Electronic supplementary information (ESI)

Synthesis, anticancer evaluation and docking study of vadimezan derivatives with carboxyl substitution

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Experimental Section (with full characterization)

Chemistry

Melting points were taken on an X-4 apparatus and are uncorrected. Infrared spectra (IR) were obtained on a Thermo Nicolet Avatar 370 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a Brucker AVANCE III spectrometer operating at 500 MHz or a Brucker AC 400 spectrometer at 400 MHz. Mass spectra (MS) were run on an HP 5989B instrument at an ionizing voltage of 70 eV or a Waters GCT Premier with EI source. High resolution mass spectra (HRMS) were measured on Waters GCT Premier with EI mode or on Agilent 6210 TOF LC/MS instrument with ESI mode. Elemental analyses of C, H, N were performed on an Elementar Vario EL3 instrument. Optical rotations were determined in a 1.5 cm^3 cell with a path length of 1 dm using a Rudolph

autopol IV automatic polarimeter (Na_D line). All the chemicals and solvents were of analytical reagent and used as received.

2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)acetic acid (**6**)

Compound **6** was synthesized according to known method as white solid, total yield: 38.4% from 2,3-dimethylaniline; Mp: 256-259 °C (lit. 259-261 °C); P_{HPLC} 98.2%, t_R = 3.53 min, (CH_3CN : H_2O = 8 : 2, T_f = 1.0, λ = 240 nm); IR ν_{max} (KBr)/cm^{-1}: 2970, 1708, 1650, 1602, 1411, 1330, 1212, 768; ^1H NMR (DMSO-d_6, 500 MHz) δ: 12.60 (s, 1H, COOH), 8.07 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.89 (d, J = 8.0 Hz, 1H, Ar-H8), 7.78 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.40 (t, J = 7.5 Hz, 1H, Ar-H2), 7.24 (d, J = 8.5 Hz, 1H, Ar-H7), 3.95 (s, 2H, Ar-CH_2), 2.39 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Ar-CH_3); EI-MS m/z(%): 282 (M^+, 77), 238 (42), 237 (100), 236 (26), 223 (17), 209 (37), 195 (12), 165 (28).

CCDC 788450, triclinic, space group *P*-1 with a = 6.7854(19), b = 9.826(3), c = 10.532(3) Å, α = 71.435(7), β = 82.741(9), γ = 83.142(9)°, V = 658.0(3) $Å^3$, Z = 2, Dc = 1.425 g/cm^{-3}, the final R = 0.040 and wR = 0.094.

Methyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7a**)

Vadimezan **6** (141 mg, 0.5 mmol), methanol (32 mg, 1.0 mmol) and DPAT (32 mg, 0.1 mmol) in toluene (15 mL) were heated to reflux for 2 h. Evaporation of solvent under reduced pressure gave crude product, which was purified by recrystallization from ethanol to give **7a** as white solid, 146 mg (yield: 98.6%); Mp: 188-189 °C; IR ν_{max} (KBr)/cm^{-1}: 2952, 1736, 1651, 1601, 1414, 1333, 1226, 1173, 771; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.35 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 4.00 (s, 2H, Ar-CH_2), 3.74 (s, 3H, OCH_3), 2.46 (s, 3H, Ar-CH_3), 2.45 (s, 3H, Ar-CH_3); EI-MS m/z(%): 296 (M^+, 61), 238 (18), 237 (100), 236 (45), 209 (26), 165 (20).

Compounds **7b-7q** were prepared by using the same procedure for **7a**, with the corresponding alcohols.

Ethyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7b**)

White solid, 148 mg (yield: 95.4%); Mp: 171-173 °C; P_{HPLC} 95.3%, t_R = 7.19 min, (CH_3CN : H_2O = 8 : 2, T_f = 1.0, λ = 240 nm); IR ν_{max} (KBr)/cm^{-1}: 2979, 1731, 1650, 1602, 1412, 1330, 1223, 1181, 769; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.5 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.0 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.35 (t, J = 7.8 Hz, 1H, Ar-H2), 7.20 (d, J = 8.0 Hz, 1H, Ar-H7), 4.20 (q, J = 7.0 Hz, 2H, C$H_2$$CH_3$), 3.99 (s, 2H, Ar-$CH_2$), 2.46 (s, 6H, 2 × Ar-$CH_3$), 1.26 (t, J = 7.0 Hz, 3H, CH_3); EI-MS m/z(%): 310 (M^+, 66), 238 (27), 237 (100), 236 (25), 209 (24), 165 (18); Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85%; Found: C, 73.37; H, 5.91%.

Propyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7c**)

White solid, 160 mg (yield: 98.7%); Mp: 101-103 °C; IR ν_{max} (KBr)/cm^{-1}: 2968, 1734, 1645, 1602, 1412, 1334, 1230, 1176, 766; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.34 (t, J = 7.5 Hz, 1H, Ar-H2), 7.19 (d, J = 8.0 Hz, 1H, Ar-H7), 4.09 (t, J = 6.8 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.45 (s, 6H, 2 × Ar-CH_3), 1.63 (q, J = 7.2 Hz, 2H, $\underline{CH_2}CH_3$), 0.86 (t, J = 7.3 Hz, 3H, CH_3); EI-MS m/z(%): 324 (M^+, 98), 282 (51), 253 (22), 238 (54), 237 (100), 236 (23), 209 (30), 165 (23); Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21%; Found: C, 74.01; H, 6.21%.

Isopropyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7d**)

White solid, 119 mg (yield: 73.4%); Mp: 108-111 °C; IR ν_{max} (KBr)/cm^{-1}: 2979, 1722, 1651, 1601, 1412, 1330, 1224, 1176, 768; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.10 (d, J = 8.0 Hz, 1H, Ar-H8), 7.63 (dd, J_1 = 1.0 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.35 (t, J = 7.8 Hz, 1H, Ar-H2), 7.21 (d, J = 8.5 Hz, 1H, Ar-H7), 5.09-5.04 (m, 1H, OCH), 3.97 (s, 2H, Ar-CH_2), 2.47 (s, 3H, Ar-CH_3), 2.46 (s, 3H, Ar-

CH_3), 1.23 (s, 3H, CH_3), 1.22 (s, 3H, CH_3); EI-MS m/z(%): 324 (M^+, 68), 282 (79), 238 (44), 237 (100), 209 (29), 165 (23); Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21%; Found: C, 73.77; H, 6.24%.

Butyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7e**)

White solid, 162 mg (yield: 95.8%); Mp: 83-85 °C; IR ν_{max} (KBr)/cm^{-1}: 2956, 1734, 1650, 1603, 1411, 1333, 1230, 1175, 759; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.34 (t, J = 7.8 Hz, 1H, Ar-H2), 7.20 (d, J = 8.5 Hz, 1H, Ar-H7), 4.13 (t, J = 6.5 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.45 (s, 6H, 2 × Ar-CH_3), 1.61-1.55 (m, 2H, $\underline{CH_2}CH_2CH_3$), 1.31-1.26 (m, 2H, $\underline{CH_2}CH_3$), 0.84 (t, J = 7.3 Hz, 3H, CH_3); EI-MS m/z(%): 338 (M^+, 94), 283 (20), 282 (100), 238 (61), 237 (82), 209 (28), 165 (22); Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55%; Found: C, 74.72; H, 6.51%.

Pentyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7f**)

White solid, 142 mg (yield: 80.6%); Mp: 83-84 °C; IR ν_{max} (KBr)/cm^{-1}: 2953, 1731, 1655, 1601, 1409, 1330, 1224, 1177, 766; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.10 (d, J = 8.0 Hz, 1H, Ar-H8), 7.65 (dd, J_1 = 1.8 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.35 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 4.13 (t, J = 6.5 Hz, 2H, OCH_2), 4.00 (s, 2H, Ar-CH_2), 2.46 (s, 6H, 2 × Ar-CH_3), 1.61-1.58 (m, 2H, $OCH_2\underline{CH_2}$), 1.26-1.21 (m, 4H, $\underline{CH_2CH_2}CH_3$), 0.80 (t, J = 6.8 Hz, 3H, CH_3); EI-MS m/z(%): 352 (M^+, 33), 282 (60), 239 (18), 238 (100), 237 (52), 209 (22), 165 (17); Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86%; Found: C, 75.21; H, 7.01%.

Isopentyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7g**)

White solid, 154 mg (yield: 87.4%); Mp: 56-59 °C; IR ν_{max} (KBr)/cm^{-1}: 2958, 1732, 1653, 1603, 1411, 1332, 1224, 1171, 761; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 =

1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.34 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 4.15 (t, J = 6.8 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.45 (s, 6H, 2 × Ar-CH_3), 1.59-1.54 (m, 1H, CH), 1.50-1.46 (m, 2H, $\underline{CH_2}CH$), 0.82 (s, 3H, CH_3), 0.81 (s, 3H, CH_3); EI-MS m/z(%): 352 (M^+, 47), 283 (27), 282 (100), 238 (35), 237 (41), 209 (18), 165 (14); Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86%; Found: C, 75.04; H, 6.88%.

Heptyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7h**)

White solid, 167 mg (yield: 87.8%); Mp: 68-69 °C; IR ν_{max} (KBr)/cm^{-1}: 2949, 1716, 1650, 1597, 1411, 1333, 1230, 766; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.34 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 4.11 (t, J = 6.8 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.45 (s, 6H, 2 × Ar-CH_3), 1.59-1.56 (m, 2H, $OCH_2\underline{CH_2}$), 1.21-1.19 (m, 6H, $\underline{CH_2CH_2CH_2}CH_2CH_3$), 1.13-1.12 (m, 2H, $\underline{CH_2}CH_3$), 0.84 (t, J = 7.3 Hz, 3H, CH_3); EI-MS m/z(%): 380 (M^+, 25), 282 (16), 239 (18), 238 (100), 237 (27), 209 (11); EI-HRMS: M^+ 380.1972 for $C_{24}H_{28}O_4$ (Calcd 380.1988).

8-Methylnonyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7i**)

White wax-like solid, 184 mg (yield: 87.1%); Mp: low mp; IR ν_{max} (KBr)/cm^{-1}: 2957, 1739, 1658, 1603, 1414, 1332, 1228, 1171, 764; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (d, J = 8.0 Hz, 1H, Ar-H1), 8.00 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H8), 7.58 (d, J = 7.0 Hz, 1H, Ar-H3), 7.28 (t, J = 7.5 Hz, 1H, Ar-H2), 7.12 (d, J = 8.0 Hz, 1H, Ar-H7), 4.07 (t, J = 6.8 Hz, 2H, OCH_2), 3.92 (s, 2H, Ar-CH_2), 2.38 (s, 6H, 2 × Ar-CH_3), 1.62-1.02 (m, 13H, 6 × CH_2 + CH), 0.84 (d, J = 7.0 Hz, 6H, 2 × CH_3); EI-MS m/z(%): 422 (M^+, 7), 283 (21), 238 (63), 237 (22), 169 (100), 168 (91), 167 (55); EI-HRMS: M^+ 422.2462 for $C_{27}H_{34}O_4$ (Calcd 422.2457).

Octadecyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7j**)

White solid, 197 mg (yield: 73.7%); Mp: 57-59 °C; IR ν_{max} (KBr)/cm^{-1}: 2917, 2849, 1731, 1602, 1413, 1336, 1230, 1182, 760; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.34 (t, J = 7.5 Hz, 1H, Ar-H2), 7.20 (d, J = 8.5 Hz, 1H, Ar-H7), 4.11 (t, J = 6.8 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.45 (s, 6H, 2 × Ar-CH_3), 1.59-1.55 (m, 2H, $OCH_2\underline{CH_2}$), 1.35-1.14 (m, 30H, $\underline{(CH_2)_{15}}CH_3$), 0.88 (t, J = 6.8 Hz, 3H, CH_3); EI-MS m/z(%): 534 (M^+, 25), 283 (34), 238 (100), 237 (21), 225 (14); EI-HRMS: M^+ 534.3720 for $C_{35}H_{50}O_4$ (Calcd 534.3709).

Cyclohexyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7k**)

White solid, 165 mg (yield: 90.6%); Mp: 59-61 °C; IR ν_{max} (KBr)/cm^{-1}: 2938, 1728, 1655, 1601, 1412, 1331, 1224, 1172, 757; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.34 (t, J = 7.5 Hz, 1H, Ar-H2), 7.20 (d, J = 8.0 Hz, 1H, Ar-H7), 4.84-4.80 (m, 1H, OCH), 3.98 (s, 2H, Ar-CH_2), 2.46 (s, 3H, Ar-CH_3), 2.45 (s, 3H, Ar-CH_3), 1.82-1.78 (m, 2H, 2 × CH), 1.63-1.60 (m, 2H, 2 × CH), 1.40-1.29 (m, 4H, 4 × CH), 1.29-1.20 (m, 2H, 2 × CH); EI-MS m/z(%): 364 (M^+, 29), 283 (19), 282 (100), 238 (41), 237 (29), 223 (10), 209 (14), 165 (11); Anal. Calcd. for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64%; Found: C, 75.64; H, 6.68%.

Allyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7l**)

Light brown solid, 93 mg (yield: 57.7%); Mp: 125-128 °C; IR ν_{max} (KBr)/cm^{-1}: 3081, 2966, 1734, 1646, 1602, 1412, 1333, 1230, 1175, 761; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.65 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.35 (t, J = 7.8 Hz, 1H, Ar-H2), 7.20 (d, J = 8.5 Hz, 1H, Ar-H7), 5.89 (ddt, J_1 = 6.0 Hz, J_2 = 10.5 Hz, J_3 =17.0Hz, 1H, $\underline{CH}$=CH_2), 5.27 (dq, J_1

= 1.3 Hz, J_2 = 17.0 Hz, 1H, CH=C<u>H</u>H), 5.20 (dq, J_1 = 1.3 Hz, J_2 = 10.5 Hz, 1H, CH=CH<u>H</u>), 4.64 (dt, J_1 = 1.3 Hz, J_2 = 6.0 Hz, 2H, OCH_2), 4.03 (s, 2H, Ar-CH_2), 2.45 (s, 3H, Ar-CH_3), 2.44 (s, 3H, Ar-CH_3); EI-MS m/z(%): 322 (M^+, 72), 281 (68), 254 (18), 253 (100), 238 (18), 237 (93), 209 (42), 165 (31); Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63%; Found: C, 74.55; H, 5.62%.

Prop-2-ynyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7m**)

Light yellow solid, 78 mg (yield: 48.7%); Mp: 146-148 °C; IR ν_{max} (KBr)/cm^{-1}: 3223, 2950, 1739, 1647, 1602, 1412, 1332, 1154, 768; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.30 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.65 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.35 (t, J = 7.5 Hz, 1H, Ar-H2), 7.20 (d, J = 8.0 Hz, 1H, Ar-H7), 4.74 (d, J = 2.5 Hz, 2H, OCH_2), 4.05 (s, 2H, Ar-CH_2), 2.46 (s, 6H, 2 × Ar-CH_3), 2.44 (t, J = 2.5 Hz, 1H, CH); EI-MS m/z(%): 320 (M^+,100), 305 (23), 281 (17), 253 (63), 238 (20), 237 (99), 209 (44), 165 (31); Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%; Found: C, 74.81; H, 5.06%.

Benzyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7n**)

White solid, 152 mg (yield: 81.7%); Mp: 118-120 °C; IR ν_{max} (KBr)/cm^{-1}: 1735, 1652, 1604, 1411, 1333, 1172, 765; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.64 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.34 (t, J = 7.8 Hz, 1H, Ar-H2), 7.23-7.21 (m, 5H, Ar'), 7.19 (d, J = 8.5 Hz, 1H, Ar-H7), 5.15 (s, 2H, OCH_2), 4.03 (s, 2H, Ar-CH_2), 2.41 (s, 3H, Ar-CH_3), 2.26 (s, 3H, Ar-CH_3); EI-MS m/z(%): 372 (M^+, 56), 282 (24), 281 (100), 253 (54), 237 (100), 209 (36), 165 (26), 91 (28); Anal. Calcd. for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41%; Found: C, 77.37; H, 5.43%.

4-Chlorobenzyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7o**)

White solid, 54 mg (yield: 26.6%); Mp: 125-127 °C; IR ν_{max} (KBr)/cm^{-1}: 1742, 1648, 1604, 1412, 1330, 1169, 769; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.30 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.63 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.35 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 7.15-7.11 (m, 4H, Ar'), 5.09 (s, 2H, OCH_2), 4.02 (s, 2H, Ar-CH_2), 2.42 (s, 3H, Ar-CH_3), 2.19 (s, 3H, Ar-CH_3); EI-MS m/z(%): 406/408 (M^+, 29/11), 282 (24), 281 (100), 253 (39), 238 (16), 237 (71), 209 (22), 165 (16); EI-HRMS: M^+ 406.0981 for $C_{24}H_{19}{}^{35}ClO_4$ (Calcd 406.0972).

1-Phenylethyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7p**)

White solid, 192 mg (yield: 99.4%); Mp: 114-115 °C; IR ν_{max} (KBr)/cm^{-1}: 1727, 1654, 1600, 1327, 1229, 1149, 762; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.59 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.33 (t, J = 7.5 Hz, 1H, Ar-H2), 7.20 (d, J = 8.0 Hz, 1H, Ar-H7), 7.13-7.08 (m, 3H, Ar'),7.03-7.01 (m, 2H, Ar'), 4.36-4.33 (m, 1H, OCH), 3.97 (s, 2H, Ar-CH_2), 2.89-2.86 (m, 3H, CH$\underline{CH_3}$), 2.44 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Ar-CH_3); EI-MS m/z(%): 386 (M^+, 4), 283 (19), 282 (100), 238 (18), 237 (31), 209 (11), 165 (10); Anal. Calcd. for $C_{25}H_{22}O_4$: C, 77.70; H, 5.74%; Found: C, 77.67; H, 5.73%.

4-Phenylbutyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate (**7q**)

White solid, 163 mg (yield: 78.7%); Mp: 67-69 °C; IR ν_{max} (KBr)/cm^{-1}: 2949, 1732, 1650, 1601, 1411, 1332, 1175, 762; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.63 (dd, J_1 = 1.8 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.34 (t, J = 7.8 Hz, 1H, Ar-H2), 7.25 (t, J = 7.5 Hz, 1H, Ar-H4'), 7.20 (d, J = 8.0 Hz, 1H, Ar-H7), 7.17 (t, J = 7.3 Hz, 2H, Ar-H3' and Ar-H5'), 7.07 (d, J = 7.0 Hz, 2H, Ar-H2' and Ar-H6'), 4.14 (t, J = 6.3 Hz, 2H, OCH_2), 3.99 (s, 2H, Ar-CH_2), 2.54 (t, J = 7.3 Hz, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3), 1.65-1.56 (m, 4H, $OCH_2\underline{CH_2}\underline{CH_2}$); EI-MS m/z(%): 414 ($M^+$, 57), 283 (15), 282 (24), 239 (18), 238 (100),

237 (28), 209 (13), 91 (11); EI-HRMS: M^+ 414.1834 for $C_{27}H_{26}O_4$ (Calcd 414.1831).

2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)-*N*-propylacetamide (**8a**)

Vadimezan **6** (141 mg, 0.5 mmol), DCC (124 mg, 0.6 mmol), HOBt (81 mg, 0.6 mmol) and propan-1-amine (36 mg, 0.6 mmol) were heated to 60 °C in DMF (20 mL) for 24 h, and the mixture was cooled to room temperature overnight to precipitate DCU. After filtration, the filtrate was poured to ice-water to precipitate white solid. The crude product was collected by filtration and recrystallized from ethanol to afford compound **8a** as white solid, 105 mg (yield: 64.9%); Mp: 187-188 °C; P_{HPLC} 96.9%, t_R = 3.94 min, (CH_3CN : H_2O = 8 : 2, T_f = 1.0, λ = 240 nm); IR ν_{max} (KBr)/cm^{-1}: 3292, 2962, 1653, 1602, 1413, 1332, 1212, 763; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.31 (d, *J* = 8.0 Hz, 1H, Ar-H1), 8.10 (d, *J* = 8.0 Hz, 1H, Ar-H8), 7.69 (d, *J* = 6.0 Hz, 1H, Ar-H3), 7.38 (t, *J* = 7.0 Hz, 1H, Ar-H2), 7.23 (d, *J* = 8.0 Hz, 1H, Ar-H7), 5.53 (br, 1H, NH), 3.95 (s, 2H, Ar-CH_2), 3.23-3.19 (m, 2H, NH$\underline{CH_2}$), 2.47 (s, 6H, 2 × Ar-CH_3), 1.47-1.43 (m, 2H, $\underline{CH_2}CH_3$), 0.80 (t, *J* = 7.3 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 323 (M^+, 29), 239 (18), 238 (100), 237 (11), 223 (18), 209 (11), 195 (11), 165 (9); Anal. Calcd. for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33%; Found: C, 74.39; H, 6.61; N, 4.29%.

Compounds **8b**-**8p** were prepared by using the same procedure for **8a**, with the corresponding amines.

N-Butyl-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8b**)

White solid, 56 mg (yield: 33.2%); Mp: 201-204 °C; IR ν_{max} (KBr)/cm^{-1}: 3293, 2929, 1654, 1601, 1412, 1335, 1210, 761; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.31 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.11 (d, *J* = 8.0 Hz, 1H, Ar-H8), 7.68 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.39 (t, *J* = 7.5 Hz, 1H, Ar-H2), 7.24 (d, *J* = 8.0 Hz, 1H, Ar-H7), 5.47 (br, 1H, NH), 3.94 (s, 2H, Ar-CH_2), 3.26-3.22 (m, 2H, NH$\underline{CH_2}$), 2.48 (s, 6H, 2 × Ar-CH_3), 1.42-1.36 (m, 2H, $\underline{CH_2}CH_2CH_3$), 1.22-1.15 (m, 2H, $CH_2\underline{CH_2}CH_3$), 0.79 (t, *J* = 7.3 Hz, 3H,

$CH_2\underline{CH_3}$); EI-MS m/z(%): 337 (M^+, 29), 239 (18), 238 (100), 237 (12), 223 (14), 209 (10), 195 (9); Anal. Calcd. for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15%; Found: C, 74.82; H, 7.04; N, 4.12%.

2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)-*N*-heptylacetamide (**8c**)

White solid, 126 mg (yield: 66.4%); Mp: 211-214 °C; IR ν_{max} (KBr)/cm^{-1}: 3303, 2926, 1654, 1601, 1412, 1331, 1212, 761; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.30 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.5 Hz, 1H, Ar-H8), 7.67 (dd, J_1 = 1.0 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.37 (t, J = 7.5 Hz, 1H, Ar-H2), 7.22 (d, J = 8.5 Hz, 1H, Ar-H7), 5.47 (br, 1H, NH), 3.92 (s, 2H, Ar-CH_2), 3.24-3.20 (m, 2H, NH$\underline{CH_2}$), 2.46 (s, 6H, 2 × Ar-CH_3), 1.39-1.36 (m, 2H, NHCH$_2\underline{CH_2}$), 1.16-1.03 (m, 8H, $\underline{(CH_2)_4}CH_3$), 0.80 (t, J = 7.5 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 379 (M^+, 13), 239 (18), 238 (100), 237 (11), 223 (10), 209 (9), 195 (7); Anal. Calcd. for $C_{24}H_{29}NO_3$: C, 75.96; H, 7.70; N, 3.69%; Found: C, 75.76; H, 7.87; N, 3.61%.

N-Cyclohexyl-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8d**)

White solid, 89 mg (yield: 49.0%); Mp: 247-249 °C; IR ν_{max} (KBr)/cm^{-1}: 3292, 2930, 1662, 1636, 1415, 1330, 1212, 759; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.30 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.10 (d, J = 8.0 Hz, 1H, Ar-H8), 7.67 (dd, J_1 = 1.3 Hz, J_2 = 7.3 Hz, 1H, Ar-H3), 7.37 (t, J = 7.8 Hz, 1H, Ar-H2), 7.22 (d, J = 8.5 Hz, 1H, Ar-H7), 5.33-5.32 (d, J = 8.0 Hz, 1H, NH), 3.90 (s, 2H, Ar-CH_2), 3.82-3.76 (m, 1H, NH$\underline{CH}$), 2.47 (s, 6H, 2 × Ar-CH_3), 1.84-1.80 (m, 2H, 2 × CH), 1.63-1.54 (m, 4H, 4 × CH), 1.35-1.27 (m, 2H, 2 × CH), 1.09-0.94 (m, 2H, 2 × CH); EI-MS m/z(%): 363 (M^+, 18), 239 (18), 238 (100), 237 (11), 223 (10), 209 (9), 195 (7); Anal. Calcd. for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93; N, 3.85%; Found: C, 75.88; H, 6.97; N, 3.79%.

2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)-*N*-phenylacetamide (**8e**)

White solid, 143 mg (yield: 80.0%); Mp: 227-231 °C; P_{HPLC} 98.8%, t_R = 4.82 min, (CH_3CN : H_2O = 8 : 2, T_f = 1.0, λ = 240 nm); IR ν_{max} (KBr)/cm^{-1}: 3282, 1657, 1602, 1443, 1413, 1327, 765; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 10.42 (s, 1H, NH), 8.11 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.93 (d, J = 8.0 Hz, 1H, Ar-H8), 7.83 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 1H, Ar-H3), 7.62 (dd, J_1 = 1.0 Hz, J_2 = 8.5 Hz, 2H, Ar-H2' and Ar-H6'), 7.44 (t, J = 7.8 Hz, 1H, Ar-H2), 7.33-7.28 (m, 1H + 2H, Ar-H7 + Ar-H3' and Ar-H5'), 7.06 (t, J = 8.0 Hz, 1H, Ar-H4'), 4.13 (s, 2H, Ar-CH_2), 2.39 (s, 3H, Ar-CH_3), 2.35 (s, 3H, Ar-CH_3); EI-MS m/z(%): 357 (M^+, 43), 264 (21), 239 (18), 238 (100), 227 (28), 209 (28), 208 (16), 165 (26); Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92%; Found: C, 77.21; H, 5.44; N, 3.87%.

N-(3-Chlorophenyl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8f**)

White solid, 109 mg (yield: 55.7%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3280, 1655, 1595, 1414, 1334, 1229, 763; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.27 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.71 (d, J = 6.5 Hz, 1H, Ar-H3), 7.62 (s, 1H, Ar-H2'), 7.46 (br, 1H, NH), 7.36 (t, J = 7.8 Hz, 1H, Ar-H2), 7.29 (t, J = 7.5 Hz, 1H, Ar-H5'), 7.22-7.19 (m, 1H + 1H, Ar-H7 + Ar-H6'), 7.07 (d, J = 8.0 Hz, 1H, Ar-H4'), 4.07 (s, 2H, Ar-CH_2), 2.43 (s, 3H, Ar-CH_3), 2.41 (s, 3H, Ar-CH_3); EI-MS m/z(%): 391/393 (M^+, 45/14), 265 (21), 264 (98), 238 (100), 237 (71), 209 (40), 208 (23), 165 (30); Anal. Calcd. for $C_{23}H_{18}ClNO_3$: C, 70.50; H, 4.63; N, 3.57%; Found: C, 77.27; H, 5.54; N, 3.46%.

N-(4-Chlorophenyl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8g**)

White solid, 86 mg (yield: 43.9%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3275, 1655, 1597, 1492, 1399, 1334, 1230, 1091, 762; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.28 (dd, J_1 = 1.3 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.72 (d, J = 7.0 Hz, 1H, Ar-H3), 7.43-7.36 (m, 1H + 2H, Ar-H2 + Ar-H2' and Ar-H6'), 7.26-7.24 (m, 2H, Ar-H3'

and Ar-H5'), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 4.07 (s, 2H, Ar-CH_2), 2.43 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3); EI-MS m/z(%): 391/393 (M^+, 48/16), 265 (25), 264 (86), 238 (100), 237 (89), 209 (51), 208 (33), 194 (19); Anal. Calcd. for $C_{23}H_{18}ClNO_3$: C, 70.50; H, 4.63; N, 3.57%; Found: C, 70.43; H, 4.63; N, 3.59%.

N-(3,4-dichlorophenyl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8h**)

Pale white solid, 125 mg (yield: 58.6%); Mp: 216-220 °C; IR ν_{max} (KBr)/cm^{-1}: 3322, 3232, 2928, 1652, 1601, 1477, 1412, 1384, 1332, 1229, 764; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.28 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.4 Hz, 1H, Ar-H8), 7.76 (s, 1H, Ar'), 7.64 (d, J = 6.8 Hz, 1H, Ar-H3), 7.39-7.32 (m*, 1H + 2H + 1H, Ar-H2 + Ar' + NH), 7.20 (d, J = 8.4 Hz, 1H, Ar-H7), 4.00 (s, 2H, Ar-CH_2), 2.45 (s, 3H, Ar-CH_3), 2.44 (s, 3H, Ar-CH_3) *overlap; EI-MS m/z(%): 425 (M^+, 16), 282 (48), 264 (65), 251 (28), 237 (100), 223 (9), 209 (18), 165 (34); Anal. Calcd. for $C_{23}H_{17}Cl_2NO_3$: C, 64.80; H, 4.02; N, 3.29%; Found: C, 64.92; H, 3.59; N, 3.35%.

N-(3-Chloro-4-fluorophenyl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8i**)

White solid, 81 mg (yield: 39.6%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3244, 1655, 1603, 1501, 1384, 1230, 765; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.26 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.71-7.67 (m, 1H + 1H, Ar-H3 + Ar'), 7.44 (br, 1H, NH), 7.37 (t, J = 7.5 Hz, 1H, Ar-H2), 7.28-7.25 (m, 1H, Ar'), 7.21 (d, J = 8.0 Hz, 1H, Ar-H7), 7.05 (t, J = 8.8 Hz, 1H, Ar'), 4.07 (s, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.41 (s, 3H, Ar-CH_3); EI-MS m/z(%): 409/411 (M^+, 35/11), 265 (27), 264 (100), 238 (59), 237 (75), 209 (37), 208 (27), 165 (29); Anal. Calcd. for $C_{23}H_{17}ClFNO_3$: C, 67.40; H, 4.18; N, 3.42%; Found: C, 67.16; H, 4.14; N, 3.36%.

2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)-*N*-(4-nitro-3-(trifluoromethyl)phenyl)acetamide (**8j**)

Yellow solid, 68 mg (yield: 28.9%); Mp: 110-113 °C; IR ν_{max} (KBr)/cm^{-1}: 3483, 3373, 2928, 1626, 1609, 1492, 1329, 1262, 1149, 1039; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.28 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (s, 1H, Ar'), 8.07 (d*, J = 8.0 Hz, 1H + 1H, Ar-H8 + NH), 8.04-8.03 (m, 2H, Ar'), 7.66 (d, J = 6.4 Hz, 1H, Ar-H3), 7.35 (t, J = 7.8 Hz, 1H, Ar-H2), 7.19 (d, J = 8.4 Hz, 1H, Ar-H7), 4.03 (s, 2H, Ar-CH_2), 2.43 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3) *overlap; EI-MS m/z(%): 470 (M^+, 10), 440 (3), 367 (7), 282 (51), 264 (13), 237 (100), 208 (11), 165 (20); EI-HRMS: M^+ 470.1103 for $C_{24}H_{17}F_3N_2O_5$ (Calcd 470.1090).

N-(5-chloropyridin-2-yl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8k**)

Pale white solid, 60 mg (yield: 34.7%); Mp: 179-182 °C; IR ν_{max} (KBr)/cm^{-1}: 3254, 2927, 1654, 1601, 1493, 1413, 1333, 1228, 763; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.27 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.23 (d, J = 8.8 Hz, 1H, Ar'), 8.12 (d, J = 2.0 Hz, 1H, Ar'), 8.02 (d, J = 8.4 Hz, 1H, Ar-H8), 7.81 (br, 1H, NH), 7.68-7.64 (m*, 1H + 1H, Ar-H3 + Ar'), 7.33 (t, J = 7.6 Hz, 1H, Ar-H2), 7.13 (d, J = 8.4 Hz, 1H, Ar-H7), 4.03 (s, 2H, Ar-CH_2), 2.43 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3) *overlap; EI-MS m/z(%): 392 (M^+, 3), 309 (3), 296 (20), 282 (60), 264 (12), 237 (100), 209 (15), 165 (26); EI-HRMS: M^+ 392.0926 for $C_{22}H_{17}{}^{35}ClN_2O_3$ (Calcd 392.0928).

N-(5-bromopyridin-2-yl)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamide (**8l**)

Light brown solid, 36 mg (yield: 16.5%); Mp: 172-175 °C; IR ν_{max} (KBr)/cm^{-1}: 3324, 2927, 1654, 1601, 1493, 1412, 1332, 1228, 763; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.25 (d, J = 2.0 Hz, 1H, Ar'), 8.22 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.18 (d, J = 8.8 Hz, 1H, Ar'), 8.00 (d, J = 8.0 Hz, 1H, Ar-H8), 7.82 (br, 1H, NH), 7.77 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H, Ar'), 7.64 (d, J = 6.4 Hz, 1H, Ar-H3), 7.30 (t, J = 7.6 Hz, 1H, Ar-H2), 7.11 (d, J = 8.0 Hz, 1H, Ar-H7), 4.00 (s, 2H, Ar-CH_2), 2.41 (s, 3H, Ar-CH_3), 2.40 (s, 3H, Ar-CH_3); EI-MS m/z(%): 436/438 (M^+, 2/2), 296 (13), 282 (3), 264 (4), 237 (29), 224 (6), 209 (3),

165 (5); EI-HRMS: M^+ 436.0429 for $C_{22}H_{17}{}^{79}BrN_2O_3$ (Calcd 436.0423).

N-(4-Hydroxy-3-methoxybenzyl)-2-(5,6-dimethyl-9-oxo-9H-xanthen-4-yl)acetamide (**8m**)

White solid, 109 mg (yield: 52.0%); Mp: 244-247 °C; IR ν_{max} (KBr)/cm^{-1}: 3507, 3283, 2925, 1653, 1631, 1601, 1515, 1276, 1209, 763; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.31 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.10 (d, J = 8.5 Hz, 1H, Ar-H8), 7.69 (d, J = 6.5 Hz, 1H, Ar-H3), 7.38 (t, J = 7.5 Hz, 1H, Ar-H2), 7.23 (d, J = 8.0 Hz, 1H, Ar-H7), 6.68 (d, J = 8.5 Hz, 1H, Ar'), 6.61 (d, J = 7.5 Hz, 1H, Ar'), 6.58 (s, 1H, Ar'), 5.77 (br, 1H, OH), 5.49 (s, 1H, NH), 4.33 (d, J = 6.0 Hz, 2H, $\underline{CH_2}$NH), 3.97 (s, 2H, Ar-CH_2), 3.62 (s, 3H, OCH_3), 2.44 (s, 3H, Ar-CH_3), 2.31 (s, 3H, Ar-CH_3); EI-MS m/z(%): 417 (M^+, 57), 281 (20), 238 (97), 209 (14), 165 (19), 152 (17), 137 (100), 122 (19); EI-HRMS: M^+ 417.1568 for $C_{25}H_{23}NO_5$ (Calcd 417.1576).

Ethyl 2-(2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamido)acetate (**8j**)

White solid, 177 mg (yield: 96.5%); Mp: 132-134 °C; IR ν_{max} (KBr)/cm^{-1}: 3297, 2928, 1750, 1654, 1601, 1412, 1213, 763; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.15 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.98 (d, J = 8.0 Hz, 1H, Ar-H8), 7.67 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.28 (t, J = 7.5 Hz, 1H, Ar-H2), 7.14 (d, J = 8.5 Hz, 1H, Ar-H7), 6.49 (br, 1H, NH), 4.15 (q, J = 7.0 Hz, 2H, O$\underline{CH_2}CH_3$), 4.04 (d, J = 6.0 Hz, 2H, NH$\underline{CH_2}$), 3.94 (s, 2H, Ar-CH_2), 2.40 (s, 3H, Ar-CH_3), 2.38 (s, 3H, Ar-CH_3), 1.22 (t, J = 7.0 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 367 (M^+, 35), 296 (11), 264 (29), 238 (94), 224 (35), 209 (7), 195 (6), 165 (14); EI-HRMS: M^+ 367.1416 for $C_{21}H_{21}NO_5$ (Calcd 367.1420).

Ethyl 3-(2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamido)propanoate (**8k**)

White solid, 176 mg (yield: 92.4%); Mp: 120-123 °C; IR ν_{max} (KBr)/cm^{-1}: 3290, 2927, 1727, 1662, 1640, 1414, 1213, 766; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.30 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.08 (d, J = 8.0 Hz, 1H, Ar-H8), 7.65 (dd, J_1 = 1.5 Hz, J_2 = 7.5

Hz, 1H, Ar-H3), 7.36 (t, J = 7.5 Hz, 1H, Ar-H2), 7.21 (d, J = 8.5 Hz, 1H, Ar-H7), 6.16 (br, 1H, NH), 3.90 (s, 2H, Ar-CH_2), 3.82 (q, J = 7.2 Hz, 2H, O$\underline{CH_2}CH_3$), 3.52-3.45 (m, 2H, NH$\underline{CH_2}$), 2.453 (s*, 6H, 2 × Ar-CH_3), 2.449 (t*, J = 6.8 Hz, 2H, NHCH$_2\underline{CH_2}$), 1.07 (t, J = 7.3 Hz, 3H, $CH_2\underline{CH_3}$) *overlap; EI-MS m/z(%): 381 (M^+, 28), 367 (4), 336 (5), 264 (10), 238 (100), 223 (5), 209 (5), 195 (4); EI-HRMS: M^+ 381.1566 for $C_{22}H_{23}NO_5$ (Calcd 381.1576).

Ethyl 4-(2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetamido)benzoate (**8l**)

White solid, 170 mg (yield: 79.3%); Mp: 271-273 °C; IR ν_{max} (KBr)/cm^{-1}: 3238, 1716, 1668, 1654, 1596, 1530, 1406, 1268, 1175, 1099, 763; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.29 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.09 (d, J = 8.0 Hz, 1H, Ar-H8), 7.99 (d, J = 8.5 Hz, 2H, Ar'), 7.73 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H, Ar-H3), 7.63 (br, 1H, NH), 7.57 (d, J = 8.5 Hz, 2H, Ar'), 7.39 (t, J = 7.8 Hz, 1H, Ar-H2), 7.22 (d, J = 7.5 Hz, 1H, Ar-H7), 4.36 (q, J = 7.0 Hz, 2H, O$\underline{CH_2}CH_3$), 4.11 (s, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3), 1.38 (t, J = 6.8 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 429 (M^+, 86), 384 (15), 264 (57), 238 (100), 209 (12), 192 (11), 165 (52), 120 (21); ESI-MS: 430.2 $[M+H]^+$, 452.2 $[M+Na]^+$; EI-HRMS: M^+ 429.1561 for $C_{26}H_{23}NO_5$ (Calcd 429.1576).

2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**9**)

A mixture of ethyl 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetate **7b** (155 mg, 0.5 mmol), ethanol (10 mL) and 85% hydrazine hydrate (2.3 mL) was refluxed for 24 h, and more hydrazine hydrate was added if necessary to reach completion. The mixture was cooled and filtrated to give compound **9** as white solid, 140 mg (yield: 94.6%); Mp: 239-241 °C; IR ν_{max} (KBr)/cm^{-1}: 3290, 3063, 2915, 1654, 1639, 1618, 1602, 1413, 1332, 1228, 758; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 9.34 (s, 1H, $\underline{NH}NH_2$), 8.08 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.93 (d, J = 8.0 Hz, 1H, Ar-H8), 7.77 (d, J = 6.5 Hz, 1H, Ar-H3), 7.41 (t, J = 7.5 Hz, 1H, Ar-H2), 7.31 (d, J = 8.0 Hz, 1H, Ar-H7), 4.27 (s, 2H, NH$\underline{NH_2}$),

3.82 (s, 2H, Ar-CH_2), 2.450 (s, 3H, Ar-CH_3), 2.446 (s, 3H, Ar-CH_3); EI-MS m/z(%): 296 (M^+, 53), 265 (72), 237 (100), 209 (10), 194 (6), 178 (6), 165 (17), 152 (4); Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45%; Found: C, 68.83; H, 5.38; N, 9.61%.

N′-(2-Hydroxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10a**)

A mixture of 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide **9** (44 mg, 0.15 mmol) and 2-hydroxybenzaldehyde (20 mg, 0.165 mmol) in ethanol (20 mL) was heated at reflux for 6 h. The reaction mixture was cooled and the precipitated solid was filtered, dried and recrystallized from ethanol to give compound **10a** as white solid, 59 mg (yield: 99.2%); Mp: 247-249°C; IR ν_{max} (KBr)/cm^{-1}: 3247, 3031, 1688, 1639, 1620, 1490, 1414, 1273, 1226, 752; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 12.03 and 11.54 (both s, total 1H, NH), 11.10 and 10.12 (both s, total 1H, OH), 8.47 and 8.37 (both s, total 1H, N=CH), 8.11 and 8.09 (both d, J = 8.8 Hz, total 1H, Ar-H1), 7.93 (d, J = 8.0 Hz, 1H, Ar-H8), 7.84 and 7.83 (both d, J = 6.5 Hz, total 1H, Ar-H3), 7.69 and 7.54 (both d, J = 7.6 Hz, total 1H, Ar'), 7.45 and 7.43 (both t, J = 7.6 Hz, total 1H, Ar-H2), 7.30-7.23 (m*, 1H + 1H, Ar-H7 + Ar'), 6.91 and 6.77 (both t, J = 7.5 Hz, total 2H, Ar'), 4.40 and 4.03 (both s, total 2H, Ar-CH_2), 2.44, 2.40, 2.39 and 2.33 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 400 (M^+, 28), 296 (11), 281 (9), 265 (30), 238 (100), 209 (15), 194 (9), 165 (28); Anal. Calcd. for $C_{24}H_{20}N_2O_4$: C, 71.99; H, 5.03; N, 7.00%; Found: C, 71.86; H, 4.97; N, 7.11%.

Compounds **10b**-**10k** were prepared by using the same procedure for **10a**, with the corresponding aldehydes.

N′-(4-Hydroxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10b**)

Light brown solid, 31 mg (yield: 52.1%); Mp: 259-262°C; IR ν_{max} (KBr)/cm^{-1}: 3360, 2964, 1676, 1638, 1604, 1496, 1413, 1228, 762; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.59 and 11.38 (both s, total 1H, NH), 9.90 and 9.87 (both s, total 1H, OH), 8.16 and 7.97 (both s, total 1H, N=CH), 8.10 and 8.08 (both dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, total 1H, Ar-

H1), 7.94 (d, J = 8.0 Hz, 1H, Ar-H8), 7.82 (d, J = 7.2 Hz, 1H, Ar-H3), 7.53 and 7.52 (both d, J = 8.4 Hz, total 2H, Ar'), 7.43 and 7.42 (both t, J = 7.6 Hz, total 1H, Ar-H2), 7.30 (d, J = 8.0 Hz, 1H, Ar-H7), 6.82 and 6.77 (both d, J = 8.8 Hz, total 2H, Ar'), 4.39 and 3.98 (both s, total 2H, Ar-CH_2), 2.44, 2.41, 2.40 and 2.33 (all s, total 6H, 2 × Ar-CH_3); EI-MS m/z(%): 400 (M^+, 26), 281 (14), 265 (21), 237 (100), 209 (15), 194 (9), 165 (30), 136 (25); EI-HRMS: M^+ 400.1425 for $C_{24}H_{20}N_2O_4$ (Calcd 400.1423).

N′-(3-Methoxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10c**)

Light yellow solid, 50 mg (yield: 81.2%); Mp: 240-241 °C; IR ν_{max} (KBr)/cm^{-1}: 3182, 3077, 2966, 1667, 1599, 1409, 1269, 764; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.81 and 11.62 (both s, total 1H, NH), 8.25 and 8.05 (both s, total 1H, N=CH), 8.10 and 8.09 (both dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, total 1H, Ar-H1), 7.93 (d, J = 8.0 Hz, 1H, Ar-H8), 7.84 (d, J = 6.8 Hz, 1H, Ar-H3), 7.44 and 7.43 (both t, J = 7.2 Hz, total 1H, Ar-H2), 7.38-7.26 (m*, 1H + 3H, Ar-H7 + Ar'), 7.01-6.97 (m, 1H, Ar'), 4.44 and 4.02 (both s, total 2H, Ar-CH_2), 3.79 and 3.77 (both s, total 3H, CH_3O), 2.41, 2.40 and 2.33 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 414 (M^+, 36), 281 (28), 265 (29), 237 (100), 209 (11), 194 (6), 165 (16), 150 (14); Anal. Calcd. for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76%; Found: C, 72.56; H, 5.27; N, 6.81%.

N′-(4-Methoxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10d**)

White solid, 53 mg (yield: 86.1%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3075, 2968, 1669, 1648, 1384, 1246, 1173, 764; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.21 and 8.02 (both s, total 1H, N=CH), 8.11 and 8.09 (both dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, total 1H, Ar-H1), 7.94 (d, J = 8.4 Hz, 1H, Ar-H8), 7.83 (d, J = 8.0 Hz, 1H, Ar-H3), 7.65 and 7.64 (both d, J = 8.8 Hz, total 2H, Ar'), 7.44 and 7.43 (both t, J = 7.6 Hz, total 1H, Ar-H2), 7.31 (d, J = 8.8 Hz, 1H, Ar-H7), 7.01-6.94 (both d, J = 8.8 Hz, total 2H, Ar'), 4.42 and 4.00 (both s, total 2H, Ar-CH_2), 3.80 and 3.79 (both s, total 3H, CH_3O), 2.41, 2.40 and

2.34 (all s, total 6H, 2 × Ar-CH_3); EI-MS m/z(%): 414 (M^+, 26), 281 (21), 264 (18), 237 (100), 209 (13), 165 (25), 150 (50), 134 (19); Anal. Calcd. for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76%; Found: C, 72.27; H, 5.46; N, 6.82%.

N′-(5-Chloro-2-hydroxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10e**)

Light yellow solid, 51 mg (yield: 79.0%); Mp: 257-260 °C; IR ν_{max} (KBr)/cm^{-1}: 3188, 2959, 1673, 1630, 1410, 1341, 1230, 763; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 12.12 and 11.62 (both s, total 1H, NH), 11.14 and 10.42 (both s, total 1H, OH), 8.44 and 8.31 (both s, total 1H, N=CH), 8.10 and 8.08 (both dd, J_1 = 2.0 Hz, J_2 = 8.2 Hz, total 1H, Ar-H1), 7.92 and 7.91 (both d, J = 8.0 Hz, total 1H, Ar-H8), 7.83 and 7.81 (both d, J = 6.8 Hz, total 1H, Ar-H3), 7.69 and 7.64 (both d, J = 2.6 Hz, total 1H, Ar'), 7.44 and 7.42 (both t, J = 8.0 Hz, total 1H, Ar-H2), 7.31-7.23 (m*, 1H + 1H, Ar-H7 + Ar'), 6.93-6.90 (m, 1H, Ar'), 4.40 and 4.02 (both s, total 2H, Ar-CH_2), 2.39, 2.38, 2.36 and 2.31 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 434/436 (M^+, 14/5), 368 (20), 296 (28), 265 (51), 237 (100), 209 (13), 194 (10), 165 (21); Anal. Calcd. for $C_{24}H_{19}ClN_2O_4$: C, 66.29; H, 4.40; N, 6.44%; Found: C, 66.23; H, 4.36; N, 6.41%.

N′-(3,4,5-Trimethoxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10f**)

White solid, 66 mg (yield: 93.7%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3199, 3014, 2941, 1660, 1577, 1416, 1329, 1234, 1129, 762; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.20 and 8.00 (both s, total 1H, N=CH), 8.12 and 8.10 (both d, J = 8.0 Hz, total 1H, Ar-H1), 7.94 (d, J = 8.4 Hz, 1H, Ar-H8), 7.85 and 7.83 (both d, J = 6.8 Hz, total 1H, Ar-H3), 7.45 and 7.44 (both t, J = 8.0 Hz, total 1H, Ar-H2), 7.31 (d, J = 8.4 Hz, 1H, Ar-H7), 7.03 and 7.02 (both s, total 2H, Ar'), 4.45 and 4.02 (both s, total 2H, Ar-CH_2), 3.81, 3.79 and 3.69 (all s, total 9H, 3 × OCH_3), 2.42, 2.41, 2.34 and 2.33 (all s, total 6H, 2 × Ar-CH_3); EI-MS

m/z(%): 474 (M^+, 89), 368 (32), 265 (17), 237 (100), 209 (26), 193 (92), 178 (29), 165 (24); Anal. Calcd. for $C_{27}H_{26}N_2O_6$: C, 68.34; H, 5.52; N, 5.90%; Found: C, 68.56; H, 5.47; N, 6.11%.

N′-(3,4-Dihydroxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10g**)

Light yellow solid, 43 mg (yield: 69.5%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3480, 3246, 2965, 1666, 1601, 1444, 1284, 762; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.56 and 11.34 (both s, total 1H, NH), 9.41, 9.38, 9.26 and 9.19 (all s, total 2H, 2 × OH), 8.11-8.06 (m*, total 1H, Ar-H1), 8.08 and 7.91 (both s, total 1H, N=CH), 7.91 (d, J = 8.0 Hz, 1H, Ar-H8), 7.83 and 7.81 (both d, J = 7.2 Hz, total 1H, Ar-H3), 7.43 and 7.42 (both t, J = 7.6 Hz, total 1H, Ar-H2), 7.27 (d, J = 7.6 Hz, 1H, Ar-H7), 7.22 and 7.20 (both d, J = 2.0 Hz, total 1H, Ar'), 6.94 and 6.92 (both dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, total 1H, Ar'), 6.78 and 6.76 (both d, J = 8.0 Hz, 1H, Ar'), 4.38 and 3.96 (both s, total 2H, Ar-CH_2), 2.39, 2.38 and 2.30 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 416 (M^+, 16), 368 (5), 282 (8), 265 (20), 237 (60), 209 (10), 165 (19), 152 (18); EI-HRMS: M^+ 416.1384 for $C_{24}H_{20}N_2O_5$ (Calcd 416.1372).

N′-(4-Hydroxy-3-methoxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10h**)

White solid, 49 mg (yield: 76.7%); Mp: 230-232 °C; IR ν_{max} (KBr)/cm^{-1}: 3440, 3041, 1650, 1601, 1512, 1413, 1384, 1273, 763; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.63 and 11.40 (both s, total 1H, NH), 9.52 and 9.49 (both s, total 1H, OH), 8.15 and 7.96 (both s, total 1H, N=CH), 8.09 and 8.08 (both dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, total 1H, Ar-H1), 7.92 and 7.91 (both d, J = 8.0 Hz, total 1H, Ar-H8), 7.82 and 7.81 (both dd, J_1 = 2.0 Hz, J_2 = 6.8 Hz, total 1H, Ar-H3), 7.43 and 7.42 (both t, J = 7.6 Hz, total 1H, Ar-H2), 7.29-7.26 (m*, 1H + 1H, Ar-H7 + Ar'), 7.10 and 7.08 (both dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, total 1H,

Ar'), 6.83 and 6.80 (both d, J = 8.4 Hz, total 1H, Ar'), 4.40 and 3.97 (both s, total 2H, Ar-CH_2), 3.79 and 3.78 (both s, total 3H, OCH_3), 2.39, 2.38 and 2.31 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 430 (M^+, 35), 282 (17), 265 (13), 237 (100), 209 (14), 194 (9), 165 (43), 149 (22); Anal. Calcd. for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51%; Found: C, 69.91; H, 5.19; N, 6.58%.

N′-(4-Hydroxy-3-methoxy-2-nitrobenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10i**)

Light yellow solid, 68 mg (yield: 96.3%); Mp: > 260 °C; IR ν_{max} (KBr)/cm^{-1}: 3184, 2949, 1684, 1634, 1603, 1528, 1307, 1229, 756; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.62 and 10.98 (both s, total 1H, NH), 9.73 (s, 1H, OH), 8.13 and 7.91 (both s, total 1H, N=CH), 8.10 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H, Ar-H1), 7.94 (d, J = 8.4 Hz, 1H, Ar-H8), 7.80 (d, J = 7.2 Hz, total 1H, Ar-H3), 7.45-7.38 (m*, 1H + 1H, Ar-H2 + Ar'), 7.31 (d, J = 8.0 Hz, 1H, Ar-H7), 7.10 (d, J = 9.2 Hz, 1H, Ar'), 4.24 and 3.98 (both s, total 2H, Ar-CH_2), 3.85 and 3.83 (both s, total 3H, OCH_3), 2.45, 2.41, 2.33 and 2.31 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 475 (M^+, 12), 281 (4), 265 (19), 237 (100), 209 (11), 194 (7), 178 (6), 165 (21); Anal. Calcd. for $C_{25}H_{21}N_3O_7$: C, 63.15; H, 4.45; N, 8.84%; Found: C, 63.32; H, 4.46; N, 8.62%.

N′-(3-Hydroxy-4-methoxybenzylidene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10j**)

Light yellow solid, 37 mg (yield: 57.9%); Mp: 259-262 °C; IR ν_{max} (KBr)/cm^{-1}: 3289, 3080, 2952, 1673, 1644, 1602, 1412, 1276, 1213, 764; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.62 and 11.42 (both s, total 1H, NH), 9.26 and 9.21 (both s, total 1H, OH), 8.12 and 7.95 (both s, total 1H, N=CH), 8.08 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.91 (d, J = 8.0 Hz, 1H, Ar-H8), 7.83 and 7.81 (both d, J = 7.6 Hz, total 1H, Ar-H3), 7.43 and 7.42 (both t, J = 8.0 Hz, total 1H, Ar-H2), 7.27-7.22 (m*, 1H + 1H, Ar-H7 + Ar'), 7.06 and

7.04 (both dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, total 1H, Ar'), 6.96 and 6.94 (both d, J = 8.0 Hz, total 1H, Ar'), 4.40 and 3.97 (both s, total 2H, Ar-CH_2), 3.81 and 3.80 (both s, total 3H, OCH_3), 2.42, 2.39, 2.37 and 2.30 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 430 (M^+, 31), 282 (23), 265 (15), 237 (100), 209 (13), 194 (8), 165 (41), 149 (20); EI-HRMS: M^+ 430.1541 for $C_{25}H_{22}N_2O_5$ (Calcd 430.1529).

N'-(Benzo[*d*][1,3]dioxol-5-ylmethylene)-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**10k**)

White solid, 58 mg (yield: 91.2%); Mp: 250-253 °C; IR ν_{max} (KBr)/cm^{-1}: 3204, 3040, 2908, 1670, 1654, 1451, 1260, 1036, 760; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.71 and 11.48 (both s, total 1H, NH), 8.18 and 7.98 (both s, total 1H, N=CH), 8.10 and 8.08 (both d, J = 8.0 Hz, total 1H, Ar-H1), 7.92 (d, J = 8.4 Hz, 1H, Ar-H8), 7.82 (d, J = 6.8 Hz, 1H, Ar-H3), 7.44 and 7.42 (both t, J = 7.2 Hz, total 1H, Ar-H2), 7.33-7.26 (m*, 1H + 1H, Ar-H7 + Ar'), 7.15 and 7.13 (both d, J = 8.0 Hz, total 1H, Ar'), 6.98 and 6.94 (both d, J = 8.0 Hz, total 1H, Ar'), 6.07 and 6.06 (both s, total 2H, OCH_2O), 4.40 and 3.98 (both s, total 2H, Ar-CH_2), 2.40, 2.38 and 2.31 (all s, total 6H, 2 × Ar-CH_3) *overlap; EI-MS m/z(%): 428 (M^+, 55), 281 (17), 264 (20), 237 (100), 209 (11), 194 (6), 164 (42), 147 (17); Anal. Calcd. for $C_{25}H_{20}N_2O_5$: C, 70.08; H, 4.71; N, 6.54%; Found: C, 69.87; H, 4.66; N, 6.62%.

(*E*)-*N'*-Pent-3-enoyl-*N*-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**11a**)

Hydrazide **9** (44.4 mg, 0.15 mmol), DCC (37.1 mg, 0.18 mmol), HOBt (24.3 mg, 0.18 mmol) and (*E*)-pent-3-enoic acid (15.0 mg, 0.15 mmol) were heated to 50 °C in DMF (15 mL) for 12 h, and the mixture was cooled in refrigerator overnight to precipitate DCU. After filtration, the filtrate was poured to ice-water to precipitate white solid. The crude product was collected by filtration and recrystallized from ethanol to afford compound **11a** as pale white solid, 55.8 mg (yield: 98.4%); Mp: 187-190 °C; IR ν_{max} (KBr)/cm^{-1}: 3327, 2928, 2851, 1627, 1602, 1576, 763; ^{1}H NMR (DMSO-d_6, 400

MHz) δ: 10.17 (d, J = 1.6 Hz, 1H, NH), 9.86 (d, J = 1.6 Hz, 1H, NH), 8.08 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.92 (d, J = 8.4 Hz, 1H, Ar-H8), 7.83 (d, J = 7.0 Hz, 1H, Ar-H3), 7.42 (t, J = 7.6 Hz, 1H, Ar-H2), 7.30 (d, J = 8.4 Hz, 1H, Ar-H7), 5.58-5.43 (m, 2H, CH=CH), 3.92 (s, 2H, Ar-CH_2), 2.83 (d, J = 6.0 Hz, 2H, $COCH_2$), 2.46 (s, 3H, Ar-CH_3), 2.44 (s, 3H, Ar-CH_3), 1.60 (d, J = 6.0 Hz, 3H, CH_3); EI-MS m/z(%): 378 (M^+, 65), 323 (11), 296 (49), 265 (100), 237 (100), 209 (20), 194 (11), 165 (31); EI-HRMS: M^+ 378.1587 for $C_{22}H_{22}N_2O_4$ (Calcd 378.1580).

Compounds **11b**-**11e** were prepared by using the same procedure for **11a**, with the corresponding acids.

N′-4-Methylpent-3-enoyl-*N*-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**11b**)

Pale white solid, 40.3 mg (yield: 68.5%); Mp: 202-205 °C; IR ν_{max} (KBr)/cm^{-1}: 3327, 2928, 2851, 1628, 1602, 1575, 1413, 1228, 763; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.28 (br, 1H, NH), 10.00 (br, 1H, NH), 8.05 (d, J = 7.6 Hz, 1H, Ar-H1), 7.88 (d, J = 8.0 Hz, 1H, Ar-H8), 7.81 (d, J = 7.2 Hz, 1H, Ar-H3), 7.38 (t, J = 7.4 Hz, 1H, Ar-H2), 7.24 (d, J = 8.0 Hz, 1H, Ar-H7), 6.81-6.68 (m, 2H, CH=C), 3.91 (s, 2H, Ar-CH_2), 3.31 (brs*, 2H, $COCH_2$), 2.42 (s, 3H, Ar-CH_3), 2.39 (s, 3H, Ar-CH_3), 1.70 (s, 3H, CH_3), 1.59 (s, 3H, CH_3) *overlapped with water residue; EI-MS m/z(%): 392 (M^+, 9), 320 (18), 296 (24), 265 (63), 237 (100), 209 (14), 194 (10), 165 (29); EI-HRMS: M^+ 392.1733 for $C_{23}H_{24}N_2O_4$ (Calcd 392.1736).

N′-Hexanoyl-*N*-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**11c**)

Pale white solid, 46.5 mg (yield: 78.7%); Mp: 226-228 °C; IR ν_{max} (KBr)/cm^{-1}: 3324, 2928, 2852, 1620, 1603, 1492, 1413, 762; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.16 (br, 1H, NH), 9.81 (br, 1H, NH), 8.07 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.90 (d, J = 8.4 Hz, 1H, Ar-H8), 7.82 (dd, J_1 = 1.2 Hz, J_2 = 7.4 Hz, 1H, Ar-H3), 7.41 (t, J = 7.6 Hz, 1H, Ar-H2), 7.26 (d, J = 8.0 Hz, 1H, Ar-H7), 3.91 (s, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3),

2.41 (s, 3H, Ar-CH_3), 2.12 (t, J = 7.4 Hz, 2H, $COCH_2$), 1.51 (m, 2H, $COCH_2\underline{CH_2}$), 1.29-1.21 (m, 4H, 2 × $\underline{CH_2}\underline{CH_2}CH_3$), 0.85 (t, J = 7.0 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 394 (M^+, 29), 296 (75), 265 (74), 237 (100), 209 (13), 194 (8), 178 (8), 165 (26); EI-HRMS: M^+ 394.1903 for $C_{23}H_{26}N_2O_4$ (Calcd 394.1893).

(*E*)-*N*′-Hex-3-enoyl-*N*-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**11d**)

Pale white solid, 34.0 mg (yield: 57.8%); Mp: 172-176 °C; IR ν_{max} (KBr)/cm^{-1}: 3326, 2963, 1657, 1602, 1492, 1413, 1229, 763; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.15 (br, 1H, NH), 9.85 (br, 1H, NH), 8.06 (d, J = 7.6 Hz, 1H, Ar-H1), 7.90 (d, J = 8.0 Hz, 1H, Ar-H8), 7.81 (d, J = 6.8 Hz, 1H, Ar-H3), 7.39 (t, J = 7.4 Hz, 1H, Ar-H2), 7.27 (d, J = 8.0 Hz, 1H, Ar-H7), 5.60-5.51 (m, 1H, $\underline{CH}$=$CHCH_2CH_3$), 5.46-5.38 (m, 1H, CH=$\underline{CH}CH_2CH_3$), 3.90 (s, 2H, Ar-CH_2), 2.84 (d, J = 6.4 Hz, 2H, $COCH_2$), 2.44 (s, 3H, Ar-CH_3), 2.41 (s, 3H, Ar-CH_3), 1.98-1.93 (m, 2H, $\underline{CH_2}CH_3$), 0.90 (t, J = 7.6 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 392 (M^+, 21), 296 (27), 265 (63), 237 (100), 209 (13), 194 (8), 178 (8), 165 (26); EI-HRMS: M^+ 392.1742 for $C_{23}H_{24}N_2O_4$ (Calcd 392.1736).

(*E*)-*N*′-Hex-2-enoyl-*N*-2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide (**11e**)

Pale white solid, 51.5 mg (yield: 87.6%); Mp: 188-191 °C; IR ν_{max} (KBr)/cm^{-1}: 3327, 2928, 1653, 1627, 1602, 1493, 1384, 763; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.29 (d, J = 1.6 Hz, 1H, NH), 9.97 (d, J = 1.6 Hz, 1H, NH), 8.06 (dd, J_1 = 1.4 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.90 (d, J = 8.0 Hz, 1H, Ar-H8), 7.82 (d, J = 6.8 Hz, 1H, Ar-H3), 7.40 (t, J = 7.6 Hz, 1H, Ar-H2), 7.28 (d, J = 8.0 Hz, 1H, Ar-H7), 6.71 (dt, J_1 = 7.2 Hz, J_2 = 15.2 Hz, 1H, CH=$\underline{CH}CH_2$), 5.94 (dt, J_1 = 1.2 Hz, J_2 = 15.2 Hz, 1H, $\underline{CH}$=$CHCH_2$), 3.93 (s, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3), 2.14 (qd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 2H, $\underline{CH_2}CH_2CH_3$), 1.47-1.38 (m, 2H, $CH_2\underline{CH_2}CH_3$), 0.89 (t, J = 7.4 Hz, 3H, $CH_2\underline{CH_3}$); EI-MS m/z(%): 392 (M^+, 22), 296 (20), 265 (42), 237 (66), 209 (9), 194 (6), 178 (6), 165 (20); EI-HRMS: M^+ 392.1746 for $C_{23}H_{24}N_2O_4$ (Calcd 392.1736).

4-Allyl-1-(2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetyl)thiosemicarbazide (**12a**)

A mixture of 2-(5,6-dimethyl-9-oxo-9*H*-xanthen-4-yl)acetohydrazide **9** (59 mg, 0.2 mmol) and 3-isothiocyanatoprop-1-ene (20 mg, 0.2 mmol) in ethanol (10 mL) was refluxed for 12 h. The mixture was cooled and the precipitated solid was filtered, dried and recrystallized from ethanol to give compound **12a** as white solid, 19 mg (yield: 24.1%); Mp: 167-170 °C; IR ν_{max} (KBr)/cm^{-1}: 3250, 3068, 2973, 1698, 1644, 1601, 1542, 1494, 1414, 1336, 1215, 763; ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 10.11 (brs, 1H, C(O)NHNH), 9.39 (s, 1H, C(O)NHNH), 8.13 (brs, 1H, C(S)NH), 8.10 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 7.94 (d, J = 8.0 Hz, 1H, Ar-H8), 7.81 (d, J = 7.0 Hz, 1H, Ar-H3), 7.43 (t, J = 7.5 Hz, 1H, Ar-H2), 7.32 (d, J = 8.5 Hz, 1H, Ar-H7), 5.87-5.79 (m, 1H, $CH_2CH=CH_2$), 5.14 (dd, J_1 = 1.5 Hz, J_2 = 17.5 Hz, 1H, =CHH, *cis*), 5.06 (dd, J_1 = 1.0 Hz, J_2 = 10.0 Hz, 1H, =CHH, *trans*), 4.13-4.09 (brs, 2H, $CH_2CH=CH_2$), 3.97 (s, 1H, Ar-CHH), 3.96 (s, 1H, Ar-CHH), 2.48 (s, 3H, Ar-CH_3), 2.46 (s, 3H, Ar-CH_3); EI-MS m/z(%): 384 ([M-C+H]$^+$, 3), 368 (3), 353 (2), 339 (1), 296 (14), 265 (21), 256 (15), 237 (36); ESI-HRMS: [M-H]$^-$ 394.1229 for $C_{21}H_{21}N_3O_3S$-H (Calcd 394.1225).

Compounds **12b**-**12c** were prepared by using the same procedure for **12a**, with the corresponding isothiocyanates.

(*R*)-1-(2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)acetyl)-4-(1-phenylethyl)thiosemicarbazide (**12b**)

White solid, 35 mg (yield: 38.3%); Mp: 229-232 °C; $[\alpha]_D^{25}$ +88.5° (*c* 0.1, EtOH); IR ν_{max} (KBr)/cm^{-1}: 3242, 3027, 2974, 1681, 1647, 1602, 1537, 1414, 1216, 760; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.13 (br, 1H, C(O)NHNH), 9.37 (s, 1H, C(O)NHNH), 8.08 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, Ar-H1), 8.06 (brs, 1H, C(S)NH), 7.92 (d, J = 8.4 Hz, 1H, Ar-H8), 7.82 (d, J = 7.2 Hz, 1H, Ar-H3), 7.41 (t, J = 7.6 Hz, 1H, Ar-H2), 7.32-7.28 (m, 1H + 4H, Ar-H7 + Ar'), 7.22 (t, J = 6.8 Hz, 1H, Ar'), 5.64-5.60 (m, 1H, $CHCH_3$), 3.96 (s,

2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3), 1.44 (d, *J* = 7.2 Hz, 3H, CH$\underline{CH_3}$); EI-MS m/z(%): 459 (M^+, 1), 338 (5), 321 (2), 305 (2), 296 (77), 265 (100), 237 (100), 209 (17); ESI-HRMS: $[M-H]^-$ 458.1546 for $C_{26}H_{25}N_3O_3S$-H (Calcd 458.1538).

(*S*)-1-(2-(5,6-Dimethyl-9-oxo-9*H*-xanthen-4-yl)acetyl)-4-(1-phenylethyl)thiosemicarbazide (**12c**)

White solid, 38 mg (yield: 41.5%); Mp: 230-234 °C; $[\alpha]_D^{25}$ –81.1° (*c* 0.1, EtOH); IR ν_{max} (KBr)/cm^{-1}: 3244, 3027, 2975, 1682, 1648, 1602, 1537, 1414, 1216, 759; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.13 (br, 1H, C(O)$\underline{NH}$NH), 9.37 (s, 1H, C(O)NH$\underline{NH}$), 8.08 (dd*, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H + 1H, Ar-H1 + C(S)$\underline{NH}$), 7.92 (d, *J* = 8.0 Hz, 1H, Ar-H8), 7.82 (d, *J* = 6.8 Hz, 1H, Ar-H3), 7.41 (t, *J* = 7.6 Hz, 1H, Ar-H2), 7.32-7.27 (m, 1H + 4H, Ar-H7 + Ar'), 7.22 (t, *J* = 6.8 Hz, 1H, Ar'), 5.64-5.60 (m, 1H, $\underline{CH}CH_3$), 3.96 (s, 2H, Ar-CH_2), 2.44 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Ar-CH_3), 1.44 (d, *J* = 7.2 Hz, 3H, CH$\underline{CH_3}$) *overlap; EI-MS m/z(%): 382 ($[M-C_6H_5]^+$, 1), 368 (10), 353 (1), 340 (1), 296 (49), 265 (70), 237 (100), 209 (11); ESI-HRMS: $[M-H]^-$ 458.1543 for $C_{26}H_{25}N_3O_3S$-H (Calcd 458.1538).