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A concise approach to polysubstituted oxazoles from *N*-acyl-2-bromo enamides *via* a copper(I)/amino acid-catalyzed intramolecular C–O bond formation†

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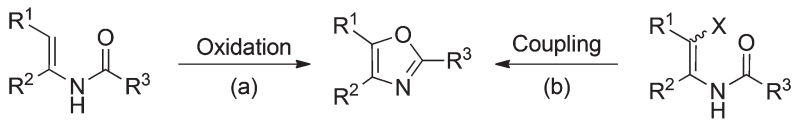
A straightforward and efficient copper(I)/amino acid-catalyzed intramolecular Ullmann-type C–O coupling reaction has been developed. This protocol affords a facile methodology for the synthesis of a series of novel 2,4,5-substituted oxazoles from readily accessible *N*-acyl-2-bromo enamides under mild conditions.

1. Introduction

Oxazoles represent one of the most important pharmacophores in drug discovery. Because of their diverse biological activities,[1–6] their synthesis has received considerable attention in recent years, with numerous new synthetic methods developed. In addition to Robinson–Gabriel condensation,[7,8] the most straightforward strategies for formation of the oxazole ring system are oxidative or coupling cyclization of enamide derivatives (eqn (1)). Recently, many oxidative cyclization approaches were developed using TBHP,[9–12] I_2,[13–17] hypervalent iodine(III) reagents,[18–20] $K_2S_2O_8$,[21] NBS,[22] or *via* the Cu(II)-catalyzed aerobic oxidation[23] (path a). However, despite the elegance of these oxidative strategies, the non-oxidative coupling strategy (path b) remains an important alternative, particularly in the context of constructing oxazoles containing oxidant-sensitive substructures, which is still not sufficiently developed. Transformation of *N*-(2-halovinyl)amides (isolated or generated *in situ*) to oxazoles could be achieved by using organic or inorganic bases,[24–27] which, nevertheless, were limited by scope of the substrates and/or efficiency of the transformation. Recently, Ila *et al.* developed the synthesis of 2,4,5-substituted oxazoles from *N*-(2-methylthiovinyl)benzamides mediated by Ag_2CO_3 [28] or catalyzed by CuI.[29] In addition, Glorius *et al.* reported copper-catalyzed coupling of primary amides with 1,2-dihalogenated olefins to synthesize 2,4- and 2,5-substituted oxazoles in 2007.[30]



X = Br, I, SMe, etc. (1)

Alternatively, we envisioned a facile copper(I)/amino acid-catalyzed oxazole synthesis methodology from readily accessible *N*-acyl-2-bromo enamides (path b) under mild conditions, which constitutes an intramolecular Ullmann coupling (IUC) strategy. Copper-assisted Ullmann-type reactions are valuable tools for the construction of C–C and C–X (X = N, O, S, *etc.*) bonds both in academic and industrial synthesis. In the past decade, these transformations have been greatly facilitated by the development of the ligands such as amino acid,[31–35] pyridine,[36–41] polyalcohol[42–44] and diamine[45–47] derivatives. With these readily available ligands, the coupling of aryl (or vinyl) halides with amines, phenols, amides, azide and other nucleophiles could occur under relatively mild conditions using a catalytic amount of copper. On the other hand, the intramolecular Ullmann coupling (IUC) strategy utilizing the above ligands also resulted in the discovery of many methodologies for the synthesis of small-,[38,48,49] medium-[50–55] and

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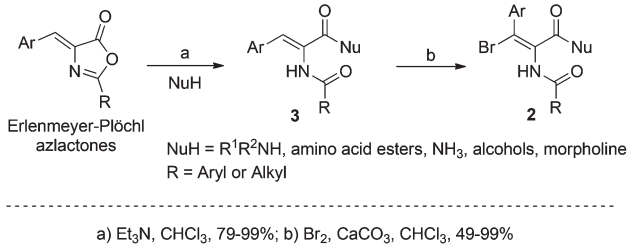
even large-sized[34,56] heterocycles. However, to the best of our knowledge, reports on constructing an oxazole framework with this strategy are rare. Herein, we wish to report a highly efficient IUC reaction catalyzed by copper(I) and *N*,*N*-dimethylglycine for polysubstituted oxazole synthesis.

2. Results and discussion

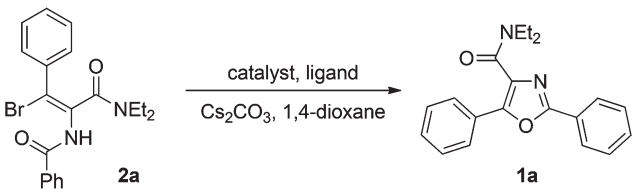
The required substrates **2** for this work were readily prepared *via* a two-step reaction from Erlenmeyer–Plöchl azlactones (Scheme 1). Firstly, the azlactone rings were opened by different nucleophiles (such as primary amines, cyclic or acyclic secondary amines, amino acid esters, ammonia, alcohols, and morpholine) to give a series of enamide derivatives **3** in good yields (79–99%). Then, treatment of enamides **3** with bromine in the presence of calcium carbonate in chloroform yielded the (*Z*)-isomer bromides **2** as the major products,[57] which were isolated for the follow-up research.

We commenced our study by using β-bromo enamide **2a** as the model substrate for the coupling cyclization to oxazole **1a** (Table 1). Initially, this transformation was performed in the presence of cesium carbonate (Cs_2CO_3) using 1,4-dioxane as a solvent with no catalyst or ligand. The conversion was completed after 24 h stirring at the refluxing temperature, giving



Scheme 1 Preparation of substrates **2**.

Table 1 Optimization of the reaction conditions for the transformation of substrate **2a** to oxazole **1a**[a]



Entry	Catalyst, ligand	Temp./°C	Time/h	Yield[b]
1	—	Reflux	24	50%
2	CuI	Reflux	1	58%[c]
3	CuI	90 °C	1	92%[c]
4	CuI, **L**	80 °C	1	98%[c]
5	CuI, **L**	60 °C	5	79%

[a] The optimal reaction conditions: CuI (10 mol%), *N*,*N*-dimethylglycine hydrochloride (**L**, 30 mol%), Cs_2CO_3 (210 mol%), 1,4-dioxane, 80 °C. [b] Isolated yields after silica gel chromatography. [c] Average yield of duplicate experiments.

product **1a** in moderate yield (50%, entry 1). Addition of copper(I) iodide (CuI, 10 mol%) as a catalyst could greatly accelerate the transformation with a slightly increased yield of **1a** (58%, entry 2). On this basis, lowering the reaction temperature to 90 °C could significantly improve the yield up to 92% (entry 3) with the conversion rate not affected (it became very slow when the reaction was carried out at temperatures lower than 90 °C). Inspired by the discovery of amino acids as ligands for copper-catalyzed Ullman-type reactions,[31,34] we utilized *N*,*N*-dimethyl-glycine hydrochloride (**L**, 30 mol%) as the ligand for our reaction, with which the reaction worked well at a relatively lower temperature (80 °C) and afforded the desired oxazole **1a** in an even better yield (98%, entry 4). However, further decreasing the reaction temperature will affect both the transformation rate and the yield of products (entry 5).

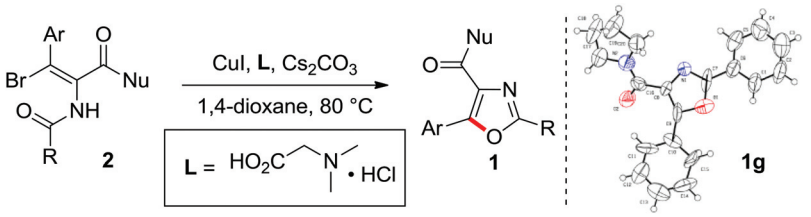
With the optimal reaction conditions (10 mol% of CuI, 30 mol% of **L**, 210 mol% of Cs_2CO_3 in 1,4-dioxane at 80 °C) in hand, we sought to probe the scope and generality of this protocol for oxazole synthesis (Table 2). Firstly, the substituents on the Ar ring of the substrate were examined. As the results shown in Table 2, this methodology is compatible with both electron-donating (**2b** and **2d**) and -withdrawing (**2c** and **2e**) groups on the Ar ring. All the bromides were smoothly converted to the corresponding oxazoles (**1a–f**) in good to excellent yields (86–99%), including the one with bulky 1-naphthyl substitution (**1f**). Encouraged by these positive results, we then prepared the substrates (**2g–s**) bearing different Nu (such as substituted amino, morpholino, and alkoxy) groups. Under the optimal coupling conditions, cyclization of these β-bromo enamides produced a series of 4-functionalized-2,5-diaryl oxazoles (**1g–s**) in 86–99% yield. The structure of oxazole **1g** was further confirmed by X-ray crystallography. In addition, the acetamide substrates (**2t–u**, R = acetyl) were successfully transformed to the desired oxazoles **1t–u** in excellent yield as well.

To further examine the feasibility of this method, *N*-(2-bromo-3-oxocyclohex-1-en-1-yl) benzamide (**2v**) was prepared (see "Experimental section"), and then subjected to the optimal cyclization conditions. To our delight, it was also converted to the expected fused-ring oxazole (**1v**) in good yield (Scheme 2).

3. Conclusions

In summary, a straightforward and facile copper(I)/amino acid-catalyzed intramolecular Ullmann-type C–O coupling reaction was developed for oxazole synthesis. The required substrates (**2**) were prepared from readily available Erlenmeyer–Plöchl azlactones *via* a two-step reaction. Under the optimal cyclization conditions, this new oxazole synthesis strategy afforded a series of novel 2,4,5-substituted oxazoles in an efficient manner. As a non-oxidative cyclization process, this high-yield methodology is an attractive alternative for the synthesis of oxazole-containing natural products and pharmaceutical compounds, especially for the ones containing oxidant-sensitive substructures.

Table 2 Scope of substrates 2[a]



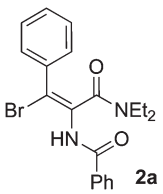
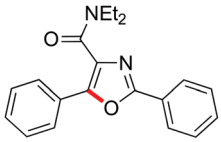
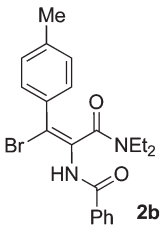
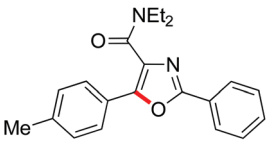
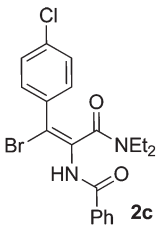
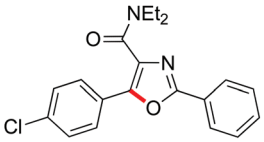
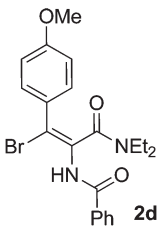
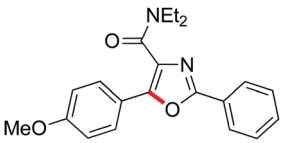
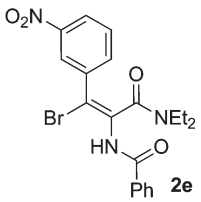
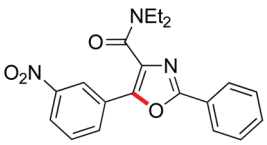
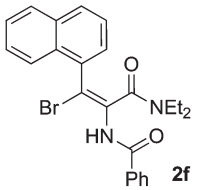
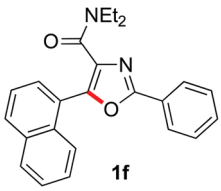
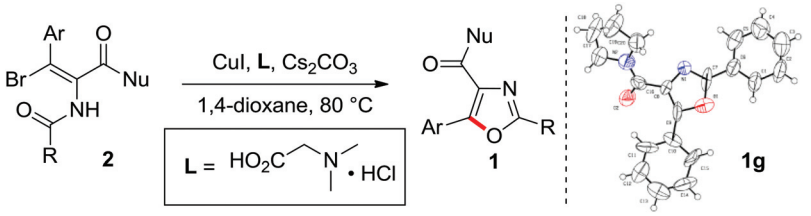
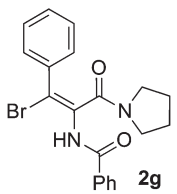
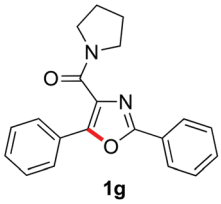
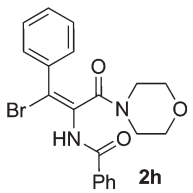
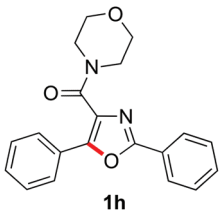
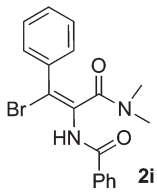
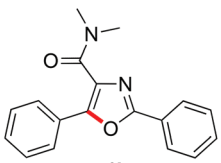
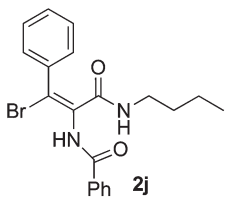
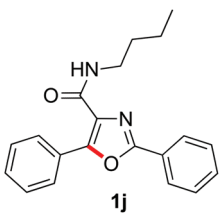
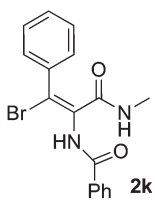
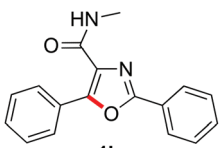
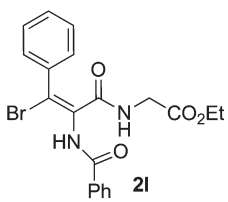
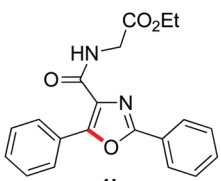
Entry	Substrate 2	Product 1	Yield[b]
1	 2a	 1a	98%
2	 2b	 1b	99%
3	 2c	 1c	86%
4	 2d	 1d	99%
5	 2e	 1e	95%
6	 2f	 1f	99%

Table 2 *(Contd.)*



Entry	Substrate **2**	Product **1**	Yield[b]
7	 **2g**	 **1g**	99%
8	 **2h**	 **1h**	99%
9	 **2i**	 **1i**	97%
10	 **2j**	 **1j**	91%
11	 **2k**	 **1k**	99%
12	 **2l**	 **1l**	95%

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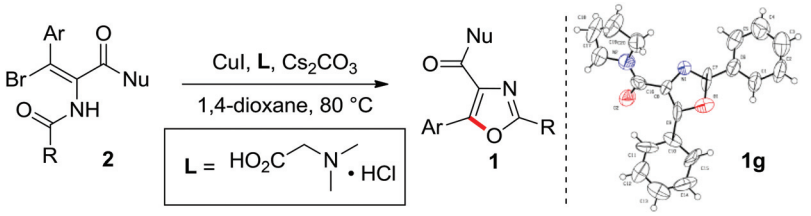

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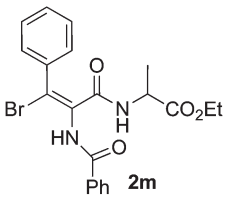
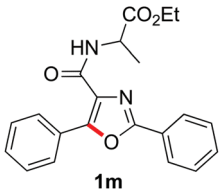
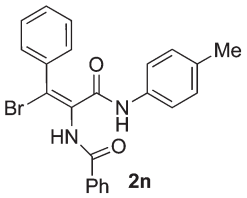
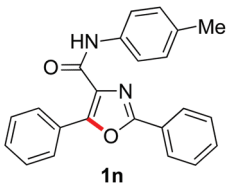
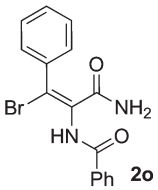
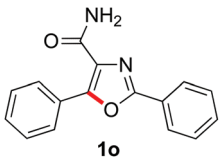
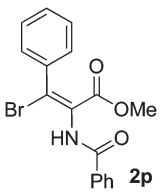
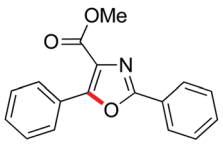
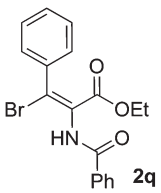
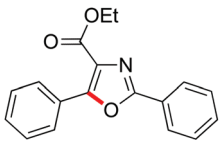
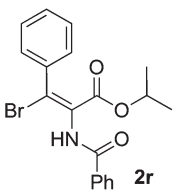
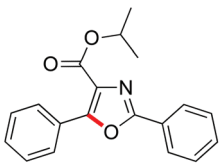
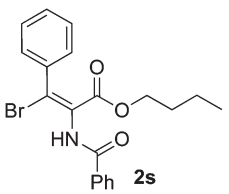
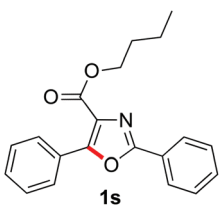
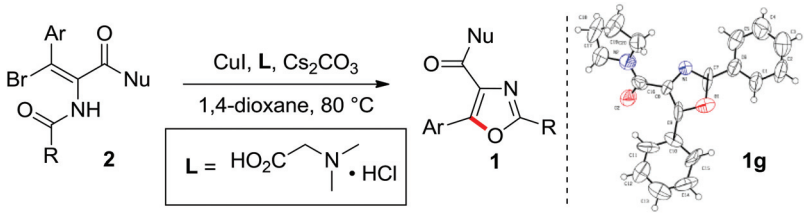
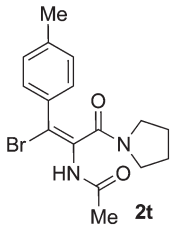
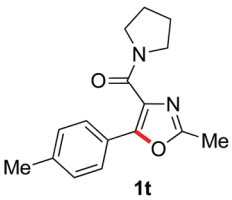
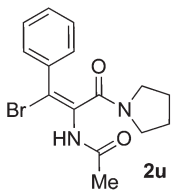
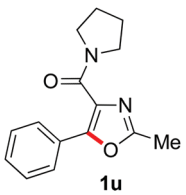
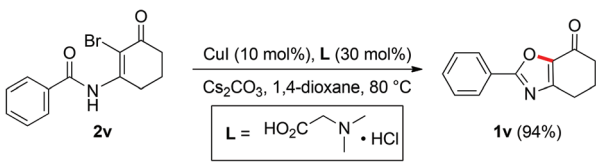
13	 2m	 1m	99%
14	 2n	 1n	89%
15	 2o	 1o	99%
16	 2p	 1p	90%
17	 2q	 1q	92%
18	 2r	 1r	95%
19	 2s	 1s	86%

Table 2 *(Contd.)*



Entry	Substrate **2**	Product **1**	Yield[b]
20[c]	 **2t**	 **1t**	99%
21[c]	 **2u**	 **1u**	99%

[a] The optimal reaction conditions: CuI (10 mol%), **L** (30 mol%), Cs_2CO_3 (210 mol%), 1,4-dioxane, 80 °C. [b] Isolated yields after silica gel chromatography. [c] The reaction was carried out at 90 °C.



Scheme 2 Synthesis of bicyclic oxazole **1v** from bromide **2v**.

4. Experimental section

4.1. General information

^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz or 300 MHz (100 MHz or 75 MHz for ^{13}C NMR) spectrometer. Chemical shift values are given in ppm with tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet; dd, doublet of doublets. The coupling constants (*J*) are reported in hertz (Hz). Melting points were determined on a micromelting point apparatus without corrections. Flash column chromatography was performed over 200–300 mesh silica gel, and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE). High-resolution mass spectra (HRMS-ESI) were recorded on a Q-TOF Mass Spectrometer. Infrared (IR) spectra were recorded on a FTIR spectrometer. 1,4-Dioxane, used for the synthesis of oxazoles **1**, was dried over 4 Å molecular sieves.

4.2. Preparation of enamides 3a–m, 3o and 3t–u

General procedure A: To a stirred solution of the corresponding Erlenmeyer–Plöchl azlactone (2 mmol, obtained *via* the reaction of the aryl aldehyde and *N*-benzoyl/acetyl glycine in acetic anhydride at 100 °C) in chloroform (20 mL) was added substituted amines (4 mmol; for **3o**, sat. ammonia solution (in methanol) was used; for **3l** and **3m**, acetonitrile was used instead of chloroform; when HCl salts were used, 6 mmol of triethylamines were added to neutralize the HCl). The reaction mixture was stirred at 0 °C until the reaction was complete (monitored by TLC, 1–12 h), and then it was washed with 2 N HCl (20 mL), followed by sat. sodium bicarbonate (20 mL). The separated organic layer was dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified through silica gel column chromatography to give enamides **3** in 79–99% yield.

4.3. Preparation of enamide 3n[29]

A suspension of (*Z*)-4-benzylidene-2-phenyloxazol-5(4*H*)-one (499 mg, 2 mmol) in ethanol (20 mL) was treated with 4-methylbenzenamine (321 mg, 3 mmol) and acetic acid (2 drops), and then heated to reflux for 5 h. After the reaction was complete, the solvent was removed by evaporation under reduced pressure, and the resulting residue was recrystallized in a mixture of EA and PE (25 : 75) to give enamide **3n** as a white solid in 92% yield.

4.4. Preparation of enamides 3p–s

General procedure B: A reaction mixture of (*Z*)-4-benzylidene-2-phenyloxazol-5(4*H*)-one (2 mmol) and potassium carbonate (6 mmol) in the corresponding alcohol (5 mL) was stirred at room temperature until the reaction was complete (monitored by TLC, 1–20 h). The reaction was quenched with water (10 mL), and then extracted with chloroform (4 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified through silica gel column chromatography to give enamides **3p–s** in 92–99% yield.

4.5. Preparation of substrates 2a–u

General procedure C: At 0 °C, to a stirred solution or suspension of the enamide (**3**, 1 mmol) and calcium carbonate (1.4 mmol) in chloroform, bromine (1.2 mmol) was added dropwise. After stirring at 0 °C for 1 h, the reaction mixture was allowed to warm up to room temperature until the bromination was complete (monitored by TLC, 3–5 h). It was then washed with 5% sodium bisulfite (30 mL), and the aqueous layer was extracted with dichloromethane (3 × 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified through silica gel column chromatography to afford the *Z*-isomer bromides **2** in 49–99% yield.

(*Z*)-*N*-(1-Bromo-3-(diethylamino)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2a). New compound, a white solid (396 mg, 0.99 mmol, 99%); mp 128–131 °C; R_f = 0.39 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3209, 3063, 2981, 2939, 1666, 1618, 1519, 1482, 1273, 1137, 706, 741, 696; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (br, s, 1H), 7.92–7.89 (m, 2H), 7.59–7.46 (m, 5H), 7.34–7.31 (m, 3H), 3.49–3.10 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 162.9, 136.3, 132.9, 132.4, 131.1 129.6, 129.2, 128.8, 128.2, 127.4, 109.6, 42.8, 38.3, 12.2, 11.4; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{21}BrN_2O_2Na$ 423.0679, found 423.0690.

(*Z*)-*N*-(1-Bromo-3-(diethylamino)-3-oxo-1-(*p*-tolyl)prop-1-en-2-yl)benzamide (2b). New compound, a white solid (348 mg, 0.84 mmol, 84%); mp 176–178 °C; R_f = 0.30 (EA–PE 65 : 35); IR (KBr, cm^{-1}) 3204, 3051, 2989, 2942, 1665, 1614, 1524, 1485, 1278, 824, 800, 739, 706; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (br, s, 1H), 7.91–7.88 (m, 2H), 7.59–7.41 (m, 5H), 7.13 (d, J = 8.4 Hz, 2H), 3.48–3.13 (m, 4H), 2.35 (s, 3H), 0.93 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 162.6, 139.0, 133.1, 132.5, 132.0, 130.2, 129.1, 128.5, 128.4, 127.0, 109.9, 42.4, 38.0, 20.9, 11.9, 11.1; HRMS (*m*/*z*) (M + Na) calcd for $C_{21}H_{23}BrN_2O_2Na$ 437.0835, found 437.0844.

(*Z*)-*N*-(1-Bromo-1-(4-chlorophenyl)-3-(diethylamino)-3-oxoprop-1-en-2-yl)benzamide (2c). New compound, a white solid (373 mg, 0.86 mmol, 86%); mp 176–178 °C; R_f = 0.44 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3206, 3063, 2981, 1668, 1616, 1520, 1479, 1273, 1089, 1014, 838, 799, 749, 702, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (br, s, 1H), 7.89 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.50–7.46 (m, 4H), 7.30 (d, J = 8.4 Hz, 2H), 3.46–3.12 (m, 4H), 0.96 (t, J = 7.2 Hz, 3H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 162.3, 134.7, 134.4, 132.3, 132.1, 131.2, 130.5, 128.4, 128.0, 127.0, 107.2, 42.5, 38.0, 12.0, 12.1; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{20}BrClN_2O_2Na$ 457.0289, found 457.0292.

(*Z*)-*N*-(1-Bromo-3-(diethylamino)-1-(4-methoxyphenyl)-3-oxoprop-1-en-2-yl)benzamide (2d). New compound, a white solid (387 mg, 0.90 mmol, 90%); mp 149–151 °C; R_f = 0.22 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3210, 2972, 2935, 2835, 1662, 1615, 1507, 1484, 1295, 1253, 1177, 1033, 835, 798, 739, 692; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (br, s, 1H), 7.89 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.49–7.46 (m, 4H), 6.84 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.48–3.13 (m, 4H), 0.95 (t, J = 7.2 Hz, 3H), 0.81 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 163.2, 160.2, 132.9, 132.3, 131.0, 130.2, 128.77, 128.75, 127.4, 113.5, 110.3, 55.3, 42.9, 38.4, 12.4, 11.6; HRMS (*m*/*z*) (M + Na) calcd for $C_{21}H_{23}BrN_2O_3Na$ 453.0784, found 453.0784.

(*Z*)-*N*-(1-Bromo-3-(diethylamino)-1-(3-nitrophenyl)-3-oxoprop-1-en-2-yl)benzamide (2e). New compound, a white solid (412 mg, 0.93 mmol, 93%); mp 125–127 °C; R_f = 0.24 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3210, 3067, 2976, 2939, 2360, 1664, 1618, 1521, 1468, 1346, 1274, 798, 736, 696; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (t, J = 2.0 Hz, 1H), 8.24 (br, s, 1H), 8.18 (dd, J = 4.0, 1.6 Hz, 1H), 7.92–7.89 (m, 3H), 7.62–7.58 (m, 1H), 7.54–7.49 (m, 3H), 3.43–3.21 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 162.2, 148.0, 138.1, 135.4, 133.4, 132.8, 132.5, 129.3, 128.9, 127.4, 124.6, 123.7, 104.7, 43.0, 38.6, 12.4, 11.4; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{20}BrN_3O_4Na$ 468.0529, found 468.0532.

(*Z*)-*N*-(1-Bromo-3-(diethylamino)-1-(naphthalen-1-yl)-3-oxoprop-1-en-2-yl)benzamide (2f). New compound, a white solid (445 mg, 0.99 mmol, 99%); mp 189–191 °C; R_f = 0.28 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3198, 3061, 2978, 2936, 1665, 1607, 1514, 1485, 1299, 1281, 801, 782, 733, 709, 692; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (br, s, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 7.2 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.65–7.50 (m, 6H), 7.42 (t, J = 8.0 Hz, 1H), 3.38 (br, s, 2H), 2.84 (br, s, 2H), 0.50 (br, s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.0, 162.5, 133.7, 133.1, 132.9, 132.5, 131.2, 130.2, 128.8, 128.6, 127.5, 126.4, 126.2, 125.6, 125.2, 107.2, 42.9, 37.5, 12.1, 11.2; HRMS (*m*/*z*) (M + Na) calcd for $C_{24}H_{23}BrN_2O_2Na$ 473.0835, found 473.0840.

(*Z*)-*N*-(1-Bromo-3-oxo-1-phenyl-3-(pyrrolidin-1-yl)prop-1-en-2-yl)benzamide (2g). New compound, a white solid (299 mg, 0.75 mmol, 75%); mp 201–203 °C; R_f = 0.42 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3159, 3054, 2957, 2883, 2802, 1666, 1616, 1519, 1484, 1445, 1289, 796, 754, 693; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (br, s, 1H), 7.92–7.90 (m, 2H), 7.60–7.55 (m, 3H), 7.51–7.47 (m, 2H), 7.36–7.32 (m, 3H), 3.32 (br, s, 2H), 3.26 (br, s, 2H), 1.60 (br, s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 162.1, 136.3, 132.6, 132.5, 131.9, 129.3, 129.1, 128.8, 128.1, 127.5, 111.8 47.4, 45.4, 25.2, 24.1; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{19}BrN_2O_2Na$ 421.0522, found 421.0520.

(*Z*)-*N*-(1-Bromo-3-morpholino-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2h). New compound, a white solid (373 mg, 0.90 mmol, 90%); mp 208–210 °C; R_f = 0.49 (EA–PE 50 : 50);

IR (KBr, cm^{-1}) 3211, 2974, 2857, 1670, 1619, 1519, 1440, 1305, 1276, 1110, 1028, 765, 746, 699; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (br, s, 1H), 7.91–7.88 (m, 2H), 7.60–7.46 (m, 5H), 7.39–7.35 (m, 3H), 3.65–2.66 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 162.7, 136.2, 132.6, 132.4, 130.0, 129.6, 129.2, 128.8, 128.4, 127.5, 111.5, 65.7, 65.6, 46.9, 41.9; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{19}BrN_2O_3Na$ 437.0471, found 437.0476.

(*Z*)-*N*-(1-Bromo-3-(dimethylamino)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2i). New compound, a white solid (368 mg, 0.99 mmol, 99%); mp 200–203 °C; R_f = 0.25 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3206, 3055, 2927, 1665, 1628, 1515, 1482, 1400, 1288, 798, 769, 753, 703; ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (br, s, 1H), 7.92–7.90 (m, 2H), 7.61–7.56 (m, 1H), 7.53–7.48 (m, 4H), 7.37–7.33 (m, 3H), 2.77 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 163.9, 136.3, 132.6, 132.5, 130.7, 129.3, 129.1, 128.8, 128.2, 127.4, 110.9, 37.9, 34.6; HRMS (*m*/*z*) (M + Na) calcd for $C_{18}H_{17}BrN_2O_2Na$ 395.0366, found 395.0370.

(*Z*)-*N*-(1-Bromo-3-(butylamino)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2j). New compound, a white solid (208 mg, 0.52 mmol, 52%); mp 168–171 °C; R_f = 0.27 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3325, 3060, 2959, 2929, 2359, 1639, 1525, 1483, 1286, 714, 693; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (br, s, 1H), 7.92 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.50–7.46 (m, 4H), 7.37–7.35 (m, 3H), 5.52 (t, J = 5.6 Hz, 1H), 3.10 (q, J = 6.8 Hz, 2H), 1.13–1.06 (m, 2H), 0.99–0.90 (m, 2H), 0.74 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 162.6, 136.9, 133.2, 132.6, 132.5, 129.4, 129.1, 128.8, 128.6, 127.6, 116.3, 39.6, 30.5, 19.7, 13.6; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{21}BrN_2O_2Na$ 423.0679, found 423.0680.

(*Z*)-*N*-(1-Bromo-3-(methylamino)-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2k). New compound, a white solid (197 mg, 0.55 mmol, 55%); mp 201–203 °C; R_f = 0.30 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3346, 3228, 3051, 1644, 1522, 1482, 1284, 714, 695; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (br, s, 1H), 7.92–7.90 (m, 2H), 7.59–7.54 (m, 1H), 7.49–7.44 (m, 4H), 7.37–7.32 (m, 3H), 5.70 (q, J = 4.8 Hz, 1H), 2.60 (d, J = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 163.6, 136.8, 132.8, 132.53, 132.47, 129.5, 129.0, 128.8, 128.5, 127.6, 116.9, 26.7; HRMS (*m*/*z*) (M + Na) calcd for $C_{17}H_{15}BrN_2O_2Na$ 381.0209, found 381.0207.

(*Z*)-Ethyl 2-(2-benzamido-3-bromo-3-phenylacrylamido)acetate (2l). New compound, a white solid (215 mg, 0.50 mmol, 50%); mp 159–161 °C; R_f = 0.41 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3250, 3060, 2978, 2933, 1758, 1729, 1647, 1520, 1480, 1191, 1027, 760, 714, 694; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (br, s, 1H), 7.92–7.90 (m, 2H), 7.60–7.56 (m, 1H), 7.51–7.46 (m, 4H), 7.38–7.33 (m, 3H), 6.11 (t, J = 4.4 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 3.88 (d, J = 4.8 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 164.9, 162.5, 136.6, 132.6, 132.5, 132.0, 129.5, 129.1, 128.8, 128.6, 127.5, 117.1, 61.5, 41.9, 14.0; HRMS (*m*/*z*) (M + Na) calcd for $C_{20}H_{19}BrN_2O_4Na$ 453.0420, found 453.0422.

(*Z*)-Ethyl 2-(2-benzamido-3-bromo-3-phenylacrylamido)propanoate (2m). New compound, a white solid (320 mg, 0.72 mmol, 72%); mp 158–161 °C; R_f = 0.25 (EA–PE 35 : 65); IR (KBr, cm^{-1}) 3257, 3076, 2982, 1752, 1651, 1562, 1517, 1484, 1331, 1288, 1204, 1163, 760, 693; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (br, s, 1H), 7.92–7.90 (m, 2H), 7.60–7.56 (m, 1H), 7.51–7.45 (m, 4H), 7.38–7.33 (m, 3H), 6.19 (d, J = 7.2 Hz, 1H), 4.44 (m, 1H), 4.13–4.01 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 164.8, 161.6, 136.8, 132.7, 132.6, 132.5, 129.4, 129.2, 128.8, 128.6, 127.5, 116.3, 61.5, 48.4, 17.7, 14.0; HRMS (*m*/*z*) (M + Na) calcd for $C_{21}H_{21}BrN_2O_4Na$ 467.0577, found 467.0587.

(*Z*)-*N*-(1-Bromo-3-oxo-1-phenyl-3-(*p*-tolylamino)prop-1-en-2-yl)benzamide (2n). New compound, a white solid (369 mg, 0.85 mmol, 85%); mp 217–219 °C; R_f = 0.35 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3345, 3237, 3057, 2923, 1643, 1601, 1514, 1479, 1334, 1290, 820, 719, 696; ^1H NMR (400 MHz, DMSO-d_6): δ 10.07 (br, s, 1H), 9.93 (br, s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.33–7.24 (m, 3H), 7.17 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.4, 161.9, 138.1, 136.7, 134.2, 133.2, 132.8, 132.6, 129.54, 129.45, 129.1, 128.9, 128.5, 128.3, 120.3, 119.8, 20.8; HRMS (*m*/*z*) (M + Na) calcd for $C_{23}H_{19}BrN_2O_2Na$ 457.0522, found 457.0523.

(*Z*)-*N*-(3-Amino-1-bromo-3-oxo-1-phenylprop-1-en-2-yl)benzamide (2o). New compound, a white solid (169 mg, 0.49 mmol, 49%); mp 223–225 °C; R_f = 0.25 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3419, 3259, 1647, 1578, 1498, 1477, 1399, 1285, 757, 719, 692; ^1H NMR (400 MHz, DMSO-d_6): δ 9.89 (br, s, 1H), 8.00 (dd, J = 7.6, 0.4 Hz, 2H), 7.63–7.59 (m, 1H), 7.54–7.51 (m, 2H), 7.44–7.34 (m, 6H), 7.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.3, 165.0, 138.6, 133.9, 133.5, 132.4, 129.6, 129.4, 128.9, 128.5, 128.3, 120.9; HRMS (*m*/*z*) (M + Na) calcd for $C_{16}H_{13}BrN_2O_2Na$ 367.0053, found 367.0058.

(*Z*)-Methyl 2-benzamido-3-bromo-3-phenylacrylate (2p). Known compound, a white solid (352 mg, 0.98 mmol, 98%); mp 138–139 °C (lit.,[58] mp 138.5–139.0 °C); R_f = 0.32 (EA–PE 20 : 80); IR (KBr, cm^{-1}) 3321, 3054, 2947, 1731, 1650, 1508, 1479, 1318, 1274, 719, 693; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (br, s, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.41–7.38 (m, 2H), 7.35–7.34 (m, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 163.3, 137.0, 132.7, 132.3, 129.5, 129.1, 129.0, 128.9, 128.3, 127.5, 117.7, 52.7; HRMS (*m*/*z*) (M + Na) calcd for $C_{17}H_{14}BrNO_3Na$ 382.0049, found 382.0057.

(*Z*)-Ethyl 2-benzamido-3-bromo-3-phenylacrylate (2q). Known compound, a white solid (298 mg, 0.80 mmol, 80%); mp 111–112 °C; R_f = 0.36 (EA–PE 20 : 80); IR (KBr, cm^{-1}) 3227, 3064, 2970, 2924, 1734, 1648, 1507, 1478, 1308, 1272, 1180, 1156, 1021, 723, 696; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (br, s, 1H), 7.91–7.89 (m, 2H), 7.60–7.56 (m, 1H), 7.51–7.47 (m, 2H), 7.42–7.38 (m, 2H), 7.36–7.32 (m, 3H), 4.05 (q, J = 7.2 Hz, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 162.7, 137.2, 132.6, 132.4, 129.6, 129.4, 129.1, 128.9, 128.3, 127.5, 117.7, 61.9, 13.4; HRMS (*m*/*z*) (M + Na) calcd for $C_{18}H_{16}BrNO_3Na$ 396.0206, found 396.0209.

(*Z*)-Isopropyl 2-benzamido-3-bromo-3-phenylacrylate (2r). New compound, a white solid (290 mg, 0.75 mmol, 75%); mp 147–148 °C; R_f = 0.43 (EA–PE 20 : 80); IR (KBr, cm^{-1}) 3315, 3273, 3053, 2975, 1697, 1673, 1621, 1518, 1480, 1358, 1315,

1273, 1201, 1106, 717, 702, 690; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (br, s, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.42–7.40 (m, 2H), 7.36–7.34 (m, 3H), 4.96–4.87 (m, 1H), 0.97 (d, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 162.7, 137.3, 132.6, 132.5, 130.0, 129.3, 129.2, 128.8, 128.3, 127.5, 117.0, 69.8, 21.0; HRMS (m/z) (M + Na) calcd for $C_{19}H_{18}BrNO_3Na$ 410.0362, found 410.0366.

(*Z*)-Butyl 2-benzamido-3-bromo-3-phenylacrylate (2s). New compound, a white solid (313 mg, 0.78 mmol, 78%); mp 82–84 °C; R_f = 0.27 (EA–PE 10 : 90); IR (KBr, cm^{-1}) 3244, 3056, 2958, 2872, 1731, 1644, 1512, 1481, 1310, 1275, 1171, 723, 694; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (br, s, 1H), 7.90 (dd, J = 8.4, 2.0 Hz, 2H), 7.60–7.56 (m, 1H), 7.51–7.47 (m, 2H), 7.42–7.39 (m, 2H), 7.35–7.33 (m, 3H), 4.02–3.98 (m, 2H), 1.34–1.25 (m, 2H), 1.06–0.96 (m, 2H), 0.77–0.72 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 162.9, 137.2, 132.6, 132.4, 129.5, 129.4, 129.1, 128.9, 128.3, 127.5, 117.6, 65.9, 29.9, 18.7, 13.6; HRMS (m/z) (M + Na) calcd for $C_{20}H_{20}BrNO_3Na$ 424.0519, found 424.0520.

(*Z*)-*N*-(1-Bromo-3-oxo-3-(pyrrolidin-1-yl)-1-(*p*-tolyl)prop-1-en-2-yl)acetamide (2t). New compound, a white solid (312 mg, 0.89 mmol, 89%); mp 207–209 °C; R_f = 0.25 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3164, 2972, 2886, 1687, 1610, 1528, 1445, 1368, 1282, 717, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (br, s, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 3.27–3.08 (m, 4H), 2.34 (s, 3H), 2.16 (s, 3H), 1.57 (br, s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 162.3, 139.0, 133.1, 130.8, 128.6, 128.4, 111.8, 46.9, 44.9, 24.7, 23.7, 22.7, 20.9; HRMS (m/z) (M + Na) calcd for $C_{16}H_{19}BrN_2O_2Na$ 373.0522, found 373.0530.

(*Z*)-*N*-(1-Bromo-3-oxo-1-phenyl-3-(pyrrolidin-1-yl)prop-1-en-2-yl)acetamide (2u). New compound, a white solid (320 mg, 0.95 mmol, 95%); mp 188–190 °C; R_f = 0.25 (EA–PE 65 : 35); IR (KBr, cm^{-1}) 3222, 2973, 2879, 1685, 1619, 1446, 1274, 707; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (br, s, 1H), 7.53–7.50 (m, 2H), 7.31–7.28 (m, 3H), 3.25–3.07 (m, 4H), 2.16 (s, 3H), 1.54 (br, s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 162.7, 136.4, 131.9, 129.2, 129.1, 128.0, 112.0, 47.4, 45.3, 25.1, 24.1, 23.1; HRMS (m/z) (M + Na) calcd for $C_{15}H_{17}BrN_2O_2Na$ 359.0366, found 359.0370.

4.6. Preparation of substrates 2v

Benzamide (4.74 g, 39.1 mmol) and a catalytic amount of *p*-toluenesulfonic acid (TsOH, 503 mg, 2.61 mmol) were added to a stirred solution of 1,3-cyclohexanedione (2.93 g, 26.1 mmol) in toluene (30 mL). The reaction mixture was heated under reflux using a Dean–Stark apparatus for 2 h.[59] Then, it was allowed to cool to room temperature, neutralized with saturated sodium bicarbonate solution (~15 mL), and treated with brine (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (30 mL × 3). All the organic layers were combined, dried over anhydrous sodium sulfate, and concentrated. The resulting residue was purified through silica gel column chromatography (EA–PE = 50 : 50) to give enamide **3v** (4.58 g) as a yellow solid in 81% yield. To a stirred solution of **3v** (200 mg, 0.93 mmol) in DMF (5 mL) was added *N*-bromosuccinimide (NBS, 178 mg, 1 mmol) and potassium carbonate (152 mg, 1.1 mmol) in sequence. The reaction mixture was stirred at room temperature for 30 min, quenched by water (20 mL), and then extracted with ethyl acetate (3 × 20 mL). The combined organic layer was washed with brine (20 mL), dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified through silica gel column chromatography to afford bromide **2v** in 59% yield. New compound, a white solid (161 mg, 0.55 mmol, 59%); mp 130–131 °C; R_f = 0.38 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3380, 2948, 1697, 1670, 1578, 1475, 1372, 1279, 1192, 804, 701; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (br, s, 1H), 7.90–7.88 (m, 2H), 7.66–7.62 (m, 1H), 7.56–7.52 (m, 2H), 3.41 (t, J = 6.4 Hz, 2H), 2.66–2.63 (m, 2H), 2.14–2.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 165.3, 155.6, 133.3, 133.2, 129.2, 127.4, 106.9, 37.3, 28.8, 21.3; HRMS (m/z) (M + Na) calcd for $C_{13}H_{12}BrNO_2Na$ 315.9944, found 315.9947.

4.7. Synthesis of oxazoles 1

General procedure D: A 50 mL round-bottom flask, equipped with a magnetic stir bar and a reflux condenser, was charged with the substrate (**2**, 0.5 mmol), cesium carbonate (1.05 mmol), copper iodide (0.05 mmol) and *N*,*N*-dimethylglycine hydrochloride (0.15 mmol), followed by addition of 1,4-dioxane (10 mL). The resulting mixture was vacuumed and refilled with nitrogen for three cycles, and then heated to 80 °C (for the preparation of **1t–u**, the reactions were carried out at 90 °C) until the conversion was complete (monitored by TLC, 1–4 h). After cooling to room temperature, it was quenched with water, and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated. The resulting residue was purified through silica gel column chromatography to yield the oxazole **1**.

***N*,*N*-Diethyl-2,5-diphenyloxazole-4-carboxamide (1a).** Known compound, a white solid (157 mg, 0.49 mmol, 98%); mp 89–90 °C; R_f = 0.40 (EA–PE 15 : 85); IR (KBr, cm^{-1}) 3061, 2970, 2925, 1630, 1496, 1486, 1444, 1261, 862, 774, 705, 693, 684; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13–8.11 (m, 2H), 7.87–7.84 (m, 2H), 7.51–7.47 (m, 3H), 7.46–7.42 (m, 2H), 7.39–7.35 (m, 1H), 3.62 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 159.5, 148.3, 131.7, 130.7, 129.0, 128.82, 128.79, 127.4, 126.9, 126.5, 125.8, 43.4, 40.0, 14.4, 12.8; HRMS (m/z) (M + H) calcd for $C_{20}H_{21}N_2O_2$ 321.1598, found 321.1603.

***N*,*N*-Diethyl-2-phenyl-5-(*p*-tolyl)oxazole-4-carboxamide (1b).** New compound, a white solid (165 mg, 0.49 mmol, 99%); mp 107–108 °C; R_f = 0.36 (EA–PE 20 : 80); IR (KBr, cm^{-1}) 3063, 2975, 2932, 1631, 1512, 1262, 863, 822, 780, 715; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11–8.08 (m, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.47–7.43 (m, 3H), 7.23 (d, J = 8.0 Hz, 2H), 3.60 (q, J = 7.2 Hz, 2H), 3.37 (q, J = 7.2 Hz, 2H), 2.36 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 159.1, 148.5, 139.1, 131.0, 130.5, 129.4, 128.7, 126.9, 126.3, 125.7, 124.6, 43.3, 39.9, 21.3, 14.3, 12.7; HRMS (m/z) (M + H) calcd for $C_{21}H_{23}N_2O_2$ 335.1754, found 335.1758.

5-(4-Chlorophenyl)-*N*,*N*-diethyl-2-phenyloxazole-4-carboxamide (1c). New compound, a light-yellow solid (152 mg, 0.43 mmol, 86%); mp 129–130 °C; R_f = 0.25 (EA–PE 10 : 90); IR (KBr, cm^{-1})

3058, 2975, 2934, 1623, 1557, 1495, 1451, 1259, 1212, 1090, 861, 839, 784, 713; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (dd, J = 6.8, 2.8 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.50–7.49 (m, 3H), 7.41 (d, J = 8.8 Hz, 2H), 3.61 (q, J = 7.2 Hz, 2H), 3.42 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 159.1, 147.3, 134.5, 131.7, 130.4, 128.6, 128.4, 126.7, 126.3, 126.1, 125.5, 43.0, 39.7, 14.0, 12.4; HRMS (m/z) (M + H) calcd for $C_{20}H_{20}ClN_2O_2$ 355.1208, found 355.1213.

***N*,*N*-Diethyl-5-(4-methoxyphenyl)-2-phenyloxazole-4-carboxamide (1d).** New compound, a light-yellow solid (173 mg, 0.49 mmol, 99%); mp 94–96 °C; R_f = 0.42 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3070, 2968, 2937, 1640, 1612, 1508, 1253, 1176, 1086, 1025, 865, 832, 776, 705, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–8.08 (m, 2H), 7.83–7.79 (m, 2H), 7.50–7.45 (m, 3H), 6.98–6.94 (m, 2H), 3.84 (s, 3H) 3.61 (q, J = 7.2 Hz, 2H), 3.41 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 160.2, 158.8, 148.8, 130.4, 130.2, 128.8, 127.5, 127.0, 126.4, 120.2, 114.2, 55.3, 55.3, 43.4, 40.0, 14.4, 12.8; HRMS (m/z) (M + H) calcd for $C_{21}H_{23}N_2O_3$ 351.1703, found 351.1709.

***N*,*N*-Diethyl-5-(3-nitrophenyl)-2-phenyloxazole-4-carboxamide (1e).** New compound, a light-yellow solid (173 mg, 0.47 mmol, 95%); mp 102–103 °C; R_f = 0.42 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3076, 2982, 2939, 1630, 1535, 1350, 1483, 1443, 1263, 1215, 1094, 856, 800, 779, 756, 707, 690; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72–8.71 (m, 1H), 8.28–8.25 (m, 1H), 8.21–8.18 (m, 1H), 8.15–8.12 (m, 2H), 7.65–7.60 (m, 1H), 7.53–7.51 (m, 3H), 3.64 (q, J = 7.2 Hz, 2H), 3.48 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 160.1, 148.5, 146.6, 133.7, 131.5, 131.2, 129.9, 129.01, 128.95, 126.7, 126.3, 123.3, 120.6, 43.6, 40.3, 14.5, 12.8; HRMS (m/z) (M + Na) calcd for $C_{20}H_{19}N_3O_4Na$ 388.1268, found 388.1268.

***N*,*N*-Diethyl-5-(naphthalen-1-yl)-2-phenyloxazole-4-carboxamide (1f).** New compound, a white solid (183 mg, 0.49 mmol, 99%); mp 109–111 °C; R_f = 0.43 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3057, 2982, 2932, 1635, 1552, 1509, 1448, 1263, 862, 810, 776, 776, 714, 694; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16–8.14 (m, 2H), 8.11–8.08 (m, 1H), 7.95–7.90 (m, 2H), 7.84 (dd, J = 7.2 Hz, 1.2 Hz, 1H), 7.56–7.52 (m, 3H), 7.50–7.47 (m, 3H), 3.46 (q, J = 7.2 Hz, 2H), 3.37 (q, J = 7.2 Hz, 2H), 1.12 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 160.5, 148.8, 134.1, 133.7, 131.0, 130.7, 130.5, 128.9, 128.8, 128.6, 127.0, 126.6, 126.3, 125.2, 125.1, 124.8, 43.2, 39.8, 14.1, 12.6; HRMS (m/z) (M + H) calcd for $C_{24}H_{23}N_2O_2$ 371.1754, found 371.1747.

(2,5-Diphenyloxazol-4-yl)(pyrrolidin-1-yl)methanone (1g). New compound, a white solid (157 mg, 0.49 mmol, 99%); mp 107–108 °C; R_f = 0.32 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3061, 2976, 2873, 1621, 1558, 1494, 1423, 888, 772, 706, 685; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13–8.10 (m, 2H), 8.00 (d, J = 7.6 Hz, 2H), 7.50–7.44 (m, 5H), 7.38 (t, J = 7.2 Hz, 1H), 3.71 (t, J = 6.8 Hz, 2H), 3.64 (t, J = 6.8 Hz, 2H), 1.97–1.89 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 159.3, 149.8, 132.2, 130.9, 129.4, 129.0, 128.9, 127.7, 127.0, 126.631, 126.626, 48.4, 46.5, 26.3, 24.4; HRMS (m/z) (M + Na) calcd for $C_{20}H_{18}N_2O_2Na$ 341.1260, found 341.1267.

(2,5-Diphenyloxazol-4-yl)(morpholino)methanone (1h). Known compound, a white solid (165 mg, 0.49 mmol, 99%); mp 155–157 °C; R_f = 0.27 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3442, 2958, 2926, 2854, 1642, 1549, 1494, 1113, 778, 707, 693; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–8.10 (m, 2H), 7.90–7.88 (m, 2H), 7.50–7.38 (m, 6H), 3.87–3.80 (m, 4H), 3.65–3.61 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 159.6, 149.9, 130.9, 130.3, 129.4, 128.9, 127.1, 126.6, 126.5 126.3, 66.9, 66.7, 47.5, 42.6; HRMS (m/z) (M + Na) calcd for $C_{20}H_{18}N_2O_3Na$ 357.1210, found 357.1221.

***N*,*N*-Dimethyl-2,5-diphenyloxazole-4-carboxamide (1i).** New compound, a white solid (142 mg, 0.49 mmol, 97%); mp 86–88 °C; R_f = 0.50 (EA–PE 33 : 67); IR (KBr, cm^{-1}) 3063, 2923, 1634, 1556, 1489, 1444, 1402, 1217, 1085, 1067, 900, 775, 758, 706, 684, 672; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–8.10 (m, 2H), 7.88–7.86 (m, 2H), 7.48–7.42 (m, 5H), 7.38–7.35 (m, 1H), 3.17 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 159.5, 148.9, 131.1, 130.8, 129.2, 128.8, 127.3, 126.7, 126.5, 125.9, 38.5, 35.3; HRMS (m/z) (M + Na) calcd for $C_{18}H_{16}N_2O_2Na$ 315.1104, found 315.1103.

***N*-Butyl-2,5-diphenyloxazole-4-carboxamide (1j).** New compound, a white solid (146 mg, 0.46 mmol, 91%); mp 90–92 °C; R_f = 0.46 (EA–PE 10 : 90); IR (KBr, cm^{-1}) 3329, 3066, 2960, 2929, 2871, 1644, 1588, 1530, 841, 775, 703, 688; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40–8.38 (m, 2H), 8.10–8.08 (m, 2H), 7.49–7.39 (m, 7H), 3.47 (q, J = 7.2 Hz, 2H), 1.68–1.61 (m, 2H), 1.44 (sext, J = 7.6 Hz, 2H), 0.97 (t, J = 7.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 157.9, 151.6, 130.5, 130.1, 129.4, 128.5, 127.9, 127.8, 126.9, 126.13, 126.09, 38.7, 31.4, 19.8, 13.4; HRMS (m/z) (M + Na) calcd for $C_{20}H_{20}N_2O_2Na$ 343.1417, found 343.1417.

***N*-Methyl-2,5-diphenyloxazole-4-carboxamide (1k).** New compound, a white solid (138 mg, 0.50 mmol, 99%); mp 153–155 °C; R_f = 0.29 (EA–PE 20 : 80); IR (KBr, cm^{-1}) 3324, 3062, 2928, 1649, 1589, 1537, 1224, 705, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, J = 7.6 Hz, 2H), 8.08 (m, 2H), 7.50–7.42 (m, 7H), 3.03 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 158.4, 152.0, 130.9, 130.4, 129.8, 128.9, 128.4, 128.2, 127.3, 126.50, 126.48, 25.9; HRMS (m/z) (M + Na) calcd for $C_{17}H_{14}N_2O_2Na$ 301.0947, found 301.0945.

Ethyl 2-(2,5-diphenyloxazole-4-carboxamido)acetate (1l). New compound, a white solid (166 mg, 0.47 mmol, 95%); mp 95–96 °C; R_f = 0.30 (EA–PE 15 : 85); IR (KBr, cm^{-1}) 3403, 3060, 2978, 2926, 1751, 1661, 1520, 1212, 780, 760. 707, 688; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J = 7.6 Hz, 2H), 8.12–8.10 (m, 2H), 7.89 (t, J = 5.2 Hz, 1H), 7.51–7.41 (m, 6H), 4.30–4.25 (m, 4H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 161.7, 158.7, 152.7, 131.1, 130.1, 130.0, 129.0, 128.5, 128.3, 127.3, 126.7, 126.5, 61.7, 41.3, 14.3; HRMS (m/z) (M + Na) calcd for $C_{20}H_{18}N_2O_4Na$ 373.1159, found 373.1148.

Ethyl 2-(2,5-diphenyloxazole-4-carboxamido)propanoate (1m). New compound, a white solid (180 mg, 0.49 mmol, 99%); mp 92–94 °C; R_f = 0.50 (EA–PE 15 : 85); IR (KBr, cm^{-1}) 3289, 3059, 2987, 2933, 1737, 1651, 1590, 1531, 1226, 777, 704, 692, 683; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38–8.34 (m, 2H), 8.16–8.11 (m,

2H), 7.91 (d, J = 7.8 Hz, 1H), 7.53–7.40 (m, 6H), 4.84–4.74 (m, 1H), 4.26 (q, J = 7.2 Hz, 2H), 1.57 (d, J = 7.2 Hz, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 160.4, 158.0, 152.0, 130.5, 129.5, 129.4, 128.4, 127.9, 127.7, 126.7, 126.1, 125.9, 61.0, 47.5, 18.0, 13.7; HRMS (m/z) (M + Na) calcd for $C_{21}H_{20}N_2O_4Na$ 387.1315, found 387.1314.

2,5-Diphenyl-*N*-(*p*-tolyl)oxazole-4-carboxamide (1n). New compound, a white solid (158 mg, 0.45 mmol, 89%); mp 156–157 °C; R_f = 0.27 (EA–PE 5 : 95); IR (KBr, cm^{-1}) 3363, 3335, 3064, 2918, 1676, 1663, 1597, 1525, 815, 704, 687; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.19 (br, s, 1H), 8.41–8.38 (m, 2H), 8.15–8.13 (m, 2H), 7.64–7.61 (m, 2H), 7.53–7.48 (m, 5H), 7.46–7.42 (m, 1H), 7.18 (d, J = 8.4 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 158.3, 153.0, 135.2, 134.0, 131.1, 130.5, 130.0, 129.5, 128.9, 128.4, 128.3, 127.2, 126.6, 126.3, 120.0, 20.9; HRMS (m/z) (M + Na) calcd for $C_{23}H_{18}N_2O_2Na$ 377.1260, found 377.1254.

2,5-Diphenyloxazole-4-carboxamide (1o). Known compound, a white solid (131 mg, 0.50 mmol, 99%); mp 180–182 °C; R_f = 0.35 (EA–PE 33 : 67); IR (KBr, cm^{-1}) 3451, 3216, 2918, 1697, 1653, 1603, 1488, 1223, 761, 709, 682; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38–8.35 (m, 2H), 8.11–8.07 (m, 2H), 7.51–7.41 (m, 6H), 7.26 (br, s, 1H, overlapped with the peak of chloroform), 5.96 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 158.5, 152.9, 131.0, 130.0, 129.8, 128.9, 128.4, 128.2, 127.1, 126.5, 126.4; HRMS (m/z) (M + Na) calcd for $C_{16}H_{12}N_2O_2Na$ 287.0791, found 287.0791.

Methyl 2,5-diphenyloxazole-4-carboxylate (1p). Known compound, a white solid (126 mg, 0.45 mmol, 90%); mp 85–87 °C; R_f = 0.30 (EA–PE 10 : 90); IR (KBr, cm^{-1}) 3412, 3077, 2951, 1714, 1563, 1489, 1447, 1358, 1227, 1109, 777, 708, 687; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18–8.13 (m, 4H), 7.53–7.47 (m, 6H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 159.3, 154.8, 130.6, 129.9, 128.3, 128.0, 127.9, 127.4, 126.4, 126.3, 125.8, 51.9; HRMS (m/z) (M + Na) calcd for $C_{17}H_{13}NO_3Na$ 302.0788, found 302.0782.

Ethyl 2,5-diphenyloxazole-4-carboxylate (1q). Known compound, a white solid (135 mg, 0.46 mmol, 92%); mp 96–97 °C; R_f = 0.38 (EA–PE 10 : 90); IR (KBr, cm^{-1}) 3408, 3054, 2988, 1716, 1585, 1492, 1445, 1374, 1239, 1224, 1108, 1100, 762, 711, 691; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18–8.15 (m, 2H), 8.13–8.10 (m, 2H), 7.53–7.45 (m, 6H), 4.46 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 159.4, 154.6, 130.6, 129.9, 128.4, 128.1, 128.0, 127.9, 126.7, 126.4, 126.0, 61.1, 13.9; HRMS (m/z) (M + Na) calcd for $C_{18}H_{15}NO_3Na$ 316.0944, found 316.0944.

Isopropyl 2,5-diphenyloxazole-4-carboxylate (1r). New compound, a white solid (146 mg, 0.48 mmol, 95%); mp 61–62 °C; R_f = 0.46 (EA–PE 10 : 90); IR (KBr, cm^{-1}) 3448, 3070, 2977, 2925, 1703, 1560, 1491, 1368, 1222, 1097, 775, 706, 689; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18–8.15 (m, 2H), 8.07–8.05 (m, 2H), 7.51–7.47 (m, 6H), 5.31 (heptet, J = 6.4 Hz, 1H), 1.40 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 160.0, 154.8, 131.1, 130.3, 128.9, 128.8, 128.4, 127.4, 127.0, 126.6, 69.4, 21.9; HRMS (m/z) (M + Na) calcd for $C_{19}H_{17}NO_3Na$ 330.1101, found 330.1101.

Butyl 2,5-diphenyloxazole-4-carboxylate (1s). New compound, a light-yellow solid (138 mg, 0.43 mmol, 86%); mp 55–57 °C; R_f = 0.24 (EA–PE 5 : 95); IR (KBr, cm^{-1}) 3436, 3061, 2959, 2928, 2872, 1718, 1563, 1491, 1212, 1096, 766, 711, 690; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19–8.14 (m, 2H), 8.10–8.07 (m, 2H), 7.53–7.46 (m, 6H), 4.39 (t, J = 7.2 Hz, 2H), 1.81–1.74 (m, 2H), 1.47–1.37 (m, 2H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 159.4, 154.5, 130.6, 129.8, 128.3, 128.1, 127.9, 126.7, 126.4, 126.0, 64.9, 30.2, 18.7, 13.3; HRMS (m/z) (M + Na) calcd for $C_{20}H_{19}NO_3Na$ 344.1257, found 344.1252.

(2-Methyl-5-(*p*-tolyl)oxazol-4-yl)(pyrrolidin-1-yl)methanone (1t). New compound, a colorless semi-solid (134 mg, 0.50 mmol, 99%); R_f = 0.32 (EA–PE 50 : 50); IR (KBr, cm^{-1}) 3423, 2977, 2922, 2869, 1622, 1578, 1509, 1435, 1264, 1100, 895, 831; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 3.65 (t, J = 6.8 Hz, 2H), 3.50 (t, J = 6.8 Hz, 2H), 2.51 (s, 3H), 2.37 (s, 3H), 1.94–1.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 159.1, 149.8, 139.2, 130.1, 129.4, 126.3, 124.9, 48.2, 46.3, 26.2, 24.3, 21.5, 13.9; HRMS (m/z) (M + Na) calcd for $C_{16}H_{18}N_2O_2Na$ 293.1260, found 293.1260.

(2-Methyl-5-phenyloxazol-4-yl)(pyrrolidin-1-yl)methanone (1u). New compound, a white solid (127 mg, 0.50 mmol, 99%); mp 106–108 °C; R_f = 0.45 (EA–PE 80 : 20); IR (KBr, cm^{-1}) 3442, 3070, 2967, 2871, 1623, 1585, 1431, 889, 768; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.36–7.32 (m, 1H), 3.66 (t, J = 6.4 Hz, 2H), 3.52 (t, J = 6.4 Hz, 2H), 2.52 (s, 3H), 1.96–1.84 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 158.9, 149.0, 130.3, 128.5, 128.2, 127.2, 125.8, 47.7, 45.8, 25.7, 23.8, 13.5; HRMS (m/z) (M + Na) calcd for $C_{15}H_{16}N_2O_2Na$ 279.1104, found 279.1104.

2-Phenyl-5,6-dihydrobenzo[*d*]oxazol-7(4*H*)-one (1v). New compound, a white solid (100 mg, 0.47 mmol, 94%); mp 112–114 °C; R_f = 0.38 (EA–PE 25 : 75); IR (KBr, cm^{-1}) 3067, 2944, 1676, 1595, 1536, 1476, 1448, 1401, 1273, 1091, 895, 785, 720, 691; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17–8.15 (m, 2H), 7.56–7.46 (m, 3H), 2.94 (t, J = 6.4 Hz, 2H), 2.66–2.63 (m, 2H), 2.27–2.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.7, 164.6, 156.9, 143.8, 132.1, 128.9, 127.6, 126.1, 38.2, 24.0, 23.2; HRMS (m/z) (M + Na) calcd for $C_{13}H_{11}NO_2Na$ 236.0682, found 236.0689.

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