Cascade Reaction between Methyl 3-Dehydroshikimate, Arylamines, and 2-Chloroalkyl Esters under Microwave Conditions: A Practical and Biomass-Based Synthesis of *N*-Aryl-1,4-benzoxazin-3-ones

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Abstract: A biomass-based, metal- and ligand-free assembly of *N*-aryl-1,4-benzoxazin-3-ones from methyl 3-dehydroshikimate (3-MHDS), involving aliphatic to aromatic transformation followed by C–O and C–N forming reactions, is presented. A variety of *N*-aryl-1,4-benzoxazin-3-ones were efficiently synthesized in a one-pot consecutive manner under microwave conditions.

Key words: methyl 3-dehydroshikimate, *N*-aryl-1,4-benzoxazin-3-ones, metal-free, cascade reaction, cyclization

N-Substituted 1,4-benzoxazin-3-ones are an intriguing class of privileged scaffold for a variety of biologically interesting molecules, ranging from potential drugs, natural products, and agrochemicals.[1] For example, various bioactive molecules (Figure 1) such as mineralocorticoid receptor modulating agents,[2] SGLT2 inhibitors,[3] thrombin inhibitors,[4] and the herbicide flumioxazin,[5] are all characterized by the N-substituted 1,4-benzoxazin-3-one motif. As a result, considerable efforts have been made to synthesize these compounds.[6] Generally, methods to access this scaffold involve the treatment of 2-halophenols and 2-aminophenols with bifunctional reagents such as 2-haloamides,[7] 2-haloalkanoyl halides,[8] or excess 2-bromoalkanoates[9] through palladium- or copper-catalyzed and ligand-involved processes. The reaction of 2-nitrophenols with a bifunctional reagent can also lead to 1,4-benzoxazin-3-ones, but a reductive process is further required to convert the nitro group into an amino group.[10] However, the aforementioned methods for the assembly of *N*-aryl-1,4-benzoxazin-3-ones are indirect, require preformed coupling partners such as 2-(2-halophenoxy)alkanoates or *N*-aryl-2-haloacetamides, and use transition-metal catalysts.[7,9b] In addition, iodo-substituted precursors and long reaction times are required to obtain satisfactory yields.[7b] Very recently, the Qi group reported an impressive, one-pot, three-component protocol for the construction of *N*-aryl-1,4-benzoxazin-3-ones through palladium(II) acetate and XPhos-catalyzed reactions between 2-halophenols, ethyl 2-bromoalkanoates, and arylamines under microwave conditions.[11] However, this method still suffered from drawbacks such as the requirements for transition-metal catalysts, phosphine ligands, and high temperatures (150 °C). Moreover, from the perspective of sustainable chemistry, the utilization of renewable biomass, the construction of platform compounds, and the development of cost-efficient methods to convert platform compounds into various value-added chemicals, are fundamental tasks for chemists.[12] To the best of our knowledge, no metal- and ligand-free protocol for the synthesis of *N*-aryl-1,4-benzoxazin-3-ones has been reported that is based on renewably sourced materials. Therefore, an alternative method that is facile, efficient, and makes use of biomass-derived starting materials to access N-substituted 1,4-benzoxazin-3-ones is of genuine interest.

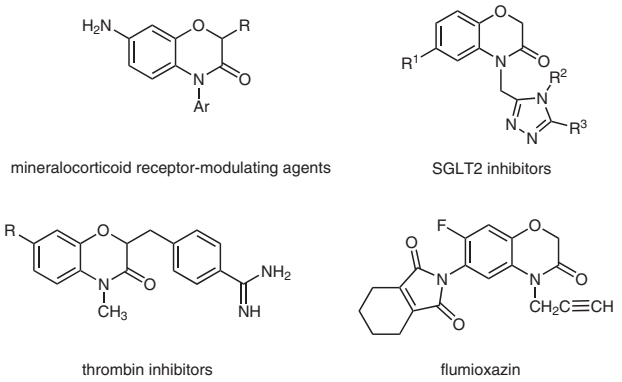

Figure 1 Examples of bioactive N-substituted 1,4-benzoxazin-3-ones

Over the past few years, a novel strategy to access to N-substituted anilines from nonaromatic cyclohexenones via sequential amination/aromatization reactions has emerged as an effective and alternative synthetic pathway.[13] Our group has also recently demonstrated the feasibility of a biomass-derived, cost-competitive cyclohexenone, methyl 3-dehydroshikimate (3-MDHS, **1**), in the facile synthesis of N-substituted 2-aminophenols via tandem cross-coupling and aromatization reactions.[14a] In the course of our study, we envisioned that this aliphatic to aromatic methodology for generating N-substituted 2-aminophenols could further be exploited for the syn-

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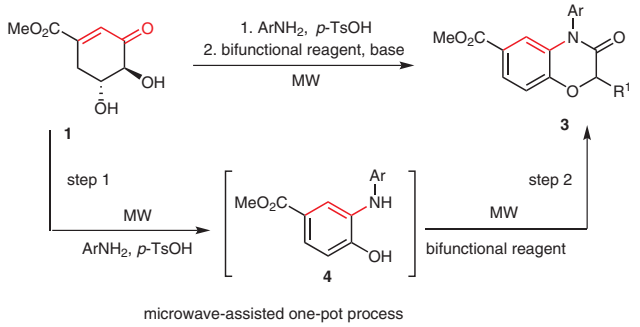
thesis of *N*-aryl-1,4-benzoxazin-3-ones **3** through a cascade process by using inexpensive and readily accessible 3-MDHS (**1**), primary amines, and bifunctional reagents, such as chloroacetyl chloride or 2-chloroalkyl esters, as the reactants (Scheme 1). This approach may be metal- and ligand-free, for the pivotal C_{Ar}-NH-$C_{Ar'}$ subunit is generated by the formation of N-arylated 2-aminophenols **4** in the absence of a metal catalyst and ligand.[14a] Hence, these N-arylated 2-aminophenols, which are generated in situ and highly functionalized, could serve as platform compounds for further transformations. In continuation of our work on the development of novel and practical methods for biomass conversion and utilization,[14] we herein describe a facile, metal- and ligand-free protocol utilizing 3-MDHS (**1**) for the one-pot synthesis of *N*-aryl-1,4-benzoxazin-3-ones under microwave irradiation.



Scheme 1 Strategy utilizing 3-MDHS (**1**) for the construction of *N*-aryl-1,4-benzoxazin-3-ones

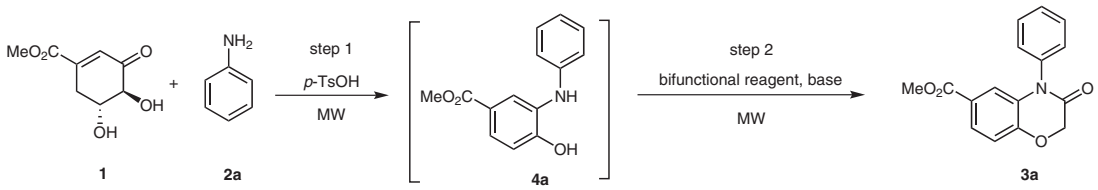
Based on an improved method from our previous findings[14a] for the synthesis of **1** (see the Supporting Information), we started our investigation by using aniline (**2a**) as a model substrate in the reaction with **1** and 2-halogenated bifunctional reagents (Table 1). As expected, the cascade reaction between **1** and aniline (**2a**) catalyzed by 4-toluenesulfonic acid under microwave conditions in *N*,*N*-dimethylformamide, dimethyl sulfoxide, or *N*-methylpyrrolidin-2-one gave intermediate **4a** (Step 1), followed by subsequent metal-free C–O and C–N forming reaction with chloroacetyl chloride to afford the desired product **3a** in good yields (entries 1–3). Although chloroacetyl chloride seemed to be highly reactive and effective in this process, it is a moisture-sensitive, corrosive, and irritating substrate. Alternatively, we then carried out the reaction by using the more benign methyl chloroacetate as the bifunctional reagent and ethanol as the solvent. To our delight, **3a** was obtained in 69% isolated yield (entry 4). Subsequently, various solvents such as dimethyl sulfoxide, *N*,*N*-dimethylformamide, *N*-methylpyrrolidin-2-one, *N*,*N*-dimethylacetamide, PEG-200, PEG-400, and 1,4-dioxane were screened. We were pleased to find that the desired product **3a** could be obtained in these solvents with yields ranging from 52–93%, among which *N*,*N*-dimethylformamide was optimal (entries 4–10). The effect of different bases on step 2 was also investigated. Results showed that both potassium and cesium carbonate gave excellent yields (entries 6 and 11), while other bases such as triethylamine, pyridine, DBU, sodium methoxide, and sodium hydroxide delivered low to moderate yields (entries 14–18). In contrast, the desired product **3a** was not obtained and only the intermediate **4a** was isolated in the absence of a base (entry 19). Temperature studies showed that 110 °C was favorable for this two-step conversion (entries 6, 20, and 21). In addition, results showed that microwave irradiation was advantageous over conventional heating in terms of yield and reaction time (entry 6 vs. 22). Therefore, the optimized reaction conditions consist of **1** (2.2 mmol) and arylamine **2** (2.0 mmol) in *N*,*N*-dimethylformamide (3 mL) using 4-toluenesulfonic acid (0.10 mmol) as the catalyst for step 1, and methyl chloroacetate (2.4 mmol) using potassium carbonate (4.0 mmol) as the base for step 2, both under microwave conditions at 110 °C (entry 6).

With the optimized reaction conditions in hand, a variety of arylamines were examined to explore the scope of the substrates. As summarized in Table 2, this one-pot, two-step transformation showed good compatibility with various functional groups such as Me, OMe, F, Cl, Br, I, NO_2, CF_3, Ac, and CO_2Me, affording the desired products in moderate to high yields. In general, electron-rich anilines required shorter reaction times and afforded higher yields compared to electron-deficient substrates. For example, anilines possessing an electron-donating group such as methyl or methoxy gave excellent yields of **3b** and **3c** (entries 2 and 3), whereas substrates bearing electron-withdrawing groups such as acetyl, nitro, methoxycarbonyl, and trifluoromethyl afforded moderate yields of products **3h**,**i**,**q**,**r**,**t** (entries 8, 9, 17, 18, and 20). No reaction took place when 2,4-dinitroaniline was used as the substrate, which might be due to the reduced nucleophilicity of the corresponding substrate (entry 16). It could be concluded that the reactivity of halogen-substituted anilines decreased in the order I > Br > Cl > F by comparing the product yields of **3d**–**g**, respectively (entries 4–7). The steric effect of the substrates was also observed. For instance, the *ortho*-substituted anilines afforded lower yields of the desired products **3j**–**m** compared to the substrates bearing the same substituents at the *para*-position **3b**,**c**,**e**,**f** (entries 10–13 vs. 2, 3, 5, 6). Moreover, 2,4,6-trimethylaniline exhibited relative low reactivity in this reaction and gave **3o** in 68% yield. It was noteworthy that the diamino substrate 4,4′-benzidine reacted smoothly with two equivalents of 3-MDHS (**1**) and methyl chloroacetate to afford the corresponding symmetrical bi-*N*-aryl-1,4-benzoxazin-3-one **3v** (entry 22). Additionally, benzophenone hydrazone and 1-naphthylamine also readily underwent this consecutive transformation and gave the desired products **3w**,**x**, respectively, in high yields (entries 23 and 24). Notably, the workup procedure of the reaction is simple; the desired products **3** could substantially be separated in pure form from the reaction mixture by precipitating with water.

Finally, the scope and generality of our protocol was further explored by using methyl 2-chloropropanoate as the bifunctional reagent (Table 3). Gratifyingly, methyl 2-

chloropropanoate coupled readily with 3-MDHS (**1**) and arylamines in this one-pot, two-step process, affording the corresponding *N*-aryl-2-methyl-1,4-benzoxazin-3-ones **5** rapidly and efficiently (entries 1–8). Both electron-rich (entry 2) and electron-deficient (entries 3–5) arylamines gave the corresponding products in satisfactory yields. It was notable that the carbonyl group survived the conditions and afforded the desired product in 82% yield (entry 6). In addition, high yields were obtained when polycyclic arylamines such as 4′-chlorobiphenyl-4-ylamine and 1-naphthylamine were used as substrates (entries 7 and 8). It is worth mentioning that compound **5h** existed as diastereoisomers in a 1:1 molar ratio as confirmed by ^{1}H NMR spectroscopy, probably owing to the steric hin-

Table 1 Optimization of the Reaction Conditions[a]



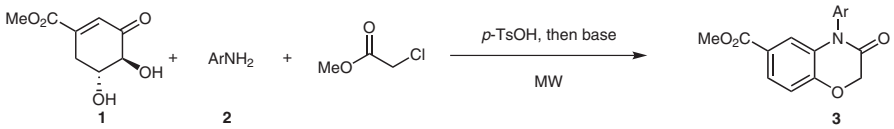
Entry	Solvent	Base	Step 1[b]	Step 2[b]	Yield[c] (%)
1	DMF	K_2CO_3	110 °C, 8 min	60 °C, 90 min	90[d]
2	DMSO	K_2CO_3	110 °C, 8 min	60 °C, 90 min	87[d]
3	NMP	K_2CO_3	110 °C, 8 min	60 °C, 90 min	89[d]
4	EtOH	K_2CO_3	78 °C, 25 min	78 °C, 30 min	69
5	DMSO	K_2CO_3	110 °C, 8 min	110 °C, 5 min	80
6	DMF	K_2CO_3	110 °C, 8 min	110 °C, 5 min	93
7	NMP	K_2CO_3	110 °C, 10 min	110 °C, 5 min	90
8	PEG-200	K_2CO_3	110 °C, 10 min	110 °C, 15 min	65
9	PEG-400	K_2CO_3	110 °C, 10 min	110 °C, 15 min	56
10	1,4-dioxane	K_2CO_3	100 °C, 20 min	100 °C, 5 min	52
11	DMF	Cs_2CO_3	110 °C, 10 min	110 °C, 5 min	93
12	DMF	Na_2CO_3	110 °C, 10 min	110 °C, 10 min	85
13	DMF	$NaHCO_3$	110 °C, 10 min	110 °C, 10 min	trace
14	DMF	Et_3N	110 °C, 10 min	110 °C, 8 min	45
15	DMF	pyridine	110 °C, 10 min	110 °C, 10 min	40
16	DMF	DBU	110 °C, 10 min	110 °C, 10 min	38
17	DMF	NaOMe	110 °C, 10 min	110 °C, 10 min	75
18	DMF	NaOH	110 °C, 10 min	110 °C, 10 min	60
19	DMF	–	110 °C, 10 min	110 °C, 110 min	–[e]
20	DMF	K_2CO_3	90 °C, 16 min	90 °C, 10 min	85
21	DMF	K_2CO_3	130 °C, 8 min	130 °C, 10 min	89
22	DMF	K_2CO_3	110 °C, 240 min	110 °C, 5 h	83[f]
23	DMF	K_2CO_3	110 °C, 8 min	60 °C, 1.5 h	90[d]

[a] Typical procedure under microwave conditions: step 1: **1** (0.41 g, 2.2 mmol), **2a** (2.0 mmol), *p*-TsOH (0.10 mmol), solvent (3.0 mL); step 2: add methyl chloroacetate (2.4 mmol), K_2CO_3 (4.0 mmol), stir.
[b] The ramp time is included as part of the reaction time.
[c] Isolated yield.
[d] Chloroacetyl chloride was used as the bifunctional reagent for step 2 under conventional heating.
[e] Not detected, only intermediate **4a** was obtained.
[f] Reaction was carried out in an oil bath.

drance of the bulky α-naphthyl group that hampers the inversion of the configuration and the rotation of the C–N bond.

In conclusion, a facile and metal-free protocol for the one-pot assembly of *N*-aryl-1,4-benzoxazin-3-ones through the sequential reaction between 3-MDHS (**1**), anilines, and bifunctional 2-chloroalkyl esters has been developed. Various *N*-aryl-1,4-benzoxazin-3-ones were readily synthesized in moderate to excellent yields. Notable features

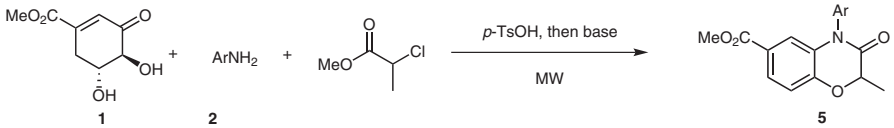
Table 2 Microwave-Assisted One-Pot Synthesis of *N*-Aryl-1,4-benzoxazin-3-ones[a]



Entry	Ar	T_1[b] (min)	T_2[b] (min)	Product	Yield[c] (%)
1	Ph	8	5	**3a**	93
2	4-$MeOC_6H_4$	8	5	**3b**	97
3	4-MeC_6H_4	8	5	**3c**	96
4	4-IC_6H_4	8	6	**3d**	90
5	4-BrC_6H_4	8	6	**3e**	87
6	4-ClC_6H_4	10	7	**3f**	83
7	4-FC_6H_4	8	8	**3g**	78
8	4-AcC_6H_4	8	7	**3h**	85
9	4-$O_2NC_6H_4$	12	6	**3i**	82
10	2-MeC_6H_4	10	6	**3j**	89
11	2-BrC_6H_4	12	7	**3k**	82
12	2-ClC_6H_4	12	7	**3l**	75
13	2-$MeOC_6H_4$	8	6	**3m**	90
14	2,5-$Cl_2C_6H_3$	13	10	**3n**	72
15	2,4,6-$Me_3C_6H_2$	12	8	**3o**	68
16	2,4-$(O_2N)_2C_6H_3$	20	0	**3p**	–[d]
17	3-$MeO_2CC_6H_4$	8	7	**3q**	80
18	3-$F_3CC_6H_4$	8	7	**3r**	71
19	3-MeC_6H_4	8	5	**3s**	92
20	3-$O_2NC_6H_4$	8	7	**3t**	83
21	3-ClC_6H_4	8	6	**3u**	85
22[e]	4-(4-$H_2NC_6H_4$)C_6H_4[f]	12	9	**3v**[g]	88
23	1-naphthyl	8	5	**3w**	87
24	N=CPh_2	8	6	**3x**	90

[a] Reactions conditions: **1** (0.41 g, 2.2 mmol), **2** (2.0 mmol), *p*-TsOH (0.10 mmol), DMF (3.0 mL), methyl chloroacetate (2.4 mmol), K_2CO_3 (4.0 mmol), microwaves, 110 °C; step 1: T_1; step 2: T_2.
[b] The ramp time is included as part of the reaction time.
[c] Isolated yield.
[d] Not detected.
[e] Reactions condition: **1** (0.82 g, 4.4 mmol), 4,4′-benzidine (2.0 mmol), *p*-TsOH (0.20 mmol), DMF (8.0 mL), methyl chloroacetate (6.0 mmol), K_2CO_3 (8.0 mmol) under typical procedures.
[f] Aniline was 4,4′-benzidine.
[g] Product is *N*,*N*′-biphenylbis[6-(methoxycarbonyl)-2*H*-1,4-benzoxazin-3(4*H*)-one].

Table 3 Expanding of Substrate Scope Using Methyl 2-chloropropanoate as the Bifunctional Reagent[a]



Entry	Ar	T_1[b] (min)	T_2[b] (min)	Product	Yield[c] (%)
1	Ph	8	5	**5a**	92
2	4-MeC_6H_4	8	5	**5b**	93
3	4-FC_6H_4	8	8	**5c**	75
4	4-BrC_6H_4	8	6	**5d**	83
5	4-$O_2NC_6H_4$	12	7	**5e**	72
6	4-AcC_6H_4	8	8	**5f**	82
7	4-(4-ClC_6H_4)C_6H_4	8	6	**5g**	87
8	1-naphthyl	8	6	**5h**	85[d]

[a] Reactions conditions: methyl 2-chloropropanoate was used as bifunctional reagent according to the typical microwave procedures.
[b] The ramp time is included as part of the reaction time.
[c] Isolated yield.
[d] ^{1}H NMR spectrum showed that **5h** existed as diastereoisomers in a 1:1 molar ratio, which may be due to the steric hindrance of the bulky α-naphthyl group, hindering the inversion of the configuration and the rotation of the C–N bond (see the Supporting Information for details).

such as the biomass-involved transformation, metal- and ligand-free reaction conditions, step-efficient procedures, and broad substrate scope have made this protocol a practical alternative to the existing transition-metal-catalyzed methods.

(–)-Shikimic acid (chromatography grade) was kindly provided as a natural product by Guangxi Wan Shan Spice Co. Ltd. (–)-Methyl 3-dehydroshikimate was readily prepared from (–)-shikimic acid through an improved method based on our previously reported protocol (see the Supporting Information for details). Petroleum ether (PE) was boiling fraction 60–90 °C. Other reagents and solvents were purchased from commercial sources and used without further purification unless otherwise stated. Reactions were monitored by TLC. Column chromatography was performed with silica gel (200–300 mesh) using a EtOAc–PE system as eluent. Melting points were measured on a Thiele apparatus and are uncorrected. Microwave experiments were carried out with a scientific WBFY microwave reactor in a flask connected with a condenser under atmosphere pressure. This microwave reactor was a monomode device with a tunable power controller. Reaction temperature was detected using an infrared thermometer and the ramp time is included as part of the reaction time. ^{1}H NMR and ^{13}C NMR spectra were measured on a 400 MHz spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz) using $CDCl_3$ or DMSO-d_6 as the solvent at r.t. calibrated using residual undeuterated solvent as an internal reference. HRMS spectra were recorded on a LC-Q-TOF (ESI) apparatus. MS spectra were measured on a Shimadzu GC-MS QP5050A in EI mode or a Thermo Finnigan LCQ DECA XP ion trap mass spectrometer in ESI mode.

Methyl 4-Aryl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylates 3a–o,q–x; General Procedure

To a mixture of 3-MDHS (**1**; 0.41 g, 2.2 mmol) and *p*-TsOH (0.10 mmol) in DMF (3 mL) was added arylamine **2** (2.0 mmol). The flask was then placed in the microwave synthesizer and the mixture was irradiated (240 W, 110 °C) with stirring for the indicated time (T_1). Then, K_2CO_3 (0.55 g, 4 mmol) and methyl chloroacetate (2.4 mmol) were added to the mixture and it was irradiated (240 W, 110 °C) with stirring for the indicated time (T_2). Upon cooling, the mixture was poured into H_2O, the resulting solid was filtered and dried to furnish the desired product in pure form in most cases. If necessary, these products could be further purified by recrystallization (EtOAc–PE) or column chromatography (silica gel, 200–300, EtOAc–PE).

Methyl 3-Oxo-4-phenyl-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3a)

White needles; yield: 0.53 g (93%); mp 161–163 °C; R_f = 0.51 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.62 (dd, J = 8.4, 1.6 Hz, 1 H), 7.60–7.53 (m, 3 H), 7.37 (d, J = 7.6 Hz, 2 H), 7.18 (d, J = 8.4 Hz, 1 H), 6.85 (d, J = 1.6 Hz, 1 H), 4.92 (s, 2 H), 3.69 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.3, 148.2, 135.4, 130.6, 130.1, 129.0, 129.0, 125.2, 123.5, 116.9, 116.6, 67.4, 52.1.

MS (EI): *m*/*z* (%) = (283 $[M]^+$, 100), 252 ($[M – OCH_3]^+$, 23), 224 ($[M – COOCH_3]^+$, 5), 198 (11), 178 (10), 77 (18).

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{13}NNaO_4$: 306.0737; found: 306.0735.

Methyl 4-(4-Methoxyphenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3b)

White solid; yield: 0.61 g (97%); mp 151–153 °C; R_f = 0.52 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 (dd, J = 8.4, 2.0 Hz, 1 H), 7.27 (d, J = 9.2 Hz, 2 H), 7.16 (d, J = 8.4 Hz, 1 H), 7.12 (d, J = 9.2 Hz, 2 H), 6.90 (d, J = 2.0 Hz, 1 H), 4.89 (s, 2 H), 3.83 (s, 3 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.4, 159.2, 148.2, 130.8, 130.1, 127.6, 125.1, 123.5, 116.8, 116.6, 115.2, 67.5, 55.4, 52.1.

MS (EI): *m*/*z* (%) = 313 ($[M]^+$, 100), 284 (73), 228 (10), 178 (8), 77 (10).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_5$: 336.0842; found: 336.0838.

Methyl 4-(4-Methylphenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3c)
White solid; yield: 0.57 g (96%); mp 174–176 °C; R_f = 0.43 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 7.23 (d, *J* = 8.4 Hz, 2 H), 7.16 (d, *J* = 8.4 Hz, 1 H), 6.88 (d, *J* = 2.0 Hz, 1 H), 4.90 (s, 2 H), 3.70 (s, 3 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.3, 148.2, 138.5, 132.7, 130.6, 128.6, 125.1, 123.5, 116.9, 116.8, 116.6, 67.4, 52.1, 20.8.

MS (EI): *m*/*z* (%) = 297 ([M]$^+$, 91), 268 (100), 266 ([M – OCH_3]$^+$, 18), 240 (9), 178 (10), 77 (23).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_4$: 320.0893; found: 320.0887.

Methyl 4-(4-Iodophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3d)
Off-white solid; yield: 0.74 g (90%); mp 165–167 °C; R_f = 0.62 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.98 (d, *J* = 8.8 Hz, 2 H), 7.64 (dd, *J* = 8.4, 1.6 Hz, 1 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.88 (d, *J* = 2.0 Hz, 1 H), 4.92 (s, 2 H), 3.74 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.3, 148.3, 139.0, 135.2, 131.3, 130.2, 125.4, 123.6, 117.0, 116.5, 95.4, 67.4, 52.1.

MS (EI): *m*/*z* (%) = 409 ([M]$^+$, 100), 380 (73), 316 (18), 77 (18).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}INNaO_4$: 431.9703; found: 431.9696.

Methyl 4-(4-Bromophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3e)
White solid; yield: 0.63 g (87%); mp 166–168 °C; R_f = 0.47 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.80 (dd, *J* = 6.8, 2.0 Hz, 2 H), 7.62 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.36 (dd, *J* = 6.8, 2.0 Hz, 2 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 4.91 (s, 2 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.3, 148.3, 134.7, 133.2, 131.3, 130.3, 125.4, 123.6, 122.2, 117.0, 116.4, 67.4, 52.1.

MS (EI): *m*/*z* (%) = 363 ([M + 2]$^+$, 100), 361 ([M]$^+$, 99), 332 ([M – OCH_3]$^+$, 73), 178 (18), 77 (8).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{79}BrNNaO_4$: 383.9842; found 383.9832.

Methyl 4-(4-Chlorophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3f)
White solid; yield: 0.53 g (83%); mp 156–158 °C; R_f = 0.61 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.67 (d, *J* = 8.8 Hz, 2 H), 7.63 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.43 (d, *J* = 8.8 Hz, 2 H), 7.19 (d, *J* = 8.4 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 4.91 (s, 2 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.4, 148.2, 134.3, 133.6, 131.0, 130.3, 130.2, 125.3, 123.6, 117.0, 116.4, 67.4, 52.1.

MS (EI): *m*/*z* (%) = 319 ([M + 2]$^+$, 100), 317 ([M]$^+$, 33), 286 ([M – OCH_3]$^+$, 14), 240 (9), 178 (10).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{35}ClNNaO_4$: 340.0347; found: 340.0340.

Methyl 4-(4-Fluorophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3g)
White solid; yield: 0.47 g (78%); mp 140–142 °C; R_f = 0.40 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.62 (dd, *J* = 8.4, 1.6 Hz, 1 H), 7.44 (d, *J* = 6.8 Hz, 4 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.84 (d, *J* = 1.6 Hz, 1 H), 4.91 (s, 2 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.4, 161.8 (d, $^1J_{FC}$ = 245 Hz, 4′C), 148.2, 131.5 (d, $^4J_{FC}$ = 2.2 Hz, 1′C), 131.3 (d, $^3J_{FC}$ = 8.9 Hz, 2′C), 130.6, 125.3, 123.6, 117.2, 117.0 (d, $^2J_{FC}$ = 22 Hz, 3′C), 116.9, 67.4, 52.1.

MS (EI): *m*/*z* (%) = 301 ([M]$^+$, 100), 272 ([M – OCH_3]$^+$, 98), 216 (7), 178 (8).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}FNNaO_4$: 324.0643; found: 324.0636.

Methyl 4-(4-Acetylphenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3h)
White solid; yield: 0.55 g (85%); mp 160–162 °C; R_f = 0.32 (EtOAc–PE, 1:2.5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.16 (d, *J* = 8.4 Hz, 2 H), 7.63 (dd, *J* = 8.4, 2.00 Hz, 1 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.21 (d, *J* = 8.4 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 4.93 (s, 2 H), 3.70 (s, 3 H), 2.66 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 197.3, 165.2, 163.3, 148.4, 139.5, 137.0, 130.2, 130.0, 129.4. 125.5, 123.6, 117.1, 116.6, 67.5, 52.1, 26.9.

MS (EI): *m*/*z* (%) = 325 ([M]$^+$, 100), 294 ([M – OCH_3]$^+$, 14), 254 (9), 178 (6).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NNaO_5$: 348.0842; found: 348.0839.

Methyl 4-(4-Nitrophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3i)
Faint yellow solid; yield: 0.54 g (82%); mp 183–185 °C; R_f = 0.52 (EtOAc–PE, 1:2.5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.47 (d, *J* = 8.8 Hz, 2 H), 7.74 (d, *J* = 8.8 Hz, 2 H), 7.66 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 1 H), 6.88 (d, *J* = 2.0 Hz, 1 H), 4.96 (s, 2 H), 3.72 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 163.4, 148.4, 147.4, 141.3, 130.6, 129.9, 125.6, 125.3, 123.7, 117.2, 116.5, 67.5, 52.1.

MS (EI): *m*/*z* (%) = 328 ([M]$^+$, 100), 297 ([M – OCH_3]$^+$, 18), 269 ([M – $COOCH_3$]$^+$, 7), 178 (6), 77 (4).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_6$: 351.0588; found: 351.0583.

Methyl 4-(2-Methylphenyl)-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3j)
White solid; yield: 0.53 g (89%); mp 93–95 °C; R_f = 0.66 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.49–7.39 (m, 3 H), 7.29 (d, *J* = 7.6 Hz, 1 H), 7.20 (d, *J* = 8.4 Hz, 1 H), 6.73 (d, *J* = 2.0 Hz, 1 H), 4.95 (q, *J* = 27.60 Hz, 2 H), 3.69 (s, 3 H), 2.02 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 162.9, 148.3, 136.3, 134.1, 131.5, 129.7, 129.5, 129.2, 127.8, 125.4, 123.8, 117.0, 116.1, 67.4, 52.1, 16.8.

MS (EI): *m*/*z* (%) = 297 ([M]$^+$, 100), 268 ([M – OCH_3]$^+$, 38), 240 ([M – $COOCH_3$]$^+$, 9), 178 (5), 77 (7).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_4$: 320.0893; found: 320.0896.

Methyl 4-(2-Bromophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3k)
Off-white solid; yield: 0.59 g (82%); mp 81–83 °C; R_f = 0.54 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.91 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.67–7.63 (m, 2 H), 7.62–7.58 (m, 1 H), 7.56–7.50 (m, 1 H), 7.23

(d, J = 8.4 Hz, 1 H), 6.71 (d, J = 2.0 Hz, 1 H), 4.96 (s, 2 H), 3.70 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 162.9, 148.2, 134.2, 133.9, 131.7, 131.5, 129.7, 129.2, 125.6, 123.8, 122.8, 117.2, 115.9, 67.4, 52.2.

MS (EI): m/z (%) = 363 ([M + 2]$^+$, 27), 361 ([M]$^+$, 25), 332 ([M – OCH_3]$^+$, 9), 282 (100), 75 (18).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_{12}BrNNaO_4$: 383.9842; found: 383.9844.

Methyl 4-(2-Chlorophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3l)
White solid; yield: 0.47 g (75%); mp 106–108 °C; R_f = 0.63 (EtOAc–PE, 1:2.5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.78–7.75 (m, 1 H), 7.65 (dd, J = 8.4, 2.0 Hz, 1 H), 7.61–7.59 (m, 3 H), 7.22 (d, J = 8.4 Hz, 1 H), 6.74 (d, J = 2.0 Hz, 1 H), 4.97 (s, 2 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 163.0, 148.2, 132.5, 132.3, 131.7, 131.4, 130.7, 129.3, 129.2, 125.7, 123.9, 117.2, 115.8, 67.3, 52.2.

MS (EI): m/z (%) = 319 ([M + 2]$^+$, 18), 317 ([M]$^+$, 55), 286 ([M – OCH_3]$^+$, 9), 282 (100), 240 (5), 178 (7), 75 (14).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_{12}ClNNaO_4$: 340.0347; found: 340.0349.

Methyl 4-(2-Methoxyphenyl)-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3m)
White solid; yield: 0.56 g (90%); mp 148–150 °C; R_f = 0.29 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 (dd, J = 8.4, 2.0 Hz, 1 H), 7.53 (m, 1 H), 7.33 (dd, J = 8.0, 1.6 Hz, 1 H), 7.28 (dd, J = 8.0, 0.8 Hz, 1 H), 7.12–7.17 (m, 2 H), 6.83 (d, J = 2.0 Hz, 1 H), 4.91 (s, 2 H), 3.70 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.1, 155.2, 148.2, 130.9, 130.6, 130.3, 125.2, 123.7, 123.1, 121.4, 116.9, 116.2, 113.0, 67.3, 55.8, 52.1.

MS (EI): m/z (%) = 313 ([M]$^+$, 100), 282 ([M – OCH_3]$^+$, 23), 254 ([M – $COOCH_3$]$^+$, 6), 178 (4), 75 (7).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_5$: 336.0842; found: 336.0845.

Methyl 4-(2,5-Dichlorophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3n)
White solid; yield: 0.51 g (72%); mp 136–138 °C; R_f = 0.71 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.87 (d, J = 2.4 Hz, 1 H), 7.83 (d, J = 8.8 Hz, 1 H), 7.72 (dd, J = 8.8, 2.4 Hz, 1 H), 7.67 (dd, J = 8.4, 2.0 Hz, 1 H), 7.24 (d, J = 8.4 Hz, 1 H), 6.77 (d, J = 2.0 Hz, 1 H), 5.03–4.93 (dd, J = 15.2 Hz, 2 H), 3.75 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.1 (C=O), 163.0 (C=O), 148.0, 133.7, 132.8, 132.0, 131.8, 131.6, 131.4, 128.9, 125.8, 123.9, 117.3, 115.6, 67.2, 52.2.

MS (EI): m/z (%) = 351 ([M]$^+$, 25), 320 ([M – OCH_3]$^+$, 7), 316 (100), 178 (7).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{16}H_{11}{}^{35}Cl_2NNaO_4$: 373.9957; found: 373.9951.

Methyl 3-Oxo-4-(2,4,6-trimethylphenyl)-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3o)
White solid; yield: 0.44 g (68%); mp 120–122 °C; R_f = 0.57 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.63 (dd, J = 8.4, 2.0 Hz, 1 H), 7.21 (d, J = 8.4 Hz, 1 H), 7.10 (s, 2 H), 6.71 (d, J = 2.0 Hz, 1 H), 4.98 (s, 2 H), 3.71 (s, 3 H), 2.32 (s, 3 H), 1.95 (s, 6 H).

MS (EI): m/z (%) = 325 ([M]$^+$, 100), 294 ([M – OCH_3]$^+$, 9), 266 ([M – $COOCH_3$]$^+$, 6), 238 (11), 77 (8).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{19}H_{19}NNaO_4$: 348.1206; found: 348.1215.

Methyl 4-[3-(Methoxycarbonyl)phenyl]-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3q)
White solid; yield: 0.54 g (80%); mp 119–121 °C; R_f = 0.48 (EtOAc–PE, 1:2.5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.11 (d, J = 8.0 Hz, 1 H), 7.98 (s, 1 H), 7.76 (t, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.62 (dd, J = 8.4, 2.0 Hz, 1 H), 7.19 (d, J_1 = 8.4 Hz, 1 H), 6.79 (d, J = 1.6 Hz, 1 H), 4.93 (s, 2 H), 3.87 (s, 3 H), 3.69 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.4, 165.2, 163.5, 148.3, 135.9, 133.9, 131.6, 130.8, 130.4, 130.0, 129.7, 125.4, 123.6, 117.0, 116.4, 67.5, 52.4, 52.1.

MS (EI): m/z (%) = 341 ([M]$^+$, 100), 310 ([M – OCH_3]$^+$, 16), 282 ([M – $COOCH_3$]$^+$, 3), 178 (5).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{18}H_{15}NNaO_6$: 364.0792; found: 364.0792.

Methyl 3-Oxo-4-[3-(trifluoromethyl)phenyl]-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3r)
White solid; yield: 0.50 g (71%); mp 108–110 °C; R_f = 0.40 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.94–7.73 (m, 4 H), 7.63 (dd, J = 8.4, 1.6 Hz, 1 H), 7.20 (d, J = 8.4 Hz, 1 H), 6.80 (d, J = 1.6 Hz, 1 H), 4.93 (s, 2 H), 3.71 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 163.5, 148.2, 136.3, 133.5, 131.5, 130.9 (q, $^2J_{CF}$ = 34 Hz, 1 C), 130.2, 126.3, 126.0, 125.9, 125.4, 123.6 (q, $^1J_{CF}$ = 274 Hz, CF_3), 117.1, 116.3, 67.4, 52.1.

MS (EI): m/z (%) = 351 ([M]$^+$, 100), 320 ([M – OCH_3]$^+$, 18), 292 ([M – $COOCH_3$]$^+$, 3), 178 (6).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{17}H_{12}F_3NNaO_4$: 374.0611; found: 374.0602.

Methyl 4-(3-Methylphenyl)-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3s)
White solid; yield: 0.55 g (92%); mp 137–139 °C; R_f = 0.44 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 (dd, J = 8.4, 2.0 Hz, 1 H), 7.48 (t, 1 H), 7.34 (d, J = 8.0 Hz, 1 H), 7.15 (t, 3 H), 6.88 (d, J = 2.0 Hz, 1 H), 4.91 (s, 2 H), 3.70 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.3, 148.3, 139.8, 135.3, 130.6, 129.9, 129.7, 129.3, 125.9, 125.2, 123.6, 116.9, 116.7, 67.5, 52.1, 20.8.

MS (EI): m/z (%) = 297 ([M]$^+$, 100), 266 ([M – OCH_3]$^+$, 73), 238 ([M – $COOCH_3$]$^+$, 5), 178 (9), 77 (6).

HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_4$: 320.0893; found: 320.0894.

Methyl 4-(3-Nitrophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3t)
White solid, yield: 0.54 g (83%); mp >200 °C; R_f = 0.44 (EtOAc–PE, 1:2.5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.40 (m, 2 H), 7.90 (d, J = 4.8 Hz, 2 H), 7.64 (dd, J = 8.4, 2.0 Hz, 1 H), 7.21 (d, J = 8.4 Hz, 1 H), 6.82 (d, J = 1.6 Hz, 1 H), 4.93 (s, 2 H), 3.70 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.6, 148.8, 148.3, 136.5, 136.0, 131.6, 130.2, 125.5, 124.7, 124.1, 123.7, 117.2, 116.4, 67.5, 52.2.

MS (EI): m/z (%) = 328 ([M]$^+$, 100), 297 ([M – OCH_3]$^+$, 23), 253 (18).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_6$: 351.0588; found: 351.0585.

Methyl 4-(3-Chlorophenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3u)
White solid; yield: 0.54 g (85%); mp 146–148 °C; R_f = 0.62 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.64–7.51 (m, 3 H), 7.58 (s, 1 H), 7.40–7.38 (m, 1 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.84 (d, *J* = 2.0 Hz, 1 H), 4.91 (s, 2 H), 3.72 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 163.4, 148.2, 136.8, 134.0, 131.7, 130.3, 129.3, 129.3, 128.0, 125.4, 123.6, 117.0, 116.4, 67.4, 52.2.

MS (EI): *m*/*z* (%) = 319 ([M + 2]$^+$, 33), 317 ([M]$^+$, 100), 286 ([M – OCH_3]$^+$, 98), 258 ([M – $COOCH_3$]$^+$, 3), 178 (9).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}ClNNaO_4$: 340.0347; found: 340.0348.

***N*,*N*′-Biphenylbis[6-(methoxycarbonyl)-2*H*-1,4-benzoxazin-3(4*H*)-one] (3v)**
White solid; yield: 0.99 g (88%); mp >200 °C; R_f = 0.24 (EtOAc–PE, 1:2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.03 (d, *J* = 8.4 Hz, 4 H), 7.64 (dd, *J* = 8.4, 2.0 Hz, 2 H), 7.53 (d, *J* = 8.4 Hz, 4 H), 7.21 (t, *J* = 8.4 Hz, 2 H), 6.98 (d, *J* = 2.0 Hz, 2 H), 4.96 (s, 4 H), 3.71 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.3, 163.4, 148.4, 139.5, 135.1, 130.5, 129.7, 128.6, 125.4, 123.6, 117.0, 116.7, 67.5, 52.1.

MS (ESI): *m*/*z* = 565 [M + H]$^+$.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{24}N_2NaO_8$: 587.1425; found: 587.1416.

Methyl 4-(1-Naphthyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3w)
Pink crystals; yield: 0.58 g (87%); mp 157–159 °C; R_f = 0.53 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.4 Hz, 1 H), 7.95 (d, *J* = 8.0 Hz, 1 H), 7.69 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 7.43–7.56 (m, 4 H), 7.12 (d, *J* = 8.4 Hz, 1 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 5.00–4.89 (dd, *J* = 15.2 Hz, 2 H), 3.68 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 163.7, 148.3, 134.9, 131.4, 130.4, 130.1, 129.8, 128.8, 127.5, 127.4, 126.7, 126.1, 125.9, 124.9, 121.8, 118.0, 116.9, 68.0, 52.0.

MS (EI): *m*/*z* (%) = 333 ([M]$^+$, 100), 302 ([M – OCH_3]$^+$, 9), 291 (8), 244 (9), 178 (7), 77 (9).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_4$: 356.0893; found: 356.0888.

Methyl 4-[(Diphenylmethylene)amino]-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (3x)
White solid; yield: 0.69 g (90%); mp 146–148 °C; R_f = 0.68 (EtOAc–PE, 1:3).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.84 (d, *J* = 2.0 Hz, 1 H), 7.77–7.73 (m, 3 H), 7.56–7.52 (m, 1 H), 7.44–7.30 (m, 5 H), 7.20–7.17 (m, 2 H), 6.96 (d, *J* = 8.4 Hz, 1 H), 4.42 (s, 2 H), 3.86 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.2, 166.3, 155.9, 147.8, 136.0, 134.7, 132.1, 129.9, 129.8, 129.1, 128.3, 128.1, 127.4, 126.3, 124.9, 116.6, 116.3, 67.5, 52.1.

MS (ESI): *m*/*z* (%) = 386 ([M]$^+$, 21), 355 ([M – OCH_3]$^+$, 3), 180 (100), 77 (53).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}N_2NaO_4$: 409.1159; found: 409.1152.

Methyl 4-Aryl-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylates 5a–h; General Procedure
To a mixture of 3-MDHS (**1**; 0.41 g, 2.2 mmol) and *p*-TsOH (0.10 mmol) in DMF (3 mL) was added arylamine **2** (2.0 mmol). The flask was then placed into the microwave synthesizer and the mixture was irradiated (240 W, 110 °C) with stirring for the indicated time (T_1). Then, K_2CO_3 (0.55 g, 4 mmol) and methyl 2-chloropropanoate (2.4 mmol) were added to the mixture and it was irradiated (240 W, 110 °C) with stirring for the indicated time (T_2). Upon cooling, the mixture was poured into H_2O, the resulting solid was filtered and dried to furnish the desired product in pure form.

Methyl 2-Methyl-4-phenyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5a)
White solid; yield: 0.55 g (92%); mp 145–147 °C; R_f = 0.65 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.62 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.58 (t, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 7.2 Hz, 1 H), 7.35 (d, *J* = 7.2 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 5.03 (q, *J* = 6.8 Hz, 1 H), 3.69 (s, 3 H), 1.54 (d, *J* = 6.80 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.5, 165.3, 147.8, 135.8, 130.9, 130.1, 129.0, 128.9, 125.2, 123.7, 117.2, 116.6, 73.5, 52.1, 16.2.

MS (EI): *m*/*z* (%) = 297 ([M]$^+$, 76), 266 ([M – OCH_3]$^+$, 9), 254 (100).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_4$: 320.0893; found: 320.0894.

Methyl 2-Methyl-4-(4-methylphenyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5b)
White solid; yield: 0.58 g (93%); mp 141–143 °C; R_f = 0.49 (EtOAc–PE, 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.62 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.38 (d, *J* = 8.4 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 8.4 Hz, 1 H), 6.88 (d, *J* = 2.0 Hz, 1 H), 5.01 (q, *J* = 6.8 Hz, 1 H), 3.70 (s, 3 H), 2.40 (s, 3 H), 1.53 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.5, 165.3, 147.8, 138.4, 133.1, 130.9, 130.6, 128.6, 125.2, 123.7, 117.1, 116.7, 73.5, 52.1, 20.7, 16.2.

MS (EI): *m*/*z* (%) = 311 ([M]$^+$, 71), 296 ([M – CH_3]$^+$, 2), 280 ([M – OCH_3]$^+$, 5), 268 (100), 240 (6), 182 (4).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}NNaO_4$: 334.1050; found: 334.1052.

Methyl 4-(4-Fluorophenyl)-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5c)
White solid; yield: 0.47 g (75%); mp 119–121 °C; R_f = 0.62 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.62 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.44 (d, *J* = 7.2 Hz, 4 H), 7.20 (d, *J* = 8.4 Hz, 1 H), 6.84 (d, *J* = 2.0 Hz, 1 H), 5.01 (q, *J* = 6.8 Hz, 1 H), 3.71 (s, 3 H), 1.54 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.7, 165.3, 161.8 (d, $^1J_{FC}$ = 245 Hz, 4′C), 147.8, 132.0 (d, $^4J_{FC}$ = 2.5 Hz, 1′C), 131.3 (d, $^3J_{FC}$ = 8.1 Hz, 2′C), 130.9, 125.3, 123.7, 117.3, 117.2 (d, $^2J_{FC}$ = 22.6 Hz, 3′C), 116.6, 73.5, 52.1, 16.3.

MS (EI): *m*/*z* (%) = 315 ([M]$^+$, 65), 284 ([M – OCH_3]$^+$, 7), 272 (100), 254 (2).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{14}FNNaO_4$: 338.0799; found: 338.0802.

Methyl 4-(4-Bromophenyl)-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5d)
White solid; yield: 0.62 g (83%); mp 152–154 °C; R_f = 0.51 (EtOAc–PE, 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.79 (d, *J* = 8.4 Hz, 2 H), 7.63 (dd, *J* = 8.4, 1.6 Hz, 1 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.4 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 5.01 (q, *J* = 6.8 Hz, 1 H), 3.72 (s, 3 H), 1.54 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.5, 165.3, 147.8, 135.2, 133.1, 131.3, 130.6, 125.4, 123.8, 122.0, 117.3, 116.5, 73.5, 52.1, 16.2.

MS (EI): *m*/*z* (%) = 377 ([M + 2]$^+$, 69), 375 ([M]$^+$, 65), 346 ([M – OCH_3]$^+$, 8), 334 (100), 332 (98), 253 (6).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{14}BrNNaO_4$: 397.9998; found: 397.9998.

Methyl 4-(4-Nitrophenyl)-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5e)

Gray solid; yield: 0.49 g (72%); mp 151–153 °C; R_f = 0.36 (EtOAc–PE, 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.43 (d, *J* = 8.8 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H), 7.65 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 1 H), 6.87 (d, *J* = 1.6 Hz, 1 H), 5.01 (q, *J* = 6.8 Hz, 1 H), 3.70 (s, 3 H), 1.56 (d, *J* = 6.8 Hz, 3 H).

MS (EI): *m*/*z* (%) = 342 ([M]$^+$, 82), 311 ([M – OCH_3]$^+$, 9), 299 (100), 253 (41).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{14}N_2NaO_6$: 365.0744; found: 365.0746.

Methyl 4-(4-Acetylphenyl)-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5f)

Yellow solid; yield: 0.56 g (82%); mp 193–195 °C; R_f = 0.38 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.15 (d, *J* = 8.8 Hz, 2 H), 7.64 (dd, J_1 = 8.4, 2.0 Hz, 1 H), 7.54 (d, *J* = 8.0 Hz, 2 H), 7.22 (d, *J* = 8.4 Hz, 1 H), 6.86 (d, *J* = 2.0 Hz, 1 H), 5.03 (q, *J* = 6.8 Hz, 1 H), 3.70 (s, 3 H), 2.65 (s, 3 H), 1.55 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 197.3, 165.4, 165.2, 147.9, 140.0, 136.9, 130.5, 129.9, 129.3, 125.5, 123.8, 117.3, 116.6, 73.5, 52.1, 26.9, 16.1.

MS (EI): *m*/*z* (%) = 339 ([M]$^+$, 65), 308 ([M – OCH_3]$^+$, 8), 296 (100), 253 (8), 77 (9).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}NNaO_5$: 362.0999; found: 362.1001.

Methyl 4-(4′-Chlorobiphenyl-4-yl)-2-methyl-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5g)

White solid; yield: 0.71 g (87%); mp 202–204 °C; R_f = 0.55 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.88 (d, *J* = 8.4 Hz, 2 H), 7.80 (d, *J* = 8.4 Hz, 2 H), 7.64 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.21 (d, *J* = 8.4 Hz, 1 H), 6.93 (d, *J* = 1.6 Hz, 1 H), 5.04 (q, *J* = 6.8 Hz, 1 H), 3.68 (s, 3 H), 1.55 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.9, 165.7, 148.1, 139.5, 138.0, 135.6, 133.1, 131.0, 129.8, 129.3, 128.9, 128.5, 125.7, 124.4, 117.6, 116.9, 73.8, 52.4, 16.5.

MS (EI): *m*/*z* (%) = 407 ([M]$^+$, 73), 376 ([M – OCH_3]$^+$, 4), 364 (100).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}ClNNaO_4$: 430.0817; found: 430.0822.

Methyl 2-Methyl-4-(1-naphthyl)-3-oxo-3,4-dihydro-2*H*-1,4-benzoxazine-6-carboxylate (5h)

Light pink solid; yield: 0.59 g (85%); mp 133–135 °C; R_f = 0.50 (EtOAc–PE, 1:4).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.16–8.09 (m, 4 H), 7.75–7.45 (m, 12 H), 7.28 (d, *J* = 7.2 Hz, 1 H), 7.26 (d, *J* = 7.2 Hz, 1 H), 6.66 (d, *J* = 2.0 Hz, 1 H), 6.59 (d, *J* = 2.0 Hz, 1 H), 5.35 (q, *J* = 6.8 Hz, 1 H), 5.15 (q, *J* = 6.8 Hz, 1 H), 3.60 (s, 6 H), 1.64 (d, *J* = 6.8 Hz, 3 H), 1.60 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.9, 165.7, 165.2, 147.9, 147.7, 134.2, 129.7, 128.8, 128.7, 128.0, 127.7, 127.6, 127.3, 126.9, 126.8, 126.3, 126.3, 125.5, 125.4, 122.2, 121.3, 117.3, 117.2, 116.4, 116.4, 73.8, 73.5, 52.0, 16.4, 16.2.

MS (EI): *m*/*z* (%) = 347 ([M]$^+$, 69), 316 ([M – OCH_3]$^+$, 4), 304 (100), 77 (5).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO_4$: 370.1050; found: 370.1054.

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