A New, One-Pot, Three-Component, Solvent-Free Synthesis of Amidoalkyl Dibenzofuranols and Dibenzofuran-Condensed 1,3-Oxazin-3-ones

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Abstract: A new, one-pot, three-component synthesis of amidoalkyl dibenzofuranols and dibenzofuran-condensed 1,3-oxazin-3-ones in good to excellent yields via the reaction of dibenzofuran-2-ol, an aromatic aldehyde, and an amide or urea in the presence of tin(II) chloride dihydrate as a Lewis acid catalyst is described.

Key words: dibenzofuran, multicomponent reaction, amidoalkyl dibenzofuranol, 1,3-oxazin-3-ones, solvent-free, condensation reactions, aromatic aldehyde

Reactions that generate carbon–carbon bonds, and at the same time introduce nitrogen-containing functionalities into a structural framework, are especially attractive for the rapid construction of organic molecules.[1] In recent years, the application of logic-based single reactant replacement (SRR) as a means to improve both known multicomponent reactions, and to design new routes to potentially bioactive complex structures has gained momentum.[2] In this context, the procedure for the synthesis of naphthalene-condensed heterocycles such as dibenzoxanthenes **1**,[3] amidoalkyl naphthols **2**[4] and naphthoxazin-3-ones **3**,[5] via the one-pot, three-component condensation of 2-naphthol, an aldehyde and an amide or urea, was of interest to us[6] for appropriate modification using similar, but more bioactive components as substrates.[7]

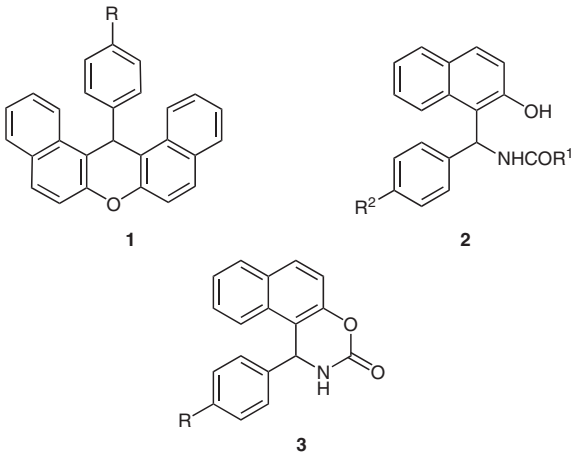

Figure 1 Examples of naphthalene-condensed heterocycles

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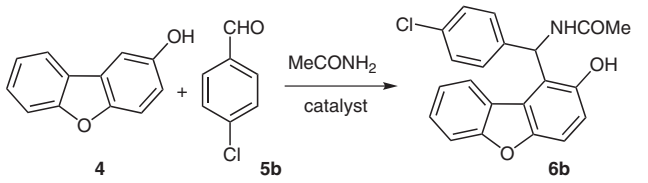
The dibenzofuran unit is the basic structural framework of several natural products with pronounced biological properties;[8] examples include fulicineroside, lucidafuran, eriobofuran, cannabifuran, ruscodibenzofuran and karnatakafurans. Simple dibenzofurans also occur in higher plants where they often act as antifungal phytoalexins.[9] Synthetic heterocycles derived from dibenzofuran display important and therapeutically useful biological activity such as antibacterial, antidepressant and antitubercular.[9] We envisaged that the preparation of heterocycles containing amidoalkyl and 1,3-oxazin-3-one groups on a dibenzofuran system, as possible drug-like candidates, would be of synthetic importance. We herein describe our investigations of a novel, one-pot, multicomponent, solvent-free condensation of dibenzofuran-2-ol (**4**), various aromatic aldehydes, and an amide or urea in the presence of a Lewis or protic acid catalyst. To the best of our knowledge, this is the first report on the synthesis of amidoalkyl dibenzofuranols **6a–n** and dibenzofuran-condensed 1,3-oxazin-3-ones **7a–e**.

The starting substrate for the study, dibenzofuran-2-ol (**4**) was prepared from dibenzofuran according to the literature procedure,[10] and was fully characterized by spectroscopic analysis.

Initially, efforts were focused on the reaction of dibenzofuran-2-ol (**4**), *p*-chlorobenzaldehyde (**5b**) and acetamide with various Lewis and protic acid catalysts (Table 1). The yields of amidoalkyl dibenzofuranol **6b**, which was obtained as racemic mixture, are shown in Table 1. The reaction proceeded efficiently with tin(II) chloride dihydrate ($SnCl_2 \cdot 2H_2O$) under solvent-free conditions (3.5 hours, 125 °C) to give the corresponding amidoalkyl dibenzofuranol **6b** in 96% yield (entry 14, Table 1). It was found that the mole ratio of tin(II) chloride dihydrate influenced the yield of the product, with 20 mol% being optimum. Furthermore, no product was detected in the absence of a catalyst. Investigation of the reaction temperature indicated that 125 °C was the most favorable for the formation of **6b**.

In order to study the general scope and versatility of this procedure for the synthesis of a series of substituted amidoalkyl dibenzofuranols **6**, the condensation of dibenzofuran-2-ol (**4**), aldehydes **5a–m**, and acetamide, benzamide or urea was examined. The three-component reaction of aryl aldehydes bearing electron-withdrawing or electron-donating substituents proceeded smoothly to give the desired amidoalkyl dibenzofuranols **6a–n** in good

Table 1 Catalyst Optimization[a]



4 5b 6b

Entry	Catalyst	mol%	Time (h)	Yield (%)[b]
1	AcOH	excess (solvent)	12	35
2	*p*-TSA	100	3.5	48
3	$HClO_4$–SiO_2	30	3.5	85
4	H_2SO_4–SiO_2	30	3.5	82
5	$InCl_3$	30	8	65
6	I_2	30	4	68
7	$BiCl_3$	20	12	56
8	$CuCl_2·4H_2O$	30	9	63
9	$Bi(OTf)_3$	20	4.5	76
10	$Zn(OTf)_2$	20	4.5	72
11	$FeCl_3$	30	10	45
12	LiBr	30	12	48
13	$CoCl_2$	30	4	46
14	$SnCl_2·2H_2O$	20	3.5	96
15	Montmorillonite-K10	20	3.5	68
16	$K_5CoW_{12}O_{40}·3H_2O$	20	6	40
17	$SnCl_2·2H_2O$	10	3.5	82
18	$SnCl_2·2H_2O$	30	3.5	96

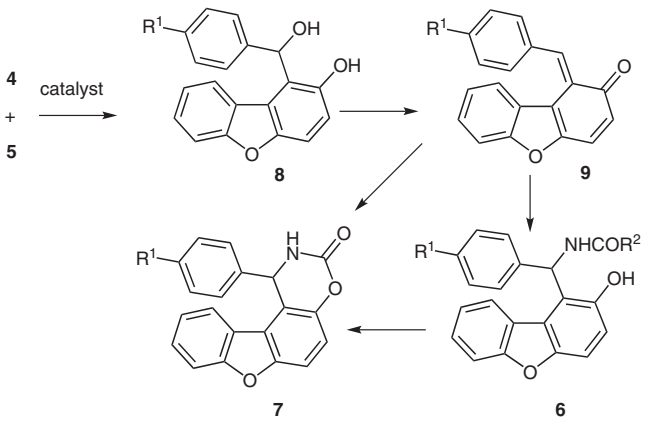
[a] Dibenzofuran-2-ol (**4**) (1 mmol), *p*-chlorobenzaldehyde (**5b**) (1 mmol), acetamide (1 mmol) and catalyst were heated at 125 °C.
[b] Yield of isolated product **6b**.

to excellent yields (Table 2). As expected, aromatic aldehydes possessing electron-withdrawing groups reacted faster than those with electron-donating groups. A large number of aryl aldehydes are readily available, hence this three-component reaction may be useful for the synthesis of various other amidoalkyl dibenzofuranols.

This three-component reaction was also carried out using the heteroaromatic aldehydes furfural and indole-3-carboxaldehyde (entries 13 and 14, Table 2). The reaction proceeded well with furfural (**5h**) (entry 13, Table 2) giving a 72% yield of the expected product. However, the reaction with indole-3-carboxaldehyde (**5i**) (entry 14, Table 2) was sluggish resulting in the formation of **6n** in a poor yield along with several unidentified by-products. The aliphatic aldehydes isobutyraldehyde (**5l**) and valeraldehyde (**5m**) (entries 17 and 18, Table 2) did not react with dibenzofuran-2-ol (**4**) and acetamide under the optimized conditions, nor with any of the catalysts specified in Table 1. Therefore, no additional aliphatic aldehydes were tested. The reaction was also unsuccessful with the sugars D-glucose and L-rhamnose (entries 15 and 16, Table 2).

Encouraged by the results obtained with aromatic aldehydes, we extended this protocol to the one-pot, three-component synthesis of dibenzofuran-condensed 1,3-oxazin-3-ones **7**. Condensation of **4** with various aromatic aldehydes and urea at elevated temperature (160 °C) gave 1,3-oxazin-3-ones **7a–e** in excellent yields (Table 3). In a typical example, reaction of dibenzofuran-2-ol (**4**), *p*-chlorobenzaldehyde (**5b**) and urea in the presence of tin(II) chloride dihydrate (20 mol%) at 160 °C for 2.5 hours gave product **7a** in 95% yield (entry 1, Table 3). Under these conditions, the corresponding amidoalkyl dibenzofuranol **6c** was not present according to thin layer chromtography. Decreasing the temperature (135 °C) resulted in formation of both amidoalkyl dibenzofuranol **6c** and 1,3-oxazin-3-one **7a** in variable yields, even after an extended reaction time (24 hours). This result indicated that the amidoalkyl dibenzofuranol **6** is formed first and then undergoes dehydration–cyclization to give the 1,3-oxazin-3-one **7**. Products **6a–n** and **7a–e** were fully characterized by IR and NMR spectroscopy, and by mass spectrometry.

A plausible mechanism for the formation of amidoalkyl dibenzofuranols **6** and 1,3-oxazin-3-ones **7** is illustrated in Scheme 1. On the basis of the established chemistry of tin(II) chloride catalyzed organic reactions, and a similar process in the literature,[5] it is reasonable to assume that *ortho*-quinone methide **9** is formed initially via addition of dibenzofuran-2-ol (**4**) to the aromatic aldehyde **5** and subsequent dehydration in the presence of the acidic catalyst. Next, Michael addition of the amide or urea leads to the formation of amidoalkyl dibenzofuranol **6**. At elevated temperature, dehydration takes place to give dibenzofuran-condensed oxazin-3-one **7**.



Scheme 1 A plausible mechanism for the formation of amidoalkyl dibenzofuranol **6** and its 1,3-oxazin-3-one analogue **7**

Table 2 Synthesis of Amidoalkyl Dibenzofuranols **6a–n**

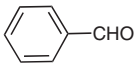
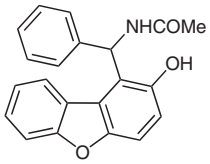
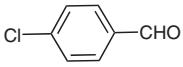
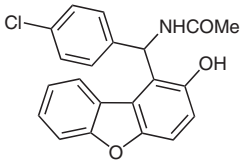
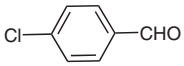
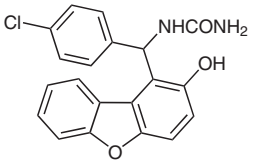
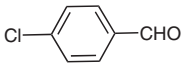
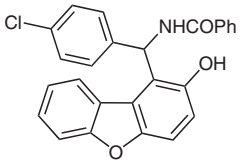
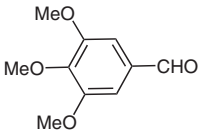
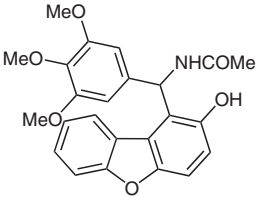
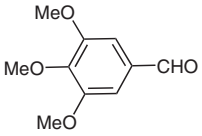
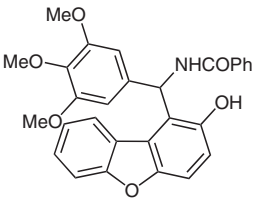
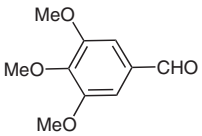
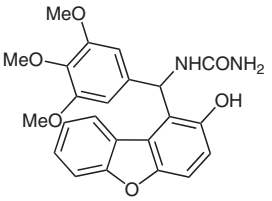
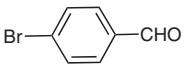
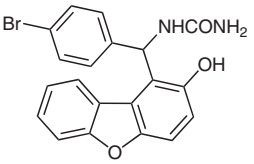
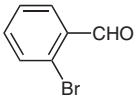
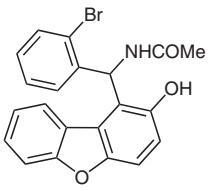
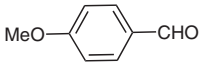
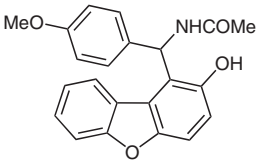
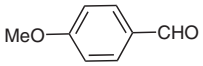
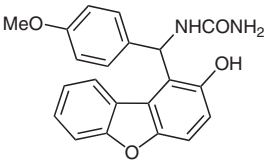
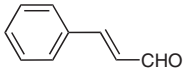
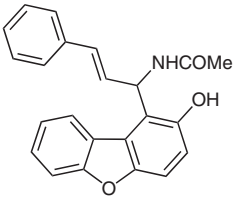
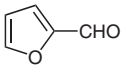
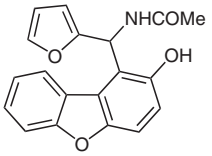
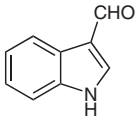
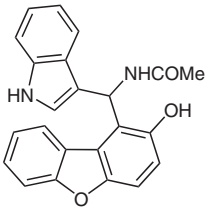
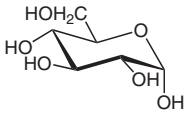
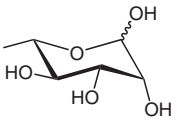
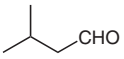
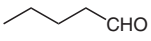
Entry	Aldehyde	Amide/Urea	Product[a]	Time (h)	Yield (%)[b]
1	**5a** 	$MeCONH_2$	**6a** 	4.5	80
2	**5b** 	$MeCONH_2$	**6b** 	3.5	96
3	**5b** 	NH_2CONH_2	**6c** 	3.5	93
4	**5b** 	$PhCONH_2$	**6d** 	3.5	91
5	**5c** 	$MeCONH_2$	**6e** 	6	85
6	**5c** 	$PhCONH_2$	**6f** 	6	82
7	**5c** 	NH_2CONH_2	**6g** 	6	85
8	**5d** 	NH_2CONH_2	**6h** 	4	90
9	**5e** 	$MeCONH_2$	**6i** 	4	82

Table 2 Synthesis of Amidoalkyl Dibenzofuranols **6a–n** (continued)

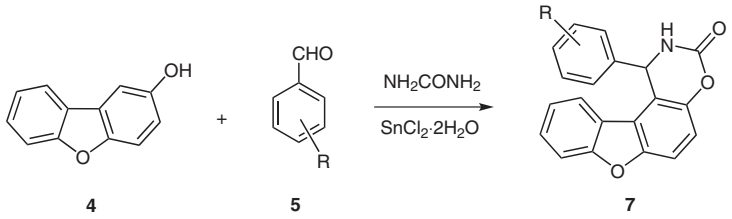
Entry	Aldehyde		Amide/Urea	Product[a]		Time (h)	Yield (%)[b]
10	**5f**		$MeCONH_2$	**6j**		5	88
11	**5f**		NH_2CONH_2	**6k**		5	83
12	**5g**		$MeCONH_2$	**6l**		5	78
13	**5h**		$MeCONH_2$	**6m**		7	72
14	**5i**		$MeCONH_2$	**6n**		7	35
15	**5j**		$MeCONH_2$		no reaction	24	–
16	**5k**		$MeCONH_2$		no reaction	24	–
17	**5l**		$MeCONH_2$		no reaction	24	–
18	**5m**		$MeCONH_2$		no reaction	24	–

[a] All reactions were performed in the presence of $SnCl_2 \cdot 2H_2O$ (20 mol%) at 125 °C under solvent-free conditions.
[b] Yield of isolated product.

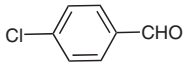
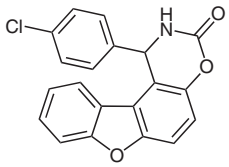
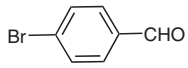
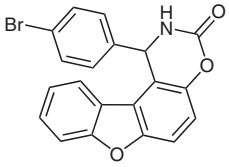
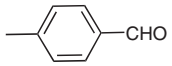
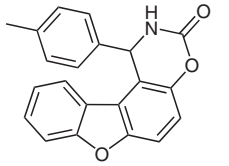
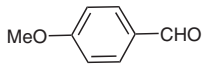
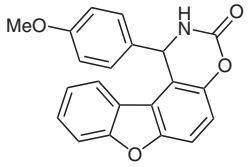
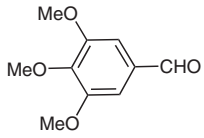
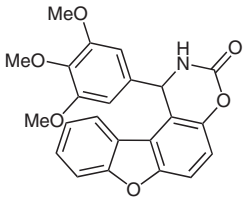
In conclusion, we have described the synthesis of novel amidoalkyl dibenzofuranols **6a–n** and dibenzofuran-condensed 1,3-oxazin-3-ones **7a–e** through an efficient one-pot, three-component condensation of dibenzofuran-2-ol (**4**), aromatic aldehydes **5**, and an amide or urea under solvent-free conditions. Among the catalysts examined, tin(II) chloride dihydrate proved to be the most effective for this transformation. The described procedure is simple and the products are easily isolated and purified in good to excellent yields. The products may show potential as drug-like candidates.

Melting points were measured with a Fischer-Johns melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer spectrophotometer. NMR spectra were recorded on Bruker (^{1}H NMR, 300 MHz; ^{13}C NMR, 75 MHz) and Varian (^{1}H NMR, 500 MHz) spectrometers with DMSO-d_6, $CDCl_3$ or a mixture of $CDCl_3$–DMSO-d_6 (8:2) and with tetramethylsilane as the internal standard. Low-resolution mass spectra were obtained using electron impact (EI), and high-resolution mass spectra (HRMS) were record-

Table 3 Synthesis of Dibenzofuran-Condensed 1,3-Oxazin-3-ones **7a–e**



4 **5** **7**

Entry	Aldehyde		Product[a]		Time (h)	Yield (%)[b]
1	**5b**		**7a**		2.5	95
2	**5d**		**7b**		3	92
3	**5n**		**7c**		2.5	90
4	**5f**		**7d**		3	89
5	**5c**		**7e**		4	85

[a] All reactions were performed in the presence of $SnCl_2·2H_2O$ (20 mol%) at 160 °C under solvent-free conditions.
[b] Yield of isolated product.

ed using electrospray ionization (ESI) on an ESI-QTOF mass spectrometer.

Amidoalkyl Dibenzofuranols 6a–n and Dibenzofuran-Condensed 1,3-Oxazin-3-ones 7a–e; General Procedure

A stirred mixture of dibenzofuran-2-ol (**4**) (1 mmol), aldehyde **5** (1 mmol), amide or urea (1 mmol) and $SnCl_2·2H_2O$ (20 mol%) was heated at 125 °C for the time specified in Table 2. The reaction mixture was cooled to r.t., H_2O (20 mL) was added, and the product was extracted with EtOAc (3 × 15 mL). The combined organic layer was washed with brine (2 × 5 mL), dried over anhyd Na_2SO_4 and evaporated under vacuum. Recrystallization of the residue from $CHCl_3$–hexane (1:3) yielded the pure amidoalkyl dibenzofuranol **6a–n** as a crystalline solid. Compounds **7a–e** were obtained by heating the reaction mixture at 160 °C for the time specified in Table 3 followed by similar work-up.

***N*-[(2-Hydroxydibenzofuran-1-yl)(phenyl)methyl]acetamide (6a)**

White solid; mp 221–224 °C.

IR (KBr): 3401, 3180, 1640, 1514, 1435, 1368, 1223 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 9.35 (s, 1 H), 8.15 (d, *J* = 7.9 Hz, 1 H), 8.05 (d, *J* = 8.4 Hz, 1 H), 7.50 (d, *J* = 8.1 Hz, 1 H), 7.45–7.10 (m, 9 H), 7.00 (d, *J* = 8.8 Hz, 1 H), 2.02 (s, 3 H).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{17}O_3NNa$: 354.1106; found: 354.1116.

***N*-[(4-Chlorophenyl)(2-hydroxydibenzofuran-1-yl)methyl]acetamide (6b)**

White solid; mp 220–222 °C.

IR (KBr): 3400, 3166, 1637, 1509, 1431, 1365, 1219, 1086 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.40 (s, 1 H), 8.15 (d, J = 7.9 Hz, 1 H), 8.02 (d, J = 8.1 Hz, 1 H), 7.50 (d, J = 8.1 Hz, 1 H), 7.43–7.15 (m, 8 H), 7.00 (d, J = 8.6 Hz, 1 H), 2.02 (s, 3 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{21}H_{16}O_3NClNa$: 388.0716; found: 388.0708.

***N*-[(4-Chlorophenyl)(2-hydroxydibenzofuran-1-yl)methyl]urea (6c)**
Light-yellow solid; mp 68–71 °C.

IR (KBr): 3384, 3063, 2922, 2852, 1701, 1638, 1590, 1461, 1431, 1216, 1154, 1092 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.32 (s, 1 H), 8.15 (d, J = 6.9 Hz, 1 H), 7.75 (s, 1 H), 7.50 (d, J = 8.1 Hz, 1 H), 7.40 (t, J = 7.9 Hz, 1 H), 7.32–7.10 (m, 7 H), 7.00 (d, J = 8.6 Hz, 1 H), 5.55 (s, 2 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{20}H_{15}O_3N_2ClNa$: 389.0668; found: 389.0685.

***N*-[(4-Chlorophenyl)(2-hydroxydibenzofuran-1-yl)methyl]benzamide (6d)**
Yellow solid; mp 210–212 °C.

IR (KBr): 3236, 2925, 1637, 1522, 1435, 1352, 1221, 1083 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.80 (s, 1 H), 8.82 (d, J = 9.6 Hz, 1 H), 8.20 (d, J = 7.5 Hz, 1 H), 7.87 (d, J = 6.6 Hz, 2 H), 7.80 (m, 1 H), 7.55–7.37 (m, 9 H), 7.20 (d, J = 8.4 Hz, 2 H), 7.07 (d, J = 8.6 Hz, 1 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{26}H_{18}O_3NClNa$: 450.0872; found: 450.0875.

***N*-[(2-Hydroxydibenzofuran-1-yl)(3,4,5-trimethoxyphenyl)methyl]acetamide (6e)**
White solid; mp 183–186 °C.

IR (KBr): 3373, 3176, 2934, 1632, 1591, 1508, 1454, 1377, 1329, 1240, 1127, 1006 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.42 (s, 1 H), 8.20–8.10 (m, 2 H), 7.55–7.20 (m, 4 H), 7.15 (d, J = 9.0 Hz, 1 H), 7.05 (d, J = 8.6 Hz, 1 H), 6.50 (s, 2 H), 3.62 (s, 9 H), 2.00 (s, 3 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{24}H_{23}O_6NNa$: 444.1429; found: 444.1426.

***N*-[(2-Hydroxydibenzofuran-1-yl)(3,4,5-trimethoxyphenyl)methyl]benzamide (6f)**
White-yellow solid; mp 122–126 °C.

IR (KBr): 3368, 3172, 2934, 2833, 1658, 1578, 1508, 1454, 1408, 1327, 1237, 1123, 1001 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.84 (s, 1 H), 8.90 (d, J = 9.0 Hz, 1 H), 8.24 (d, J = 7.9 Hz, 1 H), 7.92–7.80 (m, 3 H), 7.54–7.30 (m, 7 H), 7.10 (d, J = 8.8 Hz, 1 H), 6.62 (s, 2 H), 3.70 (s, 9 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{29}H_{25}O_6NNa$: 506.1620; found: 506.1612.

***N*-[(2-Hydroxydibenzofuran-1-yl)(3,4,5-trimethoxyphenyl)methyl]urea (6g)**
White solid; mp 161–163 °C.

IR (KBr): 3445, 3374, 2927, 2852, 1647, 1595, 1528, 1455, 1381, 1327, 1240, 1124, 1004 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.30 (d, J = 6.6 Hz, 1 H), 8.20 (br s, 1 H), 7.80 (br s, 1 H), 7.50 (d, J = 8.3 Hz, 1 H), 7.43–7.20 (m, 3 H), 7.10 (d, J = 9.6 Hz, 1 H), 7.00 (d, J = 8.4 Hz, 1 H), 6.60 (s, 2 H), 5.50 (br s, 2 H), 3.60 (s, 9 H).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{23}H_{22}O_6N_2Na$: 445.1375; found: 445.1368.

***N*-[(4-Bromophenyl)(2-hydroxydibenzofuran-1-yl)methyl]urea (6h)**
White solid; mp 78–82 °C.

IR (KBr): 3374, 2923, 2853, 1647, 1597, 1528, 1454, 1429, 1369, 1219, 1181, 1076 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.50 (s, 1 H), 8.20 (br s, 1 H), 7.60 (d, J = 8.1 Hz, 1 H), 7.50–7.23 (m, 5 H), 7.20 (d, J = 8.3 Hz, 2 H), 7.00 (s, 3 H), 5.80 (s, 2 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.4, 156.1, 151.2, 149.2, 142.7, 130.8, 129.0, 128.0, 127.2, 122.7, 122.4, 122.1, 121.8, 119.2, 116.0, 111.7, 110.8, 49.3.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{20}H_{15}O_3N_2BrNa$: 433.0163; found: 433.0152.

***N*-[(2-Bromophenyl)(2-hydroxydibenzofuran-1-yl)methyl]acetamide (6i)**
White solid; mp 208–210 °C.

IR (KBr): 3404, 3057, 2925, 1640, 1519, 1430, 1373, 1219, 1082, 1020 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.10 (s, 1 H), 8.25 (d, J = 7.3 Hz, 1 H), 7.87 (s, 1 H), 7.55 (d, J = 7.3 Hz, 1 H), 7.50 (m, 1 H), 7.45–7.23 (m, 4 H), 7.10 (d, J = 7.3 Hz, 3 H), 6.92 (d, J = 8.3 Hz, 1 H), 2.00 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$–DMSO-d_6): δ = 167.0, 158.8, 154.2, 149.9, 149.2, 138.3, 130.4, 128.4, 126.6, 121.9, 121.3, 120.4, 117.7, 114.3, 109.5, 109.1, 108.5, 49.5, 20.4.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{21}H_{16}O_3NBrNa$: 432.0207; found: 432.0211.

***N*-[(2-Hydroxydibenzofuran-1-yl)(4-methoxyphenyl)methyl]acetamide (6j)**
White solid; mp 190–192 °C.

IR (KBr): 3407, 3268, 2929, 1644, 1607, 1512, 1433, 1370, 1249, 1220, 1174 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.40 (s, 1 H), 8.10 (d, J = 7.9 Hz, 2 H), 7.50–7.17 (m, 7 H), 7.04 (d, J = 7.3 Hz, 1 H), 6.76 (d, J = 7.3 Hz, 2 H), 3.70 (s, 3 H), 2.02 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 169.0, 157.9, 156.0, 151.2, 149.1, 133.1, 128.3, 127.0, 123.5, 122.5, 121.5, 116.1, 113.4, 111.6, 110.7, 54.9, 49.0, 22.6.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{22}H_{19}O_4NNa$: 384.1211; found: 384.1217.

***N*-[(2-Hydroxydibenzofuran-1-yl)(4-methoxyphenyl)methyl]urea (6k)**
White solid; mp 76–79 °C.

IR (KBr): 3373, 2924, 2853, 1648, 1604, 1510, 1455, 1429, 1375, 1247, 1028 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.42 (s, 1 H), 8.10 (s, 1 H), 7.56 (d, J = 8.4 Hz, 1 H), 7.43–7.23 (m, 3 H), 7.20 (d, J = 8.4 Hz, 2 H), 7.00 (s, 3 H), 6.75 (d, J = 8.3 Hz, 2 H), 5.70 (s, 2 H), 3.70 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.4, 157.7, 156.0, 151.1, 149.0, 134.8, 131.7, 127.0, 123.6, 122.7, 122.0, 116.0, 114.5, 113.3, 112.8, 111.6, 110.4, 54.9, 49.3.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{21}H_{18}O_4N_2Na$: 385.1164; found: 385.1154.

***N*-[1-(2-Hydroxydibenzofuran-1-yl)-3-phenylprop-2-en-1-yl]acetamide (6l)**
White solid; mp 155–160 °C.

IR (KBr): 3399, 3066, 2924, 1639, 1513, 1451, 1429, 1371, 1271, 1219, 1087 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 9.50 (d, *J* = 6.4 Hz, 1 H), 8.30 (d, *J* = 8.6 Hz, 1 H), 7.80 (d, *J* = 10.0 Hz, 1 H), 7.50–7.05 (m, 10 H), 7.02 (d, *J* = 8.4 Hz, 1 H), 6.74–6.52 (m, 2 H), 2.00 (s, 3 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{19}O_3NNa$: 380.1262; found: 380.1273.

N-[Furyl-(2-hydroxydibenzofuran-1-yl)methyl]acetamide (6m)
White solid; mp 155–160 °C.

IR (KBr): 3407, 3181, 2924, 2853, 1645, 1514, 1430, 1369, 1335, 1302, 1272, 1223, 1145 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.30 (s, 1 H), 8.15 (d, *J* = 7.9 Hz, 1 H), 7.95 (d, *J* = 8.7 Hz, 1 H), 7.47 (m, 1 H), 7.40–7.20 (m, 5 H), 7.00 (d, *J* = 8.9 Hz, 1 H), 6.22 (s, 1 H), 6.10 (s, 1 H), 2.00 (s, 3 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{15}O_4NNa$: 344.0898; found: 344.0890.

N-[(2-Hydroxydibenzofuran-1-yl)(1*H*-indol-3-yl)methyl]acetamide (6n)
Brick-red solid; mp 125–130 °C.

IR (KBr): 3405, 2924, 1717, 1645, 1514, 1428, 1379, 1220, 1166, 744 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 10.40 (br s, 1 H), 9.30 (br s, 1 H), 8.10 (s, 1 H), 7.76 (m, 2 H), 7.60 (d, *J* = 7.7 Hz, 1 H), 7.50 (m, 1 H), 7.40–7.26 (m, 3 H), 7.20 (t, *J* = 7.9 Hz, 1 H), 7.05 (d, *J* = 8.4 Hz, 1 H), 7.00–6.95 (m, 2 H), 6.80 (s, 1 H), 2.00 (s, 3 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{18}O_3N_2Na$: 393.1215; found: 393.1213.

1-(4-Chlorophenyl)-1,2-dihydro-4,7-dioxa-2-azabenzo[*c*]fluoren-3-one (7a)
White solid; mp 127–132 °C.

IR (KBr): 3252, 2923, 1728, 1431, 1386, 1216, 1163, 1090 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.75 (s, 1 H), 7.60–7.54 (m, 3 H), 7.43 (t, *J* = 7.4 Hz, 1 H), 7.36–7.25 (m, 5 H), 7.20 (t, *J* = 7.4 Hz, 1 H), 6.20 (s, 1 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{20}H_{12}O_3NClNa$: 372.0403; found: 372.0399.

1-(4-Bromophenyl)-1,2-dihydro-4,7-dioxa-2-azabenzo[*c*]fluoren-3-one (7b)
White solid; mp 189–193 °C.

IR (KBr): 3259, 2925, 1729, 1433, 1217, 1082, 1003 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.70 (s, 1 H), 7.60–7.50 (m, 3 H), 7.48–7.40 (m, 3 H), 7.30-7.15 (m, 4 H), 6.14 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$–DMSO-d_6): δ = 156.0, 151.7, 149.4, 145.4, 139.3, 131.3, 131.2, 128.2, 126.9, 122.2, 121.8, 121.5, 121.3, 115.2, 113.4, 111.5, 111.1, 53.5.

MS (EI): *m/z* = 395 [M + 2]$^+$, 393 [M]$^+$.

1-*p*-Tolyl-1,2-dihydro-4,7-dioxa-2-azabenzo[*c*]fluoren-3-one (7c)
White solid; mp 168–172 °C.

IR (KBr): 3244, 3126, 2923, 1726, 1432, 1398, 1219, 1165 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.27 (m, 6 H), 7.20–7.00 (m, 4 H), 6.75 (s, 1 H), 6.05 (s, 1 H), 2.25 (s, 3 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{21}H_{15}O_3NNa$: 352.0950; found: 352.0956.

1-(4-Methoxyphenyl)-1,2-dihydro-4,7-dioxa-2-azabenzo[*c*]fluoren-3-one (7d)
White solid; mp 189–193 °C.

IR (KBr): 3259, 2922, 1729, 1433, 1217, 1163, 1082, 1003 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.10 (m, 9 H), 6.80 (d, *J* = 9.0 Hz, 1 H), 6.70 (s, 1 H), 6.10 (s, 1 H), 3.60 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$–DMSO-d_6): δ = 158.9, 156.1, 151.8, 149.4, 145.9, 133.5, 128.3, 127.8, 123.0, 122.8, 122.1, 119.6, 115.9, 115.5, 114.3, 112.1, 111.7, 55.0, 53.3.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{21}H_{15}O_4N$: 368.0898; found: 368.0906.

1-(3,4,5-Trimethoxyphenyl)-1,2-dihydro-4,7-dioxa-2-azabenzo[*c*]fluoren-3-one (7e)
White solid; mp 167–172 °C.

IR (KBr): 3369, 2930, 1735, 1591, 1505, 1458, 1426, 1231, 1124 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.58 (d, *J* = 2.4 Hz, 1 H), 7.70–7.50 (m, 4 H), 7.40 (t, *J* = 8.1 Hz, 1 H), 7.25–7.15 (m, 1 H), 6.55 (s, 2 H), 6.08 (d, *J* = 2.8 Hz, 1 H), 3.70 (s, 9 H).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{19}O_6NNa$: 428.1110; found: 428.1115.

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