$PhI(OAc)_2$-mediated one-pot synthesis of benzoxazinones from anthranilic acids and aromatic aldehydes

Yuanyuan Xie* and Suping Wang

Key Laboratory for Green Pharmaceutical Technologies and Related Equipment of Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China

A novel way to synthesise 2-aryl-4H-benzo[d][1,3]oxazin-4-ones has been developed by the cyclisation of Schiff bases with (diacetoxyiodo)benzene. The salient features of this new protocol which starts from an anthranilic acid and an aromatic aldehyde, are short reaction time, mild reaction conditions and good yields.

Keywords: benzoxazinones, hypervalent iodine, Schiff base, cyclisation

The benzoxazinone scaffold has been widely investigated in medicinal chemistry over the last two decades.[1–3] Benzoxazinone derivatives play an important role in the defence of the human body against infections. Substituted 4H-benzo[d][1,3]oxazin-4-ones have been well characterised as heterocyclic acylating agents of serine proteases.[4] Teshima *et al*. first reported this class of alternative substrate inhibitors in 1982 and demonstrated that they were potent irreversible inhibitors for human leukocyte elastase, porcine pancreatic elastase, cathepsin G, and chymotrypsin.[5] Since then there has been considerable interest in the development of the inhibitory effects of benzoxazinones.

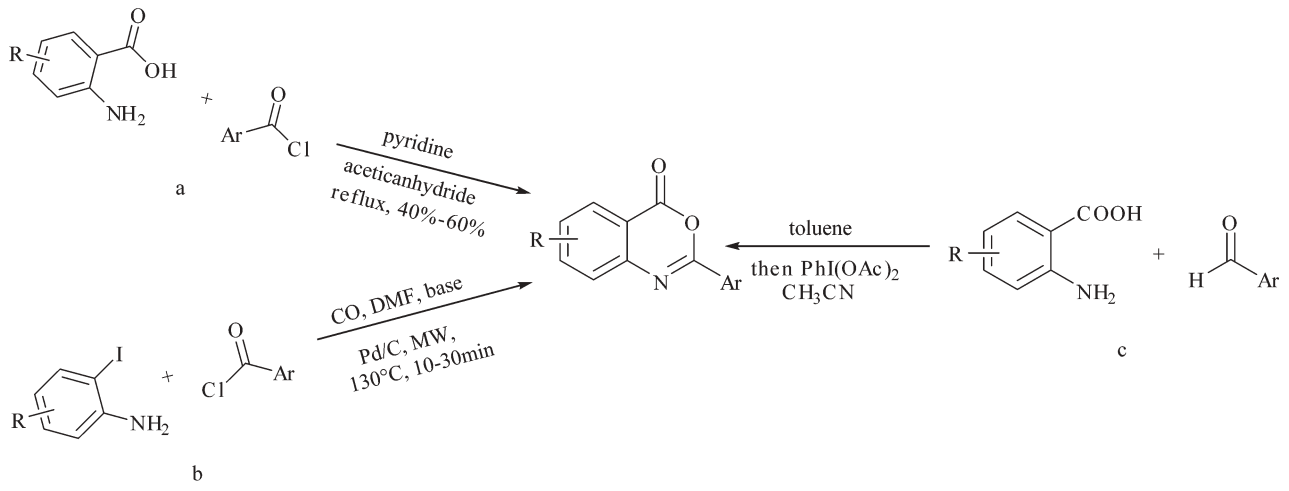
Generally, the most common method for the synthesis of benzoxazinones involves reaction of an anthranilic acid and an acyl choride followed by dehydration[6–8] (Scheme 1a). Recently the microwave-assisted cyclocarbonylation of aryl iodides (Scheme 1b) has been reported.[9] The disadvantages of these two reactions are that drastic and inconvenient conditions are required and low yields are achieved. Here, we report a novel one-pot protocol for the synthesis of benzoxazinones from anthranilic acid, aromatic aldehyde and (diacetoxyiodo) benzene [$PhI(OAc)_2$] (Scheme 1c).

During the past several decades, the chemistry of polyvalent iodine reagents has experienced an explosive development. Furthermore, many synthetic reactions using hypervalent iodine reagents have also been developed.[10,11] There has been an upsurge of interest in $PhI(OAc)_2$ one of the classical hypervalent iodine reagents, mainly due to its very useful oxidising properties, allied to its mild, highly selective, environmentally benign, and commercial availability properties.[12,13] We now propose a novel preparation of benzoxazinones by the cyclisation of a Schiff base in the presence of $PhI(OAc)_2$ (Scheme 2). This is an important improvement in the application of $PhI(OAc)_2$.

The first step in the one-pot preparation of benzoxazinones is the formation at 110 °C of a Schiff base from an anthranilic acid and an aromatic aldehyde. The second step is the Schiff base is directly oxidised by $PhI(OAc)_2$, generating the cyclic benzoxazinones.

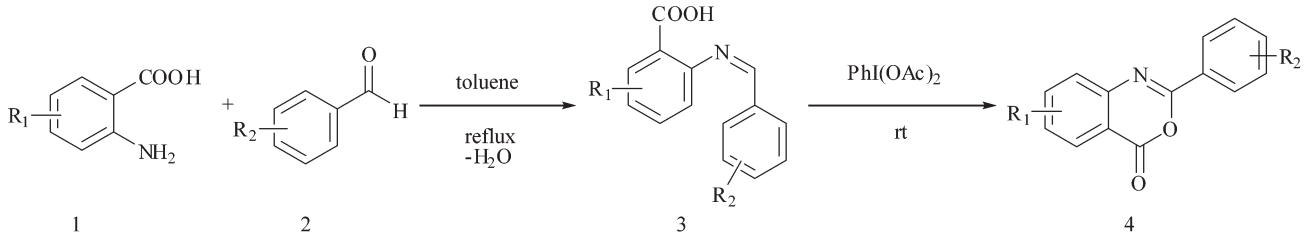
2-Phenyl-4*H*-benzo[d][1,3]oxazin-4-one (**4a**) was chosen as a candidate to optimise the reaction conditions in the second step. Initially, several solvents such as toluene, dichloromethane, MeCN, MeOH and *N,N*-dimethylformamide (DMF) were tested. The yield (83%) was observed in MeCN (Table 1, entries 1–5). According to the proposed mechanism (Scheme 3), acetic acid was produced as a by-product which, it was concluded, might slow down the reaction. Accordingly, a weak base such as Et_3N or $NaHCO_3$ was added to neutralise the reaction system.[14] However, the yields were not markedly improved (entries 6 and 7). Additionally, 1.0 equiv. 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) was tried as oxidant with 0.5 equiv. $PhI(OAc)_2$ as catalyst,[15] but this failed to improve the yield (entry 8). Furthermore, the effects of reaction temperature and time were also taken into consideration (entries 9 and 10) and it was found that a similar yield was afforded by reducing the reaction time from 60 min to 30 min. Finally the effect of the amount of $PhI(OAc)_2$ was investigated (entries 10–12), and a slightly higher yield was obtained by using 1.1 equiv. $PhI(OAc)_2$. On the basis of these results, the reaction was carried out under the optimised reaction conditions, namely, in MeCN at room temperature for 30 min (entry 11).

Having established the optimised conditions, various anthranilic acids and aromatic aldehydes were screened to explore



Scheme 1 Synthesis of benzoxazinones.

* Correspondent. E-mail: pharmlab@zjut.edu.cn



Scheme 2

Table 1 Optimisation of reaction conditions

Entry	PhI(OAc)$_2$ /equiv.	Solvent	Additive	Temp. /°C	Time /min	Yield /%[a]
1	1	PhMe	None	rt	60	25
2	1	CH_2Cl_2	None	rt	60	43
3	1	MeCN	None	rt	60	83
4	1	MeOH	None	rt	60	Trace
5	1	DMF	None	rt	60	50
6	1	MeCN	Et_3N(2equiv.)	rt	60	35
7	1	MeCN	$NaHCO_3$(2equiv.)	rt	60	83
8	0.5	MeCN	TEMPO(1equiv.)	rt	60	30
9	1	MeCN	None	60	40	86
10	1	MeCN	None	rt	30	82
11	1.1	MeCN	None	rt	30	86
12	1.3	MeCN	None	rt	30	86
13	1.5	MeCN	None	rt	30	85

[a]Isolated yield based on anthranilic acid.

Table 2 Preparation of benzoxazinones

Entry	R^1	R^2	Product	Yield/%[a]
1	H	H	**4a**	86
2	H	2-F	**4b**	81
3	H	4-Me	**4c**	85
4	H	2-Cl	**4d**	86
5	H	2,4-diCl	**4e**	84
6	H	4-Cl	**4f**	85
7	H	4-F	**4g**	84
8	H	4-Br	**4h**	88
9	3-Me	4-Me	**4i**	87
10	3-Me	3-MeO	**4j**	86
11	3-Me	2,4-diCl	**4k**	85
12	3-Me	4-F	**4l**	86
13	4-Cl	3-MeO	**4m**	68
14	4-Cl	4-MeO	**4n**	66
15	4-Cl	H	**4o**	83
16	4-Cl	4-Cl	**4p**	Trace
17	4-Cl	4-F	**4q**	Trace

[a]Isolated yield by column chromatography based on anthranilic acid.

the substrate scope. The reaction results are listed in Table 2. It was found that nonsubstituted anthranilic acid underwent the reaction with benzaldehyde derivatives containing either an electron-donating or electron-withdrawing group to obtain the corresponding products in good yields (entries 1–8). A similar result was observed when 3-methylanthranilic acid was used (entries 9–12). However, when 4-chloroanthranilic acid was tested low yields were obtained for benzaldehydes carrying electron-donating groups compared to its nonsubstituted analogue (entries 13–15), and the reaction failed for benzaldehydes carrying electron-withdrawing groups (entries 16 and 17). The reason for this result was unclear.

In addition, in order to widen the scope of the reaction, anthraldehyde and butyraldehyde were also investigated. However, none of the desired product was observed.

Based on the results described, a plausible reaction mechanism is depicted as follows (Scheme 3). Firstly, the reaction of Schiff base (**A**) and PhI(OAc)$_2$ affords the iodo complex (**B**) and 1 mole of AcO^-. The resulting AcO^- abstracts a hydrogen from the acid prompting cyclisation to form a six-membered ring intermediate (**C**). Subsequently, AcOH and PhI are spontaneously eliminated from intermediate (**C**) to generate the corresponding product benzoxazinone (**D**).

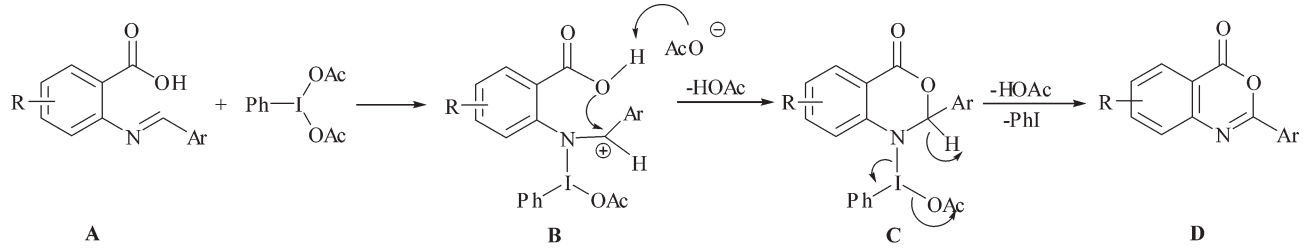
In conclusion, we have developed a novel PhI(OAc)$_2$-mediated one-pot process to synthesise benzoxazinones from anthranilic acids and benzaldehydes. A plausible mechanism for the formation of benzoxazinones was proposed. Advantages of this procedure are short reaction time, mild reaction conditions and high yields. To the best of our knowledge such a reaction is unprecedented and represents a completely new route to benzoxazinones. Further extension of this method is underway.

Experimental

^{1}H NMR and ^{13}C NMR spectra were measured on a Varian 400 (400 MHz) spectrometer (chemical shifts in δ ppm) using TMS as internal standard. Mass spectra (ESI-MS) were determined on a Thermo Finnigan LCQ-Advantage. High resolution mass spectra (ESI-HRMS) were determined on an Agilent 6210 TOF instrument. Melting points were measured on a Büchi B-540 capillary melting point apparatus.

Synthesis of benzoxazinones; general procedure

To a solution of anthranilic acid (1 mmol) in toluene (20 mL) was added aromatic aldehyde (1 mmol). The reaction mixture was heated under reflux for 2 h. After removal of solvent by rotary evaporation, the residue was dissolved in MeCN (5 mL) and PhI(OAc)$_2$ (1.1 mmol, 0.354 g) was added. The reaction mixture was stirred at room temperature for 30 min. After the completion of the reaction, the reaction mixture was evaporated under vacuum. The residue was purified by column chromatography (petroleum ether/ethyl acetate, 40:1) to



Scheme 3

afford a white solid. The six new components synthesised **4i–**n have been characterised by their spectral data.

2-Phenyl-4H-benzo[d][1,3]oxazin-4-one (**4a**): White solid; m.p. 121.8–122.3 °C (lit.[16] 123–124 °C); IR (KBr): ν_{max} = 3035, 1763, 1613, 1572, 1474, 1314, 1259, 1040, 1011, 764, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.31 (m, 2H, ArH), 8.23 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.82 (td, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.69 (d, J = 8.0 Hz, 1H, ArH), 7.59–7.56 (m, 1H, ArH), 7.52–7.49 (m, 3H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (C=O), 156.9 (C=N), 146.8, 136.4, 132.4, 130.1, 128.6 (CH×2), 128.4, 128.2 (CH×2), 128.1, 127.1, 116.9 ppm; MS (ESI): *m/z* (%) = 224 (M$^+$+1, 100).

2-(2-Fluorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4b**): White solid; m.p. 113.4–114.1 °C (lit.[16] 115–116 °C); IR (KBr): ν_{max} = 2922, 1770, 1628, 1455, 1316, 1277, 1222, 1107, 1037, 1007, 809, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, J = 7.6 Hz, 1H, ArH), 8.11 (td, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.84 (t, J = 7.6 Hz, 1H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.55 (t, J = 7.6 Hz, 2H, ArH), 7.28 (t, J = 8.0 Hz, 1H, ArH), 7.19–7.22 (m, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1 (d, $^1J_{CF}$ = 258 Hz), 159.8 (C=O), 154.6 (C=N), 146.4, 136.4, 133.8 (d, $^3J_{CF}$ = 8 Hz), 130.9, 128.6, 128.4, 127.3, 124.2, 118.9, 117.2, 117.1 (d, $^2J_{CF}$ = 22 Hz), 116.8 ppm; MS (ESI): *m/z* (%) = 242 (M$^+$+1, 100).

2-(4-Methylphenyl)-4H-benzo[d][1,3]oxazin-4-one (**4c**): White solid; m.p. 152.1–153.2 °C (lit.[17] 154–155 °C); IR (KBr): ν_{max} = 3036, 1759, 1609, 1570, 1474, 1310, 1261, 1183, 1063, 1040, 827, 769 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23–8.18 (m, 3H, ArH), 7.81 (t, J = 7.2 Hz, 1H, ArH), 7.67 (d, J = 8.0 Hz, 1H, ArH), 7.49 (t, J = 7.2 Hz, 1H, ArH), 7.31 (d, J = 8.0 Hz, 2H, ArH), 2.45 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8 (C=O), 157.4 (C=N), 147.3, 143.5, 136.7, 129.7 (CH×2), 128.7, 128.5 (CH×2), 128.2, 127.6, 127.2, 117.1, 22.1 (CH_3) ppm; MS (ESI): *m/z* (%) = 238 (M$^+$+1, 100).

2-(2-Chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4d**): White solid; m.p. 137.3–138.1 °C (lit.[17] 139–140 °C); IR (KBr): ν_{max} = 3081, 1768, 1625, 1475, 1440, 1315, 1272, 1223, 1092, 1029, 1003, 761, 730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.90–7.83 (m, 2H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.60–7.56 (m, 1H, ArH), 7.52 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.46 (td, J_1 = 1.6 Hz, J_2 = 7.2 Hz, 1H, ArH), 7.39 (td, J_1 = 1.6 Hz, J_2 = 7.2 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0 (C=O), 156.3 (C=N), 146.3, 136.5, 133.3, 132.1, 131.3, 130.9, 130.2, 128.8, 128.4, 127.3, 126.7, 116.9 ppm; MS (ESI): *m/z* (%) = 258 (M$^+$+1, 100), 260 (M$^+$+3, 30).

2-(2,4-Dichlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4e**): White solid; m.p. 131.3–132.8 °C (lit.[17] 129–130 °C); IR (KBr): ν_{max} = 3093, 1767, 1620, 1477, 1372, 1262, 1091, 1029, 1003, 858, 825, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.85-7.83 (m, 1H, ArH), 7.70 (d, J = 8.0 Hz, 1H, ArH), 7.56-7.60 (m, 1H, ArH), 7.54(d, J = 2.0 Hz, 1H, ArH), 7.38 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7 (C=O), 155.4 (C=N), 146.1, 137.9, 136.5, 134.3, 132.2, 131.0, 129.0, 128.6, 128.5, 127.3, 127.2, 116.8 ppm; MS (ESI): *m/z* (%) = 292 (M$^+$+1, 100), 294 (M$^+$+3, 62), 296 (M$^+$+5, 13).

2-(4-Chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4f**): White solid; m.p. 189.3–190.1 °C (lit.[17] 190 °C); IR (KBr): ν_{max} = 2926, 1769, 1624, 1603, 1489, 1403, 1323, 1259, 1223, 1095, 1058, 1024, 838, 761 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27–8.24 (m, 3H, ArH), 7.87–7.82 (m, 1H, ArH), 7.69 (d, J = 8.4 Hz, 1H, ArH), 7.55 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H, ArH), 7.50 (d, J = 8.8 Hz, 2H, ArH) ppm; ^{13}C NMR (100 Hz, $CDCl_3$): δ = 159.1 (C=O), 156.0 (C=N), 146.6, 138.9, 136.5, 129.5 (CH×2), 129.0 (CH×2), 128.6, 128.5, 128.3, 127.1, 116.9 ppm; MS (ESI): *m/z* (%) = 258 (M$^+$+1, 100), 260 (M$^+$+3, 368).

2-(4-Fluorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4g**): White solid; m.p. 174.8–175.3 °C (lit[18] 174–176 °C); IR (KBr): ν_{max} = 3072, 1763, 1623, 1512, 1473, 1415, 1322, 1241, 1162, 1063, 1007, 843, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (dd, J_1 = 5.2 Hz, J_2 = 8.4 Hz, 2H, ArH), 8.24 (d, J = 8.0 Hz, 1H, ArH), 7.84 (t, J = 8.0 Hz, 1H, ArH), 7.69 (d, J = 8.0 Hz, 1H, ArH), 7.53 (t, J = 8.0 Hz, 1H, ArH), 7.20 (t, J = 8.4 Hz, 2H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3 (d, $^1J_{CF}$ = 252 Hz), 159.1 (C=O), 156.0 (C=N), 146.7, 136.5, 130.5 (d, $^3J_{CF}$ = 9 Hz) (CH×2), 128.5, 128.1, 127.0, 126.2, 116.7, 115.9, 115.9 (d, $^2J_{CF}$ = 22 Hz) (CH×2) ppm; MS (ESI): *m/z* (%) = 242 (M$^+$+1, 100).

2-(4-Bromophenyl)-4H-benzo[d][1,3]oxazin-4-one (**4h**): White solid; m.p. 183.2–183.9 °C (lit.[19] 184 °C); IR (KBr): ν_{max} = 2921, 1763, 1620, 1566, 1485, 1398, 1320, 1257, 1069, 1042, 1008, 833, 775 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, ArH), 8.17 (d, J = 8.4 Hz, 2H, ArH), 7.83 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.68 (d, J = 8.0 Hz, 1H, ArH), 7.64 (d, J = 8.4 Hz, 2H, ArH), 7.52 (t, J = 7.6 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4 (C=O), 156.4 (C=N), 146.9, 136.8, 132.2 (CH×2), 129.9 (CH×2), 129.3, 128.8, 128.7, 127.9, 127.4, 117.2 ppm; MS (ESI): *m/z* (%) =274 (100), 302 (M$^+$+1, 48) , 304 (M$^+$+3, 44).

8-Methyl-2-(4-methylphenyl)-4H-benzo[d][1,3]oxazin-4-one (**4i**): White solid; m.p. 143.1–143.8 °C; IR (KBr): ν_{max} = 2917, 1749, 1621, 1598, 1311, 1240, 1176, 1048, 1019, 822, 761, 711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.4 Hz, 2H, ArH), 8.05 (d, J = 8.0 Hz, 1H, ArH), 7.64 (d, J = 7.6 Hz, 1H, ArH), 7.35 (t, J = 7.6 Hz, 1H, ArH), 7.29 (d, J = 8.0 Hz, 2H, ArH), 2.65 (s, 3H, CH_3), 2.44 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0 (C=O), 155.7 (C=N), 145.1, 142.9, 137.0, 135.8, 129.2 (CH×2), 128.0 (CH×2), 127.6, 127.2, 125.9, 116.6, 21.8 (CH_3), 17.2 (CH_3) ppm; MS (ESI): *m/z* (%) = 252 (M$^+$+1, 100); HRMS-ESI: Calcd for $C_{16}H_{14}NO_2$ (M+1)$^+$ 252.1025; found: 252.1015.

2-(3-Methoxyphenyl)-8-methyl-4H-benzo[d][1,3]oxazin-4-one (**4j**): White solid; m.p. 119.3–120.1 °C; IR (KBr): ν_{max} = 2960, 1741, 1621, 1584, 1481, 1311, 1267, 1216, 1058, 1004, 861, 773, 709 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, J = 7.6 Hz, 1H, ArH), 7.93 (d, J = 7.6 Hz, 1H, ArH), 7.84–7.83(m, 1H, ArH), 7.66 (d, J = 7.2 Hz, 1H, ArH), 7.41 (t, J = 8.0 Hz, 1H, ArH), 7.38 (t, J = 8.0 Hz, 1H, ArH), 7.10 (dd, J_1 = 2.0 Hz, J_2 = 8.0, 1H, ArH), 3.91 (s, 3H, OCH_3), 2.66 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 159.5 (C=O), 155.4 (C=N), 144.9, 137.1, 136.0, 131.6, 129.5, 127.5, 125.9, 120.6, 118.5, 116.7, 112.7, 55.5 (OCH_3), 17.1 (CH_3) ppm; MS (ESI): *m/z* (%) = 268 (M$^+$+1, 100); HRMS-ESI: Calcd for $C_{16}H_{14}NO_3$ (M+1)$^+$ 268.0974; found: 268.0965.

2-(2,4-Dichlorophenyl)-8-methyl-4H-benzo[d][1,3]oxazin-4-one (**4k**): White solid; m.p. 162.8–163.4 °C; IR (KBr): ν_{max} = 3072, 1764, 1625, 1585, 1472, 1373, 1322, 1222, 1112, 1079, 1029, 872, 800, 769 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.0 Hz, 1H, ArH), 7.96 (d, J = 8.4 Hz, 1H, ArH), 7.69 (d, J = 7.2 Hz, 1H, ArH), 7.56 (d, J = 2 Hz, 1H, ArH), 7.44 (t, J = 8.0 Hz, 1H, ArH), 7.38 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H, ArH), 2.63 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4 (C=O), 153.5 (C=N), 144.6, 137.8, 137.4, 136.6, 134.6, 132.3, 131.2, 128.4, 128.2, 127.2, 126.0, 116.9, 17.3 (CH_3) ppm; MS (ESI): *m/z* (%) = 306 (M$^+$+1, 100); HRMS-ESI: Calcd for $C_{15}H_{10}Cl_2NO_2$ (M+1)$^+$ 306.0089; found: 306.0080.

2-(4-Fluorophenyl)-8-methyl-4H-benzo[d][1,3]oxazin-4-one (**4l**): White solid; m.p. 195.3–196.1 °C; IR (KBr): ν_{max} = 2925, 1776, 1621, 1592, 1508, 1460, 1413, 1312, 1234, 1155, 1055, 1004, 842, 767, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (dd, J_1 = 5.6 Hz, J_2 = 8.0 Hz, 2H, ArH), 8.06 (d, J = 7.6 Hz, 1H, ArH), 7.65 (d, J = 7.2 Hz, 1H, ArH), 7.38 (t, J = 7.2 Hz, 1H, ArH), 7.18 (t, J = 8.0 Hz, 2H, ArH), 2.64 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.2 (d, $^1J_{CF}$ = 252 Hz), 159.6 (C=O), 154.7 (C=N), 144.9, 137.2, 135.9, 130.4 (d, $^3J_{CF}$ =9 Hz) (CH×2), 127.5, 126.6, 126.0, 116.5, 115.8 (d, $^2J_{CF}$ = 22 Hz) (CH×2), 17.2 (CH_3) ppm; MS (ESI): *m/z* (%) = 256 (M$^+$+1, 100); HRMS-ESI: Calcd for $C_{15}H_{11}FNO_2$ (M+1)$^+$ 256.0774; found: 256.0763.

7-Chloro-2-(3-methoxyphenyl)-4H-benzo[d][1,3]oxazin-4-one (**4m**): White solid; m.p. 146.3–146.9 °C; IR (KBr): ν_{max} = 2925, 1761, 1619, 1599, 1466, 1319, 1242, 1046, 1013, 874, 833, 775, 723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, J = 8.4 Hz, 1H, ArH), 7.90 (d, J = 8.0 Hz, 1H, ArH), 7.81 (s, 1H, ArH), 7.71 (d, J = 1.6 Hz, 1H, ArH), 7.48 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H, ArH), 7.43 (t, J = 8.0 Hz, 1H, ArH), 7.15 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H, ArH), 3.93 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 158.5 (C=O), 157.9 (C=N), 147.8, 142.8, 131.0, 129.74, 129.71, 128.7, 126.9, 120.9, 119.7, 115.3, 112.6, 55.6 (OCH_3) ppm; MS (ESI): *m/z* (%) = 288 (M$^+$+1, 100), 290 (M$^+$+3, 45); HRMS-ESI: Calcd for $C_{15}H_{11}ClNO_3$ (M+1)$^+$ 288.0427; found: 288.0415.

7-Chloro-2-(4-methoxyphenyl)-4H-benzo[d][1,3]oxazin-4-one (**4n**): White solid; m.p. 194.1–194.5 °C; IR (KBr): ν_{max} = 2909, 1762,

1598, 1514, 1463, 1321, 1269, 1242, 1178, 1082, 1023, 836, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 9.2 Hz, 2H, ArH), 8.12 (d, *J* = 8.4 Hz, 1H, ArH), 7.64 (d, *J* = 2.0 Hz, 1H, ArH), 7.41 (dd, J_1 = 2 Hz, J_2 = 8.4 Hz, 1H, ArH), 6.99 (d, *J* = 8.8 Hz, 2H, ArH), 3.90 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 159.1 (C=O), 158.4 (C=N), 148.6, 143.0, 130.7 (CH×2), 130.0, 128.4, 126.9, 122.3, 115.3, 114.5 (CH×2), 55.9 (OCH_3) ppm; MS (ESI): *m*/*z* (%) = 288 (M^++1, 100), 290 (M^++3, 35); HRMS-ESI: Calcd for $C_{15}H_{11}ClNO_3$ $(M+1)^+$ 288.0427; found: 288.0417.

7-Chloro-2-phenyl-4H-benzo[d][1,3]oxazin-4-one (**4o**): White solid; m.p. 193.4–194.2 °C (lit[20] 192 °C); IR (KBr): ν_{max} = 1756, 1613, 1596, 1561, 1463, 1315, 1237, 1062, 1022, 886, 833, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.29 (m, 2H, ArH), 8.17 (d, *J* = 8.4 Hz, 1H, ArH), 7.71 (d, *J* = 2.0 Hz, 1H, ArH), 7.63–7.58 (m, 1H, ArH), 7.55–7.51 (m, 2H, ArH), 7.48 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9 (C=O), 158.4 (C=N), 148.2, 143.1, 133.2, 130.04, 129.99, 129.0 (CH×2), 128.9, 128.6 (CH×2), 127.2, 115.6 ppm; MS (ESI): *m*/*z* (%) =234 (100), 258 (M^++1, 40), 260 (M^++3, 13).

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