

## A novel three-component reactions of 4-hydroxycumarine for the synthesis of oxazine derivatives in water

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**Abstract:** A simple and proficient method for the synthesis of 1,3-benzoxazine derivatives *via* three-component reaction of isocyanide and isoquinoline with 2-naphthol in water in the presence of piperidine at 70°C is reported.

**Keywords:** 1,3-benzoxazine, 2-Hydroxyacetophenone, Isocyanide, Isoquinoline, Three-component reaction.

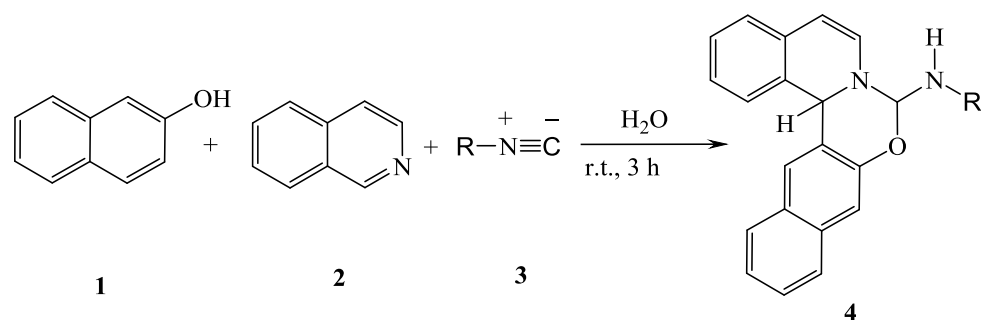
### Introduction

Multi-component reactions (MCRs), owing to their efficiency, simple procedures, junction, and facile completing, are one of the best tools in combinatorial chemistry [1, 2]. Therefore, the design of novel MCRs has attracted great attention from research groups working in areas such as drug discovery, organic synthesis and materials science. As a result, the number of new MCRs has grown rapidly [3]. Green chemistry approaches hold out momentous potential not only for reduction of byproducts, a reduction in the damage produced, and lowering of energy costs but also in the expansion of new methodologies toward previously unobtainable materials, using existing technologies [4-6]. Carrying out organic reactions in water has become highly desirable in recent years to meet environmental considerations [7- 9].

The use of water as a sole medium for organic reactions would greatly supply to the enlargement of environmentally friendly processes. Indeed, industry prefers to use water as a solvent rather than toxic organic solvents.

Also, the isoquinoline skeleton is found in a large number of naturally occurring and synthetic biologically active heterocyclic compounds [10-15]. Continuing our efforts directed towards the simple preparation of biologically active target molecules through multi-component reactions and our interest in isocyanide-based multi-component reactions [16-20], we performed the synthesis of 1,3-benzoxazine derivatives **4** *via* the reaction of 2-naphthol **1**, with isoquinoline **2** and isocyanide **3** in the presence of piperidine in water at 70 °C (Scheme 1). Hence, we describe the reaction of isoquinoline with isocyanides in the presence 2-naphthol. The reaction of 2-naphthol **1**, isoquinoline **2** and isocyanides **3** in the presence of piperidine produce 1,3-benzoxazine **4** in good yield (Scheme 1).

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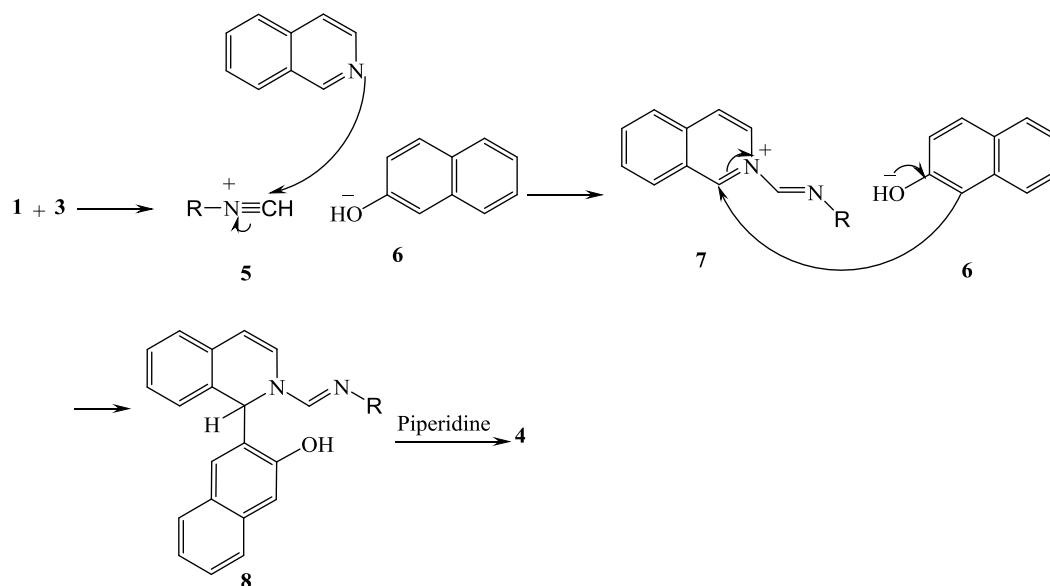
3, 4	R	Yield (%) of 4
a	<sup>t</sup> Bu	85
b	Cyclohexyl	80
c	1,1,3,3-tetramethylbutyl	80
d	CH <sub>2</sub> CO <sub>2</sub> Et	75
e	2,6-Dimethyl phenyl	83
f	Bn	78
g	2-nitrophenyl	65

**Scheme 1:** Reaction of isoquinoline, isocyanide and 2-hydroxyacetophenone.

## Results and discussion

The data obtained from elemental analysis, IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra confirmed all of the proposed products. The <sup>1</sup>H NMR spectrum of **4a** displayed one singlet at 1.38 ppm for the *tert*-butyl group, two singlet at 2.10 and 2.54 ppm for methyl protons, two singlet at 5.30 and 5.85 for CH protons, one singlet at 8.74 ppm for NH proton and two set of doublet for vicinal methine protons at 4.78 and 5.73 ppm which appeared as with <sup>2</sup>J<sub>HH</sub> of 3.5 Hz. One single resonance at δ = 196.2 ppm is observed in the <sup>13</sup>C NMR spectrum of **4a**, which is attributed to the

carbonyl group. A proposed mechanism for the formation of compound **4** is shown in Scheme 2. It is conceivable that the initial event is the formation of acid–base complex **5** from the isocyanide **3** and the 2-hydroxyacetophenone **1**. Complex **5** activates the isocyanide functional group sufficiently for further nucleophilic attack by isoquinoline to produce intermediate **7**. Finally, nucleophilic attack of the conjugated base of the 2-hydroxyacetophenone **6** on **7** affords intermediate **8** that converted to **4** by cyclization in the presence of piperidine.



**Scheme 2:** Proposed mechanism for the formation of **4**.

## Conclusion

In conclusion, we have described a new and successful strategy for the convenient synthesis of 1,3-benzoxazine *via* three-component condensation reaction of a OH-acid, isoquinoline and an isocyanide in water at 70 °C. The method offers few advantages including high yields of products and an easy experimental work-up procedure.

## Experimental Section

### General

Melting points were taken on a Kofler hot stage apparatus and are uncorrected.  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR spectra were obtained with a Bruker FT-500 spectrometer in  $\text{CDCl}_3$ , and tetramethylsilane (TMS) was used as an internal standard or 85%  $\text{H}_3\text{PO}_4$  as external standard. Mass spectra were recorded with a Finnigan Mat TSQ-70 spectrometer. Infrared (IR) spectra were acquired on a Nicolet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, N) were within  $\pm 0.4\%$  of the calculated values. Acetylenic ester, phenacyl bromide or its derivatives and triphenylphosphine were obtained from Fluka and were used without further purification.

### General procedure for preparation of compounds **4**:

To a magnetically stirred solution of isoquinoline **2** (2 mmol) and 2-hydroxyacetophenone **1** in water (5 mL) as the solvent was added isocyanide **3** (2 mmol). The

reaction mixture was stirred for 5h. After completion of reaction (monitored by TLC), piperidine was added to the mixture of reaction and the reaction mixture was stirred for 30 min. Then, the reaction mixture was filtered and the solid residue was crystallized from ethyl acetate to afford **4**.

### 7-(*tert*butylamino)-2-isopropenyl-14*b*H-furo[2,3-*ff*]isoquino[2,1-*c*][1,3]benzoxazine-5-carboxylic acid (**4a**):

pale yellow powder, m.p. 145-147 °C, 0.73 g, yield 85%. IR (KBr) ( $\nu_{\text{max}}/\text{cm}^{-1}$ ): 1727, 1675, 1548, 1228  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_3$  (428.53): C, 75.68; H, 6.59; N, 6.54%. Found: C, 75.54; H, 6.46; N, 6.47%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.38 (9 H, s,  $\text{Me}_3\text{C}$ ), 2.10 (3 H, s, Me), 2.54 (3 H, s, Me), 4.78 (1 H, d,  $^2J = 3.5$  Hz, CH), 5.30 (1 H, s, CH), 5.73 (1 H, d,  $^2J = 3.5$  Hz, CH), 5.85 (1 H, s, CH), 6.42 (1 H, d,  $^3J_{\text{HH}} = 5.8$  Hz, CH), 7.54 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH), 7.69 (1 H, t,  $^3J_{\text{HH}} = 7.2$  Hz, CH), 7.73 (1 H, t,  $^3J_{\text{HH}} = 7.2$  Hz, CH), 7.82 (1 H, s, CH), 7.93 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.74 (1 H, s, NH), 8.69 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 9.31 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  18.6 (Me), 27.3 (Me), 29.5 ( $\text{Me}_3\text{C}$ ), 48.7 (C), 52.7 (CH), 78.4 (CH), 107.8 (CH), 110.5 (C), 112.7 (CH), 114.3 ( $\text{CH}_2$ ), 117.6 (C), 121.0 (C), 121.8 (C), 122.4 (CH), 124.9 (CH), 126.1 (CH), 128.4 (CH), 129.5 (CH), 130.7 (CH), 136.8 (C), 138.2 (C), 154.5 (C), 157.6 (C), 159.4 (C), 196.2 (C=O). MS,  $m/z$  (%): 428 ( $\text{M}^+$ , 10), 371 (88), 299 (68), 129 (100), 57 (86).

**7-(cyclohexylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3]benzoxazine-5-carboxylic acid (4b):**

White powder, m.p. 152-154 °C, 0.73 g, yield 80%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1728, 1685, 1487, 1348, 1257, 1129  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{29}\text{H}_{30}\text{N}_2\text{O}_3$  (454.56): C, 76.63; H, 6.65; N, 6.16%. Found: C, 76.74; H, 6.72; N, 6.25%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.35 (2 H, m,  $\text{CH}_2$ ), 1.43 (2 H, m,  $\text{CH}_2$ ), 1.48 (2 H, m,  $\text{CH}_2$ ), 1.65 (2 H, m,  $\text{CH}_2$ ), 1.84 (2 H, m,  $\text{CH}_2$ ), 2.14 (3 H, s, Me), 2.52 (3 H, s, Me), 3.80 (1 H, m, N-CH), 4.82 (1 H, d,  $^2J = 3.0$  Hz, CH), 5.25 (1 H, s, CH), 5.70 (1 H, d,  $^2J = 3.0$  Hz, CH), 5.82 (1 H, s, CH), 6.45 (1 H, d,  $^3J_{\text{HH}} = 6.0$  Hz, CH), 7.49 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH), 7.65 (1 H, t,  $^3J_{\text{HH}} = 7.3$  Hz, CH), 7.68 (1 H, t,  $^3J_{\text{HH}} = 7.3$  Hz, CH), 7.78 (1 H, s, CH), 7.86 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.65 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.78 (1 H, s, NH), 9.27 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  18.8 (Me), 24.5 ( $\text{CH}_2$ ), 24.7 ( $\text{CH}_2$ ), 25.6 ( $\text{CH}_2$ ), 27.6 (Me), 33.4 ( $\text{CH}_2$ ), 33.7 ( $\text{CH}_2$ ), 48.7 (CH), 53.4 (CH), 80.2 (CH), 108.0 (CH), 112.2 (C), 113.4 (CH), 115.0 ( $\text{CH}_2$ ), 118.5 (C), 121.4 (C), 122.0 (C), 122.8 (CH), 125.0 (CH), 126.7 (CH), 128.7 (CH), 130.4 (CH), 131.2 (CH), 137.4 (C), 139.0 (C), 155.0 (C), 158.3 (C), 160.2 (C), 194.0 (C=O). MS,  $m/z$  (%): 454 ( $\text{M}^+$ , 15), 371 (54), 325 (78), 129 (100), 81 (48).

**7-(1,1,3,3-tetramethylbutylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3]benzoxazine-5-carboxylic acid (4c):**

Yellow crystals, m.p. 162-164 °C, 0.77 g, yield 80%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1735, 1674, 1528, 1457, 1364, 1229  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{31}\text{H}_{36}\text{N}_2\text{O}_3$  (484.64): C, 76.83; H, 7.49; N, 5.78%. Found: C, 76.92; H, 7.56; N, 5.84%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.03 (9 H, s,  $\text{CMe}_3$ ), 1.55 (3 H, s, Me), 1.62 (3 H, s, Me), 1.83 (2 H, s,  $\text{CH}_2$ ), 2.17 (3 H, s, Me), 2.48 (3 H, s, Me), 4.75 (1 H, d,  $^2J = 2.7$  Hz, CH), 5.32 (1 H, s, CH), 5.74 (1 H, d,  $^2J = 2.7$  Hz, CH), 5.93 (1 H, s, CH), 6.57 (1 H, d,  $^3J_{\text{HH}} = 5.5$  Hz, CH), 7.53 (1 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.72 (1 H, t,  $^3J_{\text{HH}} = 7.2$  Hz, CH), 7.78 (1 H, t,  $^3J_{\text{HH}} = 7.3$  Hz, CH), 7.82 (1 H, s, CH), 7.90 (1 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 8.72 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH), 8.83 (1 H, s, NH), 9.28 (1H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  19.2 (Me), 28.3 (Me), 29.7 (C), 31.6 ( $\text{CMe}_3$ ), 31.9 (2 Me), 50.4 (C), 51.2 (CH), 55.0 ( $\text{CH}_2$ ), 81.4 (CH), 108.6 (CH), 112.5 (C), 113.7 (CH), 115.4 ( $\text{CH}_2$ ), 119.2 (C), 121.8 (C), 122.5 (C), 123.0 (CH), 125.6 (CH), 127.2 (CH), 129.3 (CH), 130.8 (CH), 131.7 (CH), 137.6 (C), 139.4 (C), 155.3 (C),

159.2 (C), 160.6 (C), 196.7 (C=O). MS,  $m/z$  (%): 484 ( $\text{M}^+$ , 10), 371 (62), 129 (100), 113 (52).

**7-(2-ethoxy-2-oxoethylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3]benzoxazine-5-carboxylic acid (4d):**

Yellow powder, m.p. 158-160 °C, 0.69 g, yield 75%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1732, 1683, 1565, 1434, 1358, 1235  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}_3$  (458.51): C, 70.73; H, 5.72; N, 6.11%. Found: C, 70.65; H, 5.67; N, 6.02%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.31 (3 H, t,  $^3J = 7.4$  Hz, Me), 2.14 (3 H, s, Me), 2.50 (3 H, s, Me), 4.20 (2 H, s,  $\text{CH}_2$ ), 4.25 (2 H, q,  $^3J = 7.3$  Hz,  $\text{CH}_2\text{O}$ ), 4.75 (1 H, d,  $^2J = 2.8$  Hz, CH), 5.34 (1 H, s, CH), 5.75 (1 H, d,  $^2J = 2.8$  Hz, CH), 5.87 (1 H, s, CH), 6.62 (1 H, d,  $^3J_{\text{HH}} = 5.6$  Hz, CH), 7.58 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.74 (1 H, t,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.82 (1 H, t,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.87 (1 H, s, CH), 7.95 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.75 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.85 (1 H, s, NH), 9.24 (1H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1 (Me), 18.5 (Me), 28.4 (Me), 50.2 ( $\text{CH}_2$ ), 51.7 (CH), 60.7 ( $\text{CH}_2\text{O}$ ), 81.6 (CH), 108.5 (CH), 112.7 (C), 114.0 (CH), 115.8 ( $\text{CH}_2$ ), 119.6 (C), 122.4 (C), 122.8 (C), 123.7 (CH), 126.3 (CH), 127.8 (CH), 129.6 (CH), 131.2 (CH), 132.3 (CH), 138.0 (C), 139.7 (C), 155.6 (C), 159.8 (C), 159.4 (C), 167.2 (C=O), 195.2 (C=O). MS,  $m/z$  (%): 458 ( $\text{M}^+$ , 10), 329 (58), 129 (100), 43 (86).

**7-(2,6-dimethylphenylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3]benzoxazine-5-carboxylic acid (4e):**

Yellow powder, m.p. 164-166 °C, 0.79 g, yield 83%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1734, 1684, 1576, 1425 1374, 1247, 1129  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{31}\text{H}_{28}\text{N}_2\text{O}_3$  (476.57): C, 78.13; H, 5.92; N, 5.88%. Found: C, 78.24; H, 6.04; N, 5.94%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.10 (3 H, s, Me), 2.24 (3 H, s,  $\text{CH}_3$ ), 2.27 (3 H, s,  $\text{CH}_3$ ), 2.52 (3 H, s, Me), 4.80 (1 H, d,  $^2J = 2.6$  Hz, CH), 5.28 (1 H, s, CH), 5.78 (1 H, d,  $^2J = 2.6$  Hz, CH), 5.83 (1 H, s, CH), 6.48 (1 H, d,  $^3J_{\text{HH}} = 5.5$  Hz, CH), 7.43 (1 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.46 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.57 (1 H, t,  $^3J_{\text{HH}} = 7.3$  Hz, CH), 7.64 (1 H, t,  $^3J_{\text{HH}} = 7.2$  Hz, CH), 7.66 (2 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, 2 CH), 7.78 (1 H, s, CH), 7.82 (1 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 8.82 (1 H, s, NH), 8.92 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH), 9.27 (1 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  18.3 (Me), 18.5 (Me), 18.7 (Me), 27.5 (Me), 53.0 (CH), 78.6 (CH), 108.2 (CH), 110.7 (C), 113.4 (CH), 114.8 ( $\text{CH}_2$ ), 118.4 (C), 121.5 (C), 122.3 (C), 122.7 (CH), 125.4 (CH), 126.6 (CH), 127.3 (2 C),

128.5 (CH), 129.2 (2 CH), 130.2 (CH), 130.7 (CH), 134.0 (CH), 137.2 (C), 138.4 (C), 154.6 (C), 155.2 (C), 157.8 (C), 159.8 (C), 196.5 (C=O). MS,  $m/z$  (%): 476 ( $M^+$ , 15), 347 (68), 129 (100), 43 (86).

**7-(benzylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3]benzoxazine-5-carboxylic acid (4f):**

Yellow powder, m.p. 174-176 °C, 0.72 g, yield 78%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1735, 1678, 1556, 1367 1284  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}_3$  (462.55): C, 77.90; H, 5.67; N, 6.06%. Found: C, 77.84; H, 5.73; N, 6.14%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.15 (3 H, s, Me), 2.58 (3 H, s, Me), 4.71 (2 H, s,  $\text{CH}_2$ ), 4.83 (1 H, d,  $^2J = 2.8$  Hz, CH), 5.32 (1 H, s, CH), 5.76 (1 H, d,  $^2J = 2.8$  Hz, CH), 5.87 (1 H, s, CH), 6.52 (1 H, d,  $^3J_{\text{HH}} = 5.4$  Hz, CH), 7.25 (2 H, t,  $^3J_{\text{HH}} = 7.8$  Hz, 2 CH), 7.45 (1 H, t,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.58 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.64 (2 H, d,  $^3J_{\text{HH}} = 7.6$  Hz, 2 CH), 7.74 (1 H, t,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.75 (1 H, t,  $^3J_{\text{HH}} = 7.6$  Hz, CH), 7.80 (1 H, s, CH), 7.95 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 8.78 (1 H, s, NH), 8.94 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 9.35 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  19.2 (Me), 28.4 (Me), 51.9 ( $\text{CH}_2$ ), 53.4 (CH), 79.0 (CH), 108.4 (CH), 111.2 (C), 112.8 (CH), 114.7 ( $\text{CH}_2$ ), 118.3 (C), 122.0 (C), 122.7 (C), 123.4 (CH), 125.4 (CH), 126.7 (CH), 128.2 (2 CH), 128.6 (CH), 129.1 (2 CH), 130.4 (CH), 131.2 (CH), 134.0 (CH), 137.0 (C), 138.5 (C), 139.3 (C), 154.6 (C), 158.3 (C), 158.8 (C), 197.3 (C=O).

**7-(2-nitrophenylamino)-2-isopropenyl-14bH-furo[2,3-f]isoquino[2,1-c][1,3] benzoxazine -5-carboxylic acid (4g):**

Yellow powder, m.p. 158-160 °C, 0.32 g, yield 65%. IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 1738, 1656, 1587, 1447 1364, 1337, 1295  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{29}\text{H}_{23}\text{N}_3\text{O}_5$  (493.51): C, 70.58; H, 4.70; N, 8.51%. Found: C, 70.62; H, 7.76; N, 8.57%.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.12 (3 H, s, Me), 2.54 (3 H, s, Me), 4.78 (1 H, d,  $^2J = 3.2$  Hz, CH), 5.17 (1 H, s, CH), 5.72 (1 H, d,  $^2J = 3.2$  Hz, CH), 5.76 (1 H, s, CH), 6.52 (1 H, d,  $^3J_{\text{HH}} = 6.2$  Hz, CH), 7.45 (2 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, 2 CH), 7.48 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.62 (1 H, t,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 7.65 (1 H, t,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 7.72 (2 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, 2 CH), 7.75 (1 H, s, CH), 7.82 (1 H, d,  $^3J_{\text{HH}} = 7.4$  Hz, CH), 8.75 (1 H, s, NH), 8.87 (1 H, d,  $^3J_{\text{HH}} = 7.5$  Hz, CH), 9.25 (1 H, d,  $^3J_{\text{HH}} = 7.8$  Hz, CH) ppm.  $^{13}\text{C}$  NMR (125.7 MHz,  $\text{CDCl}_3$ ):  $\delta$  18.5 (Me), 27.8 (Me), 52.6 (CH), 78.7 (CH), 108.6 (CH), 111.2 (C), 113.6 (CH), 115.2 ( $\text{CH}_2$ ), 118.7 (C), 122.0 (C), 123.4 (C), 123.6 (CH), 125.7 (CH), 127.2 (CH), 127.8 (2 C), 128.6 (CH), 129.5 (2 CH),

130.4 (CH), 131.2 (CH), 133.8 (CH), 137.5 (C), 139.2 (C), 154.7 (C), 155.6 (C), 158.2 (C), 160.0 (C), 195.7 (C=O).

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