RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

RSC Advances

RSCPublishing

ARTICLE

Catalyst-free one-pot domino reactions for selective synthesis of functionalized 2,8-oxazabicyclo[3.3.1]-nonanes and 5*H*-indeno[1,2-*b*]pyridin-5-ones†

Cite this: DOI: 10.1039/xoxxoooooox

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

www.rsc.org/

Yin Rao, Meilin Liu, Lu Wu and Guodong Yin*

A simple and efficient method for one-pot synthesis of new functionalized 2,8-oxazabicyclo-[3.3.1]nonanes from easily accessible 2-hydroxychalcones, 4-hydroxycoumarin/1,3-cyclohexandiones and aqueous ammonia under catalyst-free conditions is described. This reaction was probably achieved via an intermolecular Michael addition/amination/intramolecular bicyclization domino process. Hydroxy-containing 5*H*-indeno[1,2-*b*]pyridin-5-ones were obtained when five-membered 1,3-indandione was employed in this reaction.

Introduction

Much attention has been paid to the functionalized oxygen- and nitrogen-containing heterobicyclo[3.3.1]nonanes in recent years due to the unique cleft-shaped structure.[1] They have been widely employed in host-guest chemistry and asymmetric catalysis.[2,3] The development of efficient synthetic routes to this type of rigid molecules has become more significant and challenging.[4–9] In a recent study, we demonstrated a stereoselective synthesis of 2,8-dioxabicyclo [3.3.1]nonanes by the reactions of 2-hydroxychalcones with 4-hydroxycoumarin (or its analogues) and naphthols/ substituted phenols.[10] 2,8-Oxazabicyclo[3.3.1]nonanes, as another kind of important hetero-bicyclic system, are frequently encountered in a variety of natural products and biologically active molecules. For example, alkaloids Larutensine, Naucleamide E and Calycinumine B show excellent antiproliferative, anti-inflammatory and cytotoxic activity against tumor cell lines (Fig. 1).[11–13] In addition, coumarin chemistry has captured the continuous attention of chemists and pharmacists for their biological activities.[14] It is well known that many synthetic drugs, such as warfarin, phenprocoumon, brodifacoum, and arisugacin A are coumarin derivatives.[15] However, only several synthetic methods have thus far been reported for the construction of 2,8-oxazabicyclo[3.3.1]nonane skeleton,[16–18] and coumarin-derived [3.3.1]hetero-bicyclic system are rarely involved. Recently, Yang reported the synthesis of coumarin-fused 2,8-oxazabicyclo[3.3.1]nonane as photochromic colorants by a one-pot multicomponent reaction of *p*-anisidine, *o*-nitrobenzaldehyde and isobutyraldehyde in the presence of *p*-TsOH to form tetrahydroquinoline, followed by treating with 4-hydroxycoumarin.[19] Zhang also reported a fluorous benzaldehyde-based green synthesis of biaryl-substituted oxazabicyclo[3.3.1]nonanes by a multi-step synthesis to form oxazabicycles, then introducing the biaryl group *via* Suzuki coupling reaction.[20] It should be noted that nitrogen-atom is connected to the aromatic ring in these reported coumarin-fused oxazabicyclo[3.3.1]nonanes. In continuation of our efforts to develop new synthetic protocols for constructing rigid bicyclic frameworks,[21] we herein described a clean synthesis of coumarin-fused 2,8-oxazabicyclo[3.3.1]nonanes from easily accessible 2-hydroxychalcones, 4-hydroxycoumarin and aqueous ammonia in a one-pot domino procedure. Nitrogen-atom is connected to the coumarin ring in these molecules. 1,3-Cyclohexanedione and its derivatives were also suitable for this reaction. Nevertheless, five-membered substrate 1,3-indandione delivered the corresponding 5*H*-indeno[1,2-*b*]pyridin-5-ones.

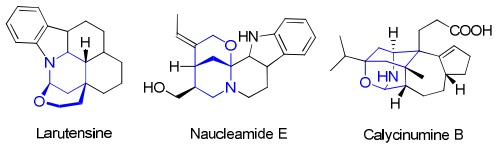


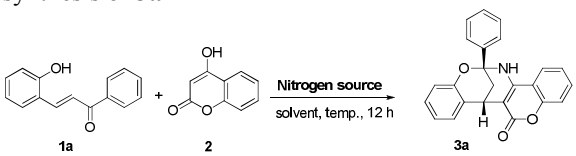
Fig. 1 Examples of natural products

Results and discussion

We initiated our studies on the synthesis of coumarin-fused oxazabicycle 8-phenyl-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (**3a**). As outlined in Table 1, various nitrogen sources, solvents and temperature were examined. When 2-hydroxychalcone (**1a**, 0.5 mmol), 4-hydroxycoumarin (**2**, 0.5 mmol) and ammonium acetate (10 mmol) were heated in ethanol under reflux for 12 h, the desired product **3a** was isolated in 20%

yield (Table 1, entry 1). The structure was confirmed by means of ^{1}H NMR, ^{13}C NMR, HRMS and IR spectra. It was found that 30% mass concentration of aqueous ammonia was more effective for this reaction, affording the product in 38% yield (Table 1, entry 2). This transformation was also attempted in other solvents, such as MeOH, *t*-BuOH, *i*-PrOH and *n*-PrOH, and we found that the higher boiling point solvent gave rise to the higher yield (*n*-PrOH, 72%, Table 1, entries 3–6). The pale yellow solid **3a** crystallized spontaneously when the reaction mixture was cooled to room temperature overnight. Increasing or decreasing the amount of aqueous ammonia both resulted in a low yield (Table 1, entries 7,8). None of the expected product was formed in THF (Table 1, entry 9). In addition, the reactions were also examined in DMSO, DMF, toluene, benzene, MeCN and 1,2-dichloroethane (DCE), **3a** was isolated in 18–41% yield (Table 1, entries 10−15). **3a** was only obtained in 40% yield when no other solvent was used (Table 1, entry 16).

Table 1. Optimization of the reaction conditions for the synthesis of **3a**

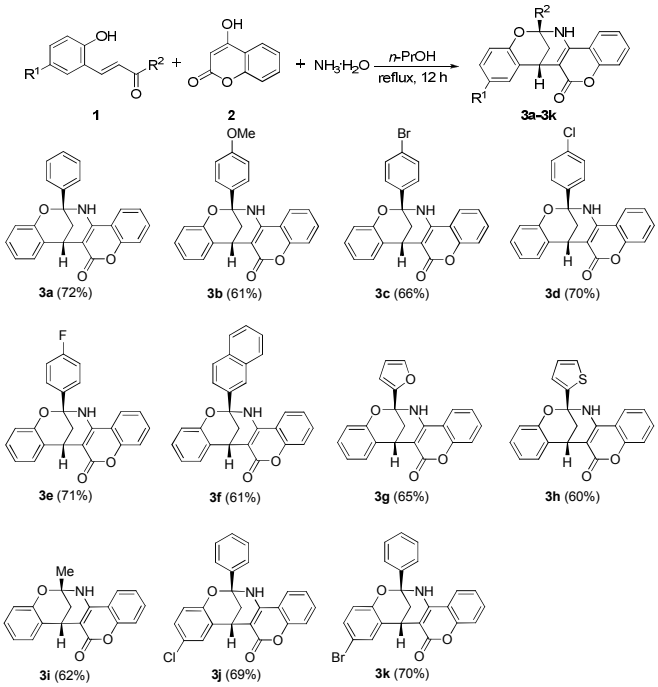


1a 2 3a

Entry[a]	Nitrogen source[b]	Solvent	Temp. (°C)	Yield[c](%)
1	NH_4OAc	EtOH	reflux	20
2	$NH_3·H_2O$	EtOH	reflux	38
3	$NH_3·H_2O$	MeOH	reflux	25
4	$NH_3·H_2O$	*t*-BuOH	reflux	44
5	$NH_3·H_2O$	*i*-PrOH	reflux	42
6	$NH_3·H_2O$	*n*-PrOH	reflux	72
7	$NH_3·H_2O$	*n*-PrOH	reflux	63[d]
8	$NH_3·H_2O$	*n*-PrOH	reflux	50[e]
9	$NH_3·H_2O$	THF	reflux	–[f]
10	$NH_3·H_2O$	DMSO	100	36
11	$NH_3·H_2O$	DMF	100	41
12	$NH_3·H_2O$	Toluene	reflux	38
13	$NH_3·H_2O$	Benzene	reflux	18
14	$NH_3·H_2O$	MeCN	reflux	35
15	$NH_3·H_2O$	DCE	reflux	23
16	$NH_3·H_2O$	none	100	40[g]

[a]All reactions were performed with 2-hydroxychalcone (**1a**, 0.5 mmol), 4-hydroxycoumarin (**2**, 0.5 mmol) and nitrogen source (10 mmol) in an appropriate solvent (5 mL) for 12 h. [b]Aqueous ammonia with a 30% (w/w) concentration. [c]Isolated yield. [d]15 mmol $NH_3·H_2O$ was used. [e]5 mmol $NH_3·H_2O$ was used. [f]None of the expected product was observed. [g]3 mL $NH_3·H_2O$ was used.

With the optimum reaction conditions in hand, a variety of substituted 2-hydroxychalcones (**1**) was subsequently investigated, and the results were summarized in Scheme 1. It was observed that substrates in which R^1 = H and R^2 was a phenyl ring bearing electron-donating substituents (–OCH_3) or electron-withdrawing substituent (–Br, –Cl and –F) gave the corresponding products **3b**–**3e** in 61–71% yields. The substrates for R^2 were naphthalene, furan, and thiophene rings, delivering **3f**–**3h** in 60–65% yields. Moreover, an alkyl group (–CH_3) substrate was also suitable for this transformation with isolation of the product **3i** in 62% yield. To our delight, 5-chloro- and 5-bromo-substituted (R^1) 2-hydroxychalcone also furnished **3j** and **3k** in 69% and 70% yields respectively.



Scheme 1 Scope of 2-hydroxychalcone derivatives. Reaction conditions: 2-hydroxychalcones (**1**, 0.5 mmol), 4-hydroxycoumarin (**2**, 0.5 mmol) and aqueous ammonia (10 mmol) in *n*-propanol (5 mL) under reflux for 12 h. Isolated yield.

Next, we further extended the substrates to 1,3-cyclohexandione (**4a**, R^3 = R^4 = H) for the preparation of the structurally diverse and functionalized 2,8-oxazabicyclo[3.3.1]nonane library (Scheme 2). It was found that the expected products **5a**–**5d** were obtained in 60–71% yields. In addition, substrates 5,5-dimethyl-1.3-cyclohexanedione (**4b**, R^3 = R^4 = CH_3) also gave the corresponding products **5e**–**5j** in satisfactory yields (63–72%). The steric configuration of **5e** was further clarified by X-ray single-crystal diffraction analysis (Fig. 2).[22] When 5-methyl-1,3-cyclohexanedione (**4c**, R^3 = CH_3, R^4 = H) was employed in this reaction, cyclohexanedione-fused 2,8-oxazabicyclo[3.3.1]nonanes **5k**–**5n** were obtained in 65–71% yields with an approximate diastereometric ratio of 1:1 according to NMR spectrum analysis.

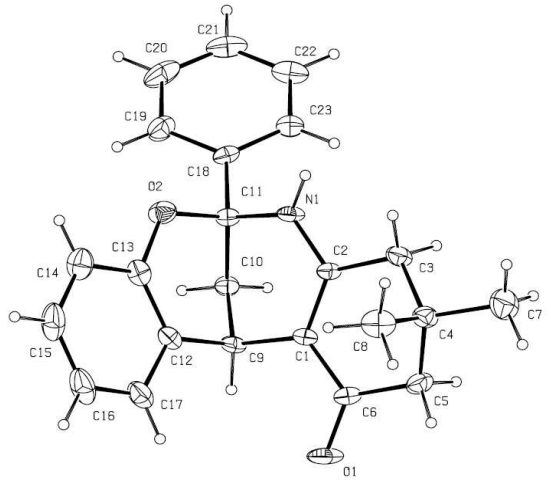
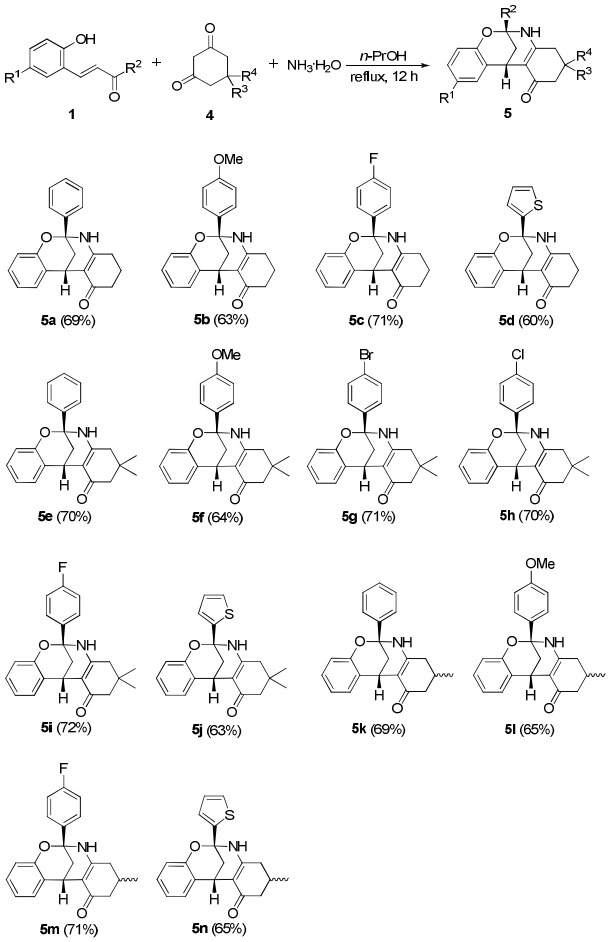
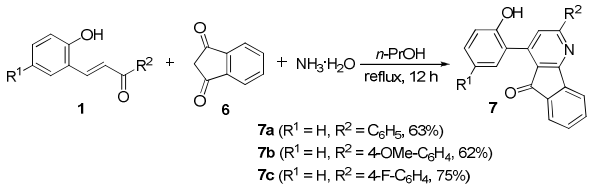


Fig. 2 X-ray structure of **5e**†.



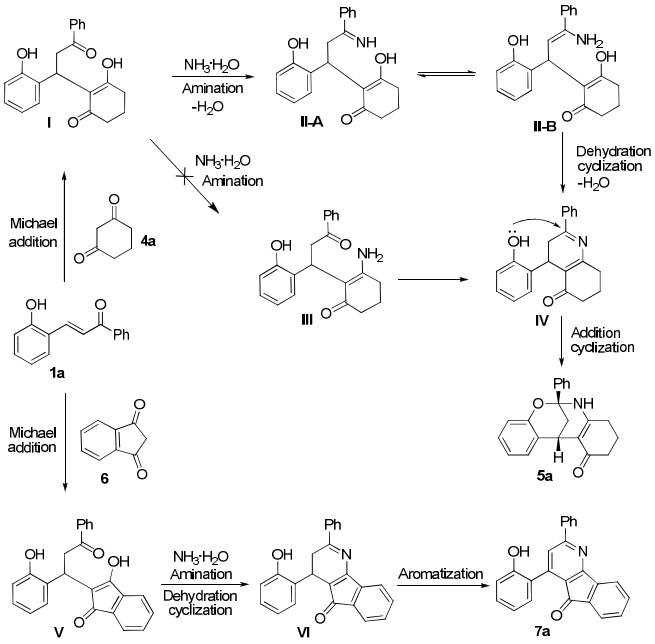
Scheme 2 Scope of 1,3-diones. Reaction conditions: 2-hydroxychalcones (**1**, 0.5 mmol), 1,3-cyclohexandiones (**4b–4c**, 0.5 mmol) and aqueous ammonia (10 mmol) in *n*-propanol (5 mL) under reflux for 12 h. Isolated yield.

Next, five-membered substrate 1,3-indandione (**6**) was also used to react with 2-hydroxychalcones in the presence of aqueous ammonia, as shown in Scheme 3. It was found that the expected oxazabicyclo[3.3.1]nonane did not form, and the reaction gave 4-(2-hydroxyphenyl)-2-phenyl-5*H*-indeno[1,2-*b*]pyridin-5-one (**7a**) in 63% yield. The 2-position hydroxyl group of **1a** did not participate in the reaction, probably due to the effect of the ring strain of 1,3-indandione. Moreover, we use the substrates in which R^1 = H and R^2 was a phenyl ring bearing electron-donating substituent (–OCH_3) or electron-withdrawing substituent (–F) also smoothly furnished the corresponding products **7b** and **7c** in 62% and 75% yields respectively.

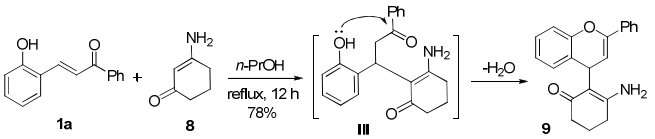


Scheme 3 Reaction conditions: 2-hydroxychalcones (**1**, 0.5 mmol), 1,3-indandione (**6**, 0.5 mmol) and aqueous ammonia (10 mmol) in *n*-propanol (5 mL) under reflux for 12 h. Isolated yield.

A possible domino reaction mechanism was proposed as shown in Scheme 4. First, intermediate **I** was formed through Michael addition reaction between 2-hydroxychalcone (**1a**) and 1,3-cyclohexanedione (**4a**).[10a,23] One possible pathway was that intermediate **I** was reacted with ammonia to form intermediate **III** by amination substitution reaction of the hydroxyl group (-OH),[24] which was converted to intermediate **IV** via an intramolecular cyclization process after loss of water. Finally, **5a** was formed by a spontaneous addition intramolecular cyclization process.[25] However, we were failed to isolate the intermediates during the reaction process. In order to further confirm this reaction process, 2-hydroxychalcone and 3-aminocyclohex-2-enone (**8**) was heated in refluxing *n*-PrOH for 12 h, and it was found the expected product **5a** was not formed. The unexpected 4-substituted 4*H*-chromene (**9**) was obtained in 78% isolated yield (Scheme 5). Obviously, intermediate **III** was formed during the reaction, but the hydroxyl group was first attacked the carbonyl group (C=O) to deliver the dehydration product **9**. Therefore, we believe that product **5a** was formed without involving the intermediate **III**. The other possible pathway was that intermediate **I** was directly converted to imine intermediate **II-A**, which could be isomerized to **II-B**. The latter gave the corresponding dehydration cyclization intermediate **IV,** sequentially delivering the target molecule **5a**. Similarly, when 1,3-indandione (**6**) was employed, the reaction afforded the corresponding intermediate **VI** by subsequent intermolecular Michael addition-amination-dehydration cyclization process, which could be easily oxidized to more thermodynamic stable π-conjugated structure 5*H*-indeno[1,2-*b*]pyridin-5-one **7a** in the presence of air.[26]



Scheme 4 The possible reaction mechanism.



Scheme 5

Conclusions

In summary, we have described a simple and efficient method for the stereoselective synthesis of new coumarin- and cyclohexandione-fused 2,8-oxazabicyclo[3.3.1]nonane derivatives from 2-hydroxychalcones, 4-hydroxy coumarin/1,3-cyclohexandiones and aqueous ammonia. This reaction was probably achieved via an intermolecular Michael addition/amination/intramolecular bicyclization domino process. Functionalized hydroxy-containing 5*H*-indeno[1,2-*b*]pyridin-5-ones were obtained when five-membered 1,3-indandione was employed in this reaction. The hydroxyl group of substrate **1** did not participate in the reaction probably due to the effect of the ring strain. All these reported compounds were unknown and characterized by means of ^{1}H NMR, ^{13}C NMR, HRMS and IR spectra. The structure and steric configuration of **5e** were further clarified by X-ray single-crystal diffraction analysis. The prominent advantages of this approach are easily available starting materials, a wide scope of substrates, mild reaction conditions, ease of purification and catalyst-free conditions. Further investigations on the applications of this transformation to other bicyclic systems are currently underway in our laboratory.

Experimental

General information

All the chemicals were commercially available and used without further purification. All the organic solvents were dried and freshly distilled before use. ^{1}H and ^{13}C NMR spectra were recorded using Bruker AV 300 MHz spectrometers with $CDCl_3$ or DMSO-d_6 as the solvent. Chemical shifts are reported relative to TMS (internal standard). High resolution mass spectra were recorded using a Waters GCT Premier (ESI) or a Bruker ultrafleXtreme MALDI-TOF/TOF (HCCA matrix). IR spectra were obtained as KBr pellet samples using a Nicolet 5700 FTIR spectrometer. Melting points were determined using an uncorrected X-4 apparatus. The X-ray crystal structure determination was performed using a Bruker SMART APEX CCD system.

General one-pot procedure for the synthesis of 3 and 5

A mixture of 2-hydroxychalcones (**1**, 0.5 mmol), 4-hydroxycoumarin (**2**, 0.5 mmol)/substituted 1,3-cyclohexandiones (**4**, 0.5 mmol) and 30% aqueous ammonia (10 mmol, w/w) was heated in *n*-propanol (5 mL) under reflux. After the reaction was completed (12 h, monitored by thin layer chromatography), the mixture was slowly cooled to room temperature overnight. Then crystals precipitated, which were filtrated and washed with a small amount of anhydrous ethanol to give the products **3** and **5** respectively.

8-Phenyl-7,8-dihydro-8,14-methanobenzo[*g*]chromeno [4,3-*d*][1,3]oxazocin-1(14*H*)-one (3a). White solid, 132 mg, yield 72%; mp 286–288 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.58–7.45 (m, 5H), 7.30–7.27 (m, 1H), 7.23–7.11 (m, 3H), 6.95–6.90 (m, 2H), 6.09 (s, 1H), 4.51 (t, *J* = 3.0 Hz, 1H), 2.43–2.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 152.5, 151.6, 146.0, 141.5, 131.5, 129.1, 128.9, 128.8, 127.8, 126.0, 125.7, 123.6, 121.3, 119.7, 117.7, 116.5, 113.3, 101.1, 83.6, 33.7, 28.6; IR (KBr) *v* 3435, 2026, 1660, 1614, 1524, 1475, 1390, 1104, 885, 751, 621 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{18}NO_3$ $[M+H]^+$ 368.1281, found 368.1278.

8-(4-Methoxyphenyl)-7,8-dihydro-8,14-methanobenzo[*g*] chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3b). White solid, 121 mg, yield 61%; mp 274–276 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71–7.66 (m, 2H), 7.50–7.45 (m, 1H), 7.30–7.27 (m, 1H), 7.24–7.11 (m, 3H), 7.04–6.99 (m, 2H), 6.95–6.90 (m, 2H), 6.08 (s, 1H), 4.50 (t, *J* = 2.9 Hz, 1H), 3.88 (s, 1H), 2.40–2.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 160.1, 152.5, 151.7, 146.0, 133.6, 131.5, 128.8, 127.8, 127.0, 126.1, 123.6, 121.2, 119.7, 117.7, 116.5, 114.1, 113.4, 101.0, 83.4, 55.4, 33.7, 28.7; IR (KBr) ν 3437, 2027, 1664, 1614, 1521, 1470, 1390, 1104, 886, 824, 754, 621 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{25}H_{20}NO_4$ $[M+H]^+$ 398.1387, found 398.1398.

8-(4-Bromophenyl)-7,8-dihydro-8,14-methanobenzo[*g*] chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3c). White

solid, 147 mg, yield 66%; mp 290–291 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.61 (m, 4H), 7.56–7.48 (m, 2H), 7.33–7.29 (m, 2H), 7.25–7.13 (m, 2H), 6.99–6.91 (m, 2H), 6.02 (s, 1H), 4.51 (s, 1H), 2.41–2.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 152.6, 151.4, 145.9, 140.6, 132.0, 131.7, 128.8, 127.9, 127.6, 125.8, 123.7, 123.4, 121.5, 119.7, 117.8, 116.5, 113.3, 101.4, 83.3, 33.6, 28.5; IR (KBr) ν 3433, 3294, 2026, 1667, 1616, 1530, 1475, 1391, 1105, 997, 890, 823, 755, 622 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{17}BrNO_3$ $[M+H]^+$ 446.0386, found 446.0397.

8-(4-Chlorophenyl)-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3d). White solid, 140 mg, yield 70%; mp 291–292 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.71 (m, 2H), 7.57–7.46 (m, 4H), 7.32–7.28 (m, 2H), 7.24–7.12 (m, 2H), 6.98–6.91 (m, 2H), 6.06 (s, 1H), 4.51 (t, *J* = 3.0 Hz, 1H), 2.40–2.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 152.6, 151.4, 145.9, 140.1, 135.2, 131.7, 129.0, 128.8, 127.9, 127.3, 125.9, 123.7, 121.5, 119.7, 117.8, 116.5, 113.3, 101.4, 83.3, 33.7, 28.5; IR (KBr) ν 3433, 2026, 1666, 1616, 1529, 1477, 1391, 1104, 757, 621 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{17}ClNO_3$ $[M+H]^+$ 402.0891, found 402.0897.

8-(4-Fluorophenyl)-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3e). White solid, 137 mg, yield 71%; mp 286–287 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.73 (m, 2H), 7.57–7.47 (m, 2H), 7.32–7.29 (m, 2H), 7.23–7.12 (m, 4H), 6.97–6.91 (m, 2H), 6.05 (s, 1H), 4.51 (t, *J* = 2.9 Hz, 1H), 2.41–2.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0 (d, $^1J_{C-F}$ = 247.2 Hz), 161.0, 152.5, 151.5, 145.9, 137.4 (d, $^4J_{C-F}$ = 2.9 Hz), 131.6, 128.8, 127.9, 127.8 (d, $^3J_{C-F}$ = 8.3 Hz), 125.9, 123.7, 121.4, 119.7, 117.8, 116.4, 115.7 (d, $^2J_{C-F}$ = 21.5 Hz), 113.3, 101.3, 83.3, 33.8, 28.6; IR (KBr) ν 3432, 2026, 1665, 1617, 1525, 1474, 1391, 1104, 755, 621 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{17}FNO_3$ $[M+H]^+$ 386.1187, found 386.1182.

8-(Naphthalen-2-yl)-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3f). Brown solid, 127 mg, yield 61%; mp 267–268 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31–8.30 (m, 1H), 7.99–7.91 (m, 3H), 7.81–7.77 (m, 1H), 7.60–7.57 (m, 3H), 7.52–7.47 (m, 1H), 7.32–7.29 (m, 2H), 7.22–7.14 (m, 2H), 7.02–6.92 (m, 2H), 6.22 (s, 1H), 4.55 (t, *J* = 2.9 Hz, 1H), 2.50–2.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 152.6, 151.7, 146.0, 138.6, 133.3, 133.0, 131.6, 128.9, 128.8, 128.5, 127.9, 127.7, 127.0, 126.8, 126.1, 125.2, 123.6, 123.2, 121.4, 119.8, 117.7, 116.5, 113.4, 101.2, 83.7, 33.6, 28.6; IR (KBr) ν 3429, 3300, 2026, 1665, 1615, 1528, 1472, 1391, 1105, 889, 815, 751, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{28}H_{20}NO_3$ $[M+H]^+$ 418.1438, found 418.1445.

8-(Furan-2-yl)-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3g). White solid, 116 mg, yield 65%; mp 257–258 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (s, 1H), 8.19–8.16 (m, 1H), 7.80–7.79 (m, 1H), 7.61–7.55 (m, 1H), 7.35–7.29 (m, 3H), 7.15–7.09 (m, 1H), 6.93–6.85 (m, 2H), 6.81–6.80 (m, 1H), 6.61–6.59 (m, 1H), 4.32 (t, *J* = 2.9 Hz, 1H), 2.45–2.40 (m, 1H), 2.31–2.26 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.5, 152.7, 152.4, 151.7, 147.0, 143.7, 132.3, 128.6, 128.1, 126.7, 124.1, 123.5, 121.3, 117.2, 116.8, 113.9, 111.2, 108.7, 100.5, 80.8, 31.0, 27.9; IR (KBr) ν 3434, 3265, 2026, 1664, 1617, 1530, 1474, 1392, 1103, 884, 749, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{22}H_{16}NO_4$ $[M+H]^+$ 358.1074, found 358.1066.

8-(Thiophen-2-yl)-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3h). Brown solid, 112 mg, yield 60%; mp 264–265 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.21 (s, 1H), 8.19–8.17 (m, 1H), 7.65–7.56 (m, 2H), 7.36–7.28 (m, 4H), 7.15–7.11 (m, 2H), 6.96–6.87 (m, 2H), 4.30 (s, 1H), 2.42–2.31 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.6, 152.5, 151.9, 147.3, 145.7, 132.4, 128.6, 128.2, 127.8, 127.0, 126.8, 126.3, 124.2, 123.6, 121.5, 117.2, 116.9, 114.0, 100.4, 83.4, 35.1, 28.8; IR (KBr) ν 3433, 2026, 1616, 1525, 1388, 1104, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{22}H_{16}NO_3S$ $[M+H]^+$ 374.0845, found 374.0851.

8-Methyl-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3i). White solid, 95 mg, yield 62%; mp 317–318 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52–7.44 (m, 2H), 7.32–7.28 (m, 2H), 7.23–7.17 (m, 1H), 7.11–7.06 (m, 1H), 6.89–6.81 (m, 2H), 5.87 (s, 1H), 4.47 (t, *J* = 2.9 Hz, 1H), 2.36–2.30 (m, 1H), 2.11–2.06 (m, 1H), 1.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 152.5, 151.7, 145.7, 131.4, 128.8, 127.7, 126.0, 123.5, 121.0, 119.7, 117.7, 116.1, 113.2, 100.9, 80.9, 31.3, 28.2, 27.6; IR (KBr) ν 3434, 2026, 1655, 1614, 1533, 1390, 1206, 1104, 874, 752, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{19}H_{16}NO_3$ $[M+H]^+$ 306.1125, found 306.1126.

12-Chloro-8-phenyl-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3j). White solid, 138 mg, yield 69%; mp 297–298 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (s, 1H), 8.20–8.18 (m, 1H), 7.76–7.73 (m, 2H), 7.62–7.56 (m, 1H), 7.54–7.43 (m, 3H), 7.36–7.28 (m, 3H), 7.20–7.17 (m, 1H), 7.07–7.04 (m, 1H), 4.28 (t, *J* = 2.9 Hz, 1H), 2.33–2.19 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.6, 152.5, 151.4, 148.0, 141.7, 132.5, 129.1, 128.9, 127.8, 127.7, 126.7, 124.5, 124.2, 123.6, 118.8, 117.3, 114.1, 99.3, 84.6, 33.8, 28.7; IR (KBr) ν 3435, 3286, 2026, 1665, 1615, 1527, 1473, 1105, 885, 756, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{17}ClNO_3$ $[M+H]^+$ 402.0891, found 402.0878.

12-Bromo-8-phenyl-7,8-dihydro-8,14-methanobenzo[*g*]chromeno[4,3-*d*][1,3]oxazocin-1(14*H*)-one (3k). White solid, 156 mg, yield 70%; mp 293–294 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (s, 1H), 8.20–8.18 (m, 1H), 7.75–7.73 (m, 2H), 7.62–7.57 (m, 1H), 7.51–7.44 (m, 4H), 7.37–7.29 (m, 3H), 7.02–6.99 (m, 1H), 4.28 (s, 1H), 2.33–2.19 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.6, 152.5, 151.8, 147.9, 141.6, 132.4, 130.6, 130.5, 129.6, 129.0, 128.8, 126.6,

124.2, 123.5, 119.2, 117.3, 114.0, 112.2, 99.3, 84.6, 33.7, 28.6; IR (KBr) ν 3434, 3290, 2026, 1664, 1616, 1527, 1474, 1399, 1107, 998, 887, 816, 757, 691, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{17}BrNO_3$ $[M+H]^+$ 446.0386, found 446.0393.

6-Phenyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo [*d*,*g*][1,3]oxazocin-11(7*H*)-one (5a). White solid, 109 mg, yield 69%; mp 268–269 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71–7.68 (m, 2H), 7.49–7.39 (m, 4H), 7.14–7.08 (m, 1H), 6.98–6.96 (m, 1H), 6.89–6.84 (m, 1H), 5.44 (s, 1H), 4.40 (t, *J* = 2.9 Hz, 1H), 2.50–1.83 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 156.1, 151.7, 141.8, 128.9, 128.8, 128.7, 127.5, 127.0, 125.5, 120.8, 116.2, 112.3, 83.7, 36.3, 34.0, 28.2, 26.6, 21.4; IR (KBr) ν 3423, 3240, 2940, 2026, 1584, 1510, 1387, 1108, 1031, 914, 757, 696, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$ 318.1489, found 318.1482.

6-(4-Methoxyphenyl)-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5b). Brown solid, 109 mg, yield 63%; mp 244–245 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63–7.58 (m, 2H), 7.42–7.39 (m, 1H), 7.13–7.08 (m, 1H), 6.98–6.93 (m, 3H), 6.89–6.83 (m, 1H), 5.37 (s, 1H), 4.39 (s, 1H), 3.85 (s, 3H), 2.48–1.87 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 159.8, 156.1, 151.8, 134.0, 128.9, 127.5, 127.0, 126.8, 120.8, 116.1, 113.9, 112.2, 83.6, 55.4, 36.3, 34.1, 28.2, 26.6, 21.4; IR (KBr) ν 3432, 3237, 2956, 2027, 1582, 1508, 1386, 1107, 1035, 928, 829, 759, 697, 617 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{22}H_{22}NO_3$ $[M+H]^+$ 348.1594, found 348.1583.

6-(4-Fluorophenyl)-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5c). White solid, 119 mg, yield 71%; mp 266–267 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.72–7.65 (m, 2H), 7.42–7.39 (m, 1H), 7.17–7.09 (m, 3H), 6.98–6.95 (m, 1H), 6.90–6.85 (m, 1H), 5.33 (s, 1H), 4.40 (t, *J* = 3.0 Hz, 1H), 2.50–1.86 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 162.8 (d, $^1J_{C-F}$ = 246.5 Hz), 155.9, 151.6, 137.7 (d, $^4J_{C-F}$ = 3.1 Hz), 128.9, 127.5 (d, $^3J_{C-F}$ = 8.2 Hz), 127.4, 127.1, 121.0, 116.1, 115.5 (d, $^2J_{C-F}$ = 21.5 Hz), 112.3, 83.4, 36.3, 34.2, 28.2, 26.6, 21.4; IR (KBr) ν 3431, 3243, 2026, 1583, 1504, 1387, 1106, 754, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{21}H_{19}FNO_2$ $[M+H]^+$ 336.1394, found 336.1384.

6-(Thiophen-2-yl)-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5d). Brown solid, 97 mg, yield 60%; mp 302–303 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.35 (m, 2H), 7.24–7.23 (m, 1H), 7.13–7.05 (m, 2H), 6.96–6.85 (m, 2H), 5.47 (s, 1H), 4.42–4.41 (m, 1H), 2.48–1.86 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.5, 155.4, 151.4, 145.8, 128.9, 127.2, 127.1, 127.0, 126.1, 124.6, 121.1, 116.2, 112.5, 82.7, 36.3, 34.7, 28.2, 26.6, 21.3; IR (KBr) ν 3439, 3221, 2026, 1586, 1507, 1387, 1103, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{19}H_{18}NO_2S$ $[M+H]^+$ 324.1053, found 324.1046.

9,9-Dimethyl-6-phenyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5e). Yellow solid, 121 mg, yield 70%; mp 248–250 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.67 (m, 2H), 7.49–7.37 (m, 4H), 7.12–7.07 (m, 1H), 6.98–6.95 (m, 1H), 6.88–6.83 (m, 1H), 5.43 (s, 1H), 4.39 (t, *J* = 2.9 Hz, 1H), 2.31–2.07 (m, 6H), 1.09 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.9, 155.0, 151.6, 141.8, 128.7, 128.6, 128.5, 127.4, 126.9, 125.5, 120.8, 116.2, 110.7, 83.8, 50.0, 41.9, 34.1, 32.8, 28.3, 28.1, 26.5; IR (KBr) ν 3434, 3247, 2026, 1596, 1389, 1105, 756, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1802, found 346.1812.

6-(4-Methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5f). White solid, 120 mg, yield 64%; mp 221–223 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62–7.57 (m, 2H), 7.41–7.38 (m, 1H), 7.12–7.06 (m, 1H), 6.99–6.94 (m, 3H), 6.88–6.82 (m, 1H), 5.28 (s, 1H), 4.39 (t, *J* = 2.9 Hz, 1H), 3.85 (s, 3H), 2.29–2.05 (m, 6H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.9, 159.8, 154.6, 151.7, 134.0, 128.7, 127.4, 126.9, 126.8, 120.8, 116.2, 113.9, 110.9, 83.7, 55.4, 50.1, 42.1, 34.2, 32.9, 28.4, 28.1, 26.6; IR (KBr) ν 3434, 3246, 2026, 1585, 1510, 1390, 1105, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{24}H_{26}NO_3$ $[M+H]^+$ 376.1907, found 376.1915.

6-(4-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5g). White solid, 150 mg, yield 71%; mp 278–279 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60–7.54 (m, 4H), 7.40–7.37 (m, 1H), 7.44–7.36 (m, 3H), 7.13–7.07 (m, 1H), 6.96–6.94 (m, 1H), 6.89–6.83 (m, 1H), 5.31 (s, 1H), 4.38 (t, *J* = 3.0 Hz, 1H), 2.31–2.05 (m, 6H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.0, 154.4, 151.4, 141.0, 131.8, 128.8, 127.4, 127.2, 127.0, 123.0, 121.0, 116.2, 111.1, 83.6, 50.1, 42.0, 34.1, 32.8, 28.4, 28.0, 26.5; IR (KBr) ν 3434, 3243, 2959, 2026, 1585, 1516, 1391, 1105, 825, 760, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{23}H_{23}BrNO_2$ $[M+H]^+$ 424.0907, found 424.0908.

6-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one (5h). White solid, 133 mg, yield 70%; mp 272–273 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.67 (m, 2H), 7.64–7.60 (m, 2H), 7.44–7.36 (m, 3H), 7.13–7.07 (m, 1H), 6.96–6.94 (m, 1H), 6.89–6.83 (m, 1H), 5.36 (s, 1H), 4.38 (t, *J* = 3.0 Hz, 1H), 2.31–2.05 (m, 6H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.0, 154.5, 151.4, 140.4, 134.8, 128.8, 128.7, 127.2, 127.1, 127.0, 121.0, 116.2, 111.0, 83.6, 50.8, 42.0, 34.2, 32.8, 28.4, 28.0, 26.5; IR (KBr) ν 3430, 3243, 3020, 2957, 2026, 1584, 1517, 1392, 1298, 1257, 1216, 1107, 1023, 974, 911, 827, 759, 719, 621 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{23}H_{23}ClNO_2$ $[M+H]^+$ 380.1412, found 380.1421.

6-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d*,*g*][1,3]oxazocin-11(7*H*)-one

(5i). White solid, 131 mg, yield 72%; mp 255–256 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.64 (m, 2H), 7.39–7.36 (m, 1H), 7.16–7.07 (m, 3H), 6.96–6.94 (m, 1H), 6.88–6.83 (m, 1H), 5.39 (s, 1H), 4.38 (t, J = 3.0 Hz, 1H), 2.31–2.04 (m, 6H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.0, 162.8 (d, $^1J_{C–F}$ = 246.5 Hz), 154.6, 151.5, 137.8 (d, $^4J_{C–F}$ = 3.2 Hz), 128.7, 127.5 (d, $^3J_{C–F}$ = 8.3 Hz), 127.3, 127.0, 121.0, 116.2, 115.5 (d, $^2J_{C–F}$ = 21.4 Hz), 110.9, 83.6, 50.1, 42.0, 34.3, 32.8, 28.4, 28.1, 26.5; IR (KBr) ν 3434, 3251, 2958, 2026, 1585, 1510, 1392, 1215, 1107, 911, 834, 759, 620 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{23}H_{23}FNO_2$ $[M+H]^+$ 364.1707, found 364.1707.

9,9-Dimethyl-6-(thiophen-2-yl)-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d,g*][1,3]oxazocin-11(7*H*)-one (5j). White solid, 111 mg, yield 63%; mp 251–253 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.34 (m, 2H), 7.23–7.22 (m, 1H), 7.11–7.04 (m, 2H), 6.94–6.83 (m, 2H), 5.50 (s, 1H), 4.40 (t, J = 2.9 Hz, 1H), 2.41–2.05 (m, 6H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.1, 154.0, 151.3, 145.8, 128.7, 127.1, 127.0, 126.9, 126.1, 124.5, 121.0, 116.2, 111.2, 82.8, 50.1, 41.9, 34.7, 32.8, 28.4, 28.1, 26.6; IR (KBr) ν 3435, 3232, 2954, 2026, 1594, 1511, 1388, 1211, 1106, 899, 835, 708, 618 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{21}H_{22}NO_2S$ $[M+H]^+$ 352.1366, found 352.1359.

9-Methyl-6-phenyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d,g*][1,3]oxazocin-11(7*H*)-one (5k). White solid, 114 mg, yield 69%; mp 256–257 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72–7.66 (m, 2H), 7.49–7.35 (m, 4H), 7.14–7.08 (m, 1H), 6.98–6.96 (m, 1H), 6.89–6.83 (m, 1H), 5.42 (s, 1H), 4.41–4.35 (m, 1H), 2.46–1.93 (m, 7H), 1.08–0.97 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.5, 193.4, 155.7, 155.6, 151.7, 151.6, 141.9, 141.8, 128.9, 128.8, 128.7, 128.6, 127.5, 127.4, 127.0, 126.9, 125.5, 125.4, 120.9, 120.8, 116.2, 116.1, 111.8, 111.7, 83.8, 83.7, 44.7, 44.6, 36.6, 36.1, 34.3, 33.8, 29.6, 28.4, 26.7, 26.5, 21.1, 21.0; IR (KBr) ν 3417, 3234, 2026, 1624, 1585, 1515, 1388, 1104, 756, 618 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{22}H_{21}NO_2Na$ $[M+Na]^+$ 354.1465, found 354.1458.

6-(4-Methoxyphenyl)-9-methyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d,g*][1,3]oxazocin-11(7*H*)-one (5l). White solid, 117 mg, yield 65%; mp 242–243 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64–7.57 (m, 2H), 7.44–7.35 (m, 1H), 7.13–7.07 (m, 1H), 6.97–6.94 (m, 3H), 6.88–6.82 (m, 1H), 5.37 (s, 1H), 4.40–4.34 (m, 1H), 3.85 (s, 1H), 2.45–1.96 (m, 7H), 1.04–0.97 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 193.3, 159.8, 155.7, 155.6, 151.8, 151.7, 134.0, 133.9, 128.8, 127.5, 127.4, 127.0, 126.8, 126.7, 120.8, 120.7, 116.2, 116.0, 113.9, 111.8, 111.7, 83.7, 83.6, 55.4, 44.7, 44.6, 36.6, 36.1, 34.4, 33.9, 29.6, 28.4, 26.8, 26.6, 21.1, 21.0; IR (KBr) ν 3419, 3235, 2026, 1622, 1585, 1511, 1389, 1103, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{23}H_{23}NO_3Na$ $[M+Na]^+$ 384.1570, found 384.1569.

6-(4-Fluorophenyl)-9-methyl-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d,g*][1,3]oxazocin-11(7*H*)-one (5m). White solid, 124 mg, yield 71%; mp 250–251 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71–7.64 (m, 2H), 7.44–7.35 (m, 1H), 7.16–7.08 (m, 3H), 6.97–6.94 (m, 1H), 6.90–6.84 (m, 1H), 5.33–5.31 (m, 1H), 4.41–4.35 (m, 1H), 2.46–1.94 (m, 7H), 1.04–0.97 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.5, 193.4, 162.8 (d, $^1J_{C–F}$ = 246.6 Hz), 155.6, 155.5, 151.6, 151.5, 137.8 (d, $^4J_{C–F}$ = 3.1 Hz), 137.7 (d, $^4J_{C–F}$ = 2.9 Hz), 128.8, 127.6 (d, $^3J_{C–F}$ = 8.2 Hz), 127.5 (d, $^3J_{C–F}$ = 8.2 Hz), 127.4, 127.3, 127.1, 127.0, 121.0, 120.9, 116.2, 116.0, 115.5 (d, $^2J_{C–F}$ = 21.4 Hz), 111.9, 111.8, 83.5, 83.4, 44.7, 44.6, 36.6, 36.1, 34.5, 34.0, 29.6, 28.4, 26.7, 26.5, 21.1, 21.0; IR (KBr) ν 3437, 3245, 2026, 1584, 1509, 1391, 1212, 1103, 619 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{22}H_{21}FNO_2$ $[M+H]^+$ 350.1551, found 350.1550.

9-Methyl-6-(thiophen-2-yl)-8,9,10,12-tetrahydro-6*H*-6,12-methanodibenzo[*d,g*][1,3]oxazocin-11(7*H*)-one (5n). Brown solid, 110 mg, yield 65%; mp 253–254 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.34 (m, 2H), 7.25–7.21 (m, 1H), 7.13–7.04 (m, 2H), 6.95–6.92 (m, 1H), 6.89–6.83 (m, 1H), 5.48 (s, 1H), 4.42–4.37 (m, 1H), 2.46–1.94 (m, 7H), 1.04–0.99 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.6, 193.5, 155.1, 155.0, 151.4, 151.3, 145.9, 145.8, 128.8, 127.3, 127.2, 127.1, 127.0, 126.1, 124.6, 124.5, 121.1, 121.0, 116.3, 116.1, 112.1, 112.0, 82.8, 82.7, 44.7, 44.6, 36.5, 36.0, 34.9, 34.5, 29.6, 28.4, 26.8, 26.5, 21.1, 21.0; IR (KBr) ν 3439, 3226, 3013, 2025, 1584, 1513, 1389, 1253, 1213, 1105, 711, 618 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{20}H_{20}NO_2S$ $[M+H]^+$ 338.1209, found 338.1209.

General one-pot procedure for the synthesis of 7

A mixture of 2-hydroxychalcones (**1**, 0.5 mmol), 1,3-indandione (**6**, 0.5 mmol) and 30% aqueous ammonia (10 mmol, w/w) was heated in *n*-propanol (5 mL) under reflux. After the reaction was completed (12 h, monitored by thin layer chromatography), the mixture was slowly cooled to room temperature and purified by column chromatography using petroleum ether–ethyl acetate (10:1, v/v) to deliver the product **7** as the yellow solids.

4-(2-Hydroxyphenyl)-2-phenyl-5*H*-indeno[1,2-*b*]pyridin-5-one (7a). Yellow solid, 110 mg, yield 63%; mp 197–199 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.75 (s, 1H), 8.29–8.26 (m, 2H), 7.99–7.97 (m, 1H), 7.80–7.71 (m, 2H), 7.65–7.63 (m, 1H), 7.57–7.52 (m, 4H), 7.39–7.28 (m, 2H), 6.98–6.89 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.4, 165.3, 160.1, 155.4, 146.5, 142.8, 138.1, 135.7, 135.5, 131.9, 131.0, 130.9, 130.7, 129.4, 127.8, 124.1, 123.8, 123.2, 122.6, 121.1, 119.2, 116.1; IR (KBr) ν 3362, 3055, 2922, 1691, 1583, 1541, 1459, 1364, 1271, 1246, 742, 686 cm^{-1}; HRMS *m/z* (ESI) calcd for $C_{24}H_{15}NO_2Na$ $[M+Na]^+$ 372.0995, found 372.0998.

4-(2-Hydroxyphenyl)-2-(4-methoxyphenyl)-5*H*-indeno [1,2-*b*]pyridin-5-one (7b). Yellow solid, 118 mg, yield 62%; mp 239–241 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.71 (s, 1H), 8.32–8.24 (m, 2H), 7.97–7.95 (m, 1H), 7.74–7.70 (m, 2H), 7.63–7.61 (m, 1H), 7.56–7.51 (m, 1H), 7.37–7.28 (m,

2H), 7.11–7.08 (m, 2H), 6.97–6.89 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.4, 165.3, 161.6, 159.9, 155.4, 146.4, 142.8, 135.6, 135.5, 131.8, 131.0, 130.8, 130.5, 129.4, 123.7, 123.4, 123.3, 121.4, 121.0, 119.2, 116.1, 114.8, 55.8; IR (KBr) ν 3421, 2948, 2835, 1718, 1604, 1553, 1460, 1368, 1238, 1177, 1034, 758 cm^{-1}; HRMS *m/z* (ESI) calcd for $C_{25}H_{17}NO_3Na$ $[M+Na]^+$ 402.1101, found 402.1102.

4-(2-Hydroxyphenyl)-2-(4-methoxyphenyl)-5*H*-indeno [1,2-*b*]pyridin-5-one (7c). Yellow solid, 138 mg, yield 75%; mp 256–255 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.76 (s, 1H), 8.38–8.33 (m, 2H), 7.99–7.96 (m, 1H), 7.80 (s, 1H), 7.76–7.71 (m, 1H), 7.65–7.63 (m, 1H), 7.57–7.52 (m, 1H), 7.41–7.28 (m, 4H), 6.98–6.89 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 190.4, 165.4 (d, $^1J_{C-F}$ = 246.6 Hz), 165.2, 159.0, 155.4, 146.6, 142.7, 135.8, 135.5, 134.6 (d, $^4J_{C-F}$ = 2.8 Hz), 131.9, 131.0, 130.9, 130.1 (d, $^3J_{C-F}$ = 8.6 Hz), 124.0, 123.9, 123.2, 122.4, 121.2, 119.2, 116.3 (d, $^2J_{C-F}$ = 21.4 Hz), 116.1; IR (KBr) ν 3369, 1705, 1594, 1550, 1357, 1223, 1159, 748 cm^{-1}; HRMS *m/z* (ESI) calcd for $C_{24}H_{14}FNO_2Na$ $[M+Na]^+$ 390.0908, found 390.0904.

Synthesis of 3-amino-2-(2-phenyl-4*H*-chromen-4-yl)-cyclohex-2-enone (9). A mixture of 2-hydroxychalcone (**1a**, 112 mg, 0.5 mmol), 3-aminocyclohex-2-enone (**8**, 56 mg, 0.5 mmol) was heated in *n*-propanol (5 mL) under reflux. After the reaction was completed (12 h, monitored by thin layer chromatography), the mixture was slowly cooled to room temperature and purified by column chromatography using petroleum ether–ethyl acetate (4:1, v/v) to deliver the product **9** (124 mg, 78%) as a white solid. mp 210–211 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.71–7.68 (m, 2H), 7.42–7.31 (m, 3H), 7.20–7.14 (m, 1H), 7.06–6.97 (m, 3H), 5.62–5.61 (m, 1H), 5.43–5.42 (m, 1H), 4.62 (br, 2H), 2.49–2.28 (m, 4H), 2.05–1.94 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 194.9, 161.1, 151.3, 148.6, 133.7, 128.8, 128.5, 128.4, 127.6, 124.4, 124.0, 122.7, 116.1, 113.8, 100.5, 36.4, 30.9, 27.9, 21.3; IR (KBr) *v* 3454, 3304, 3177, 2920, 1648, 1540, 1488, 1409, 1317, 1218, 943, 758 cm^{-1}; HRMS *m/z* (MALDI) calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$ 318.1489, found 318.1488.

Acknowledgements

We gratefully acknowledge support from the Educational Commission of Hubei Province (D20142501) and the National Natural Science Foundation of China (21102042).

Notes and references

Hubei Collaborative Innovation Center for Rare Metal Chemistry, Hubei Key Laboratory of Pollutant Analysis and Reuse Technology, Hubei Normal University, Huangshi 435002, China. E-mail: gdyin_hbnu@163.com

† Electronic Supplementary Information (ESI) available: Copies of ^{1}H NMR, ^{13}C NMR spectra for all new products **3**, **5**, **7**, **9** and CIF file of **5e** (CCDC 1023466). See DOI: 10.1039/b000000x/

1 (a) M. Presset, Y. Coquerel and J. Rodriguez, *Chem. Rev.*, 2013, **113**, 525–595; (b) M. Ruiz, P. López-Alvarado, G. Giorgi and J. C. Menéndez, *Chem. Soc. Rev.*, 2011, **40**, 3445–3454; (c) W. Zhao, *Chem. Rev.*, 2010, **110**, 1706–1745.

2 C.-J. Wallentin, T. Wixe, O. F. Wendt, K.-E. Bergquist and K. Wärnmark, *Chem. Eur. J.*, 2010, **16**, 3994–4002.

3 M. Harmata and M. Kahraman, *Tetrahedron-Asymmetry*, 2000, **11**, 2875–2879.

4 (a) F. Wang, F. Chen, M. Qu, T. Li, Y. Liu and M. Shi, *Chem. Commun.*, 2013, **49**, 3360–3362; (b) N. C. Ganguly, P. Mondal and S. Roy, *Tetrahedron Lett.*, 2013, **54**, 2386–2390; (c) M. F. Polat, L. Hettmanczyk, W. Zhang, Z. Szabo and J. Franzén, *ChemCatChem*, 2013, **5**, 1334–1339; (d) G. M. Reddy and P. R. Sridhar, *Eur. J. Org. Chem.*, 2014, 1496–1504; (e) L. Xia, H. Cai and Y. R. Lee, *Org. Biomol. Chem.*, 2014, **12**, 4386–4396; (f) X. Jiang, Z. Song, C. Xu, Q. Yao and A. Zhang, *Eur. J. Org. Chem.*, 2014, 418–425.

5 (a) L. Jurd, *J. Heterocycl. Chem.*, 1981, **18**, 429–430; (b) I. Manolov and N. Danchev, *Eur. J. Med. Chem.*, 1995, **30**, 531–535; (c) D.-U. Chen, P.-Y. Kuo and D.-Y. Yang, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 2665–2668; (d) I. Manolov, C. Maichle-Moessmer and E. Niquet, *Z. Naturforsch*, 2006, **61b**, 207–212; (e) I. Kim, S. G. Kim, J. Choi and G. H. Lee, *Tetrahedron*, 2008, **64**, 664–671; (f) D. B. Ramachary and R. Sakthidevi, *Chem. Eur. J.*, 2009, **15**, 4516–4522.

6 (a) F. M. Moghaddam, Z. Mirjafary, H. Saeidian, S. Taheri, M. Doulabi and M. Kiamehr, *Tetrahedron*, 2010, **66**, 134–138; (b) Y.-F. Wang and S. Chiba, *J. Am. Chem. Soc.*, 2009, **131**, 12570–12572; (c) E. Butkus, U. Berg, J. Malinauskienė and J. Sandström, *J. Org. Chem.*, 2000, **65**, 1353–1358.

7 (a) A. Mendoza, P. Pardo, F. Rodríguez and F. J. Fañanás, *Chem. Eur. J.*, 2010, **16**, 9758–9762; (b) T. Enomoto, Y. Yasui and Y. Takemoto, *J. Org. Chem.*, 2010, **75**, 4876–4879; (c) K. Vervisch, M. D'hooghe, K. W. Törnroos and N. D. Kimpe, *J. Org. Chem.*, 2010, **75**, 7734–7744; (d) I. N. Michaelides, B. Darses and D. J. Dixon, *Org. Lett.*, 2011, **13**, 664–667; (e) F. M. Moghaddam, S. Taheri, Z. Mirjafary and H. Saeidian, *Synlett*, 2010, 123–127.

8 (a) H. Ren, C. Wu, X. Ding, X. Chen and F. Shi, *Org. Biomol. Chem.*, 2012, **10**, 8975–8984; (b) T.-M. Teng, A. Das, D. B. Huple and R.-S. Liu, *J. Am. Chem. Soc.*, 2010, **132**, 12565–12567; (c) Y. Kuninobu, J. Morita, M. Nishi, A. Kawata and K. Takai, *Org. Lett.*, 2009, **11**, 2535–2537; (d) C.-L. Cao, X.-L. Sun, Y.-B. Kang and Y. Tang, *Org. Lett.*, 2007, **9**, 4151–4154; (e) J. M. Aurrecoechea, J. M. Gorgojo and C. Saornil, *J. Org. Chem.*, 2005, **70**, 9640–9643.

9 (a) N. R. Norcross, J. P. Melbardis, M. F. Solera, M. A. Sephton, C. Kilner, L. N. Zakharov, P. C. Astles, S. L. Warriner and P. R. Blakemore, *J. Org. Chem.*, 2008, **73**, 7939–7951; (b) P. R. Blakemore, C. Kilner, N. R. Norcross and P. C. Astles, *Org. Lett.*, 2005, **7**, 4721–4724; (c) N. K. Garg, D. D. Caspi and B. M. Stoltz, *J. Am. Chem. Soc.*, 2004, **126**, 9552–9553; (d) L. N. Mander and M. M. McLachlan, *J. Am. Chem. Soc.*, 2003, **125**, 2400–2401; (e) Y. Sun, B. Yu, X. Wang, S. Tang, X. She and X. Pan, *J. Org. Chem.*, 2010, **75**, 4224–4229; (f) D. Solé, E. Peidró and J. Bonjoch, *Org. Lett.*, 2000, **2**, 2225–2228.

10 (a) G. Yin, T. Ren, Y. Rao, Y. Zhou, Z. Li, W. Shu and A. Wu, *J. Org. Chem.*, 2013, **78**, 3132–3141; (b) Y. Rao and G. Yin, *Org. Biomol. Chem.*, 2013, **11**, 6029–6035.

11 H. Shigemori, T. Kagata, H. Ishiyama, F. Morah, A. Ohsaki and J. Kobayashi, *Chem. Pharm. Bull.*, 2003, **51**, 58–61.

12 K. Awang, M. Païs, T. Sévenet, H. Schaller, A. M. Nasir and A. H. A. Hadi, *Phytochemistry*, 1991, **30**, 3164–3167.

13 (a) C.-R. Zhang, H.-B. Liu, S.-H. Dong, J.-Y. Zhu, Y. Wu and J.-M. Yue, *Org. Lett.*, 2009, **11**, 4692–4695; (b) A. Jossang, H. E. Bitar, V. C. Pham and T. Sévenet, *J. Org. Chem.*, 2003, **68**, 300–304; (c) J. Kobayashi, H. Takatsu, Y.-C. Shen and H. Morita, *Org. Lett.*, 2003, **5**, 1733–1736.

14 P. O. Patil, S. B. Bari, S. D. Firke, P. K. Deshmukh, S. T. Donda and D. A. Patil, *Bioorg. Med. Chem.*, 2013, **21**, 2434–2450.

15 (a) Z. F. Al-Rashid and R. P. Hsung, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 2687–2691; (b) V. U. Ahmad, F. Ullah, J. Hussain, U. Farooq, M. Zubair, M. T. H. Khan and M. I. Choudhary, *Chem. Pharm. Bull.*, 2004, **52**, 1458–1461.

16 (a) D. Deredas, Ł. Albrecht, W. Maniukiewicz, J. Wojciechowski, W. M. Wolf, P. Paluch, T. Janecki, M. Różalski, U. Krajewska, A. Janecka and H. Krawczyk, *RSC Adv.*, 2013, **3**, 6821–6832; (b) X. Zhang, X. Jiang, C. Ding, Q. Yao and A. Zhang, *Org. Biomol. Chem.*,

2013, **11**, 1383–1389; (c) S. H. Sim, Y. Park and Y. K. Chung, *Synlett*, 2012, 473–477; (d) H. M. Mohamed, A. H. F. A. EL-Wahab, A. M. EL-Agrody, A. H. Bedair, F. A. Eid, M. M. Khafagy and K. A. Abd-EL-Rehem, *Beilstein J. Org. Chem.*, 2011, **7**, 1688–1696; (e) D. Jönsson, M. Erlandsson and A. Undén, *Tetrahedron Lett.*, 2001, **42**, 6953–6956.

17 (a) A. Schmidt, D. Michalik, S. Rotzoll, E. Ullah, C. Fischer, H. Reinke, H. Görls and P. Langer, *Org. Biomol. Chem.*, 2008, **6**, 2804–2814; (b) Y. Xu, E. Aldeco-Pérez, H. Rudler, A. Parlier and C. Alvarez, *Tetrahedron Lett.*, 2006, **47**, 4553–4556; (c) L. D. Raev, W. Frey and I. C. Ivanov, *Synlett*, 2004, 1584–1588; (d) H. Rudler, B. Denise, Y. Xu, A. Parlier and J. Vaissermann, *Eur. J. Org. Chem.*, 2005, 3724–3744.

18 (a) F. M. Moghaddam, S. Taheri, Z. Mirjafary, H. Saeidian, M. Kiamehr and M. Tafazzoli, *Helv. Chim. Acta*, 2011, **94**, 142–147; (b) S. Mondal, R. Paira, A. Maity, S. Naskar, K. B. Sahu, A. Hazra, P. Saha, S. Banerjee and N. B. Mondal, *Tetrahedron Lett.*, 2011, **52**, 4697–4700; (c) R. Paira, S. Mondal, A. Maity, K. B. Sahu, S. Naskar, P. Saha, A. Hazra, S. Kundu, S. Banerjee and N. B. Mondal, *Tetrahedron Lett.*, 2011, **52**, 5516–5520; (d) F. M. Moghaddam, H. Saeidian, M. Kiamehr, Z. Mirjafary and S. Taheri, *Arkivoc*, 2010, 91–100.

19 (a) W.-C. Lin and D.-Y. Yang, *J. Org. Chem.*, 2013, **78**, 11798−11806; (b) J.-T. Lai, P.-S. Shieh, W.-H. Huang and D.-Y. Yang, *J. Comb. Chem.*, 2008, **10**, 381−386.

20 S. Ding, M. Le-Nguyen, T. Xu and W. Zhang, *Green Chem.*, 2011, **13**, 847−849.

21 W.-M. Shu, Y. Yang, D.-X. Zhang, L.-M. Wu, Y.-P. Zhu, G.-D. Yin and A.-X. Wu, *Org. Lett.,* 2013, **15**, 456−459.

22 Crystal data. $C_{23}H_{23}NO_2$, M = 345.42, orthorhombic, a = 33.520(5), b = 7.236(1), c = 15.699(2) Å, U = 3807.9(9) Å^3, T = 296(2) K, space group Pca2(1), Z = 8, 32705 reflections measured, 8432unique (R_{int}=0.0518) which were used in all calculations. The final wR(F_2) was 0.1282 (all data).

23 (a) S. K. Ray, P. K. Singh, N. Molleti and V. K. Singh, *J. Org. Chem.*, 2012, **77**, 8802−8808; (b) J. Dong and D.-M. Du, *Org. Biomol. Chem.*, 2012, **10**, 8125−8131.

24 P. N. Kalaria, S. P. Satasia and D. K. Raval, *Eur. J. Med. Chem.*, 2014, **78**, 207−216.

25 J. Svetlik and L. Veizerova, *Helv. Chim. Acta*, 2011, **94**, 199−205.

26 (a) S. Tu, B. Jiang, R. Jia, J. Zhang and Y. Zhang, *Tetrahedron Lett.*, 2007, **48**, 1369–1374; (b) G. D. Yin, Q. Liu, J. R. Ma and N. F. She, *Green Chem.*, 2012, **14**, 1796−1798.

Catalyst-free one-pot domino reactions for selective synthesis of functionalized 2,8-oxazabicyclo[3.3.1]-nonanes and 5*H*-indeno[1,2-*b*]pyridin-5-ones

Yin Rao, Meilin Liu, Lu Wu and Guodong Yin*

A simple and efficient method for one-pot selective synthesis of functionalized 2,8-oxazaxabicyclo[3.3.1]nonanes and hydroxy-containing 5*H*-indeno[1,2-*b*]pyridin-5-ones under catalyst-free conditions has been developed.