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# Synthesis of anabasine-containing aminomethyl derivatives of 6-hydroxyaurones

**Antonina V. Popova[1], Svitlana P. Bondarenko[2], Valentina I. Vinogradova[3], Mykhaylo S. Frasinyuk[1]***

[1] *V. P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, 1 Murmanska St., Kyiv 02094, Ukraine; e-mail: mykhaylo.frasinyuk@ukr.net*

[2] *National University of Food Technologies, 68 Volodymyrska St., Kyiv 01601, Ukraine; e-mail: svitlana.bondarenko@ukr.net*

[3] *Academician S. Yu. Yunusov Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, 77 Mirzo Ulugbek St., Tashkent 700170, Uzbekistan; e-mail: 1946viv@mail.ru*

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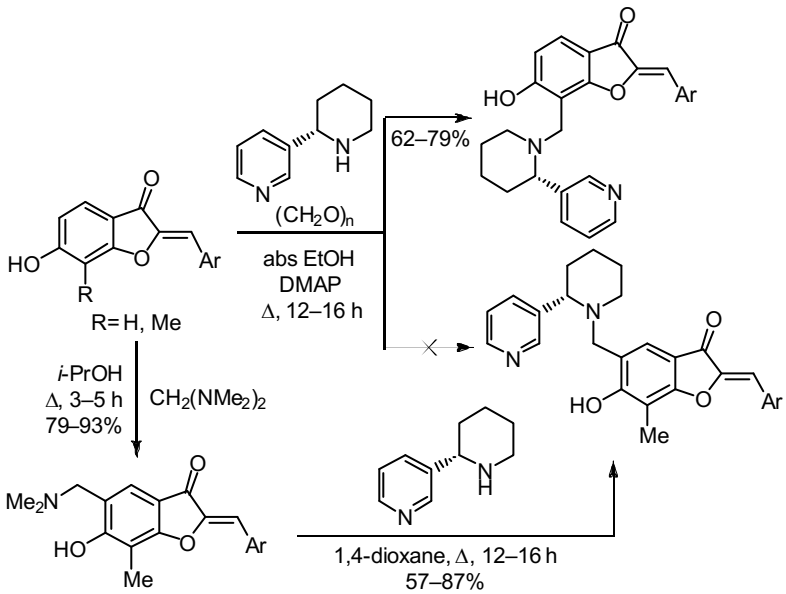



Aminomethylation of aurones was studied by using anabasine. The reaction in the case of 6-hydroxyaurones was shown to selectively provide 7-aminomethyl-6-hydroxyaurones, while 5-aminomethyl-6-hydroxy-7-methylaurones could be obtained by transamination of 5-dimethylaminomethyl derivatives of 6-hydroxy-7-methylaurones in the presence of anabasine.

**Keywords**: anabasine, benzofuran-3(2*H*)-one, 6-hydroxyaurone, aminomethylation, Mannich base.

Anabasine (3-[(2*S*)-piperidin-2-yl]pyridine) (**1**) and its derivatives have been characterized as cholinesterase inhibitors,[1] as well as agonists of nicotinic acetylcholine receptors,[2] which are currently considered as important targets in the drug discovery efforts aimed at treating neurological disorders. Due to its high toxicity, the practical applications of anabasine in medicine and agriculture are quite limited. At the same time, alkylation or acylation of this alkaloid at the piperidine ring nitrogen atom has helped to mitigate the toxicity.[2a,3] In addition, alkaloids isolated from the roots of *Alangium chinense*, identified as derivatives of (2*S*)-*N*-(2-hydroxybenzyl)-anabasine, can suppress the development of inflammatory processes in the peripheral nervous system.[4]

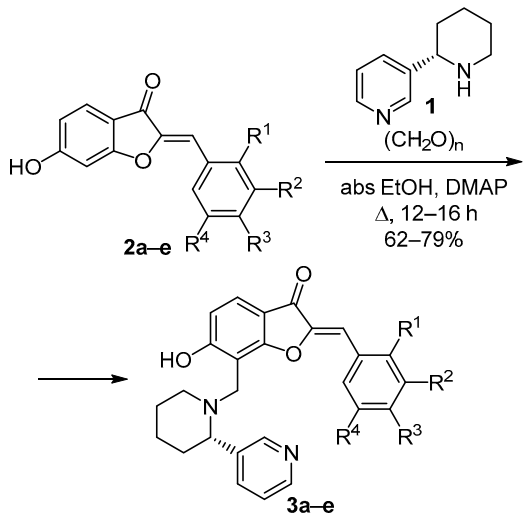
One of the promising routes for modification of anabasine involves its transformations *via* the Mannich reaction. According to the literature data, anabasine has been successfully used in aminomethylation of acetylenes

in the presence of CuCl,[5] while *N*-benzyl derivatives of anabasine have been obtained in reductive amination reactions.[6]

We selected aurones in the role of CH substrates for aminomethylation reactions involving anabasine, because aurones represent a minor subclass of flavonoids that have been previously aminomethylated in the presence of simple amines.[7] In addition, it is known that their derivatives act as cholinesterase inhibitors.[8]

It was found that our proposed method for the aminomethylation of isoflavones[9] in the presence of anabasine (**1**) was also effective for reactions involving 6-hydroxyaurones **2a**–**e**. The reactions of the starting aurones **2a**–**e** with anabasine (**1**) and paraformaldehyde in absolute EtOH in the presence of 4-(dimethylamino)pyridine (DMAP) proceeded regioselectively and were accompanied by the formation of 7-aminomethyl derivatives **3a**–**e** (Scheme 1), which was confirmed by the spin-spin coupling constant of 8.4–8.9 Hz observed between the H-4 and H-5 protons.

**Scheme 1**




**a** $R^1 = R^2 = R^4 = H$, $R^3 = OMe$; **b** $R^1 = R^3 = OMe$, $R^2 = R^4 = H$; **c** $R^1 = R^2 = OMe$, $R^3 = R^4 = H$; **d** $R^1 = R^2 = R^3 = OMe$, $R^4 = H$; **e** $R^1 = H$, $R^2 = R^3 = R^4 = OMe$

Heating of 6-hydroxy-7-methylaurones **4a**–**e** with anabasine (**1**) and paraformaldehyde either in absolute EtOH or in 1,4-dioxane did not produce the expected aminomethylation products. Apparently, the moderate reactivity of anabasine, arising from the presence of an electron-withdrawing pyridine ring, as well as caused by steric hindrance, prevented the occurrence of electrophilic substitution reaction at the C-5 atom of benzylidenebenzofuran-3(2*H*)-one ring, which exhibited less reactivity than the C-7 position.

In order to achieve aminomethylation of aurones at the C-5 position, we developed a method for transamination of 5-dimethylaminomethyl derivatives **5a**–**e** that, as we have previously demonstrated,[7b] can be synthesized in high yields by using the reactions of 6-hydroxy-7-methylaurones **4a**–**e** with bis(dimethylamino)methane. It was shown that heating Mannich bases **5a**–**e** with an excess of anabasine (**1**) in 1,4-dioxane was accompanied by the formation of aurone aminomethyl derivatives **6a**–**e** containing an anabasine moiety.

The structures of our obtained anabasine-containing Mannich bases – aurones **3a**–**e** and **6a**–**e** – were confirmed by the methods of NMR spectroscopy and mass spectrometry. $^1$H NMR spectra of these compounds contained not only the signals of aurone and anabasine moieties, but also two doublets of methylene group with spin-spin coupling constants of 13.9–15.1 Hz that were characteristic for geminal protons.

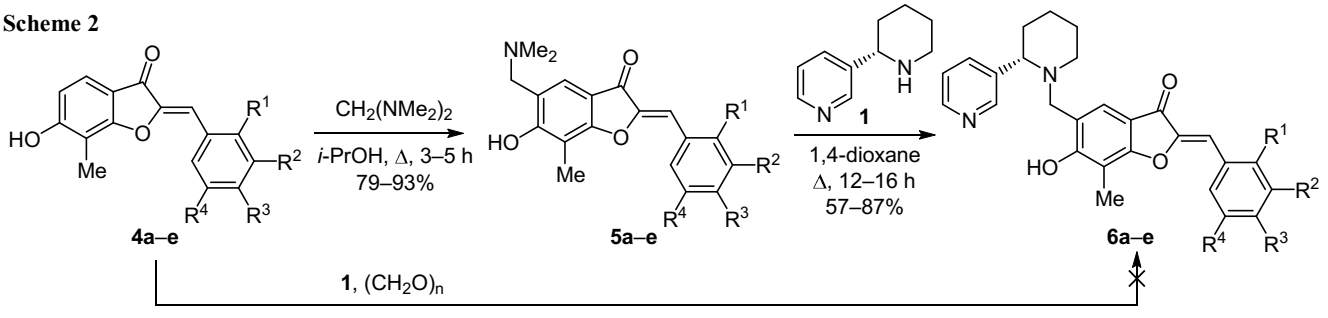
Thus, we have developed methods for the synthesis of anabasine-containing derivatives of 6-hydroxyaurones. Aminomethylation of benzylidenebenzofuran-3(2*H*)-one ring in the presence of anabasine proceeded at position 7 under Mannich reaction conditions, while transamination of 5-(dimethylaminomethyl)aurones by the action of anabasine provided convenient synthetic access to 5-(anabasin-1-yl)methyl derivatives of 6-hydroxy-7-methylaurones.

## Experimental

$^1$H and $^{13}$C NMR spectra were acquired on Varian Mercury 400 (400 and 100 MHz, respectively) and Bruker Avance 500 (500 and 125 MHz, respectively) instruments, using TMS as internal standard. Mass spectra were recorded on an Agilent 1100 HPLC system (atmospheric pressure chemical ionization). Elemental analysis was performed on a vario MICRO cube automatic CHNS-analyzer. The reaction progress and purity of the obtained compounds were controlled by TLC on Merck 60 $F_{254}$ plates, using $CHCl_3$–MeOH (9:1, 19:1) and EtOAc as eluents.

**Synthesis of 6-hydroxyaurones 2a–e and 4a–e** (General method). A solution of 6-hydroxybenzofuran-3(2*H*)-one

**Scheme 2**




**a** $R^1 = R^2 = R^4 = H$, $R^3 = OMe$; **b** $R^1 = R^3 = OMe$, $R^2 = R^4 = H$; **c** $R^1 = R^4 = H$, $R^2 = R^3 = OMe$; **d** $R^1 = R^4 = H$, $R^2 + R^3 = OCH_2O$; **e** $R^1 = R^4 = OMe$, $R^2 = R^3 = H$

(1.50 g, 10 mmol, for the synthesis of compounds **2a**–**e**) or 6-hydroxy-7-methylbenzofuran-3(2*H*)-one (1.64 g, 10 mmol, for the synthesis of compounds **4a**–**e**) and aromatic aldehyde in a 1:1 mixture of DMF–EtOH (50 ml) was treated by adding 50% aqueous solution of KOH (2.3 ml). The mixture was stirred at room temperature for 4–6 h (the completion of reaction was determined by TLC). Then the reaction mixture was poured into vigorously stirred hot $H_2O$ (50 ml) and neutralized with concentrated HCl to pH 4–5. The precipitate that formed was filtered off, washed with $H_2O$, dried, and crystallized from a 1:1 mixture of DMF–MeOH. The obtained NMR spectra of compounds **2a**–**e**[7c,8c] and **4a**,**c**[10] matched the literature data.

**(2*Z*)-2-(2,4-Dimethoxybenzylidene)-6-hydroxy-7-methyl-1-benzofuran-3(2*H*)-one (4b)**. Yield 2.59 g (83%), yellow crystals, mp 287–289°C. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$), δ, ppm (*J*, Hz): 2.20 (3H, s, 7-$CH_3$); 3.84 (3H, s) and 3.89 (3H, s, 2',4'-$OCH_3$); 6.65 (1H, d, *J* = 2.5, H-3'); 6.69–6.81 (2H, m, H-5,5'); 7.01 (1H, s, =CHAr); 7.44 (1H, d, *J* = 8.4, H-4); 8.15 (1H, d, *J* = 8.7, H-6'); 11.00 (1H, br. s, 6-OH). $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$), δ, ppm: 7.6; 55.5; 55.9; 98.2; 103.9; 106.6; 107.6; 111.9; 112.8; 113.3; 122.5; 132.2; 146.3; 159.7; 162.3; 163.7; 165.6; 181.8. Mass spectrum, *m*/*z* ($I_{rel}$, %): 313 $[M+H]^+$ (100). Found, %: C 69.37; H 5.41. $C_{18}H_{16}O_5$. Calculated, %: C 69.22; H 5.16.

**(2*Z*)-2-(1,3-Benzodioxol-5-ylmethylidene)-6-hydroxy-7-methyl-1-benzofuran-3(2*H*)-one (4d)**. Yield 2.34 g (79%), yellow crystals, mp 293–295°C. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$), δ, ppm (*J*, Hz): 2.19 (3H, s, 7-$CH_3$); 6.10 (2H, s, $OCH_2O$); 6.71 (1H, s, =CHAr); 6.76 (1H, d, *J* = 8.4, H-5); 7.03 (1H, d, *J* = 8.4, H-7'); 7.44 (1H, d, *J* = 8.4, H-4); 7.46 (2H, d, *J* = 8.4, H-6'); 7.52 (1H, d, *J* = 1.6, H-4'); 10.95 (1H, br. s, 6-OH). $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$), δ, ppm: 7.6; 101.6; 107.6; 108.9; 109.9; 110.5; 112.0; 112.6; 122.6; 126.4; 126.9; 146.5; 147.8; 148.5; 163.9; 165.7; 181.8. Mass spectrum, *m*/*z* ($I_{rel}$, %): 297 $[M+H]^+$ (100). Found, %: C 69.17; H 4.00. $C_{17}H_{12}O_5$. Calculated, %: C 68.92; H 4.08.

**(2*Z*)-2-(2,5-Dimethoxybenzylidene)-6-hydroxy-7-methyl-1-benzofuran-3(2*H*)-one (4e)**. Yield 2.84 g (91%), yellow crystals, mp 295–297°C. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$), δ, ppm (*J*, Hz): 2.18 (3H, s, 7-$CH_3$); 3.79 (3H, s) and 3.84 (3H, s, 2',5'-$OCH_3$); 6.76 (1H, d, *J* = 8.4, H-5); 6.93–7.06 (3H, m, =CHAr, H-3',4'); 7.43 (1H, d, *J* = 8.4, H-4), 7.76 (1H, d, *J* = 3.1, H-6'). $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$), δ, ppm: 7.4; 55.1; 56.1; 103.2; 107.6; 112.0; 112.4; 112.5; 114.9; 117.2; 121.0; 122.7; 147.6; 152.5; 152.9; 164.0; 165.8; 181.9. Mass spectrum, *m*/*z* ($I_{rel}$, %): 313 $[M+H]^+$ (100). Found, %: C 69.01; H 4.92. $C_{18}H_{16}O_5$. Calculated, %: C 69.22; H 5.16.

**Synthesis of 7-(anabasin-1-yl)-7-hydroxyaurones 3a–e** (General method). A hot solution of 6-hydroxyaurone **2a**–**e** (2 mmol) in absolute EtOH (15 ml) was treated by adding anabasine (**1**) (0.80 ml, 5 mmol), paraformaldehyde (150 mg, equivalent to 5 mmol of formaldehyde), and DMAP (5 mg). The reaction mixture was refluxed for 12–16 h, then cooled and the solvent was evaporated at reduced pressure. The obtained residue was purified by silica gel column chromatography using EtOAc as eluent.

**(2*Z*)-6-Hydroxy-2-(4-methoxybenzylidene)-7-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (3a)**. Yield 337 mg (76%), yellow crystals, mp 193–195°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.46–1.62 (1H, m), 1.69–1.89 (3H, m), 1.89–2.01 (2H, m), 2.28–2.41 (1H, m), 3.26–3.37 (1H, m) and 3.41–3.50 (1H, m, CH and $CH_2$ piperidine); 3.64 (1H, d, *J* = 14.9) and 3.93 (1H, d, *J* = 14.9, $CH_2$); 3.86 (3H, s, 4'-$OCH_3$); 6.60 (1H, d, *J* = 8.4, H-5); 6.72 (1H, s, =CHAr); 6.97 (2H, d, *J* = 8.4, H-3',5'); 7.31 (1H, dd, *J* = 8.0, *J* = 4.8, H-5"); 7.53 (1H, d, *J* = 8.4, H-4); 7.73 (2H, d, *J* = 8.4, H-2',6'); 7.76–7.82 (1H, m, H-4"); 8.53 (1H, dd, *J* = 4.8, *J* = 1.6, H-6"); 8.65 (1H, d, *J* = 2.3, H-2"). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 24.6; 25.6; 36.0; 51.2; 54.2; 55.5; 67.0; 104.5; 111.8; 113.5; 113.8; 114.6; 124.3; 124.8; 125.3; 133.0; 135.0; 137.6; 146.8; 149.7; 160.8; 165.4; 166.5; 182.7. Mass spectrum, *m*/*z* ($I_{rel}$, %): 443 $[M+H]^+$ (100). Found, %: C 73.05; H 6.70; N 6.56. $C_{27}H_{26}N_2O_4$. Calculated, %: C 73.28; H 5.92; N 6.33.

**(2*Z*)-2-(2,4-Dimethoxybenzylidene)-6-hydroxy-7-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (3b)**. Yield 293 mg (62%), yellow crystals, mp 193–195°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.51–1.65 (1H, m), 1.73–2.02 (5H, m), 2.28–2.40 (1H, m), 3.29–3.37 (1H, m) and 3.41–3.48 (1H, m, CH and $CH_2$ piperidin); 3.64 (1H, d, *J* = 14.9) and 3.94 (1H, d, *J* = 14.9, $CH_2$); 3.88 (3H, s) and 3.90 (3H, s, 2',4'-$OCH_3$); 6.47 (1H, d, *J* = 2.4, H-3'); 6.61 (1H, d, *J* = 8.5, H-5); 6.65 (1H, dd, *J* = 8.5, *J* = 2.4, H-5'); 7.29 (1H, s, =CHAr); 7.33 (1H, dd, *J* = 8.0, *J* = 4.8, H-5"); 7.56 (1H, d, *J* = 8.5, H-4); 7.78–7.85 (1H, m, H-4"); 8.06 (1H, d, *J* = 8.5, H-6'); 8.55 (1H, dd, *J* = 4.8, *J* = 1.6, H-6"); 8.66 (1H, d, *J* = 2.3, H-2"). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 24.6; 25.6; 36.0; 51.2; 54.1; 55.5; 55.6; 66.9; 98.1; 104.4; 105.7; 106.0; 113.2; 114.0; 114.6; 124.2; 124.6; 132.7; 134.9; 137.7; 146.8; 149.6; 160.3; 162.4; 165.2; 166.2; 182.6. Mass spectrum, *m*/*z* ($I_{rel}$, %): 473 $[M+H]^+$ (100). Found, %: C 71.40; H 6.11; N 6.02. $C_{28}H_{28}N_2O_5$. Calculated, %: C 71.17; H 5.97; N 5.93.

**(2*Z*)-2-(2,3-Dimethoxybenzylidene)-6-hydroxy-7-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (3c)**. Yield 374 mg (79%), yellow crystals, mp 184–186°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.48–1.64 (1H, m), 1.74–1.89 (3H, m), 1.92–2.01 (2H, m), 2.28–2.40 (1H, m), 3.28–3.37 (1H, m) and 3.40–3.48 (1H, m, CH and $CH_2$ piperidine); 3.63 (1H, d, *J* = 15.1) and 3.93 (1H, d, *J* = 15.1, $CH_2$); 3.89 (3H, s) and 3.90 (3H, s, 2',3'-$OCH_3$); 6.62 (1H, d, *J* = 8.4, H-5); 6.97 (1H, dd, *J* = 8.3, *J* = 1.4, H-4'); 7.15–7.22 (1H, m, H-5'); 7.23 (1H, s, =CHAr); 7.33 (1H, dd, *J* = 8.0, *J* = 4.7, H-5"); 7.57 (1H, d, *J* = 8.4, H-4); 7.70 (1H, dd, *J* = 8.0, *J* = 1.4, H-6'); 7.77–7.83 (1H, m, H-4"); 8.55 (1H, dd, *J* = 4.8, *J* = 1.6, H-6"); 8.65 (1H, d, *J* = 2.7, H-2"). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 24.6; 25.6; 36.0; 51.2; 54.2; 56.0; 61.7; 67.0; 104.5; 105.5; 113.5; 113.6; 113.7; 123.0; 124.3; 125.0; 126.9; 134.9; 137.6; 148.5; 149.2; 149.7; 152.9; 165.6; 166.8; 182.8. Mass spectrum, *m*/*z* ($I_{rel}$, %): 473 $[M+H]^+$ (100). Found, %: C 70.92; H 6.21; N 6.05. $C_{28}H_{28}N_2O_5$. Calculated, %: C 71.17; H 5.97; N 5.93.

**(2*Z*)-6-Hydroxy-7-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]-methyl}-2-(2,3,4-trimethoxybenzylidene)-1-benzofuran-**

**3(2*H*)-one (3d)**. Yield 327 mg (65%), yellow crystals, mp 121–123°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.48–1.63 (1H, m), 1.72–2.02 (5H, m), 2.27–2.39 (1H, m), 3.28–3.37 (1H, m) and 3.39–3.47 (1H, m, CH and $CH_2$ piperidine); 3.62 (1H, d, *J* = 14.9) and 3.95 (1H, d, *J* = 14.9, $CH_2$); 3.89 (3H, s), 3.95 (3H, s) and 3.96 (3H, s, 2',3',4'-$OCH_3$); 6.61 (1H, d, *J* = 8.4, H-5'); 6.84 (1H, d, *J* = 8.9, H-5); 7.16 (1H, s, =CHAr); 7.34 (1H, dd, *J* = 7.9, *J* = 4.8, H-5"); 7.56 (1H, d, *J* = 8.4, H-4); 7.78–7.83 (1H, m, H-4"); 7.85 (1H, d, *J* = 8.9, H-6'); 8.55 (1H, dd, *J* = 4.8, *J* = 1.6, H-6"); 8.65 (1H, d, *J* = 2.2, H-2"). $^{13}$C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 24.5; 25.5; 35.9; 51.1; 54.1; 56.1; 60.9; 61.9; 66.9; 104.3; 105.8; 107.8; 113.3; 113.8; 119.6; 124.2; 124.7; 126.6; 134.9; 137.6; 142.2; 147.5; 149.6; 153.8; 155.1; 165.2; 166.3; 182.5. Mass spectrum, *m*/*z* ($I_{rel}$, %): 503 $[M+H]^+$ (100). Found, %: C 69.14; H 6.24; N 5.39. $C_{29}H_{30}N_2O_6$. Calculated, %: C 69.31; H 6.02; N 5.57.

**(2*Z*)-6-Hydroxy-7-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]-methyl}-2-(3,4,5-trimethoxybenzylidene)-1-benzofuran-3(2*H*)-one (3e)**. Yield 377 mg (75%), yellow crystals, mp 194–196°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.49–1.62 (1H, m), 1.71–2.03 (5H, m), 2.18–2.29 (1H, m) and 3.20–3.38 (2H, m, CH and $CH_2$ piperidine); 3.56 (1H, d, *J* = 14.7, $CH_2$); 3.92–3.96 (7H, m, $CH_2$, 3',5'-$OCH_3$); 3.91 (3H, s, 4'-$OCH_3$); 6.61 (1H, d, *J* = 8.5, H-5); 6.67 (1H, s, =CHAr); 7.08 (2H, s, H-2',6'); 7.32 (1H, dd, *J* = 7.9, *J* = 4.8, H-5"); 7.54 (1H, d, *J* = 8.5, H-4); 7.70–7.78 (1H, m, H-4"); 8.51–8.57 (2H, m, H-2",6"). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 24.6; 25.6; 35.7; 51.3; 54.6; 56.1; 61.2; 67.7; 104.4; 108.6; 111.7; 113.6; 124.4; 125.0; 128.1; 134.9; 137.5; 139.7; 147.6; 149.5; 150.0; 153.3; 165.4; 166.4; 182.5. Mass spectrum, *m*/*z* ($I_{rel}$, %): 503 $[M+H]^+$ (100). Found, %: C 69.52; H 6.16; N 5.41. $C_{29}H_{30}N_2O_6$. Calculated, %: C 69.31; H 6.02; N 5.57.

**Synthesis of dimethylaminomethyl-6-hydroxy-7-methylaurones 5a–e** (General method). A hot solution of the appropriate 6-hydroxyaurone **4a**–**e** (2 mmol) in *i*-PrOH (15 ml) was treated by adding bis(dimethylamino)methane (0.33 ml, 2.4 mmol). The reaction mixture was refluxed for 3–5 h, then cooled, diluted with hexane (15–20 ml), the precipitate that formed was filtered off and crystallized from 1:2 mixture of *i*-PrOH–hexane. The physicochemical and spectral characteristics of compounds **5a**,**c** were described in our earlier work.[7b]

**(2*Z*)-6-Hydroxy-5-[(dimethylamino)methyl]-2-(2,4-dimethoxybenzylidene)-7-methyl-1-benzofuran-3(2*H*)-one (5b)**. Yield 583 mg (79%), yellow crystals, mp 173–175°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.28 (3H, s, 7-$CH_3$); 2.35 (6H, s, $N(CH_3)_2$); 3.67 (2H, s, $CH_2$); 3.85 (3H, s) and 3.86 (3H, s, 2',4'-$OCH_3$); 6.45 (1H, d, *J* = 2.4, H-3'); 6.61 (1H, dd, *J* = 8.7, *J* = 2.4, H-5'); 7.28 (2H, s, =CHAr, H-4); 8.26 (1H, d, *J* = 8.5, H-6'); 10.94 (1H, br. s, 6-OH). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.7; 44.1; 55.5; 55.7; 62.5; 98.1; 105.5; 105.7; 108.4; 113.1; 115.0; 117.6; 121.2; 133.0; 147.2; 160.2; 162.3; 165.2; 166.1; 183.5. Mass spectrum, *m*/*z* ($I_{rel}$, %): 370 $[M+H]^+$ (100). Found, %: C 68.52; H 6.39; N 3.52. $C_{21}H_{23}NO_5$. Calculated, %: C 68.28; H 6.28; N 3.79.

**(2*Z*)-2-(1,3-Benzodioxol-5-ylmethylidene)-5-[(dimethylamino)methyl]-6-hydroxy-7-methyl-1-benzofuran-3(2*H*)-one (5d)**. Yield 600 mg (85%), yellow crystals, mp 192–194°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.30 (3H, s, 7-$CH_3$); 2.38 (6H, s, $N(CH_3)_2$); 3.70 (2H, s, $CH_2$); 6.05 (2H, s, $OCH_2O$); 6.71 (1H, s, =CHAr); 6.89 (1H, d, *J* = 8.1, H-7'); 7.27–7.35 (2H, m, H-4',6'); 7.56 (1H, s, H-4). $^{13}$C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 7.8; 44.1; 62.5; 101.6; 108.6; 108.8; 110.5; 111.2; 112.7; 117.8; 121.3; 127.0; 127.2; 147.2; 148.2; 148.8; 165.7; 166.3; 183.4. Mass spectrum, *m*/*z* ($I_{rel}$, %): 354 $[M+H]^+$ (100). Found, %: C 67.71; H 5.19; N 4.08. $C_{20}H_{19}NO_5$. Calculated, %: C 67.98; H 5.42; N 3.96.

**(2*Z*)-5-[(Dimethylamino)methyl]-2-(2,5-dimethoxybenzylidene)-6-hydroxy-7-methyl-1-benzofuran-3(2*H*)-one (5e)**. Yield 642 mg (87%), yellow crystals, mp 155–156°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.27 (3H, s, 7-$CH_3$); 2.37 (6H, s, $N(CH_3)_2$); 3.69 (2H, s, $CH_2$); 3.85 (3H, s) and 3.87 (3H, s, 2',5'-$OCH_3$); 6.85 (1H, d, *J* = 9.0, H-3'); 6.91 (1H, dd, *J* = 9.0, *J* = 3.0, H-4'); 7.30 (1H, s, =CHAr); 7.32 (1H, s, H-4); 7.93 (1H, d, *J* = 3.0, H-6'). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.7; 44.2; 55.7; 56.3; 62.5; 105.1; 108.5; 112.1; 112.8; 115.8; 117.3; 117.8; 121.5; 122.4; 148.4; 153.4; 153.5; 165.7; 166.4; 183.5. Mass spectrum, *m*/*z* ($I_{rel}$, %): 370 $[M+H]^+$ (100). Found, %: C 68.07; H 6.44; N 3.98. $C_{21}H_{23}NO_5$. Calculated, %: C 68.28; H 6.28; N 3.79.

**Synthesis of 5-(anabasin-1-yl)-6-hydroxy-7-methylaurones 6a–e** (General method). A hot solution of the appropriate compound **5a**–**e** (1 mmol) in 1,4-dioxane (5 ml) was treated by adding anabasine (**1**) (0.32 ml, 2 mmol). The reaction mixture was refluxed for 12–16 h, then cooled, and the solvent was evaporated at reduced pressure. The obtained residue was purified by silica gel column chromatography using EtOAc as eluent.

**(2*Z*)-6-Hydroxy-2-(4-methoxybenzylidene)-7-methyl-5-{[(2*S*)-2-(pyridine-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (6a)**. Yield 315 mg (69%), yellow crystals, mp 130–132°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.50–1.56 (1H, m), 1.72–2.14 (5H, m), 2.17–2.20 (1H, m) and 3.18–3.29 (2H, m, CH and $CH_2$ piperidine); 2.30 (3H, s, 7-$CH_3$); 3.10 (1H, d, *J* = 14.0) and 3.98 (1H, d, *J* = 14.0, $CH_2$); 3.87 (3H, s, 4'-$OCH_3$); 6.75 (1H, s, =CHAr); 6.98 (2H, d, *J* = 8.6, H-3',5'); 7.18 (1H, s, H-4); 7.35 (1H, dd, *J* = 7.9, *J* = 4.8, H-5"); 7.78 (1H, d, *J* = 8.0, H-4"); 7.86 (2H, d, *J* = 8.6, H-2',6'); 8.57 (1H, d, *J* = 4.0, H-6"); 8.62 (1H, d, *J* = 2.3, H-2"). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.8; 24.6; 25.6; 35.7; 53.4; 55.4; 58.5; 67.0; 108.5; 111.4; 113.1; 114.5; 117.4; 121.5; 124.2; 125.6; 133.1; 135.0; 137.6; 147.1; 149.6; 160.7; 164.5; 166.1; 183.4. Mass spectrum, *m*/*z* ($I_{rel}$, %): 457 $[M+H]^+$ (100). Found, %: C 73.51; H 6.03; N 6.27. $C_{28}H_{28}N_2O_4$. Calculated, %: C 73.66; H 6.18; N 6.14.

**(2*Z*)-2-(2,4-Dimethoxybenzylidene)-6-hydroxy-7-methyl-5-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (6b)**. Yield 278 mg (57%), yellow crystals, mp 129–131°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.46–1.56 (1H, m), 1.72–1.95 (5H, m), 2.13–2.18 (1H, m) and 3.18–3.28 (2H, m, CH and $CH_2$ piperidine); 2.29 (3H, s, 7-$CH_3$); 3.09 (1H, d, *J* = 14.2) and 3.98 (1H, d, *J* = 14.2, $CH_2$); 3.87 (6H, s, 2',4'-$OCH_3$); 6.46 (1H, d, *J* = 2.4, H-3'); 6.63 (1H, dd, *J* = 8.7, *J* = 2.4, H-5'); 7.18 (1H, s, H-4); 7.29 (1H, s, =CHAr); 7.34 (1H, dd, *J* = 7.8,

*J* = 4.8, H-5'''); 7.74–7.83 (1H, m, H-4''); 8.26 (1H, d, *J* = 8.7, H-6'); 8.56 (1H, dd, *J* = 4.8, *J* = 1.6, H-6''); 8.62 (1H, d, *J* = 2.3, H-2''). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.8; 24.7; 25.6; 35.8; 53.4; 55.6; 55.7; 58.5; 67.1; 98.2; 105.7; 108.5; 113.4; 115.0; 117.3; 121.5; 124.2; 133.1; 135.0; 137.7; 147.2; 149.6; 160.3; 162.3; 164.1; 165.9; 183.3. Mass spectrum, *m*/*z* ($I_{rel}$, %): 487 $[M+H]^+$ (100). Found, %: C 71.33; H 6.34; N 5.71. $C_{29}H_{30}N_2O_5$. Calculated, %: C 71.59; H 6.21; N 5.76.

**(2*Z*)-2-(3,4-Dimethoxybenzylidene)-6-hydroxy-7-methyl-5-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (6c)**. Yield 424 mg (87%), yellow crystals, mp 125–127°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.46–1.56 (1H, m), 1.69–1.83 (5H, m), 1.89–1.92 (1H, m), 3.09–3.12 (1H, m) and 3.17–3.29 (1H, m, CH and $CH_2$ piperidine); 2.28 (3H, s, 7-$CH_3$); 3.11 (1H, d, *J* = 14.0, $CH_2$), 3.94 (3H, s) and 3.96–4.01 (4H, m, $CH_2$, 3',4'-$OCH_3$); 6.74 (1H, s, =CHAr); 6.93 (1H, d, *J* = 8.3, H-5'); 7.18 (1H, s, H-4); 7.31–7.40 (2H, m, H-6',5''); 7.67 (1H, d, *J* = 2.0, H-2'); 7.74–7.80 (1H, m, H-4''); 8.56 (1H, dd, *J* = 4.8, *J* = 1.6, H-6''); 8.62 (1H, d, *J* = 2.3, H-2''). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.6; 24.6; 25.6; 35.7; 53.4; 55.8; 56.0; 58.5; 67.0; 108.3; 111.2; 111.6; 113.0; 113.3; 117.5; 121.6; 124.2; 125.6; 125.8; 135.0; 137.6; 147.1; 149.0; 149.6; 150.4; 164.5; 165.9; 183.2. Mass spectrum, *m*/*z* ($I_{rel}$, %): 487 $[M+H]^+$ (100). Found, %: C 71.72; H 6.40; N 5.51. $C_{29}H_{30}N_2O_5$. Calculated, %: C 71.59; H 6.21; N 5.76.

**(2*Z*)-2-(1,3-Benzodioxol-5-ylmethylidene)-6-hydroxy-7-methyl-5-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (6d)**. Yield 301 mg (64%), yellow crystals, mp 134–136°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.48–1.56 (1H, m), 1.72–1.95 (5H, m), 2.13–2.19 (1H, m) and 3.17–3.29 (2H, m, CH and $CH_2$ piperidine); 2.29 (3H, s, 7-$CH_3$); 3.10 (1H, d, *J* = 13.9) and 3.97 (1H, d, *J* = 13.9, $CH_2$); 6.04 (2H, s, $OCH_2O$); 6.69 (1H, s, =CHAr); 6.87 (1H, d, *J* = 8.1, H-7'); 7.17 (1H, s, H-4); 7.29 (1H, dd, *J* = 8.1, *J* = 1.7, H-6'); 7.34 (1H, dd, *J* = 7.9, *J* = 4.7, H-5''); 7.54 (1H, d, *J* = 1.7, H-4'); 7.74–7.81 (1H, m, H-4''); 8.53–8.58 (1H, m, H-6''); 8.59–8.65 (1H, m, H-2''). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.8; 24.6; 25.6; 35.7; 53.4; 58.5; 67.0; 101.6; 108.6; 108.8; 110.5; 111.4; 113.0; 117.5; 121.5; 124.2; 127.1; 135.0; 137.6; 147.1; 148.2; 148.8; 149.6; 149.7; 164.6; 166.0; 183.3. Mass spectrum, *m*/*z* ($I_{rel}$, %): 471 $[M+H]^+$ (100). Found, %: C 71.71; H 5.31; N 6.20. $C_{28}H_{26}N_2O_5$. Calculated, %: C 71.48; H 5.57; N 5.95.

**(2*Z*)-2-(2,5-Dimethoxybenzylidene)-6-hydroxy-7-methyl-5-{[(2*S*)-2-(pyridin-3-yl)piperidin-1-yl]methyl}-1-benzofuran-3(2*H*)-one (6e)**. Yield 385 mg (79%), yellow crystals, mp 194–196°C. $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.50–1.56 (1H, m), 1.72–1.95 (5H, m), 2.14–2.20 (1H, m) and 3.18–3.29 (2H, m, CH and $CH_2$ piperidine); 2.28 (3H, s, 7-$CH_3$); 3.10 (1H, d, *J* = 14.0) and 3.98 (1H, d, *J* = 14.0, $CH_2$); 3.85 (3H, s) and 3.88 (3H, s, 2',5'-$OCH_3$); 6.85 (1H, d, *J* = 9.0, H-3'); 6.92 (1H, dd, *J* = 9.0, *J* = 3.1, H-4'); 7.18 (1H, s, H-4); 7.30 (1H, s, =CHAr); 7.35 (1H, dd, *J* = 8.0, *J* = 4.8, H-5''); 7.71–7.81 (1H, m, H-4''); 7.92 (1H, d, *J* = 3.1, H-6'); 8.55–8.57 (1H, m, H-6''); 8.62 (1H, s, H-2''). $^{13}$C NMR spectrum (125 MHz, $CDCl_3$), δ, ppm: 7.7; 24.6; 25.6; 35.7; 53.4; 55.7; 56.3; 58.5; 67.1; 105.2; 108.5; 112.0; 113.0; 115.8; 117.3; 117.5; 121.7; 122.3; 124.2; 135.0; 137.6; 148.2; 149.6; 149.7; 153.4; 153.5; 164.5; 166.0; 183.3. Mass spectrum, *m*/*z* ($I_{rel}$, %): 487 $[M+H]^+$ (100). Found, %: C 71.81; H 6.42; N 5.84. $C_{29}H_{30}N_2O_5$. Calculated, %: C 71.59; H 6.21; N 5.76.

Supplementary information file containing $^1$H and $^{13}$C NMR spectra of all the synthesized compounds is available at the journal website at http://link.springer.com/journal/10593.

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