*Refluxing*	
Entry	*ArCHO* ***1***	*Product* ***2***	*Time (min)*	*Yield*[b] *(%)*	*Time (h)*	*Yield*[b] *(%)*
2a			8	95	6	64
2b			10	96	3	71
2c			18	98	1.5	66
2d			25	92	2.5	55
2e			19	98	2.5	63
2f			10	97	2	64
2g			14	90	3	57
2h			17	94	2.5	74
2i			15	90	3.5	61
2j			12	94	3.5	59

(*Continued*)

TABLE 2 Continued

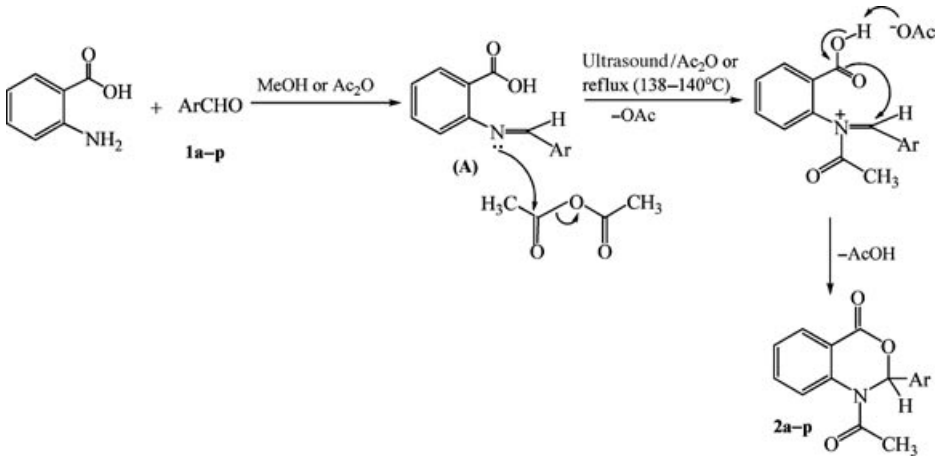
			Conditions			
			Sonication		*Refluxing*	
Entry	*ArCHO* ***1***	*Product* ***2***	*Time (min)*	*Yield*[b] *(%)*	*Time (h)*	*Yield*[b] *(%)*
2k			7	92	4	62
2l			14	95	3	55
2m			7	96	1.5	70
2n			9	98	1	75
2o			10	98	2	63
2p			30	95	6	57

[a]Anthranilic acid (1 mmol), acetic anhydride (5 mL), aldehyde (1 mmol), sonication at 35-40°C (or without sonication at 138–140°C).
[b]Isolated yields.

1366, 1051; MS, *m/z* (%): 267 (M^+, 11), 225 ($M^+ - CH_2CO$, 45), 180 ($M^+ - CH_2CO - CO_2H$, 27); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.30 (s, 3H, $COCH_3$), 7.16 (s, 1H, CH), 8.08–7.45 (m, 9H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 24.4, 85.0, 122.7, 123.4, 126.5, 129.0, 129.4, 130.4, 131.7, 132.4, 136.2, 136.5, 136.7, 140.5, 163.9, 171.3; Anal. Calcd for $C_{16}H_{13}NO_3$: C, 71.91; H, 4.86; N, 5.24%. Found: C, 71.85; H, 4.82; N, 5.18%.

*N-Acetyl-1,2-dihydro-2-(4-methylphenyl)-(4H)-3, 1-benzoxazin-4-one (***2b***).* White solid; mp = 146–148°C; IR (KBr), *ν*: 3009, 2935, 1727, 1686, 1597, 1381. MS, *m/z* (%): 281 (M^+, 45), 239 ($M^+ - CH_2CO$, 100), 194 ($M^+ - CH_2CO - CO_2H$, 55), 179 ($C_{12}H_9N^+$, 38); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.57 (s, 3H, CH_3), 3.75 (s, 3H, $COCH_3$), 7.55–6.82 (m, 8H, Ar-H), 7.62 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.7, 27.2, 84.5, 108.8, 114.6, 116.7, 122.8, 125.9, 133.0, 133.7, 134.5, 138.7, 149.8, 151.5, 156.6, 163.0, 170.6; Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.59; H, 5.33; N, 4.98%. Found: C, 72.54; H, 5.30; N, 4.95%.

*2-(2-Acetoxyphenyl)-N-acetyl-1,2-dihydro-(4H)-3, 1-benzoxazin-4-one (***2c***).* White solid; mp = 132–135°C; IR (KBr), *ν*: 3053, 2995,1764, 1739, 1709, 1583, 1349; MS, *m/z* (%): 325 (M^+, 9), 283 ($M^{+-}CH_2CO$, 47), 241 (M^{+-} $2CH_2CO$, 66), 196 (M^{+-} $2CH_2CO - CO_2H$, 30), 179 ($C_{13}H_9N^+$, 95); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.35 (s, 3H, $COCH_3$), 2.37 (s, 3H,



SCHEME 2 Mechanism of the formation of *N*-Acetyl-2-aryl-1,2-dihydro-(4*H*)-3,1-benzoxazin-4-one **2a–p**.

$OCOCH_3$), 7.10 (s, 1H, CH), 7.29 (m, 4H, Ar-H), 7.87 (m, 4H, Ar-H); ^{13}C NMR (22.5 MHz, $CDCl_3$): δ_C 22.9, 23.6, 83.7, 121.9, 122.2, 124.3, 125.2, 126.3, 129.8, 131.3, 133.2, 134.5, 137.2, 139.2, 148.8, 169.9, 170.6, 172.2; Anal. Calcd for $C_{18}H_{15}NO_5$: C, 66.46; H, 4.61; N, 4.30%. Found: C, 66.42; H, 4.56; N, 4.25%.

N-Acetyl-2-(2,3-diacetoxyphenyl)-1,2-dihydro-(4h)-3,1-benzoxazin-4-one (**2d**). Pale yellow solid; mp = 165–168°C; IR (KBr), ν: 3083, 2943, 1757, 1682, 1606, 1588, 1489, 1366; MS, *m/z* (%): 383 (M^+, 10), 299 (M^{+-} $2CH_2CO$, 19), 257 ($M^+ - 3CH_2CO$, 22), 212 ($M^+ - 3CH_2CO - CO_2H$, 30), 178 ($C_{13}H_9N^+$, 95); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.24 (s, 3H, $COCH_3$), 2.34 (s, 3H, $OCOCH_3$), 2.36 (s, 3H, $OCOCH_3$), 7.05 (m, 4H, Ar-H), 7.27 (s, 1H, CH), 7.85 (m, 3H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 20.1, 20.9, 22.2, 79.6, 119.4, 124.2, 124.6, 125.0, 126.1, 126.7, 129.0, 129.8, 135.0, 135.3, 138.3, 143.0, 161.0, 167.3, 167.7, 169.6; Anal. Calcd for $C_{20}H_{17}NO_7$: C, 62.66; H, 4.43; N, 3.65%. Found: C, 62.58; H, 4.41; N, 3.62%.

N-Acetyl-1,2-dihydro-2-(2-methoxyphenyl)-(4H)-3,1-benzoxazin-4-one (**2e**). White solid; mp = 132–135°C; IR (KBr), ν: 3003, 2926, 1718, 1675, 1597, 1373. MS, *m/z* (%): 297 (M^+, 55), 255 ($M^+ - CH_2CO$, 100), 210 ($M^{+-}CH_2CO - CO_2H$, 51), 195 ($C_{13}H_9NO^+$, 55), 167 ($C_{12}H_9N^+$, 33); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.50 (s, 3H, $COCH_3$), 3.85 (s, 3H, OCH_3), 7.35–6.62 (m, 8H, Ar-H), 7.50 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.7, 56.2, 82.5, 106.8, 110.6, 111.7, 120.8, 123.9, 130.0, 132.1, 133.0, 138.7, 147.8, 148.5, 154.6, 161.0, 170.1; Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.05; N, 4.71%. Found: C, 68.64; H, 5.03; N, 4.67%.

N-Acetyl-1,2-dihydro-2-(3,4,5-trimethoxyphenyl)-(4H)-3,1-benzoxazin-4-one (**2f**). Pale yellow solid; mp = 174–176°C; IR (KBr), ν: 3072, 2974, 2943, 1736, 1702, 1589, 1346; MS, *m/z* (%): 357 (M^+, 42), 315 ($M^{+-}CH_2{=}C{=}O$, 100), 270 ($M^+ - CH_2{=}C{=}O - CO_2H$, 57), 206 ($C_{10}H_8NO_4^+$, 37), 179 ($C_9H_9NO_3^+$, 45), 107 ($C_7H_7O^+$, 62); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.03 (s, 3H, $COCH_3$), 3.43 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 6.50 (s, 1H, CH), 7.80–7.21 (m, 6H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.5, 30.5, 55.9, 59.9, 83.0, 103.7, 106.7, 119.3, 125.1, 126.2, 129.1, 131.9, 134.9, 137.7, 139.0, 153.1, 161.5, 170.3, 191.8; Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.32; N, 3.92%. Found: C, 63.84; H, 5.28; N, 3.90%.

N-Acetyl-2-(2-bromophenyl)-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (**2g**). Pale yellow solid; mp = 80–82°C; IR (KBr), ν: 3055, 2993, 1734, 1685, 1604, 1363, 1056; MS, *m/z* (%): 347 ($M^+ + 2$, 3), 345 (M^+, 4), 305 ($M^+ + 2 - CH_2CO$, 51), 303 (M^{+-} CH_2CO, 49), 260 ($M^+ + 2 - CH_2CO - CO_2H$, 12), 258 ($M^+ - CH_2CO - CO_2H$, 27), 186 ($C_6H_5^{81}BrO^+$, 48), 184 ($C_6H_5^{79}BrO^+$, 49); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.35 (s, 3H, $COCH_3$), 7.08 (s, 1H, CH), 8.0–7.25 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.4, 83.0, 120.7, 121.4, 124.5, 127.0, 127.4, 128.4, 129.7, 130.4, 134.2, 134.5, 134.7, 138.5, 161.9, 169.3; Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.49; H, 3.46; N, 4.04%. Found: C, 55.43; H, 3.42; N, 3.97%.

N-Acetyl-2-(3-bromophenyl)-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (**2h**). White solid; mp = 180–182 °C; IR (KBr), ν: 3084, 2987, 1739, 1690, 1602, 1367, 1072; MS, m/z (%): 347 ($M^+ + 2$, 3), 345 (M^+, 7), 305 ($M^+ + 2 - CH_2CO$, 40), 303 ($M^{+-}CH_2CO$,

31), 260 ($M^+ + 2 - CH_2CO - CO_2H$, 17), 258 ($M^+ - CH_2CO - CO_2H$, 24), 158 ($C_6H_5^{81}Br^+$, 48), 156 ($C_6H_5^{79}Br^+$, 49); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.44 (s, 3H, $COCH_3$), 6.47 (s, 1H, CH), 7.58–7.17 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.4, 82.4, 123.0, 124.1, 124.6, 126.6, 129.0, 130.3, 130.5, 132.1, 132.30, 134.8, 134.9, 138.3, 138.6, 169.9; Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.49; H, 3.46; N, 4.04. Found: C, 55.41; H, 3.38; N, 4.00%.

*N-Acetyl-2-(4-bromophenyl)-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (***2i***).* Pale yellow solid; mp = 92–95°C; IR (KBr), ν: 3084, 2985, 1739, 1693, 1602, 1363, 1064; MS, *m/z* (%): 347 ($M^+ + 2$, 3), 345 (M^+, 4), 305 ($M^+ + 2 - CH_2CO$, 45), 303 ($M^{+-}CH_2CO$, 45), 260 ($M^+ + 2 - CH_2CO - CO_2H$, 16), 258 ($M^+ - CH_2CO - CO_2H$, 31), 158 ($C_6H_5^{81}Br^+$, 48), 156 ($C_6H_5^{79}Br^+$, 49); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.47 (s, 3H, $COCH_3$), 7.23 (s, 1H, CH), 7.90–7.43 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.5, 82.4, 123.0, 124.1, 124.6, 126.6, 129.0, 130.3, 131.2, 132.1, 133.1, 134.9, 135.6, 138.3, 167.6, 169.9; Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.49; H, 3.46; N, 4.04. Found: C, 55.39; H, 3.42; N, 3.93%.

*N-Acetyl-2-(2-chlorophenyl)-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (***2j***).* Colorless solid; mp = 166–169°C; IR (KBr), ν: 3082, 2995, 1749, 1680, 1602, 1357, 1066. MS, m/z (%): 303 ($M^+ + 2$, 2), 301 (M^+, 5), 261 (M^+ + 2-CH_2CO, 26), 259 ($M^{+-}CH_2CO$, 52), 216 ($M^+ + 2 - CH_2CO - CO_2H$, 23), 214 ($M^+ - CH_2CO - CO_2H$, 38), 142 ($C_7H_5^{37}ClO^+$, 46), 140 ($C_7H_5^{35}ClO^+$, 44); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.40 (s, 3H, $COCH_3$), 7.61–7.13 (m, 8H, Ar-H), 7.78 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.3, 81.6, 120.5, 124.4, 126.5, 126.8, 128.1, 129.7, 130.2, 130.7, 132.3, 132.7, 134.7, 138.4, 162.0, 169.0; Anal. Calcd for $C_{16}H_{12}ClNO_3$: C, 63.68; H, 3.98; N, 4.64%. Found: C, 63.63; H, 3.95; N, 4.58%.

*N-Acetyl-2-(4-chlorophenyl)-1,2-dihydro-(4H)-3,1-benzoxazin-4-one (***2k***).* Colorless solid; mp = 169–172°C; IR (KBr), ν: 3086, 2989, 1739, 1670, 1602, 1367, 1089; MS, *m/z* (%): 303 ($M^+ + 2$, 2), 301 (M^+, 5), 261 ($M^+ + 2 - CH_2CO$, 14), 259 ($M^{+-}CH_2CO$, 49), 216 ($M^+ + 2 - CH_2CO - CO_2H$, 16), 214 ($M^+ - CH_2CO - CO_2H$, 31), 114 ($C_6H_5^{37}Cl^+$, 46), 112 ($C_6H_5^{35}Cl^+$, 44); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.48 (s, 3H, $COCH_3$), 7.24 (s, 1H, CH), 7.91–7.49 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.2, 82.6, 119.4, 124.0, 126.2, 126.8, 127.2, 127.8, 128.1, 128.6, 129.4, 129.8, 134.6, 138.2, 161.3, 169.7; Anal. Calcd for $C_{16}H_{12}ClNO_3$: C, 63.68; H, 3.98; N, 4.64%. Found: C, 63.61; H, 3.94; N, 4.61%.

*N-Acetyl-1,2-dihydro-2-(4-fluorophenyl)-(4H)-3,1-benzoxazin-4-one (***2l***).* Pale yellow solid; mp = 133–136°C; IR (KBr), ν: 3067, 2992, 1750, 1682, 1590, 1330, 1150; MS, *m/z* (%): 285 (M^+, 10), 243 ($M^{+-}CH_2CO$, 21), 198 ($M^+ - CH_2CO - CO_2H$, 16), 179 ($C_{13}H_9N^+$, 46), 118 ($C_7H_4NO^+$, 30), 77 ($C_6H_5^+$, 23); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.45 (s, 3H, $COCH_3$), 6.91 (s, 1H, CH), 7.65- 7.24 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.5, 83.1, 115.4, 116.3, 119.8, 124.1, 126.6, 127.8, 128.2, 130.3, 131.9, 134.8, 138.6, 157.3, 161.3, 169.9; Anal. Calcd for $C_{16}H_{12}FNO_3$: C, 67.36; H, 4.21; N, 4.91%. Found: C, 67.32; H, 4.18; N, 4.87%.

*N-Acetyl-1,2-dihydro-2-(2-nitrophenyl)-(4H)-3,1-benzoxazin-4-one (***2m***).* White solid; mp = 177–180°C; IR (KBr), ν: 3065, 2991, 1737, 1703, 1616, 1522, 1494, 1372, 1314; MS, *m/z* (%): 312 (M^+, 12), 270 ($M^+ - CH_2CO$, 94), 225 ($M^+ - CH_2CO - CO_2H$, 26), 179 ($C_3H_3NO_5^+$, 41), 146 ($C_8H_4NO_2^+$, 37), 119 ($C_7H_5NO^+$, 67); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.37 (s, 3H, $COCH_3$), 7.27 (s, 1H, CH), 7.90–7.35 (m, 8H, Ar-H);^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 22.5, 82.5, 119.5, 121.0, 124.0, 124.1, 127.0, 130.1, 130.6, 132.3, 135.1, 138.2, 138.4, 149.1, 161.0, 170.9; Anal. Calcd for $C_{16}H_{12}N_2O_5$: C, 61.53; H, 3.84; N, 8.97%. Found: C, 61.48; H, 3.79; N, 8.94%.

*N-Acetyl-1,2-dihydro- 2-(3-nitrophenyl)-(4H)-3,1-benzoxazin-4-one (***2n***).* White solid; mp = 182–184°C; IR (KBr), ν: 3055, 2994, 1741, 1720, 1609, 1516, 1499, 1377, 1312; MS, *m/z* (%): 312 (M^+, 18), 270 ($M^+ - CH_2CO$, 100), 225 ($M^+ - CH_2CO - CO_2H$, 31), 179 ($C_3H_3NO_5^+$, 47), 146 ($C_8H_4NO_2^+$, 40), 119 ($C_7H_5NO^+$, 70); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.41 (s, 3H, $COCH_3$), 7.32 (s, 1H, CH), 7.94–7.45 (m, 8H, Ar-H);^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 23.5, 83.1, 121.7, 122.4, 123.8, 124.6, 127.4 130.7, 131.4, 132.8, 134.1, 139.2, 141.4, 151.1, 165.0, 168.9; Anal. Calcd for $C_{16}H_{12}N_2O_5$: C, 61.53; H, 3.84; N, 8.97%. Found: C, 61.48; H, 3.79; N, 8.94%.

*N-Acetyl-1,2-dihydro- 2-(4-nitrophenyl)-(4H)-3,1-benzoxazin-4-one (***2o***).* Pale yellow solid; mp = 190–193°C; IR (KBr), ν: 3078, 2989, 1748, 1695, 1604, 1510, 1487, 1363, 1303; MS, *m/z* (%): 312 (M^+, 8), 270 ($M^+ - CH_2CO$, 100), 225 ($M^+ - CH_2CO - CO_2H$, 19), 179 ($C_3H_3NO_5^+$, 32), 146 ($C_8H_4NO_2^+$, 31), 119 ($C_7H_5NO^+$, 75); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.47 (s, 3H, $COCH_3$), 7.24 (s, 1H, CH), 8.15–7.54 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 24.7, 80.5, 119.5, 121.0, 124.5, 125.1, 126.9, 131.0, 132.6, 134.2, 136.1, 138.6, 139.4, 148.5, 163.0, 171.9; Anal. Calcd for $C_{16}H_{12}N_2O_5$: C, 61.53; H, 3.84; N, 8.97%. Found: C, 61.51; H, 3.82; N, 8.92%.

*2 - (2 - Acetoxynaphthalen - 1 - yl) - N - acetyl - 1, 2-dihydro-2-(4H)-3,1-benzoxazin-4-one (***4p***).* Pale yellow solid; mp = 196–198°C; IR (KBr), ν: 3057, 2946, 1776, 1736, 1674, 1514, 1367; MS, *m/z* (%): 375 (M^+, 9), 315 ($M^{+-}CH_2CO$, 53), 273 (M^{+-} $2CH_2CO$, 31), 228 ($M^+ - 2CH_2CO - CO_2H$, 30), 118 ($C_7H_4NO^+$, 30), 77 ($C_6H_5^+$, 27); ^{1}H NMR ($CDCl_3$, 90 MHz): δ 2.21 (s, 3H, $COCH_3$), 2.36 (s, 3H, $COCH_3$), 6.74 (s, 1H, CH), 7.71–7.33 (m, 6H, Ar-H), 8.35–8.03 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 21.2, 22.3, 81.9, 120.1, 122.7, 122.8., 123.4, 124.9, 125.9, 127.6, 127.8, 128.7, 129.5, 131.2, 131.3, 131.6, 134.0, 138.5, 147.1, 162.7, 169.7, 169.8; Anal. Calcd for $C_{22}H_{17}NO_5$: C, 70.40; H, 4.53; N, 3.73%. Found: C, 70.36; H, 4.48; N, 3.68%.

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