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An efficient synthesis of [1,4]pyridazinooxazine[3,4-*a*]tetrahydro isoquinolines

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Abstract—A series of fused isoquinoline–pyridazinooxazine chimera were prepared in good overall yield from phenethylamide **1** and 4,5-dichloropyridazin-3-one 2 via Smiles rearrangement and Pictet–Spengler cyclization.

1. Introduction

Tetrahydroisoquinolines constitute a large and still growing class of alkaloids that display diverse biological activities.[1–5] Not surprisingly, fusion of the tetrahydroisoquinoline skeleton with other heterocyclic ring systems also leads to new entities showing significant biological activities.[6] Consequently, there has been a surge of interest in the development of versatile synthetic methods for the preparation of tetrahydroisoquinoline-heterocycle chimera, inter alia, oxazines,[7] thiazines,[8] oxathiazine,[9] benzoxazine[10] and oxazaphosphorine.[11] In the course of our development of specific inhibitors of multi-drug resistant (MDR) pumps, we needed a series of functionalized tetracycles derived from the union of tetrahydroisoquinolines and pyridazinoxazines. Herein, we wish to report a convenient, high yield synthesis of several [1,4]pyridazinooxazino[3,4-*a*]tetrahydroisoquinolines **6** and **7** from readily available precursors.

2. Results and discussion

2.1. One-pot synthesis of pyridazino[4,5-*b*][1,4]oxazine derivatives 3 via Smiles rearrangement

In a previous communication,[12] we reported an efficient, one-pot synthesis of pyridazino[4,5-*b*][1,4]oxazine derivatives **3** via Smiles rearrangement of the initial adduct between α-hydroxyphenethylamide **1** and 4,5-dichloro-2-tetrahydropyranylpyridazin-3-one (**2**) (Scheme 1). Sodium borohydride reduction of **3** in methanol gave the corresponding 3-hydroxy derivative **4** in excellent yield. Boron trifluoride-diethyl etherate induced cyclization in dichloromethane smoothly transformed **4** into **5**, obtained as a single stereoisomer. The configurations of **5a** and **5b** were established by X-ray analysis (Fig. 1).[13] These results could describe the conversion of **4** into **5** via *N*-acyliminium ion intermediate (Scheme 2).

Alkylation of **5** with alkyl halides afforded the corresponding N-alklylated isoquinolines **6** and **7** in good yield. All products were characterized by ^{1}H, ^{13}C NMR, IR, mass spectroscopy and CHN analysis.

2.2. Synthesis of halotetrahydroisoquinolines

For access to 7,8-disubstituted analogs (isoquinoline numbering), we sought to redirect the Pictet–Spengler cyclization by introduction of a blocking group at the usual site of annulation. While attempts to halogenate **3** under a variety of conditions resulted in extensive decomposition, **9a** was more amenable to functionalization (Scheme 3). Specifically, **3** was deprotected using 6 N HCl[14] and the resultant pyridazino[4,5-*b*][1,4]oxazine-8-one (**8**) was alkylated with benzyl chloride in the presence of potassium carbonate in DMF to give **9a** in good overall yield. The halogenation of **9a** was conducted in accordance with literature procedures.[15] To facilitate Pictet–Spengler cyclization, the halogenation product **10**, was firstly treated

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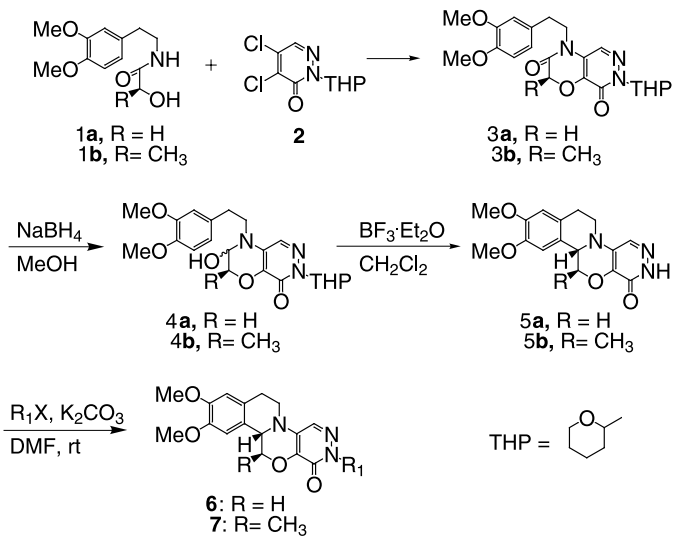


6, 7	a	b	c	d	e	f	g	h	i	j
R_1	Me	Et	Pr	i-Pr	n-Bu	Allyl	Benzyl			

6, 7	k	l	m	n	o	p	q	r	s	
R_1										

Scheme 1.

with $NaBH_4$ in methanol and then boron trifluoride diethyl etherate in methylene chloride leading to both cyclized compounds **11** (39–92%) and **6g** (1–48%). The distribution of products depended on the identity of the blocking substituent at C-2 on the aromatic moiety of dimethoxy phenethyl group. The percentage of **11** increased in the order H≪I<Br<Cl, i.e., with increasing electrophilicity (Table 1). It was gratifying to note that virtually complete regiocontrol was achieved in the case of **9a** and **10c**.[15]

3. Conclusion

In conclusion, we report herein a convenient synthetic strategy for the preparation of the title heterocycles containing a fused tetrahydroisoquinoline-pyridazino[4,5-*b*][1,4]oxazine chimera. The Pictet–Spengler cyclization of **9** was shown to depend on the identity of the substituent at C-2 on the aromatic moiety of the dimethoxyphenylethyl group. The percentage of **10** increased with increasing electrophilicity of the substituent at C-2. Further studies on the synthesis of related polyannular isoquinolines using this methodology are in progress and will be reported in due course.

4. Experimental

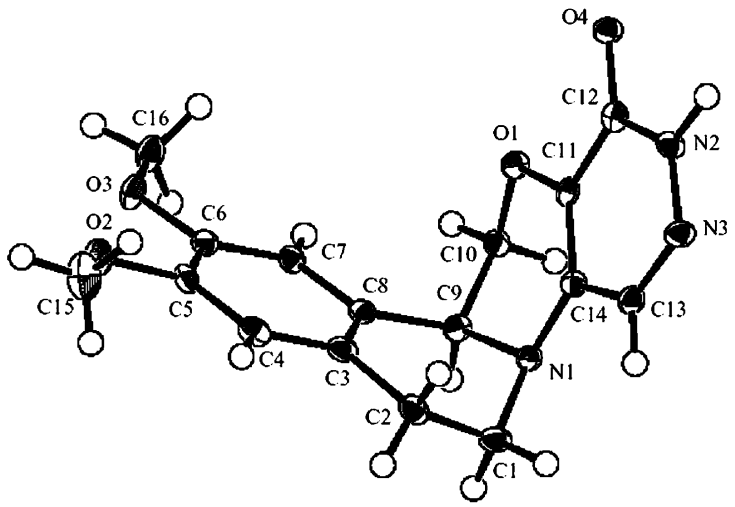
4.1. General

Melting points were determined with a Thomas–Hoover capillary apparatus and uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Jeol AL-300 spectrometer with chemical shift values reported in δ units (ppm) relative to an internal standard (TMS). IR spectra were obtained on a Hitachi 270-50 spectrophotometer. Elemental analyses were performed with a Perkin Elmer 240C. Open-bed UV-chromatography was carried out on silica gel F_{254} (70–230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent.

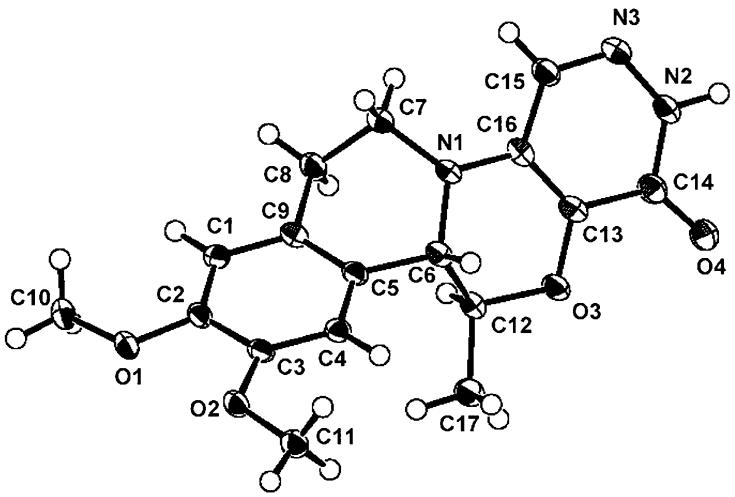
4.2. Synthesis of compound 5a and 5b

To a solution of compound **3**[12] (50 mmol) in methanol (50 mL) was added powdered sodium borohydride (125 mmol) below 10 °C. The reaction mixture was stirred for 6 h. After completion of the reaction as determined by TLC, the mixture was evaporated in vacuo. Dichloromethane and water were added sequentially. The organic layer was separated, washed with brine, dried over anhydrous magnesium sulfate, and evaporated in vacuo to give crude **4**. A solution of crude **4** in CH_2Cl_2 (50 mL) was slowly added to $BF_3{\cdot}OEt_2$ (155 mmol) at 10 °C. After completion of the reaction as determined by TLC, water added and the resulting mixture was neutralized using saturated sodium bicarbonate. The organic layer was separated, concentrated in vacuo, and the residue was purified by column chromatography on silica gel with DMF/diethyl ether (1/1, v/v) to give a white solid.

4.2.1. (10b*S*)-8,9-Dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (5a). 85%; mp 228–229 °C; $[\alpha]_D^{20}=+2.7°$ (c=1, DMSO); IR (KBr) 3048, 2974, 2890, 1642, 1618, 1520, 1422, 1330, 1260, 1108, 1042,



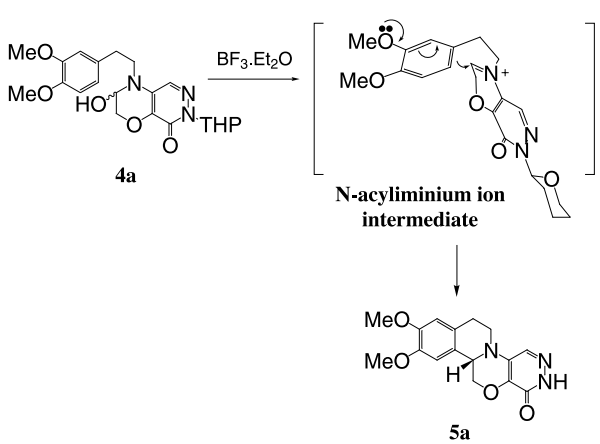
(5a)



(5b)

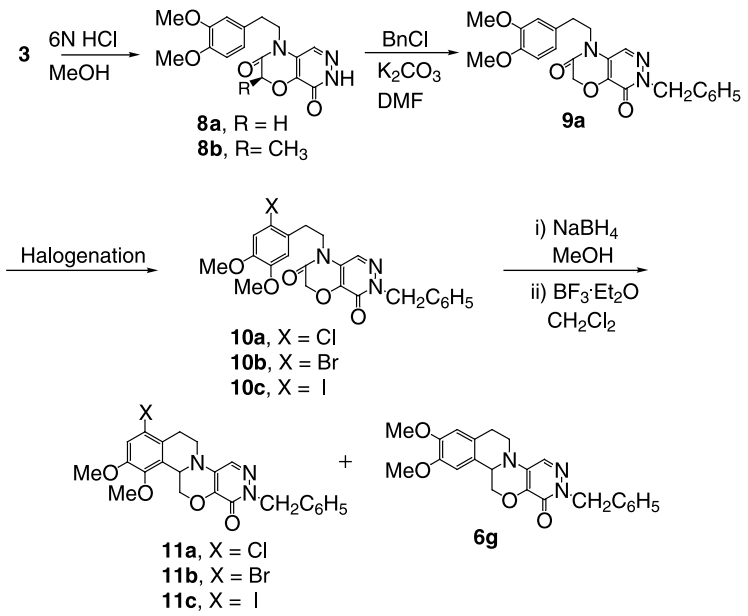
Figure 1. X-ray structure of **5a** (up) and **5b** (down)

836 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.46 (s, 1H), 7.83 (s, 1H), 6.79 (s, 1H), 6.70 (s, 1H), 4.69–4.74 (dd, J=2.70, 10.80 Hz, 1H), 4.42–4.44 (dd, J=8.12, 11.00 Hz, 1H), 3.89–3.95 (dd, J=8.10, 10.80 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.78–3.82 (m, 1H), 3.34–3.42 (m, 1H), 2.88–2.99 (m, 1H), 2.79–2.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 27.68, 42.85, 52.86, 55.36, 55.67, 68.30, 108.71, 111.50, 122.17, 126.65, 129.75, 131.75, 134.42, 147.38, 147.85, 156.60; MS (*m*/*z*) 315 (M^+); Anal. Calcd for $C_{16}H_{17}N_3O_4$: 60.94; H, 5.43; N, 13.33. Found: C, 60.92; H, 5.41; N, 13.29.



Scheme 2.

4.2.2. (10b*S*,11*S*)-8,9-Dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (5b). 82%; $[\alpha]_D^{20}=-51.9°$ (c=1, DMSO); mp 214–215 °C; IR (KBr) 3072, 2936, 1644, 1618, 1520, 1460, 1258, 1216, 1070, 1006, 902, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1H), 6.67 (s, 1H), 6.66 (s, 1H), 4.68–4.71 (dd, J=2.80, 10.85 Hz, 1H), 4.36–4.38 (dd, J=2.05, 8.10 Hz, 1H), 3.93–3.97 (dd, J=8.20, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.76 (s, 3H), 3.70–3.73 (m, 1H), 3.38–3.40 (m, 1H), 2.90–2.94 (m, 1H), 2.81–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.35, 39.60, 43.58, 53.40, 56.01, 56.28, 69.16, 108.93, 111.91, 122.43, 126.93, 128.95, 131.54, 135.70, 148.23, 148.73, 156.27; MS (*m*/*z*): 329 (M^+); Anal. Calcd for $C_{17}H_{19}N_3O_4$: C, 62.00; H, 5.81; N, 12.76. Found: C, 62.02; H, 5.78; N, 12.75.



Scheme 3.

Table 1. The yield and ratio of **11/6g** by Pictet–Spengler cyclization of **9a** and **11**

X	Ratio of **11** and **6g**[a]		Yield (%)[b] of **11/6g**
	11	**6g**	
H	0	100	0/89
I	43	57	37/48
Br	80	20	69/17
Cl	99	1	92/1

[a] Determined via GC–MS.
[b] Isolated yield after flash chromatography.

4.3. Synthesis of compounds 6 and 7

A solution of compound **5** (30 mmol), organic halide (33 mmol), K_2CO_3 (35 mmol) in DMF was stirred for 14 h at room temperature. After completion of the reaction by TLC, the reaction mixture was concentrated in vacuo. Dichloromethane (50 mL) and then water (50 mL) were added to the mixture. The organic layer was separated and subsequently washed with brine. Organic layer was dried over anhydrous magnesium sulfate, and the resultant was evaporated to give the crude product **6** and **7**. The residue was purified by column chromatography on silicagel with CH_2Cl_2/EtOAc (10/1, v/v) to give the product.

4.3.1. (10b*S*)-8,9-Dimethoxy-2-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6a). 89%; mp 214–215 °C; IR (KBr) 3072, 2936, 1644, 1618, 1520, 1460, 1258, 1216, 1070, 1006, 902, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1H), 6.67 (s, 1H), 6.66 (s, 1H), 4.68–4.71 (dd, J=2.80, 10.85 Hz, 1H), 4.36–4.38 (dd, J=2.05, 8.10 Hz, 1H), 3.93–3.97 (dd, J=8.20, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.76 (s, 3H), 3.70–3.73 (m, 1H), 3.38–3.40 (m, 1H), 2.90–2.94 (m, 1H), 2.81–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.35, 39.60, 43.58, 53.40, 56.01, 56.28, 69.16, 108.93, 111.91, 122.43, 126.93, 128.95, 131.54, 135.70, 148.23, 148.73, 156.27; MS (*m*/*z*): 329 (M^+); Anal. Calcd for $C_{17}H_{19}N_3O_4$: C, 62.00; H, 5.81; N, 12.76. Found: C, 62.02; H, 5.78; N, 12.75.

4.3.2. (10b*S*)-2-Ethyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6b). 91%; mp 195–196 °C; IR (KBr) 3064, 2952, 2926, 1640, 1608, 1514, 1450, 1420, 1256, 1020, 896, 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (s, 1H), 6.67 (s, 1H), 6.66 (s, 1H), 4.68–4.71 (dd, J=2.75, 10.80 Hz, 1H), 4.36–4.38 (dd, J=2.10, 8.10 Hz, 1H), 4.18–4.22 (q, 2H), 3.92–3.96 (dd, J=8.30, 10.75 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.70–3.73 (m, 1H), 3.38–3.40 (m, 1H), 2.89–2.94 (m, 1H), 2.83–2.85 (m, 1H), 1.34–1.37 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 13.70, 28.40, 43.52, 46.39, 53.40, 56.00, 56.27, 69.19, 108.95, 111.91, 122.47, 126.95, 129.08, 131.28, 135.71, 148.22, 148.71, 155.74; MS (*m*/*z*): 343 (M^+); Anal. Calcd for $C_{18}H_{21}N_3O_4$: C, 62.96; H, 6.16; N, 12.24. Found: C, 62.92; H, 6.15; N, 12.25.

4.3.3. (10b*S*)-2-Propyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6c). 93%; mp 166–167 °C; IR (KBr) 3062, 2940, 2872, 1646, 1618, 1514, 1462, 1258, 1028, 830, 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.71 (s, 1H), 6.67 (s, 1H), 6.66 (s, 1H), 4.69–4.72 (dd, J=2.75, 10.75 Hz, 1H), 4.36–4.38 (dd, J=2.10, 8.10 Hz, 1H), 4.01–4.13 (m, 2H), 3.92–3.95 (dd, J=8.30, 10.75 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.70–3.73 (m, 1H), 3.37–3.39 (m, 1H), 2.89–2.94 (m, 1H), 2.83–2.85 (m, 1H), 1.79–1.86 (m, 2H), 0.94–0.97 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 11.13, 21.84, 28.41, 43.48, 52.78, 53.37, 55.99, 56.24, 69.22, 108.9, 111.90, 122.46, 126.95, 128.88, 131.18, 135.63, 148.21, 148.69, 155.92; MS (*m*/*z*): 357 (M^+); Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 63.85; H, 6.49; N, 11.76. Found: C, 63.83; H, 6.46; N, 11.75.

4.3.4. (10b*S*)-2-Isopropyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6d). 91%; mp 207–208 °C; IR (KBr) 3100, 3002, 2968, 2876, 1640, 1622, 1528, 1450, 1338, 1270, 1236, 1216, 1160, 1124, 1042, 1020, 920, 876, 844, 790 cm^{-1}; ^1H NMR

($CDCl_3$) δ 7.77 (s, 1H), 6.67 (s, 1H), 6.66 (s, 1H), 5.31–5.35 (m, 1H), 4.68–4.71 (dd, J=2.75, 10.80 Hz, 1H), 4.36–4.38 (dd, J=1.95, 8.15 Hz, 1H), 3.92–3.96 (dd, J=8.25, 10.75 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.72–3.74 (m, 1H), 3.38–3.39 (m, 1H), 2.90–2.95 (m, 1H), 2.80–2.85 (m, 1H), 1.34 (d, J=1.85 Hz, 3H), 1.33 (d, J=1.85 Hz 3H); ^{13}C NMR ($CDCl_3$) δ 20.96, 21.05, 28.41, 43.40, 48.59, 53.40, 55.99, 56.26, 69.20, 108.94, 111.91, 122.55, 126.99, 128.79, 130.86, 135.27, 148.19, 148.68, 155.62; MS (*m*/*z*): 357 (M^+); Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 63.85; H, 6.49; N, 11.76. Found: C, 63.83; H, 6.46; N, 11.75.

4.3.5. (10b*S*)-2-Butyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6e). 94%; mp 150–152 °C; IR (KBr) 3058, 2950, 2864, 1644, 1618, 1516, 1456, 1360, 1320, 1260, 1218, 1114, 1078, 1028, 906, 830, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.70 (s, 1H), 6.66 (s, 2H), 4.69–4.72 (dd, J=2.80, 10.75 Hz, 1H), 4.36–4.37 (dd, J=2.15, 8.10 Hz, 1H), 4.12–4.17 (m, 2H), 3.91–3.95 (dd, J=8.10, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.69–3.73 (m, 1H), 3.35–3.38 (m, 1H), 2.90–2.94 (m, 1H), 2.84–2.86 (m, 1H), 1.75–1.79 (q, 2H), 1.36–1.40 (q, 2H), 0.93–0.96 (t, 3H); ^{13}C NMR ($CDCl_3$) δ 13.79, 19.89, 28.43, 30.63, 43.50, 51.02, 53.39, 56.01, 56.27, 69.22, 108.96, 122.47, 126.95, 128.89, 131.17, 135.70, 148.23, 148.72, 155.98; MS (*m*/*z*): 371 (M^+); Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.62; H, 6.76; N, 11.32.

4.3.6. (10b*S*)-2-Allyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6f). 92%; mp 172–173 °C; IR (KBr) 3082, 3026, 2948, 2850, 1638, 1620, 1520, 1458, 1420, 1360, 1328, 1266, 1220, 1108, 1078, 1040, 1008, 968, 916, 870, 770 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 6.66 (s, 1H), 6.65 (s, 1H), 5.98–6.01 (m, 1H), 5.21–5.27 (m, 2H), 4.72–4.81 (m, 2H), 4.69–4.72 (dd, J=2.75, 10.80 Hz, 1H), 4.37–4.39 (dd, J=1.96, 8.10 Hz, 1H), 3.91–3.95 (dd, J=8.30, 10.80 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.70–3.74 (m, 1H), 3.36–3.41 (m, 1H), 2.91–2.97 (m, 1H), 2.81–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.40, 43.50, 53.40, 53.43, 56.01, 56.28, 69.26, 108.92, 111.90, 118.09, 122.39, 126.92, 129.36, 131.35, 132.46, 135.67, 148.25, 148.73, 155.82; MS (*m*/*z*): 355 (M^+); Anal. Calcd for $C_{19}H_{21}N_3O_4$: C, 64.21; H, 5.96; N, 11.82. Found: C, 64.21; H, 5.92; N, 11.79.

4.3.7. (10b*S*)-2-Benzyl-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6g). 95%; mp 208–210 °C; IR (KBr) 3048, 2936, 1634, 1620, 1520, 1460, 1414, 1320, 1264, 1220, 1160, 1112, 1080, 836, 776, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.70 (s, 1H), 7.25–7.44 (m, 5H), 6.65 (s, 1H), 6.64 (s, 1H), 5.26–5.38 (dd, J=13.95, 44.80 Hz, 2H), 4.68–4.70 (dd, J=2.75, 10.80 Hz, 1H), 4.35–4.37 (dd, J=2.10, 8.20 Hz, 1H), 3.88–3.92 (dd, J=8.30, 10.75 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.68–3.71 (m, 1H), 3.34–3.37 (m, 1H), 2.90–2.92 (m, 1H), 2.78–2.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.05, 43.39, 53.34, 54.36, 55.99, 56.26, 69.28, 108.92, 111.89, 12235, 126.91, 127.70, 128.50, 128.76, 129.37, 131.28, 135.63, 136.88, 148.22, 148.70, 155.99; MS (*m*/*z*): 405 (M^+); Anal. Calcd for $C_{23}H_{23}N_3O_4$: C, 68.13; H, 5.72; N, 10.36. Found: C, 68.11; H, 5.69; N, 10.37.

4.3.8. (10b*S*)-2-(4-Fluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6h). 93%; mp 203–204 °C; IR (KBr) 3072, 2926, 2850, 1654, 1622, 1520, 1450, 1268, 1222, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.71 (s, 1H), 7.40–7.45 (m, 2H), 6.95–7.01 (m, 2H), 6.65 (s, 2H), 5.20–5.34 (dd, J=13.50, 30.30 Hz, 2H), 4.67–4.71 (dd, J=2.70, 11.10 Hz, 1H), 4.35–4.38 (dd, J=2.00, 8.10 Hz, 1H), 3.88–3.93 (m, 4H), 3.87 (s, 3H), 3.68–3.75 (m, 1H), 3.31–3.39 (m, 1H), 2.87–2.95 (m, 1H), 2.77–2.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.36, 43.28, 53.26, 53.69, 55.95, 56.21, 69.30, 108.77, 111.78, 115.17, 115.45, 122.20, 126.85, 129.40, 130.56, 130.67, 131.36, 132.61, 132.65, 135.44, 148.14, 148.61, 156.87; MS (*m*/*z*): 423 (M^+); Anal. Calcd for $C_{23}H_{22}FN_3O_4$: C, 65.24; H, 5.24; N, 9.92. Found: C, 65.22; H, 5.20; N, 9.88.

4.3.9. (10b*S*)-2-(3-Fluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6i). 92%; mp 208–209 °C; IR (KBr) 3096, 2952, 1640, 1524, 1466, 1280, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.19–7.31 (m, 2H), 7.10–7.14 (m, 1H), 6.92–6.99 (m, 1H), 6.65 (s, 2H), 5.24–5.38 (dd, J=14.60, 18.48 Hz, 2H), 4.68–4.73 (dd, J=2.78, 10.78 Hz, 1H), 4.37–4.40 (dd, J=2.25, 8.21 Hz, 1H), 3.89–3.94 (dd, J=8.32, 10.77 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.64–3.77 (m, 1H), 3.32–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.77–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.38, 43.28, 53.27, 53.83 (C–F), 55.96, 56.21, 69.35, 108.74, 111.76, 114.50 (C–F), 114.78 (C–F), 115.36 (C–F), 115.65 (C–F), 122.17, 124.24 (C–F), 124.28 (C–F), 126.83, 129.50, 129.93 (C–F), 130.04 (C–F), 131.39, 135.41, 139.10 (C–F), 139.20 (C–F), 148.14, 148.62, 155.92; MS (*m*/*z*): 423 (M^+); Anal. Calcd for $C_{23}H_{22}FN_3O_4$: C, 65.24; H, 5.24; N, 9.92. Found: C, 65.22; H, 5.20; N, 9.90.

4.3.10. (10b*S*)-2-(2-Fluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6j). 90%; mp 195–196 °C; IR (KBr) 3070, 2950, 2906, 2840, 1642, 1616, 1516, 1458, 1360, 1262, 1218, 1050, 764 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74 (s, 1H), 7.31–7.37 (m, 1H), 7.20–7.28 (m, 1H), 7.01–7.10 (m, 2H), 6.66 (s, 2H), 5.35–5.46 (dd, J=14.59, 18.50 Hz, 2H), 4.69–4.73 (dd, J=2.76, 10.78 Hz, 1H), 4.37–4.41 (dd, J=2.02, 8.14 Hz, 1H), 3.89–3.95 (dd, J=8.30, 10.75 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.69–3.76 (m, 1H), 3.32–3.40 (m, 1H), 2.88–2.98 (m, 1H), 2.77–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.36, 43.25, 47.86 (C–F), 47.91 (C–F), 53.27, 55.96, 56.21, 69.33, 108.74, 111.77, 115.17 (C–F), 115.46 (C–F), 122.21, 123.68 (C–F), 123.88 (C–F), 124.12 (C–F), 124.17 (C–F), 126.85, 129.30 (C–F), 129.41 (C–F), 129.47, 130.60 (C–F), 130.65 (C–F), 131.32, 135.31, 148.12, 148.60, 156.10; MS (*m*/*z*): 423 (M^+); Anal. Calcd for $C_{23}H_{22}FN_3O_4$: C, 65.24; H, 5.24; N, 9.92. Found: C, 65.21; H, 5.24; N, 9.89.

4.3.11. (10b*S*)-2-(2,3-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6k). 91%; mp 200–201 °C; IR (KBr) 3070, 2942, 1648, 1616, 1520, 1482, 1360, 1260, 1056, 768 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74 (s, 1H), 6.96–7.13 (m, 3H), 6.66 (s, 2H), 5.36–5.47 (dd, J=14.70, 19.20 Hz, 2H), 4.69–4.73 (m, 1H), 4.37–4.41 (m, 1H), 3.91–3.95 (m, 1H), 3.89 (s,

3H), 3.88 (s, 3H), 3.71–3.78 (m, 1H), 3.33–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.79–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.29, 43.13, 47.57, 53.18, 55.89, 56.13, 69.31, 108.62, 111.66, 116.38 (C–F), 116.61 (C–F), 122.05, 123.89 (C–F), 123.95 (C–F), 124.04 (C–F), 125.17, 126.04 (C–F), 126.19 (C–F), 126.75 (C–F), 129.50, 131.35, 135.35, 148.05, 148.53, 155.96; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.60; H, 4.79; N, 9.49.

4.3.12. (10b*S*)-2-(2,4-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6l). 89%; mp 220–221 °C; IR (KBr) 3082, 3026, 2960, 2926, 2850, 1656, 1620, 1520, 1454, 1470, 1270, 1222, 1060, 976 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.36–7.41 (m, 1H), 6.77–6.84 (m, 2H), 6.66 (s, 2H), 5.29–5.41 (dd, *J*=14.10, 19.80 Hz, 2H), 4.68–4.73 (dd, *J*=3.00, 10.50 Hz, 1H), 4.37–4.41 (dd, *J*=2.10, 8.10 Hz, 1H), 3.90–3.95 (dd, *J*=8.10, 10.80 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.70–3.78 (m, 1H), 3.32–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.77–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.28, 43.17, 47.41 (C–F), 47.46 (C–F), 53.19, 55.89, 56.14, 69.28, 103.31 (C–F), 103.65 (C–F), 103.98 (C–F), 108.67, 111.08 (C–F), 111.13 (C–F), 111.36 (C–F), 111.41 (C–F), 111.71, 119.57 (C–F), 119.62 (C–F), 119.77 (C–F), 119.82 (C–F), 122.09, 126.76, 129.39, 131.30, 131.76 (C–F), 131.82 (C–F), 131.88 (C–F), 131.96 (C–F), 135.20, 148.08, 148.56, 155.96; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.56; H, 4.79; N, 9.50.

4.3.13. (10b*S*)-2-(2,5-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6m). 87%; mp 215–216 °C; IR (KBr) 3098, 2950, 1638, 1520, 1264 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (s, 1H), 6.93–7.28 (m, 3H), 6.67 (s, 2H), 5.33–5.44 (dd, *J*=14.93, 18.70 Hz, 2H), 4.71–4.75 (dd, *J*=2.78, 10.78 Hz, 1H), 4.40–4.44 (dd, *J*=2.20, 8.19 Hz, 1H), 3.91–3.96 (dd, *J*=8.31, 10.75 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.73–3.80 (m, 1H), 3.35–3.43 (m, 1H), 2.90–3.00 (m, 1H), 2.79–2.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.37, 43.22, 47.74, 53.25, 55.95, 56.20, 69.41, 108.69, 111.74, 115.45 (C–F), 115.57 (C–F), 115.77 (C–F), 115.88 (C–F), 116.12 (C–F), 116.23 (C–F), 116.44 (C–F), 116.53 (C–F), 116.81 (C–F), 116.86 (C–F), 122.10, 125.27 (C–F), 125.38 (C–F), 125.51 (C–F), 125.61 (C–F), 126.81, 129.66, 131.21, 135.21, 148.13, 148.61, 156.03; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.55; H, 4.78; N, 9.50.

4.3.14. (10b*S*)-2-(2,6-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6n). 93%; mp 206–207 °C; IR (KBr) 3092, 2950, 1650, 1624, 1520, 1480, 1278, 1256, 1056, 840, 794 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.21–7.31 (m, 1H), 6.85–6.94 (m, 2H), 6.65 (s, 1H), 6.64 (s, 1H), 5.42 (s, 2H), 4.68–4.72 (dd, *J*=2.70, 10.80 Hz, 1H), 4.36–4.40 (dd, *J*=2.10, 8.10 Hz, 1H), 3.89–3.95 (dd, *J*=8.40, 11.10 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.63–3.73 (m, 1H), 3.30–3.38 (m, 1H), 2.86–2.96 (m, 1H), 2.75–2.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.32, 41.97 (C–F), 42.01 ((C–F), 43.18, 53.21, 55.90, 56.14, 69.26, 108.65, 111.03 (C–F), 111.12 (C–F), 111.26 (C–F), 111.37 (C–F), 111.67, 112.13 (C–F), 122.20, 126.78, 129.18 (C–F), 129.76, 131.13, 135.09, 148.04, 148.50, 155.78; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.56; H, 4.79; N, 9.48.

4.3.15. (10b*S*)-2-(3,4-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6o). 90%; mp 165–166 °C; IR (KBr) 3050, 2924, 2832, 1640, 1618, 1516, 1438, 1260, 1102, 762 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.04–7.13 (m, 1H), 7.16–7.20 (m, 1H), 7.24–7.31 (m, 1H), 6.66 (s, 2H), 5.18–5.32 (dd, *J*=13.99, 30.38 Hz, 2H), 4.68–4.73 (dd, *J*=2.77, 10.79 Hz, 1H), 4.37–4.41 (dd, *J*=2.14, 8.16 Hz, 1H), 3.89–3.94 (dd, *J*=8.33, 10.83 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.68–3.78 (m, 1H), 3.33–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.78–2.86 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.36, 43.24, 53.25, 53.50, 55.95, 56.20, 69.37, 108.69, 111.73, 117.06 (C–F), 117.29 (C–F), 117.72 (C–F), 117.95 (C–F), 122.09 (C–F), 124.91 (C–F), 124.96 (C–F). 125.00 (C–F), 125.04 (C–F), 126.79, 129.54, 131.45, 133.58 (C–F), 133.65 (C–F), 135.33, 148.13, 148.60, 155.83; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.56; H, 4.79; N, 9.47.

4.3.16. (10b*S*)-2-(3,5-Difluorobenzyl)-8,9-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6p). 91%; mp 208–209 °C; IR (KBr) 3100, 2950, 1638, 1520, 1462, 1324, 1274, 1124, 992, 836, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74 (s, 1H), 6.90–6.94 (m, 2H), 6.66–7.72 (m, 3H), 5.20–5.34 (dd, *J*=14.40, 26.10 Hz, 2H), 4.69–4.73 (dd, *J*=2.40, 10.50 Hz, 1H), 4.37–4.41 (dd, *J*=2.10, 8.10 Hz, 1H), 3.89–3.94 (dd, *J*=8.40, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.72–3.79 (m, 1H), 3.34–3.42 (m, 1H), 2.89–2.97 (m, 1H), 2.78–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.30, 43.17, 53.19, 53.54, 55.89, 56.14, 69.32, 102.73 (C–F), 103.07 (C–F), 103.40 (C–F), 108.68, 111.15 (C–F), 111.25 (C–F), 111.37 (C–F), 111.48 (C–F), 111.71, 122.03, 126.75, 129.56, 131.42, 135.20, 139.10 (C–F), 140.35 (C–F), 140.26 (C–F), 148.10, 148.58, 155.79; MS (*m*/*z*): 441 (M^+); Anal. Calcd for $C_{23}H_{21}F_2N_3O_4$: C, 62.58; H, 4.80; N, 9.52. Found: C, 62.57; H, 4.81; N, 9.49.

4.3.17. (10b*S*)-8,9-Dimethoxy-2-(4-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6q). 92%; mp 215–216 °C; IR (KBr) 3072, 2948, 1620, 1522, 1464, 1430, 1340, 1260, 1120, 838, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.52–7.58 (m, 4H), 6.65 (s, 2H), 5.29–5.43 (dd, *J*=13.80, 28.80 Hz, 2H), 4.68–4.72 (dd, *J*=2.70, 10.80 Hz, 1H), 4.37–4.40 (dd, *J*=1.80, 8.10 Hz, 1H), 3.89–3.94 (dd, *J*=8.40, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.70–3.77 (m, 1H), 3.32–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.77–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.38, 43.28, 53.28, 53.95, 55.97, 56.22, 69.37, 108.75, 111.78, 122.13, 125.39 (C–F), 125.45 (C–F), 125.50 (C–F), 125.54 (C–F), 126.81, 128.99, 129.58, 131.44, 135.39, 140.65, 148.19, 148.66, 155.94; MS (*m*/*z*): 473 (M^+); Anal. Calcd for $C_{24}H_{22}F_3N_3O_4$: C, 60.89; H, 4.68; N, 8.88. Found: C, 60.86; H, 4.68; N, 8.85.

4.3.18. (10b*S*)-8,9-Dimethoxy-2-(3-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6r). 92%; mp 155–156 °C; IR (KBr) 3076, 2952, 2846, 1638, 1610, 1512, 1320, 1258, 1168, 1120, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74 (s, 1H), 7.68 (s, 1H),

7.63–7.65 (d, 1H), 7.51–7.54 (d, 1H), 7.40–7.45 (t, 1H), 6.65 (s, 2H), 5.29–5.43 (dd, *J*=14.40, 27.90 Hz, 2H), 4.68–4.73 (dd, *J*=2.70, 10.50 Hz, 1H), 4.37–4.41 (dd, *J*=1.80, 8.10 Hz, 1H), 3.89–3.94 (dd, *J*=8.40, 10.80 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.70–3.78 (m, 1H), 3.33–3.41 (m, 1H), 2.88–2.98 (m, 1H), 2.77–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.38, 43.26, 53.27, 53.94, 55.96, 56.22, 69.39, 108.76, 111.78, 122.15, 124.59 (C–F), 124.64 (C–F), 125.40 (C–F), 125.45 (C–F), 125.50 (C–F), 126.85, 129.00, 129.58, 131.45, 132.29, 132.30, 135.35, 137.65, 148.16, 148.65, 155.91; MS (*m*/*z*): 473 (M^+); Anal. Calcd for $C_{24}H_{22}F_3N_3O_4$: C, 60.89; H, 4.68; N, 8.88. Found: C, 60.86; H, 4.67; N, 8.85.

4.3.19. (10b*S*)-8,9-Dimethoxy-2-(2-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (6s). 93%; mp 220–221 °C; IR (KBr) 3062, 2942, 1646, 1618, 1516, 1312, 1100, 770 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.77 (s, 1H), 7.65–7.68 (d, 1H), 7.31–7.47 (m, 2H), 7.07–7.09 (d, 1H), 6.68 (s, 1H), 6.67 (s, 1H), 5.57 (s, 2H), 4.72–4.77 (dd, *J*=3.00, 11.10 Hz, 1H), 4.42–4.46 (dd, *J*=2.00, 8.10 Hz, 1H), 3.92–3.97 (dd, *J*=8.40, 11.10 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.74–3.81 (m, 1H), 3.35–3.43 (m, 1H), 2.91–3.01 (m, 1H), 2.78–2.86 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 28.28, 43.12, 50.11, 53.19, 55.87, 56.13, 69.35, 108.67, 111.71, 122.06, 127.77 (C–F), 125.84 (C–F), 125.91 (C–F), 126.76, 127.12, 128.08, 129.66, 131.39, 131.96, 135.09, 135.34, 148.08, 148.56, 156.27; MS (*m*/*z*): 473 (M^+); Anal. Calcd for $C_{24}H_{22}F_3N_3O_4$: C, 60.89; H, 4.68; N, 8.88. Found: C, 60.87; H, 4.66; N, 8.87.

4.3.20. (10b*S*,11*S*)-8,9-Dimethoxy-2,11-dimethyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7a). 94%; mp 183–184 °C; IR (KBr) 3100, 2976, 1642, 1620, 1520, 1422, 1220, 1110, 1018, 980, 838, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (s, 1H), 6.76 (s, 1H), 6.61 (s, 1H), 4.39–4.47 (m, 1H), 4.09 (d, *J*=4.20 Hz, 1H), 3.88–3.91 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.68–3.77 (s, 3H), 3.37–3.49 (m, 1H), 2.91–3.01 (m, 1H), 2.65–2.72 (m, 1H), 1.50 (d, *J*=6.60 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.48, 27.11, 39.49, 45.63, 55.79, 55.98, 58.84, 72.69, 110.24, 111.45, 123.99, 127.37, 129.41, 130.86, 135.24, 147.49, 148.45, 156.20; MS (*m*/*z*): 343 (M^+); Anal. Calcd for $C_{18}H_{21}N_3O_4$: C, 62.96; H, 6.16; N, 12.24. Found: C, 62.92; H, 6.17; N, 12.24.

4.3.21. (10b*S*,11*S*)-2-Ethyl-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7b). 90%; mp 150–151 °C; IR (KBr) 3094, 2984, 2950, 1636, 1620, 1526, 1440, 1264, 1220, 1200, 1106, 1038, 1016, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.70 (s, 1H), 6.76 (s, 1H), 6.62 (s, 1H), 4.30–4.38 (m, 1H), 4.11–4.24 (m, 2H), 4.07 (d, *J*=5.10 Hz, 1H), 3.88–3.91 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.37–3.49 (m, 1H), 2.88–3.01 (m, 1H), 2.66–2.73 (m, 1H), 1.50 (d, *J*=6.60 Hz, 3H), 1.32–1.37 (t, *J*=7.50 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 15.56, 18.49, 27.29, 45.58, 46.25, 55.79, 55.99, 58.98, 72.89, 110.50, 111.42, 123.81, 127.51, 129.64, 130.68, 135.23, 147.46, 148.45, 155.67; MS (*m*/*z*): 357 (M^+); Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 63.85; H, 6.49; N, 11.76; N, 12.24. Found: C, 63.82; H, 6.47; N, 11.74.

4.3.22. (10b*S*,11*S*)-8,9-Dimethoxy-11-methyl-2-propyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7c). 92%; mp 198–199 °C; IR (KBr) 3050, 2976, 2948, 1648, 1622, 1526, 1430, 1260, 1218, 1104, 1040, 1010, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (s, 1H), 6.76 (s, 1H), 6.62 (s, 1H), 4.25–4.31 (m, 1H), 4.01–4.12 (m, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.82–3.86 (m, 1H), 3.36–3.49 (m, 1H), 2.88–3.00 (m, 1H), 2.65–2.73 (m, 1H), 1.75–1.87 (m, 2H), 1.50 (d, *J*=6.30 Hz, 3H), 0.92–0.97 (t, *J*=7.20 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 11.07, 18.53, 21.72, 27.43, 45.61, 52.70, 55.84, 56.04, 59.10, 73.07, 110.68, 111.43, 123.75, 127.60, 129.54, 130.65, 135.26, 147.49, 148.50, 155.95; MS (*m*/*z*): 371 (M^+); Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.66; H, 6.76; N, 11.30.

4.3.23. (10b*S*,11*S*)-2-Isopropyl-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7d). 91%; mp 242–243 °C; IR (KBr) 3074, 2962, 2924, 1626, 1600, 1510, 1418, 1248, 1200, 1180, 1086, 1020, 990, 824 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.74 (s, 1H), 6.76 (s, 1H), 6.62 (s, 1H), 5.27–5.36 (m, 1H), 4.30–4.38 (m, 1H), 4.07 (d, *J*=5.10 Hz, 1H), 3.88–3.91 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.36–3.46 (m, 1H), 2.88–3.01 (m, 1H), 2.65–2.73 (m, 1H), 1.50 (d, *J*=6.60 Hz, 3H), 1.30–1.35 (t, *J*=6.60 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 18.66, 20.95, 21.07, 27.45, 45.64, 48.54, 55.93, 56.13, 59.13, 72.95, 110.60, 111.54, 124.05, 127.66, 129.48, 130.36, 135.00, 147.60, 148.57, 155.70; MS (*m*/*z*): 371 (M^+); Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.63; H, 6.77; N, 11.29.

4.3.24. (10b*S*,11*S*)-2-Butyl-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7e). 88%; mp 126–127 °C; IR (KBr) 3074, 2952, 2874, 1640, 1620, 1522, 1428, 1360, 1278, 1216, 1104, 1012, 838, 778 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.68 (s, 1H), 6.76 (s, 1H), 6.62 (s, 1H), 4.25–4.31 (m, 1H), 4.05–4.13 (m, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.78–3.84 (m, 1H), 3.37–3.49 (m, 1H), 2.89–3.01 (m, 1H), 2.66–2.73 (m, 1H), 1.73–1.80 (m, 2H), 1.50 (d, *J*=6.00 Hz, 3H), 1.33–1.41 (m, 2H), 0.92–0.96 (t, *J*=7.20 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 13.72, 18.53, 19.80, 27.44, 30.52, 45.62, 50.94, 55.84, 56.05, 59.12, 73.08, 110.70, 111.43, 123.76, 127.60, 129.55, 130.65, 135.29, 147.50, 148.51, 155.92; MS (*m*/*z*): 385 (M^+); Anal. Calcd for $C_{21}H_{27}N_3O_4$: C, 65.44; H, 7.06; N, 10.90. Found: C, 65.43; H, 7.05; N, 10.87.

4.3.25. (10b*S*,11*S*)-2-Allyl-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7f). 91%; mp 195–196 °C; IR (KBr) 3142, 3026, 2986, 2800, 1646, 1618, 1260, 1100, 1030, 1002, 836, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.71 (s, 1H), 6.76 (s, 1H), 6.62 (s, 1H), 5.93–6.04 (m, 1H), 5.19–5.28 (m, 2H), 4.66–4.80 (m, 2H), 4.28–4.34 (m, 1H), 4.07 (d, *J*=5.1 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.82–3.84 (m, 1H), 3.36–3.46 (m, 1H), 2.88–3.00 (m, 1H), 2.66–2.73 (m, 1H), 1.50 (d, *J*=6.60 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.61, 27.47, 45.71, 53.43, 55.94, 56.13, 59.17, 73.15, 110.68, 111.54, 118.08, 123.84, 127.63, 130.09, 130.89, 132.49, 135.37, 147.61, 148.61, 155.86; MS (*m*/*z*): 369 (M^+); Anal. Calcd for $C_{20}H_{23}N_3O_4$: C, 65.03; H, 6.28; N, 11.37. Found: C, 65.01; H, 6.26; N, 11.38.

4.3.26. (10b*S*,11*S*)-2-Benzyl-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7g). 92%; mp 183–184 °C; IR (KBr) 3072, 2950, 1634, 1612, 1516, 1458, 1410, 1354, 1260, 1208, 1100, 1006, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67 (s, 1H), 7.41–7.45 (m, 2H), 7.22–7.32 (m, 3H), 6.74 (s, 1H), 6.61 (s, 1H), 5.21–5.37 (dd, *J*=14.10, 33.30 Hz, 2H), 4.15–4.23 (m, 1H), 4.02 (d, *J*=5.4 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.76–3.83 (m, 1H), 3.31–3.41 (m, 1H), 2.85–2.96 (m, 1H), 2.62–2.70 (m, 1H), 1.49 (d, *J*=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.60, 27.60, 45.59, 54.34, 55.91, 56.13, 59.27, 73.37, 110.92, 111.50, 123.58, 127.64, 127.75, 128.44, 128.82, 130.21, 130.92, 135.31, 136.87, 147.53, 148.59, 156.01; MS (*m/z*): 419 (M^+); Anal. Calcd for $C_{24}H_{25}N_3O_4$: C, 68.72; H, 6.01; N, 10.02. Found: C, 68.69; H, 6.00; N, 10.01.

4.3.27. (10b*S*,11*S*)-2-(4-Fluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7h). 90%; mp 186–187 °C; IR (KBr) 3098, 2970, 1640, 1622, 1520, 1436, 1362, 1280, 1238, 1210, 1102, 1036, 1020, 826, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.41–7.46 (m, 2H), 6.94–7.01 (m, 2H), 6.74 (s, 1H), 6.61 (s, 1H), 5.17–5.33 (dd, *J*=13.80, 35.40 Hz, 2H), 4.14–4.23 (m, 1H), 4.03 (d, *J*=5.40 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.78–3.83 (m, 1H), 3.33–3.42 (m, 1H), 2.86–2.97 (m, 1H), 2.64–2.71 (m, 1H), 1.48 (d, *J*=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.53, 27.56, 45.52, 53.64, 55.84, 56.04, 59.21, 73.37, 100.49 (C–F), 110.80, 111.36, 115.06 (C–F), 115.34 (C–F), 123.42, 127.64, 130.20, 130.60 (C–F), 130.72 (C–F), 130.91 (C–F), 132.57 (C–F), 132.60, 135.22, 147.46, 148.51, 155.86; MS (*m/z*): 437 (M^+); Anal. Calcd for $C_{24}H_{24}F_1N_3O_4$: C, 65.89; H, 5.53; N, 9.61. Found: C, 65.85; H, 5.50; N, 9.58.

4.3.28. (10b*S*,11*S*)-2-(3-Fluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7i). 94%; mp 202–203 °C; IR (KBr) 3096, 2952, 1642, 1520, 1460, 1280, 1258, 1102, 1030, 776 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1H), 7.19–7.30 (m, 2H), 7.10–7.14 (m, 1H), 6.92–6.98 (m, 1H), 6.74 (s, 1H), 6.62 (s, 1H), 5.20–5.36 (dd, *J*=13.80, 32.70 Hz, 2H), 4.14–4.22 (m, 1H), 4.04 (d, *J*=5.70 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.79–3.84 (m, 1H), 3.34–3.44 (m, 1H), 2.89–2.98 (m, 1H), 2.66–2.72 (m, 1H), 1.48 (d, *J*=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.55, 27.63, 45.55, 53.83 (C–F), 53.85 (C–F), 55.88, 56.08, 59.28, 73.48, 110.88, 111.41, 114.42 (C–F), 114.70 (C–F), 115.42 (C–F), 115.71 (C–F), 123.41, 124.31 (C–F), 124.35 (C–F), 127.69, 129.85 (C–F), 129.95 (C–F), 130.35 (C–F), 131.00, 135.22, 139.18, 147.52, 148.57, 155.93; MS (*m/z*): 437 (M^+); Anal. Calcd for $C_{24}H_{24}F_1N_3O_4$: C, 65.89; H, 5.53; N, 9.61. Found: C, 65.86; H, 5.52; N, 9.59.

4.3.29. (10b*S*,11*S*)-2-(2-Fluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7j). 93%; mp 177–178 °C; IR (KBr) 3078, 2970, 2900, 1644, 1620, 1522, 1470, 1438, 1364, 1280, 1240, 1214, 1100, 1032, 1018, 776 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (s, 1H), 7.22–7.37 (m, 2H), 7.00–7.08 (m, 2H), 6.75 (s, 1H), 6.62 (s, 1H), 5.33–5.43 (dd, *J*=15.00, 15.90 Hz, 2H), 4.19–4.23 (m, 1H), 4.04–4.06 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.80–3.83 (m, 1H), 3.35–3.42 (m, 1H), 2.87–2.92 (m, 1H), 2.64–2.71 (m, 1H), 1.50 (d, *J*=6.00 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.49, 27.52, 45.47, 47.74 (C–F), 47.80 (C–F), 55.81, 56.03, 59.18, 73.34, 110.82, 111.40, 115.01 (C–F), 115.30 (C–F), 123.45, 123.61 (C–F), 123.80 (C–F), 123.99 (C–F), 124.04 (C–F), 135.05, 147.46, 148.50, 156.05; MS (*m/z*): 437 (M^+); Anal. Calcd for $C_{24}H_{24}F_1N_3O_4$: C, 65.89; H, 5.53; N, 9.61. Found: C, 65.87; H, 5.50; N, 9.61.

4.3.30. (10b*S*,11*S*)-2-(2,3-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7k). 91%; mp 190–192 °C; IR (KBr) 3050, 2948, 1638, 1516, 1500, 1460, 1274, 1100, 1032, 830, 768 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.71 (s, 1H), 6.96–7.15 (m, 3H), 6.74 (s, 1H), 6.63 (s, 1H), 5.39 (d, *J*=3.30 Hz, 2H), 4.17–4.25 (m, 1H), 4.06 (d, *J*=5.40 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.81–3.84 (m, 1H), 3.35–3.44 (m, 1H), 2.88–2.99 (m, 1H), 2.66–2.72 (m, 1H), 1.48 (d, *J*=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.54, 27.61, 45.52, 47.60, 55.87, 56.07, 59.26, 73.48, 110.81, 111.39, 116.36 (C–F), 116.59 (C–F), 123.39, 124.03 (C–F), 125.40 (C–F), 125.43 (C–F), 126.23 (C–F), 127.67, 130.41, 131.01, 135.04, 138.26, 147.51, 156.18; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.26; H, 5.07; N, 9.24.

4.3.31. (10b*S*,11*S*)-2-(2,4-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7l). 90%; mp 190–191 °C; IR (KBr) 3058, 2948, 1638, 1518, 1430, 1264, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.63 (s, 1H), 7.37–7.42 (m, 1H), 6.69–6.82 (m, 2H), 6.67 (s, 1H), 6.62 (s, 1H), 5.36 (d, *J*=3.30 Hz, 2H), 4.22–4.32 (m, 1H), 4.05 (d, *J*=5.68 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.76–3.82 (m, 1H), 3.34–3.43 (m, 1H), 2.82–2.94 (m, 1H), 2.61–2.74 (m, 1H), 1.47 (d, *J*=6.50 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.55, 27.61, 45.53, 47.48, 55.88, 56.08, 59.26, 73.46, 103.31 (C–F), 103.65 (C–F), 103.98 (C–F), 110.82, 111.10 (C–F), 111.16 (C–F), 111.24 (C–F), 111.40 (C–F), 111.56, 119.63 (C–F), 123.43, 127.67, 130.32 (C–F), 130.98, 132.06, 147.52, 148.57, 156.08; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.28; H, 5.05; N, 9.22.

4.3.32. (10b*S*,11*S*)-2-(2,5-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7m). 92%; mp 204–205 °C; IR (KBr) 3100, 2974, 1648, 1516, 1476, 1292, 1016, 1040, 842 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (s, 1H), 6.97–7.05 (m, 2H), 6.87–6.95 (m, 1H), 6.75 (s, 1H), 6.63 (s, 1H), 5.32–5.37 (dd, *J*=2.03, 8.14 Hz, 2H), 4.16–4.24 (m, 1H), 4.06 (d, *J*=5.55 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.81–3.85 (m, 1H), 3.36–3.45 (m, 1H), 2.91–3.00 (m, 1H), 2.66–2.73 (m, 1H), 1.49 (d, *J*=6.31 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.61, 27.71, 45.59, 47.78 (C–F), 47.83 (C–F), 55.94, 56.16, 59.37, 73.63, 110.99, 111.49, 115.43 (C–F), 115.55 (C–F), 115.76 (C–F), 115.87 (C–F), 116.08 (C–F), 116.19 (C–F), 116.40 (C–F), 116.52 (C–F), 116.68 (C–F), 116.73 (C–F), 117.01 (C–F), 117.06 (C–F), 123.43, 125.30 (C–F), 125.42 (C–F), 125.54 (C–F), 125.66 (C–F), 127.77, 130.59, 131.14, 135.14, 147.61, 148.67, 156.11; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.28; H, 5.08; N, 9.21.

4.3.33. (10b*S*,11*S*)-2-(2,6-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7n). 92%; mp 240–241 °C;

IR (KBr) 3100, 2998, 2954, 1664, 1624, 1522, 1480, 1250, 1038, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (s, 1H), 7.21–7.28 (m, 1H), 6.86–6.91 (m, 2H), 6.74 (s, 1H), 6.61 (s, 1H), 5.39 (s, 2H), 4.19–4.27 (m, 1H), 4.04 (d, J=5.70 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.77–3.83 (m, 1H), 3.32–3.41 (m, 1H), 2.87–2.97 (m, 1H), 2.63–2.70 (m, 1H), 1.48 (d, J=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.52, 27.49, 42.09, 45.49, 55.84, 56.03, 59.17, 73.26, 110.71, 110.97 (C–F), 110.99 (C–F), 111.07 (C–F), 111.31, 111.38 (C–F), 111.86 (C–F), 112.11 (C–F), 123.58, 127.63, 129.56 (C–F), 129.69 (C–F), 129.83 (C–F), 129.98 (C–F), 130.74, 134.93, 147.46, 148.49, 155.82; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.25; H, 5.08; N, 9.21.

4.3.34. (10b*S*,11*S*)-2-(3,4-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7o). 91%; mp 143–144 °C; IR (KBr) 3060, 2942, 2842, 1630, 1516, 1438, 1356, 1270, 1100, 1018, 826, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1H), 7.25–7.32 (m, 1H), 7.16–7.21 (m, 1H), 7.03–7.12 (m, 1H), 6.74 (s, 1H), 6.62 (s, 1H), 5.14–5.30 (dd, J=13.94, 34.11 Hz, 2H), 4.14–4.22 (m, 1H), 4.04 (d, J=5.53 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.80–3.84 (m, 1H), 3.35–3.44 (m, 1H), 2.87–2.98 (m, 1H), 2.65–2.72 (m, 1H), 1.48 (d, J=6.31 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.60, 27.69, 45.60, 53.54, 55.93, 56.15, 59.35, 73.57, 110.96, 111.47, 117.02 (C–F), 117.25 (C–F), 117.84 (C–F), 118.07 (C–F), 123.43, 125.02 (C–F), 125.07 (C–F), 125.11 (C–F), 125.16 (C–F), 127.74, 130.44, 131.11, 133.64 (C–F), 133.72 (C–F), 133.76 (C–F), 133.77 (C–F), 135.24, 147.60, 148.21 (C–F), 148.45 (C–F), 148.66, 151.60 (C–F), 151.73 (C–F), 151.85 (C–F), 155.89; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.28; H, 5.06; N, 9.22.

4.3.35. (10b*S*,11*S*)-2-(3,5-Difluorobenzyl)-8,9-dimethoxy-11-methyl-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7p). 91%; mp 230–231 °C; IR (KBr) 3076, 2950, 1640, 1522, 1464, 1278, 1126, 1032, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (s, 1H), 6.90–7.00 (m, 2H), 6.78 (s, 1H), 6.65–6.74 (m, 1H), 6.63 (s, 1H), 5.17–5.32 (dd, J=2.02, 8.14 Hz, 2H), 4.14–4.22 (m, 1H), 4.05 (d, J=5.70 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.81–3.84 (m, 1H), 3.36–3.45 (m, 1H), 2.88–2.99 (m, 1H), 2.66–2.73 (m, 1H), 1.49 (d, J=6.60 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.54, 27.65, 45.53, 53.60, 55.87, 56.07, 59.30, 73.57, 102.73 (C–F), 103.07 (C–F), 103.40 (C–F), 110.89, 111.28, 111.38 (C–F), 111.51 (C–F), 111.62 (C–F), 123.30, 127.68, 130.50, 131.10, 135.11, 140.24 (C–F), 140.36 (C–F), 147.52, 148.58, 155.86; MS (*m/z*): 455 (M^+); Anal. Calcd for $C_{24}H_{23}F_2N_3O_4$: C, 63.29; H, 5.09; N, 9.23. Found: C, 63.24; H, 5.07; N, 9.21.

4.3.36. (10b*S*,11*S*)-8,9-Dimethoxy-11-methyl-2-(4-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7q). 89%; mp 130–131 °C; IR (KBr) 3072, 2948, 1622, 1520, 1466, 1430, 1338, 1260, 1140, 1120, 1076, 1030, 836, 776 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (m, 1H), 7.55–7.62 (m, 4H), 6.74 (s, 1H), 6.62 (s, 1H), 5.26–5.42 (dd, J=13.80, 33.30 Hz, 2H), 4.17–4.19 (m, 1H), 4.06 (d, J=5.40 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.81–3.84 (m, 1H), 3.35–3.42 (m, 1H), 2.90–2.94 (m, 1H), 2.65–2.72 (m, 1H), 1.48 (d, J=5.70 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.51, 27.60, 45.51, 53.92, 55.85, 56.07, 59.26, 73.51, 110.90, 111.42, 123.35, 125.33, 125.38, 127.66, 129.00, 130.42, 131.07, 135.15, 140.63, 147.54, 148.60, 155.93; MS (*m/z*): 487 (M^+); Anal. Calcd for $C_{25}H_{24}F_3N_3O_4$: C, 61.60; H, 4.96; N, 8.62. Found: C, 61.59; H, 4.92; N, 8.60.

4.3.37. (10b*S*,11*S*)-8,9-Dimethoxy-11-methyl-2-(3-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7r). 90%; mp 145–147 °C; IR (KBr) 3098, 2972, 1644, 1626, 1526, 1478, 1342, 1284, 1138, 1040, 780, 714 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.70 (m, 5H), 6.74 (s, 1H), 6.62 (s, 1H), 5.26–5.41 (dd, J=14.10, 30.60 Hz, 2H), 4.14–4.22 (m, 1H), 4.04 (d, J=5.40 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.81–3.84 (m, 1H), 3.35–3.49 (m, 1H), 2.88–2.98 (m, 1H), 2.64–2.72 (m, 1H), 1.48 (d, J=6.30 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.54, 27.65, 45.53, 53.92, 55.87, 56.08, 59.29, 73.55, 110.89, 111.39, 123.35, 124.51 (C–F), 124.56 (C–F), 125.46 (C–F), 125.51 (C–F), 127.69, 128.93, 130.44, 131.07 (C–F), 132.38 (C–F), 137.59, 147.52, 148.58, 155.60; MS (*m/z*): 487 (M^+); Anal. Calcd for $C_{25}H_{24}F_3N_3O_4$: C, 61.60; H, 4.96; N, 8.62. Found: C, 61.58; H, 4.93; N, 8.60.

4.3.38. (10b*S*,11*S*)-8,9-Dimethoxy-11-methyl-2-(2-trifluoromethylbenzyl)-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (7s). 91%; mp 203–204 °C; IR (KBr) 3048, 2974, 1656, 1624, 1522, 1440, 1330, 1286, 1050, 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.74 (s, 1H), 7.65–7.68 (d, J=7.80 Hz, 1H), 7.31–7.47 (m, 2H), 7.0–7.11 (d, J=7.8 Hz, 1H), 6.76 (s, 1H), 6.64 (s, 1H), 5.55 (s, 2H), 4.18–4.27 (m, 1H), 4.09 (d, J=5.40 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.76–3.85 (m, 1H), 3.37–3.51 (m, 1H), 2.88–3.01 (m, 1H), 2.67–2.73 (m, 1H), 1.51 (d, J=6.00 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 18.56, 27.67, 45.52, 50.56 (C–F), 50.60 (C–F), 55.89, 56.09, 59.33, 73.63, 110.91, 111.42, 123.37, 125.84 (C–F), 125.91 (C–F), 127.12, 127.72 (C–F), 128.29 (C–F), 130.66, 131.10, 132.00 (C–F), 135.05, 135.46 (C–F), 147.55, 148.60, 156.40; MS (*m/z*): 487 (M^+); Anal. Calcd for $C_{25}H_{24}F_3N_3O_4$: C, 61.60; H, 4.96; N, 8.62. Found: C, 61.57; H, 4.98; N, 8.61.

4.4. Synthesis of compound 8

To a solution of compound **3** (30 mmol) in methanol was added 6 N hydrochloric acid (120 mmol). The mixture was warmed to 40 °C for 10 min and heated to reflux for 4 h. The reaction mixture was slowly cooled to 30 °C. The mixture was made basic (pH 7.5) by addition of 50% sodium hydroxide in portion. The product in the mixture was filtered, and dried at 50 °C.

4.4.1. 4-[2-(3,4-Dimethoxyphenyl)ethyl]-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (8a). 92%; mp 234–235 °C; IR (KBr) 3270, 3100, 3064, 3022, 2908, 2840, 1700, 1658, 1630, 1510, 1418, 1374, 1320, 1250, 1228, 1134, 1018, 984, 802, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 13.04 (s, 1H), 7.96 (s, 1H), 6.71–6.84 (m, 3H), 4.73 (s, 2H), 4.07–4.12 (t, 2H), 3.76 (s, 3H), 3.74 (s, 3H), 2.78–2.83 (t, 2H); ^{13}C NMR ($CDCl_3$) δ 32.90, 41.87, 55.29, 55.36, 66.78, 111.57, 112.53, 120.74, 125.72, 128.60, 129.92, 136.65,

147.39, 148.51, 155.91, 162.00; MS (*m*/*z*): 331 (M^+); Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: C, 57.98; H, 5.15; N, 12.65.

4.4.2. (11*S*)-4-[2-(3,4-Dimethoxyphenyl)ethyl]-2-methyl-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (8b). 90%; mp 180–182 °C; IR (KBr) 3320, 2974, 2850, 1642, 1620, 1514, 1450, 1408, 1360, 1266, 1222, 1094, 1016, 950, 926, 884, 820, 782, 762 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.67 (s, 1H), 7.71 (s, 1H), 6.71–6.81 (m, 3H), 4.79–4.85 (m, 1H), 4.00–4.18 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.87–2.92 (t, 2H), 1.62 (d, J=6.90 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 16.72, 33.73, 43.31, 55.97, 55.99, 74.51, 111.55, 112.00, 120.91, 126.83, 128.66, 129.32, 136.56, 148.25, 149.23, 157.89, 164.67; MS (*m*/*z*): 487 (M^+); Anal. Calcd for $C_{17}H_{19}N_3O_5$: C, 59.12; H, 5.55; N, 12.17. Found: C, 59.11; H, 5.53; N, 12.15.

4.4.3. 7-Benzyl-4-[2-(3,4-dimethoxyphenyl)ethyl]-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (9a). 89%; mp 164–165 °C; IR (KBr) 3100, 3020, 2952, 2848, 1706, 1656, 1630, 1522, 1430, 1394, 1350, 1270, 1240, 1184, 1140, 1030, 1000, 836, 816, 760, 706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (s, 1H), 7.19–7.35 (m, 5H), 6.71 (d, 1H), 6.61–6.65 (m, 2H), 5.25 (s, 2H), 4.68 (s, 2H), 3.96–3.99 (t, J=7.52 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 2.78–2.81 (t, J=7.71 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 34.10, 43.29, 55.40, 56.35, 56.37, 67.85, 111.91, 112.29, 121.23, 125.43, 127.23, 128.55, 129.07, 129.28, 129.71, 136.22, 137.64, 148.65, 149.66, 155.77, 162.27; MS (*m*/*z*): 421 (M^+); Anal. Calcd for $C_{23}H_{23}N_3O_5$: C, 65.55; H, 5.50; N, 9.97. Found: C, 65.53; H, 6.49; N, 9.96.

4.4.4. 7-Benzyl-4-[2-(2-chloro-4,5-dimethoxyphenyl)-ethyl]-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (10a). 89%; mp 175–176 °C; IR (KBr) 3028, 2960, 2850, 1700, 1660, 1626, 1506, 1422, 1388, 1348, 1256, 1210, 1170, 1038, 960, 820, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (s, 1H), 7.26–7.41 (m, 5H), 6.84 (s, 1H), 6.69 (s, 1H), 5.32 (s, 2H), 4.76 (s, 2H), 4.03–4.06 (t, J=7.52 Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.98–3.01 (t, J=7.72 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 31.78, 41.31, 55.06, 56.22, 56.32, 67.47, 112.79, 113.56, 124.91, 125.18, 126.40, 126.89, 128.09, 128.66, 128.81, 135.88, 137.21, 148.38, 149.02, 155.36, 162.05; MS (*m*/*z*): 456 (M^+); Anal. Calcd for $C_{23}H_{22}ClN_3O_5$: C, 60.59; H, 4.86; N, 9.22. Found: C, 60.55; H, 4.85; N, 9.20.

4.4.5. 7-Benzyl-4-[2-(2-bromo-4,5-dimethoxyphenyl)-ethyl]-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (10b). 92%; mp 176–177 °C; IR (KBr) 3050, 3012, 2952, 2846, 1698, 1644, 1618, 1510, 1420, 1388, 1344, 1260, 1214, 1164, 1030, 880, 820, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.73 (s, 1H), 7.19–7.35 (m, 5H), 6.91 (s, 1H), 6.64 (s, 1H), 5.24 (s, 2H), 4.69 (s, 2H), 3.95–3.99 (t, J=7.44 Hz, 2H), 3.76 (s, 3H), 3.75 (s, 3H), 2.92–2.95 (t, J=7.71 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 34.50, 41.83, 55.45, 56.62, 67.85, 113.99, 114.55, 116.13, 125.60, 127.42, 128.46, 128.76, 129.02, 129.16, 136.24, 137.57, 149.33, 149.42, 155.74, 162.45; MS (*m*/*z*): 500 (M^+); Anal. Calcd for $C_{23}H_{22}BrN_3O_5$: C, 55.21; H, 4.43; N, 8.40. Found: C, 55.19; H, 4.40; N, 8.41.

4.4.6. 7-Benzyl-4-[2-(2-iodo-4,5-dimethoxyphenyl)ethyl]-4*H*,7*H*-pyridazino[4,5-*b*][1,4]oxazine-3,8-dione (10c). 91%; mp 178–179 °C; IR (KBr) 3082, 3046, 2962, 2850, 1718, 1664, 1636, 1510, 1422, 1384, 1368, 1260, 1234, 1170, 1036, 858, 708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.83 (s, 1H), 7.26–7.41 (m, 5H), 7.18 (s, 1H), 6.72 (s, 1H), 5.32 (s, 2H), 4.76 (s, 2H), 4.01–4.04 (t, J=7.43 Hz, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 3.00–3.03 (t, J=7.70 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 38.40, 41.75, 55.09, 56.13, 56.24, 67.50, 87.87, 112.90, 121.86, 125.26, 127.25, 128.09, 128.65, 128.80, 132.44, 135.88, 137.23, 148.93, 149.90, 155.35, 162.11; MS (*m*/*z*): 547 (M^+); Anal. Calcd for $C_{23}H_{22}IN_3O_5$: C, 50.47; H, 4.05; N, 7.68. Found: C, 50.48; H, 4.04; N, 7.62.

4.4.7. (10b*S*)-2-Benzyl-7-chloro-9,10-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (11a). 90%; mp 178–179 °C; IR (KBr) 3004, 2946, 2844, 1638, 1600, 1480, 1450, 1332, 1298, 1230, 1156, 1100, 1070, 1044, 942, 782 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.26–7.44 (m, 5H), 6.95 (s, 1H), 5.28–5.40 (dd, J=13.90, 48.20 Hz, 2H), 4.92–4.95 (dd, J=2.50, 10.15 Hz, 1H), 4.41–4.43 (dd, J=2.15, 8.30 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.59–3.63 (dd, J=8.45, 10.10 Hz, 1H), 3.41–3.43 (m, 1H), 3.34–3.38 (m, 1H), 2.95–3.00 (m, 1H), 2.78–2.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 26.45, 44.25, 51.56, 54.40, 56.14, 60.72, 66.79, 113.28, 125.31, 125.57, 127.72, 128.41, 128.51, 128.76, 131.26, 131.28, 136.86, 137.34, 145.34, 151.19, 156.26; MS (*m*/*z*): 440 (M^+); Anal. Calcd for $C_{23}H_{22}ClN_3O_4$: C, 62.80; H, 5.04; N, 9.55. Found: C, 62.78; H, 5.04; N, 9.52.

4.4.8. (10b*S*)-2-Benzyl-7-bromo-9,10-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (11b). 87%; mp 167–168 °C; IR (KBr) 3014, 2920, 2858, 1636, 1480, 1444, 1430, 1348, 1298, 1220, 1090, 1036, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67 (s, 1H), 7.24–7.44 (m, 5H), 7.13 (s, 1H), 5.27–5.40 (dd, J=13.90, 47.30 Hz, 2H), 4.91–4.94 (dd, J=2.40, 10.15 Hz, 1H), 4.41–4.43 (dd, J=2.00, 8.36 Hz, 1H), 3.87 (s, 3H), 3. 86 (s, 3H), 3.58–3.62 (dd, J=8.50, 10.05 Hz, 1H), 3.41–3.44 (m, 1H), 3.34–3.37 (m, 1H), 2.94–2.96 (m, 1H), 2.78–2.81 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 29.33, 44.51, 51.57, 54.40, 56.17, 60.67, 66.80, 116.41, 118.45, 125.86, 127.09, 127.71, 128.50, 128.76, 131.22, 131.26, 136.86, 137.32, 145.94, 151.33, 156.25; MS (*m*/*z*): 484 (M^+); Anal. Calcd for $C_{23}H_{22}BrN_3O_4$: C, 57.04; H, 4.58; N, 8.68. Found: C, 57.03; H, 4.54; N, 8.66.

4.4.9. (10b*S*)-2-Benzyl-7-iodo-9,10-dimethoxy-5,6,10b,11-tetrahydro-2*H*-12-oxa-2,3,4b-triazachrysen-1-one (11c). 89%; mp 225–226 °C; IR (KBr) 3048, 2944, 2868, 1648, 1620, 1482, 1422, 1320, 1256, 1106, 1036, 1002, 836, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (s, 1H), 7,22–7.44 (m, 5H), 6.73 (s, 1H), 5.27–5.36 (dd, J=13.90, 30.20 Hz, 2H), 4.66–4.69 (dd, J=2.75, 10.90 Hz, 1H), 4.35–4.37 (dd, J=1.85, 7.90 Hz, 1H), 3.96–4.00 (dd, J=8.00, 10.90 Hz, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.69–3.72 (m, 1H), 3.30–3.33 (m, 1H), 2.87–2.92 (m, 1H), 2.78–2.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 34.40, 44.16, 53.54, 54.45, 56.36, 60.29, 68.92, 100.99, 110.38, 127.76, 128.11, 128.52, 128.79, 129.34, 130.32, 131.01, 135.94, 136.75, 148.79, 151.29, 155.92; MS (*m*/*z*): 531 (M^+); Anal. Calcd for $C_{23}H_{22}IN_3O_4$: C, 51.99; H, 4.17; N, 7.91. Found: C, 51.96; H, 4.15; N, 7.88.

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13. Crystal data for **5a**: $C_{16}H_{17}N_3O_4$, FW=315.32, monoclinic, space group *P*1 (No. 2), a=9.725 (6) Å, b=9.870 (5) Å, c=10.034 (4) Å, α=113.69 (2)°, β=103.18 (3)°, γ=99.22 (3)°, V=823.8 (8) Å^3; Z=2, D_c=1.449 g/cm^3, F_{000}=380.00, μ (Mo Kα)=1.07 cm^{-1}, Temperature=−180 °C. Data were collected on a Rigaku RAXIS-RAPID Imaging Plate diffractometer using $2\theta_{max}$=60.1° with graphite monochromated Mo Kα radiation (λ=0.71075 Å). Of 8700 reflections collected, 4627 reflections with $I>-3.00\sigma$ (I), $2\theta<60.07°$ were used in the solution. Structure refined to R=0.087, $R1$=0.046 and Rw=0.091., Crystal data for **5b**: $C_{17}H_{19}N_3O_4$, FW=329.35, orthorhombic, space group $P2_12_12_1$ (No. 19), a=7.9375 (5) Å, b=8.2717 (6) Å, c=23.9023 Å, V=1569.3 (2) Å^3, Z=4, D_c=1.394 g/cm^3, F_{000}=696.00, ((Mo Kα)=8.37 cm^{-1}, Temperature=23.0 °C. Data were collected on a Rigaku RAXIS-RAPID Imaging Plate diffractometer using $2\theta_{max}$=136.4° with graphite monochromated Mo Kα radiation (λ=1.54186 Å). Of 18088 reflections collected, 1676 reflections with $2\sigma>136.39°$ were used in the solution. Structure refined to R=0.064, $R1$=0.033 and Rw=0.077..
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