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Novel aurone-type compounds with an extended π-system: Synthesis and optical properties

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ABSTRACT

In this paper, a novel family of (*E*,*E*)-aminoaurone-type compounds with an extended π-system has been developed, prepared *via* copper catalysed aza-Michael addition, ring opening, and cyclization between (*E*)-3-bromo-2-styrylchromones and aniline derivatives in the presence of base under mild reaction conditions. All derivatives showed strong solvatochromic absorption and emission properties, which make them potential compounds for sensing applications. The presence of electron-withdrawing substituents in the aromatic ring had a strong influence on the fluorescence behavior of the aurone-type derivatives. In particular, aurone **3h** has promising characteristics, not only for the large Stokes observed, but also for the presence of the *C*-glycosyl moiety. We conclude that appropriately substituted π-extended aminoaurones are potentially useful as biological probes.

1. Introduction

Aurones are a subclass of the flavonoid family characterized by the presence of a 2-benzylidenebenzofuran-3(2*H*)-one moiety **1** (Fig. 1) and responsible for the vibrant yellow colour of some plants and flowers. Although they have a very limited presence in nature, interest in these flavonoids has been growing steadily in the past few years mostly due to their importance in medicinal chemistry [1,2]. Aurones display a wide variety of biological activities, including anticancer [3,4], antibacterial [5], antifungal [6], antimalarial [7], antileishmanial [8], anti-Alzheimer [9,10], anti-inflammatory [11] and antioxidant [12].

More recently, aurones have shown great potential to be used as chemical sensors and fluorescent labels or probes in biological and medical fields. This is because their absorption and fluorescent properties fall in the visible range, absorbing light at longer wavelengths than other flavonoid pigments. In addition, some derivatives exhibit efficient fluorescent emission with large quantum yields and sizable Stokes shifts [13]. Thus, the relatively small size of aurones is an evident advantage over other chromophores typical used for fluorescent probes, such as xanthenes (fluorescein, rhodamine) or cyanine and boron dipyrromethanes [14].

The photophysical properties of aurones are directly related with its molecular structure. Thus, the maximum absorption wavelength λ_{max} can be tailored by substituting its basic structure with electron withdrawing/donating functional groups [13]. On other hand, the maximum absorption λ_{max} was described as a HOMO→LUMO transition (π→π*) with charge-transfer (CT) character [15]. It is widely assumed that, as the number of conjugated double bonds increases, the π→π* band shifts bathochromically. As a consequence, a vinylogous extension would shift λ_{max} to the visible region of the electromagnetic spectrum.

Due to their huge chemical and biological relevance, many efforts have been devoted to the synthesis of aurones [16]. The most common synthetic methodologies for the preparation of aurones are: the oxidative cyclization of (*E*)-2′-hydroxychalcones by thallium (III) nitrate [17] or $Hg(OAc)_2$ [18]; the intramolecular cyclization of 2-hydroxyaryl phenylethynyl ketones [19]; and the condensation of benzofuran-3(2*H*)-ones with aromatic aldehydes catalysed by acid [20] or base [21], or alumina [22]. Along with those methods other improved strategies have also been recently reported for the synthesis of aurones. A representative example is the high yielding stereoselective synthesis of aurones from arylacetylenes and salicylaldehydes by the means of silver (I) nitrate mediated cyclization/oxidation developed by Jung [23] et al. Yu and co-authors have also successfully developed alkynylation/cyclization of terminal alkynes with salicylaldehydes by using Cy_3P-silver

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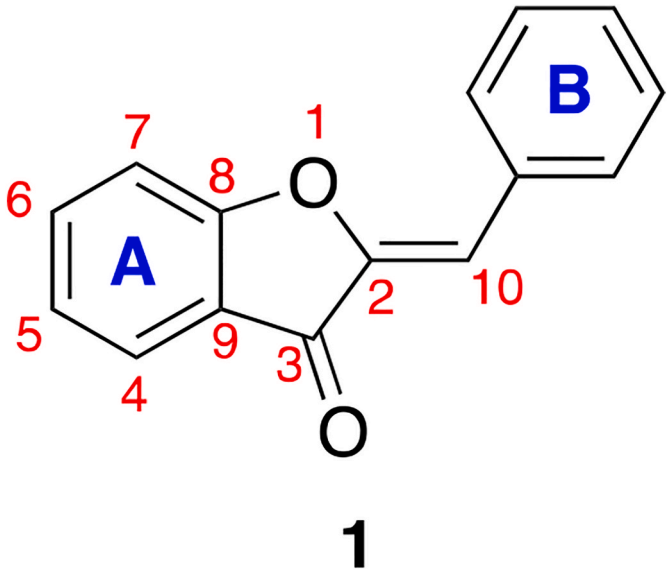


1

Fig. 1. Aurone [2-benzylidenebenzofuran-3(2*H*)-one] scaffold.

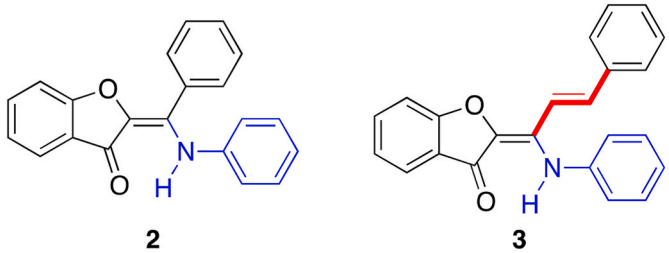
complex [24]. However, the reported cyclization strategies for the construction of the aurone core have some drawbacks, such as harsh reaction condition, long reaction time, expensive catalyst loading, among others. In 2019, Parveen and co-workers reported a facile synthesis of aurones based on a Cu(I)-catalysed cascade aza-Michael addition, ring opening, and oxidative cyclization reactions in one-pot under basic reaction condition, which afforded (*E*)-aminated aurone derivatives **2** (Fig. 2) in moderate to good yields and excellent stereoselectivities [25].

Considering that the optical properties of aurones depend on the level of conjugation between the benzene and benzofuranone moieties, we envisioned the study of the impact of a vinylogous extension on the optical properties of aminoaurone derivatives. For this purpose, we developed the synthesis of a novel type of aminoaurone derivatives with extended π-system **3** (Fig. 2) through the copper-catalysed stereoselective reaction of (*E*)-3-bromo-2-styrylchromones with anilines.

2. Results and discussion

2.1. Synthesis of aurone-type derivatives

We have previously reported in our group the synthesis of a significant number of 3-bromo-2-styrylchromones by way of a Baker-Venkataraman rearrangement of 2′-cinnamoyloxyacetophenones [26,27], followed by a one-pot cyclization/bromination reaction with phenyltrimethylammonium tribromide (PTT) [28]. To explore the effect of both the extended π-system and the substitution of the aromatic rings on the optical properties of aurones, a series of (*E*)-3-bromo-2-styryl-4*H*-chromen-4-ones with different substitution patterns were prepared. The synthesis itself was performed *via* the copper-catalysed reaction of (*E*)-3-bromo-2-styrylchromone starting materials **4a-b** with differently substituted anilines **5a-e** in the presence of KO^{t}Bu as base in DMF for 5 h at room temperature (Scheme 1). For the adopted reaction conditions, 2-(3-arylallylidene)benzofuran-3(2*H*)-ones **3a-g** were obtained in all cases with total (*E*,*E*)-selectivity in moderate yields (31–47%).



2 **3**

Fig. 2. (*E*)-Aminoaurones **2** and π-extended (*E*,*E*)-aminoaurone-type compounds **3**.

In nature, flavonoids are typically bound to sugars. Therefore, we decided to investigate the synthesis of a derivative containing a carbohydrate residue and its effect on the optical properties. For this purpose, we employed a strategy based on the Heck reaction. Thus, a mixture of 1 equiv of galactose derived alkene **6**, 1 equiv of iodoaurone **3f**, 0.15 equiv of $Pd(OAc)_2$, 3 equiv of K_2CO_3 and 2.5 equiv of Bu_4NBr in DMF was stirred at 100 °C overnight, affording aurone–sugar hybrid compound **3h** in 43% yield (Scheme 1).

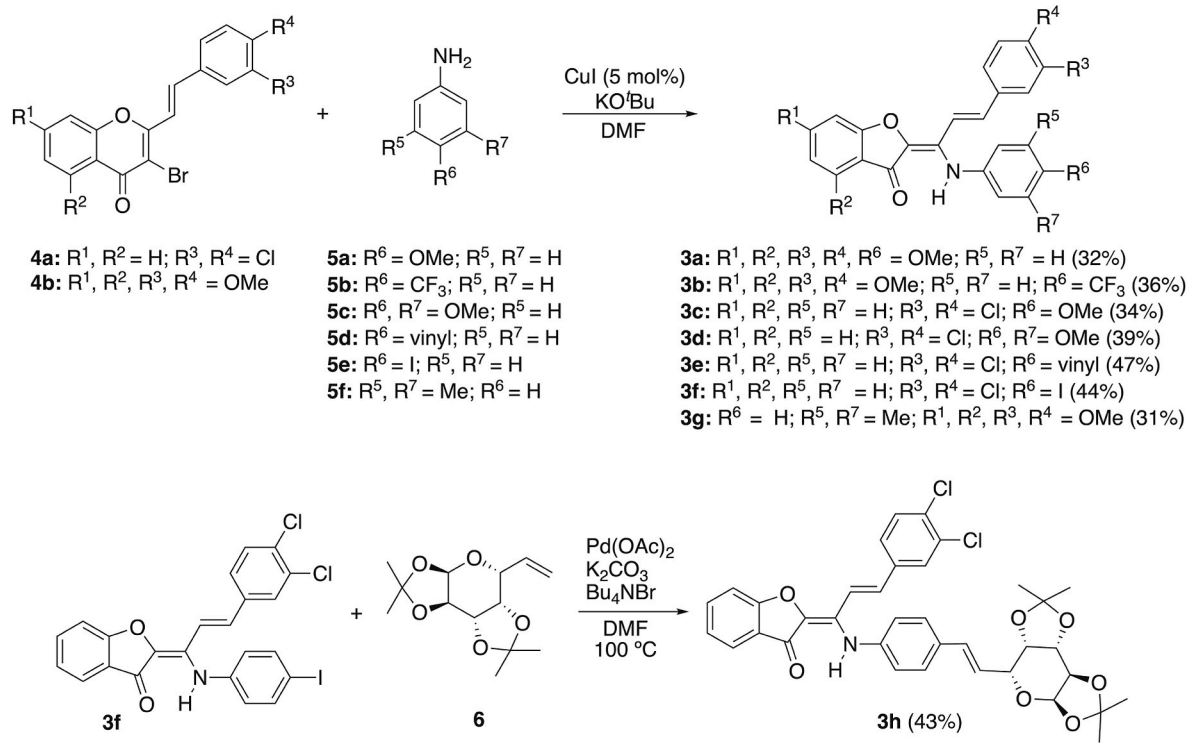
2.2. Absorption and emission spectra for aurone-type derivatives

Table 1 summarizes the excitation and emission energies of **3a-h** in acetonitrile. Aurone-type derivatives **3a-h** showed absorption maxima in the visible range in acetonitrile (Fig. 3), which is consistent with the experimental and theoretical data reported in the literature and [13,29] the extended conjugated π-system of these molecules [30]. While not all substituents were prepared at every position, some interesting trends were observed. Derivative **3a** with a *p*-OMe group in the aniline ring afforded a typical excitation maximum for an aurone (385 nm) but derivative **3b** with an electron-withdrawing *p*-CF_3 resulted in a hypsochromic shift of this maximum wavelength to around 366 nm, behavior in concordance with theoretical data reported previously for other aurones [29] On the other hand, the presence of chlorine atoms at positions 3 and 4 of the B ring in derivative **3d** resulted in a significant hypsochromic shift of roughly 23 nm (362 nm). The replacement of the *p*-OMe in the aniline ring for an iodine atom resulting in derivative **3f** has little effect. Interestingly, whereas the presence of a vinyl group in the aniline ring of derivative **3e** afforded essentially identical lambda maxima (365 nm), an additional chromophore was observed. Unexpectedly, this additional chromophore was not observed in vinyl sugar derivative **3h**. Replacement of the *p*-OMe group in the aniline ring for two methyl groups at positions 3 and 5 in derivative **3g** also had little effect (390 nm).

The π-extended (*E*,*E*)-aminoaurone-type derivatives fluoresce in the visible region of the electromagnetic spectrum; emission spectra in acetonitrile showed maxima between 433 nm and 509 nm depending on the structure. Notable features include the large Stokes shift exhibited by all aminoaurone-type compounds **3**. The emission maxima showed similar values for the aminoaurone-type derivatives, ranging from 464 to 484 nm, with the exception of **3b** and **3f** (Supporting Information). When the 4-substituent of the aniline ring is a CF_3 group for **3b**, a bathochromic shift in the emission maximum was observed (509 nm) (Fig. 4a). On the contrary, a quite significant hypsochromic shift was observed for iodine-containing derivative **3f** (433 nm). The influence of the *p*-CF_3 substitution in the aniline ring is also evidenced in the Stokes shift. As the electron-withdrawing character of the substituents increase, the polarization of the structure also increases, resulting in larger Stokes shifts. As a result, –CF_3 substituent is responsible for the larger Stokes shift in all the series (Δ_{Stokes} = 143). This result is in accordance with what has been reported for –CF_3 substituted aminoaurone derivatives [15].

Carbohydrate derived fluorescent probes have many advantages: they are neutral, hydrophilic and usually display good biocompatibility. On account of these attractive features, sugar-based probes have gained much attention concerning ion detection [31,32], interaction with proteins [33,34] and biological imaging [35]. Considering the importance of the presence of a C-glycoside moiety and the interesting fluorescence properties (Fig. 4b), derivative **3h** was further investigated.

Solvent polarity showed a small effect on the emission maxima



4a: R^1, R^2 = H; R^3, R^4 = Cl
4b: R^1, R^2, R^3, R^4 = OMe

5a: R^6 = OMe; R^5, R^7 = H
5b: R^6 = CF_3; R^5, R^7 = H
5c: R^6, R^7 = OMe; R^5 = H
5d: R^6 = vinyl; R^5, R^7 = H
5e: R^6 = I; R^5, R^7 = H
5f: R^5, R^7 = Me; R^6 = H

3a: R^1, R^2, R^3, R^4, R^6 = OMe; R^5, R^7 = H (32%)
3b: R^1, R^2, R^3, R^4 = OMe; R^5, R^7 = H; R^6 = CF_3 (36%)
3c: R^1, R^2, R^5, R^7 = H; R^3, R^4 = Cl; R^6 = OMe (34%)
3d: R^1, R^2, R^5 = H; R^3, R^4 = Cl; R^6, R^7= OMe (39%)
3e: R^1, R^2, R^5, R^7 = H; R^3, R^4 = Cl; R^6 = vinyl (47%)
3f: R^1, R^2, R^5, R^7 = H; R^3, R^4 = Cl; R^6 = I (44%)
3g: R^6 = H; R^5, R^7 = Me; R^1, R^2, R^3, R^4 = OMe (31%)

Scheme 1. Synthesis of π-extended (*E*,*E*)-aminoaurone-type compounds **3**.

Table 1
Spectral data for π-extended (*E*,*E*)-aminoaurone-type compounds.

Compound	λ_{exc}, nm		λ_{em}, nm		Φ_F
3a	315	385	480		0.0035 ± 0.0008
3b	366		509		0.012 ± 0.004
3c	362		464		0.016 ± 0.004
3d	381		484		0.001 ± 0.001
3e	–	365	411(s)	485	
	–	345	410	485	0.005 ± 0.001
	315(s)	–	377	485	
3f	304(s)	364	433		0.006 ± 0.001
3g	390		475		0.010 ± 0.003
3h	278	348 (365 s)	475	505	0.018 ± 0.004

[a] In acetonitrile.

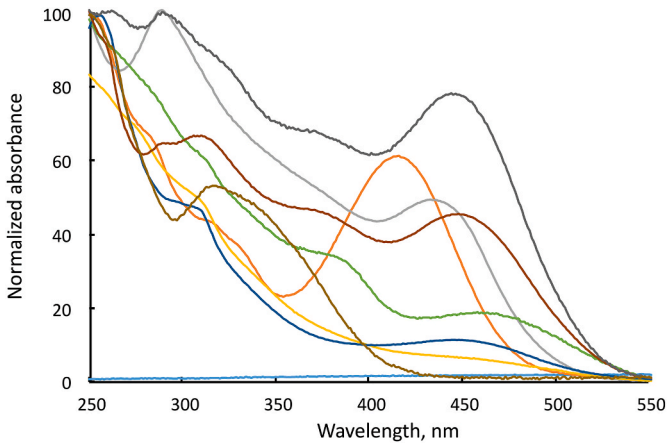


Fig. 3. Absorption spectra for π-extended (*E*,*E*)-aminoaurone-type derivatives **3a** (orange), **3b** (light grey), **3c** (yellow), **3d** (green), **3e** (dark blue), **3f** (dark red), **3g** (dark grey) and **3h** (brown) in acetonitrile (light blue).

(Table 2). However, the emission intensities showed a marked dependence on the solvent polarity as seen in Fig. 5. Interestingly, aurone **3h** is less fluorescent in methanol and highly fluorescent in non-polar dichloromethane and the hydrophobic alcohol 1-pentanol, making it a good probe for biological applications.

It is worth mentioning that the quantum yields of derivative **3h** are larger than those of other aurone derivatives which showed potential to serve as probes for proteins and nucleic acids [13]. In this regard, this novel C-glycosyl aurone-type fluorescent probe is complementary to other dye classes such as xanthenes and cyanines, with lower quantum yields but significantly larger Stokes shifts.

3. Conclusions

In summary, we have developed a copper-catalysed one-pot cascade *via* aza-Michael addition, ring opening and cyclization reactions between (*E*)-3-bromo-2-styrylchromones and anilines for the stereoselective synthesis of (*E*,*E*)-aminated aurone derivatives with a vinylogous extension between the benzylidene and benzofuranone moieties. To the best of our knowledge, this is the first example of the synthesis of (*E*,*E*)-2-[styryl (arylamino)methylene]benzofuran-3(2*H*)-ones, a novel family of non-natural flavonoids. This new family of aurone-type derivatives displays strong solvatochromic absorption and emission properties, which may be tuned to suit a particular application through functional group selection. The aurone-type scaffold **3h** bearing a sugar derivative is interesting for developing further fluorescence applications such as visible-range optical sensors.

4. Experimental section

4.1. Materials and methods

All non-aqueous reactions were carried out under a positive atmosphere of nitrogen in flame-dried glassware unless otherwise stated. Air- and moisture-sensitive liquid reagents were added by dry syringe or cannula. Anhydrous tetrahydrofuran (THF) was freshly distilled from

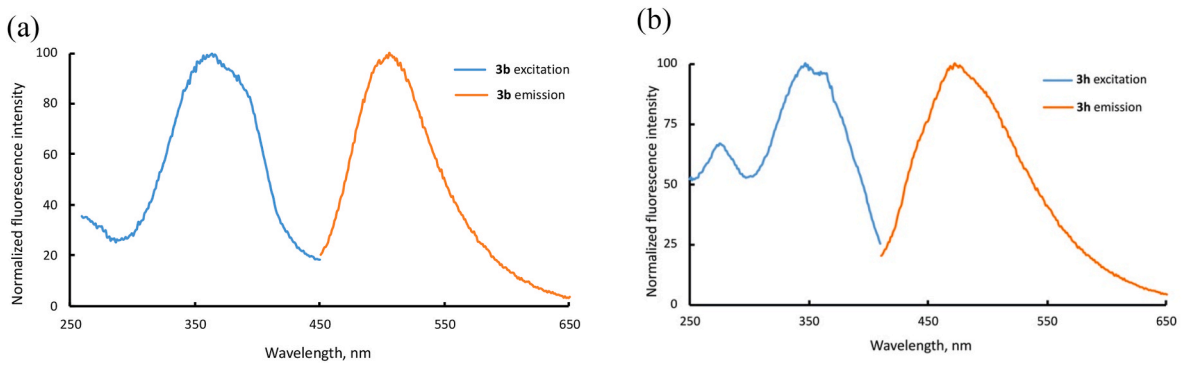


Fig. 4. Fluorescence excitation and emission spectra for (a) **3b** and (b) **3h**.

Table 2
Excitation and fluorescence emission maxima for derivative **3h** in different solvents.

Solvent	Relative polarity [36]	λ_{exc1}	λ_{exc1}	λ_{exc1}	λ_{em}	Δ_{Stokes}	I	I_{rel}[a]	Φ_F
Ether	0.117	271	346	360	487	127	303	0.6	0.020 ± 0.005
dichloromethane	0.309	277	350	363	476	113	925	1.8	0.027 ± 0.007
Acetone	0.355	n.d.	350	362	475	113	554	1.1	0.017 ± 0.004
Acetonitrile	0.460	278	347	360	472	112	515	1.0	0.018 ± 0.004
pentan-1-ol	0.568	276	349	362	482	120	807	1.6	0.030 ± 0.007
propan-1-ol	0.617	277	348	361	481	120	521	1.0	0.024 ± 0.007
Methanol	0.762	277	348	361	474	113	416	0.8	0.016 ± 0.004
Water	1.000	n.d.	n.d.	n.d.	n.d.	n.d.	0	0.0	n.d.

[a] $I_{rel} = I / I_{acetonitrile}$

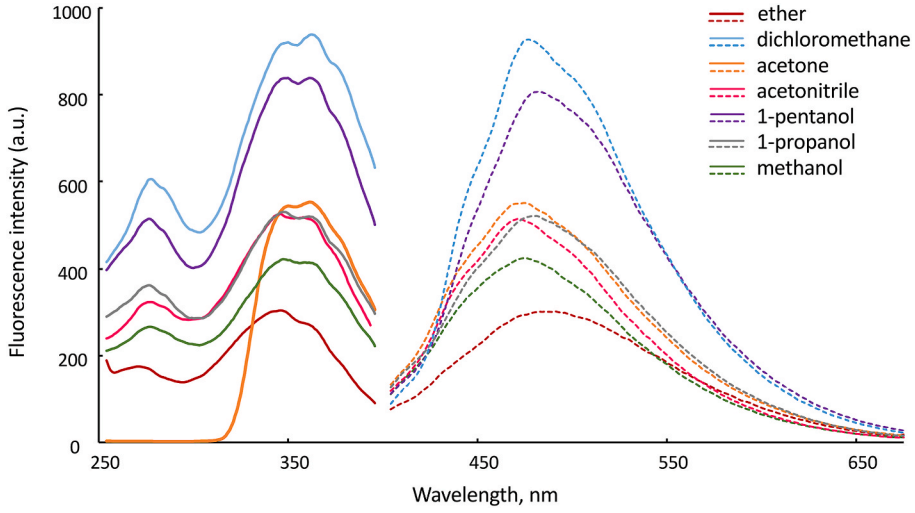


Fig. 5. Fluorescence emission spectra for **3h** in different solvents.

sodium/benzophenone under nitrogen and all other solvents and reagents were used as obtained from commercial sources without further purification unless stated. Flash chromatography was performed using 60 Merck 230–400 mesh (flash, 0.04–0.063) silica. Thin layer chromatography (tlc) was carried out on aluminum backed sheets coated with 60 GF254 silica. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C at room temperature. All chemical shifts are quoted on the δ scale using residual solvent as internal standard; s, d, t, q, m, and br designate singlet, doublet, triplet, quadruplet, multiplet, and broad, respectively. Coupling constants (*J*) are measured in Hz. Mass spectra analysis (ESI-MS) and high resolution mass spectra analysis (ESI-HRMS, 70eV) were carried out on an electrospray ionization mass spectrometer with a micro-TOF analyzer. Absorption measurements were taken in a Cary 60 UV–Vis spectrophotometer from Agilent Technologies (Palo Alto, CA, USA). Excitation and emission luminescence spectra were obtained with a Varian Cary Eclipse (Agilent Technologies).

4.2. General procedure for the synthesis of aurone-type derivatives 3a-h

To a solution of the corresponding (*E*)-3-bromo-2-aryl-4*H*-chromen-4-one **4** (1 mmol) in DMF (10 mL), the appropriate aniline **5** (1.5 mmol, 1.5 equiv), KO^{t}Bu (3 mmol, 3 equiv) and CuI (5 mol%) were added. The reaction mixture was stirred at room temperature for 5 h and then poured into ice and water. The precipitate was filtered and then the obtained solid was taken up in dichloromethane (50 mL), washed with water (3 × 50 mL), dried (Na_2SO_4) and filtered. The organic layer was evaporated to dryness and the obtained residue was purified by column chromatography by using 1:1 hexane/ethyl acetate as eluent affording (*E*,*E*)-2-(3-arylallylidene)benzofuran-3(2*H*)-ones **3a-h**.

*(E,E)-4,6-Dimethoxy-2-[(3,4-dimethoxystyryl) (4-methoxyphenylamino)methylene]benzofuran-3(2H)-one (**3a**):* 32% yield (156 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.17 (d, *J* 1.9 Hz, 1H), 6.70 (d, *J* 16.5 Hz, 1H), 6.88 (d, *J* 8.9 Hz, 2H), 7.00–7.15 (m, 4H), 7.56 (d, *J* 16.5 Hz, 1H), 11.36 (bs, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 55.5 (CH_3), 55.8 (CH_3), 55.97 (CH_3), 56.01 (2 x CH_3), 88.4 (CH), 93.4 (CH), 109.6 (CH), 111.2 (CH), 114.5 (2 x CH), 115.8 (CH), 121.3 (CH), 124.6 (2 x CH), 129.2 (C), 132.7 (C), 133.3 (C), 133.5 (C), 141.1 (C), 141.2 (CH), 149.3 (C), 150.5 (C), 156.7 (C), 158.3 (C), 164.1 (C), 165.9 (C), 177.1 (C═O) ppm; HRMS (ESI^+): $C_{28}H_{28}NO_7$: calcd 490.1860 $[M+H]^+$, found: 490.1869.

*(E)-4,6-Dimethoxy-2-[(E)-(3,4-Dimethoxystyryl) (4-trifluoromethylphenylamino)methylene]benzofuran-3(2H)-one (**3b**):* 36% yield (190 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 3.91 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 6.18 (d, *J* 1.6 Hz, 1H), 6.42 (s, 1H), 6.77–6.96 (m, 3H), 7.03–7.09 (m, 2H), 7.32–7.50 (m, 4H), 10.88 (bs, 1H, NH) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 55.5 (CH_3), 55.8 (CH_3), 55.9 (CH_3), 56.0 (CH_3), 88.5 (CH), 93.4 (CH), 109.7 (CH), 111.6 (CH), 114.5 (2 x CH), 116.0 (CH), 121.3 (CH), 124.8 (C), 125.5 (2 x CH), 127.3 (C), 132.7 (C), 133.3 (C), 133.7 (C), 141.1 (C), 146.1 (C), 149.3 (C), 151.0 (C), 156.7 (C), 158.5 (C), 164.2 (C), 177.9 (C═O) ppm; HRMS (ESI^+): $C_{23}H_{17}^{35}Cl^{35}ClNO_2$: calcd 528.1628 $[M+H]^+$, found: 528.1619.

*(E,E)-2-[(3,4-Dichlorostyryl) (4-methoxyphenylamino)methylene]benzofuran-3(2H)-one (**3c**):* 34% yield (179 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 3.83 (s, 3H, OCH_3); 6.79 (d, *J* 16.5 Hz, 1H), 6.91 (dd, *J* 8.9 and 2.1 Hz, 2H), 7.15 (dd, *J* 8.9 and 2.1 Hz, 2H), 7.20 (d, *J* 7.5 Hz, 1H), 7.22 (d, *J* 7.2 Hz, 1H), 7.34 (d, *J* 8.3 Hz, 1H), 7.45 (d, *J* 1.6 Hz, 1H), 7.47 (d, *J* 7.2 Hz, 1H), 7.56 (ddd, *J* 8.3, 7.5 and 0.9 Hz, 1H), 7.88 (dd, *J* 7.5 and 0.9 Hz, 1H), 8.12 (d, *J* 16.5 Hz, 1H), 11.36 (br s, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 55.6 (CH_3), 112.6 (CH), 114.7 (2 x CH), 120.3 (CH), 122.3 (CH), 123.2 (CH), 124.1 (C), 125.7 (2 x CH), 127.6 (2 x CH), 129.9 (CH), 131.5 (C), 132.8 (C), 132.9 (CH), 133.4 (C), 135.1 (C), 135.7 (C), 137.4 (CH), 142.5 (C), 157.6 (C), 161.2 (C), 179.0 (C═O) ppm; HRMS (ESI^+): $C_{25}H_{17}^{35}Cl^{35}ClNO_2$: calcd 438.0658 $[M+H]^+$, found: 438.0660.

*(E)-2-[(E)-(3,4-Dichlorostyryl) (3,4-dimethoxyphenylamino)methylene]benzofuran-3(2H)-one (**3d**):* 39% yield (183 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 3.84 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.78 (d, *J* 8.0 Hz, 1H), 6.78 (d, *J* 1.9 Hz, 1H), 6.82 (d, *J* 16.6 Hz, 1H), 6.86 (br d, *J* 8.0 Hz, 1H), 7.21 (br d, *J* 7.4 Hz, 1H), 7.23 (d, *J* 7.5 Hz, 1H), 7.23 (br d, *J* 7.5 Hz, 1H), 7.46 (d, *J* 2.3 Hz, 1H), 7.48 (br d, *J* 7.5 Hz, 1H), 7.56 (ddd, *J* 8.4, 7.4 and 1.3 Hz, 1H), 7.88 (br d, *J* 7.4 Hz, 1H), 8.12 (d, *J* 16.6 Hz, 1H), 11.36 (bs, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 56.0 (CH_3), 56.1 (CH_3), 108.3 (CH), 111.5 (CH), 112.6 (CH), 116.4 (CH), 120.4 (CH), 122.3 (CH), 123.2 (CH), 124.0 (C), 127.5 (CH), 127.6 (CH), 130.0 (CH), 131.8 (C), 132.8 (C), 133.0 (CH), 133.5 (C), 135.1 (C), 135.7 (C), 137.2 (CH), 142.3 (C), 147.1 (C), 149.5 (C), 161.3 (C), 179.0 (C═O) ppm; HRMS (ESI+): $C_{25}H_{19}^{35}Cl^{35}ClNO_4$: calcd 468.0764 $[M+H]^+$, found: 468.0762.

*(E,E)-2-[(3,4-Dichlorostyryl) (4-vinylphenylamino)methylene]benzofuran-3(2H)-one (**3e**):* 47% yield (204 mg); red oil. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 5.25 (d, *J* 10.9 Hz, 1H), 5.72 (d, *J* 17.5 Hz, 1H), 6.70 (dd, *J* 17.5 and 10.9 Hz, 1H), 6.85 (d, *J* 16.5 Hz, 1H), 7.16 (d, *J* 8.0 Hz, 2H), 7.23 (d, *J* 7.7 Hz, 1H), 7.25 (d, *J* 7.2 Hz, 1H), 7.33 (d, *J* 8.1 Hz, 1H), 7.41 (d, *J* 8.0 Hz, 2H), 7.46 (d, *J* 1.9 Hz, 1H), 7.54 (d, *J* 7.2 Hz, 1H), 7.52–7.58 (m, 1H), 7.87 (d, *J* 7.7 Hz, 1H), 8.11 (d, *J* 16.5 Hz, 1H), 11.33 (bs, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 112.7 (CH), 113.8 (=CH_2), 120.4 (CH), 122.4 (CH), 123.3 (2 x CH), 123.4 (CH), 123.9 (C), 127.2 (2 x CH), 127.6 (CH), 127.7 (CH), 130.0 (CH), 132.7 (C), 133.4 (CH), 134.0 (C), 134.4 (C), 135.1 (C), 135.7 (C), 135.9 (CH), 137.2 (CH), 138.5 (C), 140.9 (C), 161.6 (C), 179.6 (C═O) ppm; HRMS (ESI^+): $C_{25}H_{17}^{35}Cl^{35}ClNO_2$: calcd 434.0714 $[M+H]^+$, found: 434.0705.

*(E)-2-[(E)-3,4-(Dichlorostyryl) (4-iodophenylamino)methylene]benzofuran-3(2H)-one (**3f**):* 44% yield (235 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 6.82 (d, *J* 16.5 Hz, 1H), 6.95 (dd, *J* 8.8 and 2.2 Hz, 2H), 7.21 (d, *J* 7.3 Hz, 1H), 7.23 (d, *J* 7.8 Hz, 1H), 7.39 (d, *J* 8.5 Hz, 1H), 7.47 (d, *J* 2.0 Hz, 1H), 7.52 (d, *J* 7.8 Hz, 1H), 7.58 (ddd, *J* 8.5, 7.3 and 1.3 Hz, 1H), 7.65 (dd, *J* 8.8 and 2.2 Hz, 2H), 7.86 (d, *J* 7.3 Hz, 1H), 8.04 (d, *J* 16.5 Hz, 1H), 11.10 (bs, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 88.5 (C), 117.6 (CH), 119.9 (CH), 122.6 (CH), 123.5 (CH), 123.7 (C), 125.0 (2 x CH), 127.6 (CH), 127.7 (CH), 130.0 (CH), 132.6 (C), 133.8 (CH), 134.3 (C), 135.1 (C), 135.9 (C), 137.3 (CH), 138.4 (2 x CH), 139.1 (C), 140.1 (C). 161.9 (C), 180.2 (C═O) ppm; HRMS (ESI^+): $C_{23}H_{14}^{35}Cl^{37}ClINO_2$: calcd 535.9495 $[M+H]^+$, found: 535.9480.

*(E,E)-4,6-Dimethoxy-2-[(3,4-Dimethoxystyryl) (5,7-dimethylphenylamino)methylene]benzofuran-3(2H)-one (**3g**):* 31% yield (151 mg); dark orange oil; ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.27 (s, 6H, 2 x CH_3), 3.88 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 6.15 (d, *J* 1.8 Hz, 1H), 6.40 (s, 1H), 6.64–6.93 (m, 5H), 6.96–7.15 (m, 2H), 7.57 (d, *J* 16.4 Hz, 1H), 11.11 (bs, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 21.4 (2 x CH_3), 55.9, 56.0 (4 x CH_3), 88.5 (CH), 93.5 (CH), 109.3 (CH), 111.2 (CH), 116.2 (CH), 120.2 (2 x CH), 121.4 (CH), 125.6 (C), 129.3 (C), 133.8 (C), 133.3 (C), 138.9 (2 x –CH), 140.2 (C), 140.8 (C), 149.3 (C), 150.4 (C), 158.4 (C), 164.4 (C), 166.0 (C), 177.3 (C═O) ppm; HRMS (ESI^+): $C_{23}H_{17}^{35}Cl^{35}ClNO_2$: calcd 488.2068 $[M+H]^+$, found: 488.2068.

4.3. Synthesis of C-glycosyl aurone-type derivative **3h**

A mixture of the iodo aurone-type derivative **3f** (0.22 mmol, 117.4 mg) and sugar alkene **6** (0.22 mmol, 56.4 mg), $Pd(OAc)_2$ (7 mg, 0.15 equiv), Bu_4NBr (0.18 g, 2.5 equiv) and K_2CO_3 (92 mg, 3 equiv) in dry DMF (5 mL) was heated at 100 °C for 2 days. After this period, water was added (10 mL), and the mixture was extracted with ethyl acetate (15 mL). The organic layer was washed with water (2 × 10 mL) and brine (2 × 10 mL), dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography eluting with a mixture of ethyl acetate/hexane to afford *C*-glycosylated (*E,E*)-2-(3-arylallylidene)benzofuran-3(2*H*)-one **3h** as a dark orange oil (61.2 mg, 43%).

(E,E,E)-2-{[2-(3,4-Dichlorophenyl)ethenyl][4-((6,7-dideoxy-1,2:3,4-di-O-isopropylidene-β-D-galacto-hept-6-enopyranos-7yl)phenylamino]methylene}benzofuran-3(2H)-one (**3h**).

^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.25 (s, 3H), 1.38 (s, 3H), 1.45 (s, 3H), 1.59 (s, 3H), 4.36 (dd, *J* 7.7 and 2.2 Hz, 1H), 4.38 (dd, *J* 5.0 and 2.4 Hz, 1H), 4.56 (d, *J* 5.8 Hz, 1H), 4.69 (dd, *J* 7.7 and 2.4 Hz, 1H), 5.64 (d, *J* 5.0 Hz, 1H), 6.31 (dd, *J* 16.1 and 5.8 Hz, 1H), 6.83 (dd, *J* 16.1 and 1.4 Hz, 1H), 7.26 (dd, *J* 8.1 and 2.4 Hz, 1H), 7.26 (d, *J* 8.1 Hz, 1H), 7.38 (d, *J* 7.7 and 0.6 Hz, 1H), 7.47 (d, *J* 7.5 Hz, 2H), 7.48 (d, *J* 16.0 Hz, 1H), 7.48 (d, *J* 2.4 Hz, 1H), 7.54 (d, *J* 8.0 Hz, 1H), 7.66–7.71 (m, 1H), 7.72 (d, *J* 7.5 Hz, 2H), 7.99 (d, *J* 16.0 Hz, 1H), 8.21 (dd, *J* 7.7 and 1.6 Hz, 1H) ppm; ^{13}C NMR (75.47 MHz; $CDCl_3$): δ 24.7 (CH_3), 25.0 (CH_3), 26.1 (CH_3), 26.2 (CH_3), 68.9 (CH), 70.4 (CH), 71.0 (CH), 73.8 (CH), 96.4 (C), 108.7 (C), 109.3 (C), 117.7 (CH), 120.2 (C), 122.0 (2 x CH), 123.0 (2 x CH), 124.9 (CH), 126.0 (CH), 127.5 (2 x CH), 128.0 (2 x CH), 129.9 (C–H), 131.2 (CH), 132.5 (2 x C), 133.8 (CH), 134.1 (CH), 135.2 (C), 135.4 (C), 143.0 (C), 149.1 (C), 151.7 (C), 177.6 (C═O) ppm. HRMS (ESI^+): $C_{36}H_{37}^{35}Cl^{35}N_2O_7$: calcd 644.2284 $[M + NH_3–Cl]^+$, found: 644.2160.

4.4. Determination of the quantum yields

The luminescence quantum yield (Φ) of the compounds in different solvents was calculated according to the procedure described by Parker and Rees [37] and the protocol from Jobin Yvon-Horiba [38]. The luminescence quantum yield (Φ) was calculated using the equation:

$$\Phi_i = \Phi_{std}\frac{m_i}{m_{std}}.\left(\frac{n_i}{n_{std}}\right)^2$$

where Φ_{std} is the quantum yield of a quinine sulfate standard solution

($\Phi_{std} = 0.54$) [39] m_i the slope of the integrated emission luminescence spectrum vs absorbance and n the refractive index od de solvent. All results have been expressed with a confidence interval of 99%

The refractive indices for the solvents were obtained from the literature [40].

4.5. Notes

The manuscript was written through the contributions of all authors. All authors have approved the final version of the manuscript.

CRediT authorship contribution statement

Sara M. Tomé: Writing – original draft, performed the aurone synthesis, All authors contributed to the overall scientific interpretation. **Raquel G. Soengas:** Writing – original draft, supervised the project, All authors contributed to the overall scientific interpretation. **Rosana Badía-Laíño:** performed the absorption and emission studies, All authors contributed to the overall scientific interpretation. **Artur M.S. Silva:** Methodology, Supervision, Project administration, Funding acquisition, Writing – review & editing, All authors contributed to the overall scientific interpretation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

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