

# SUPPLEMENTARY INFORMATION

## Synthesis, biological evaluation and *in silico* studies of novel aminated xanthones as potential p53-activating agents

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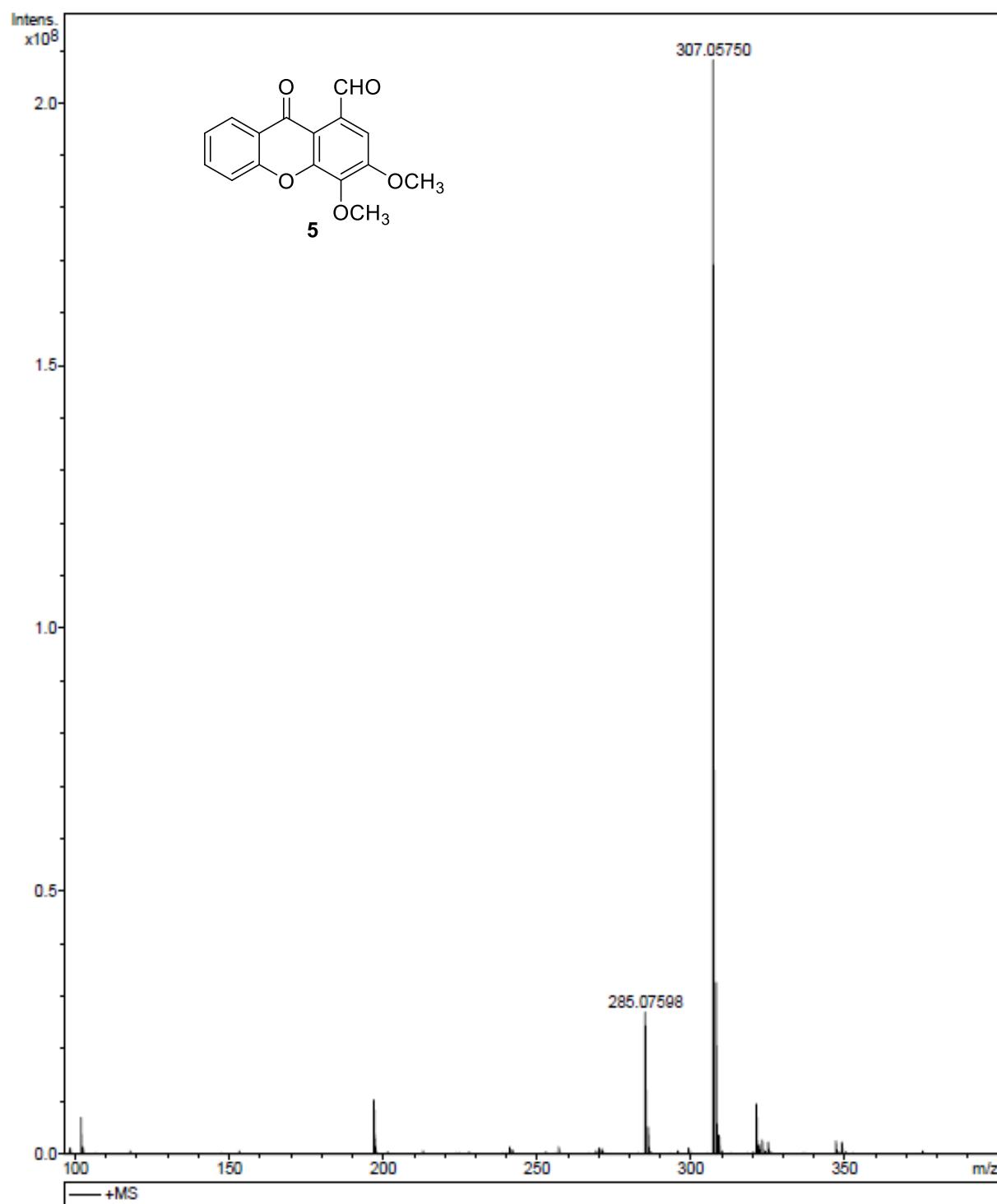
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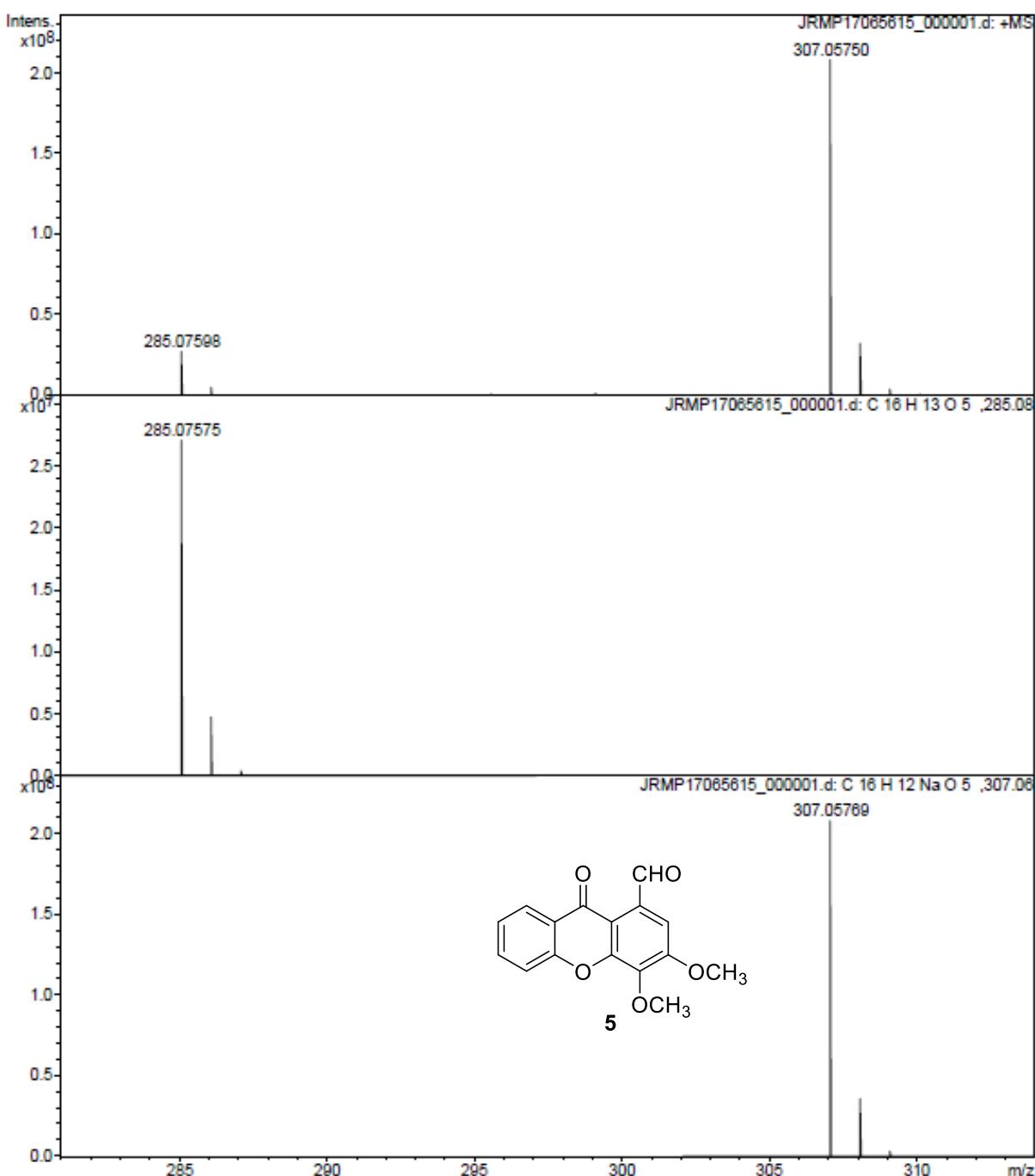
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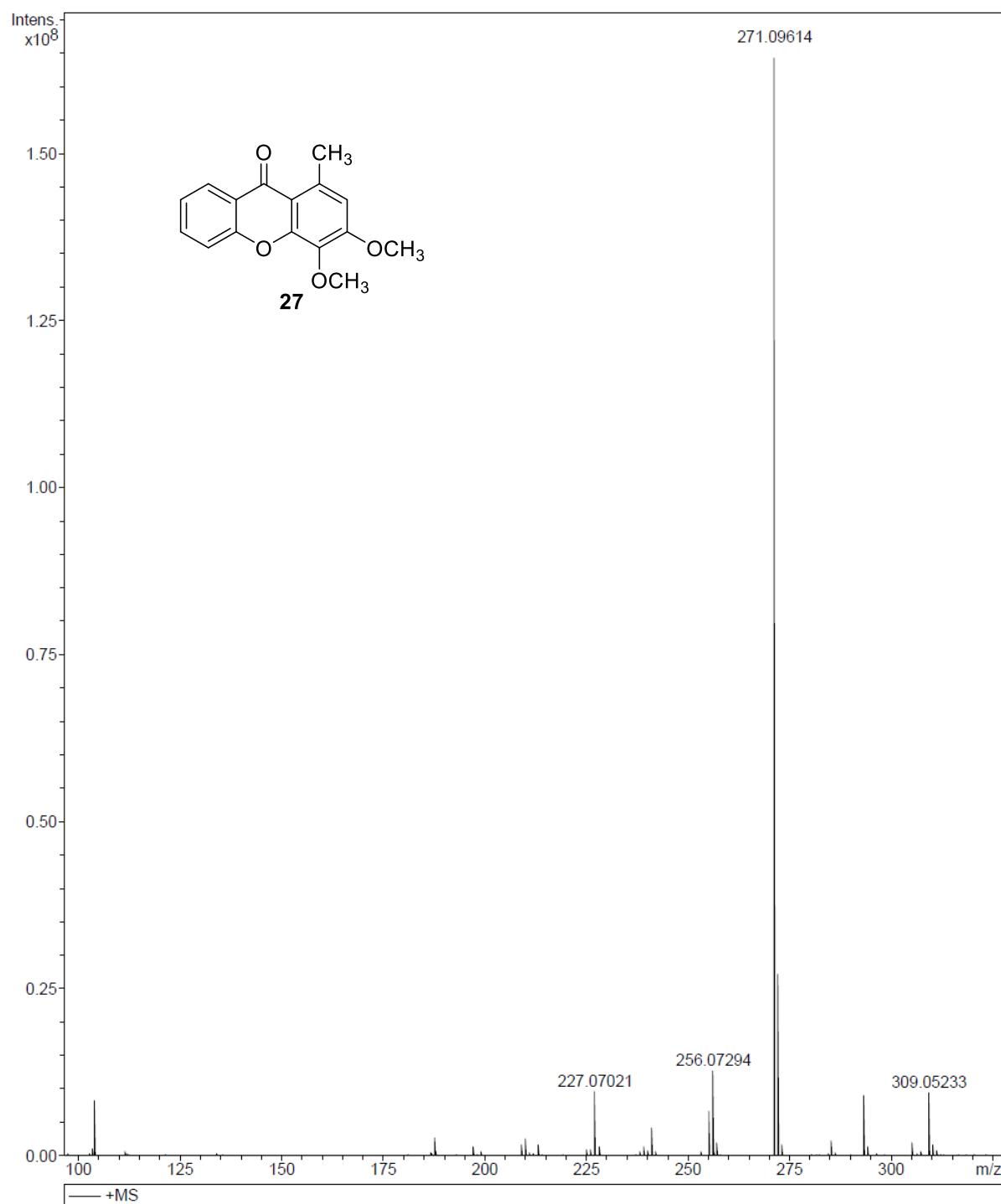
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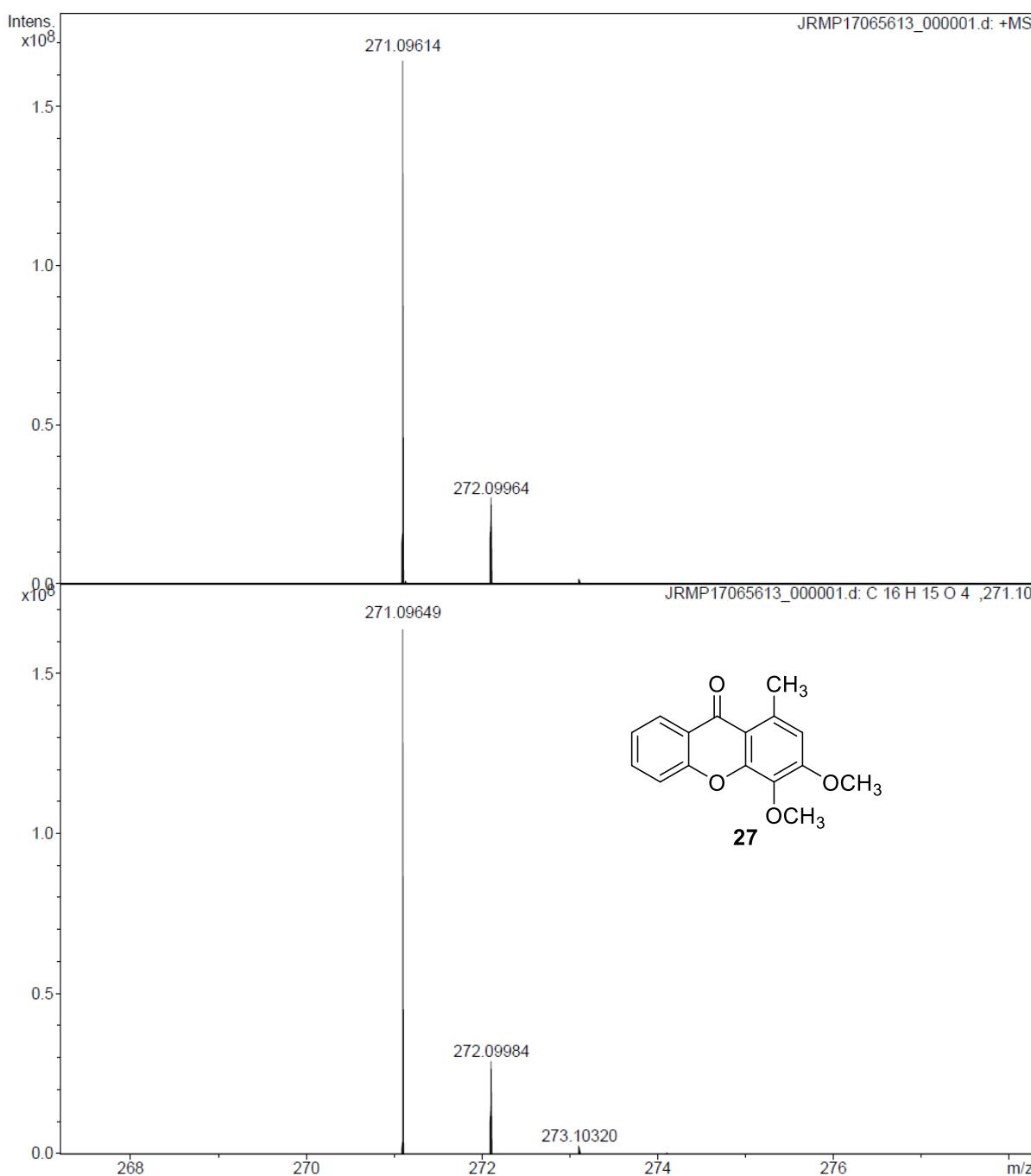
1. HRMS spectra of the described xanthone derivatives



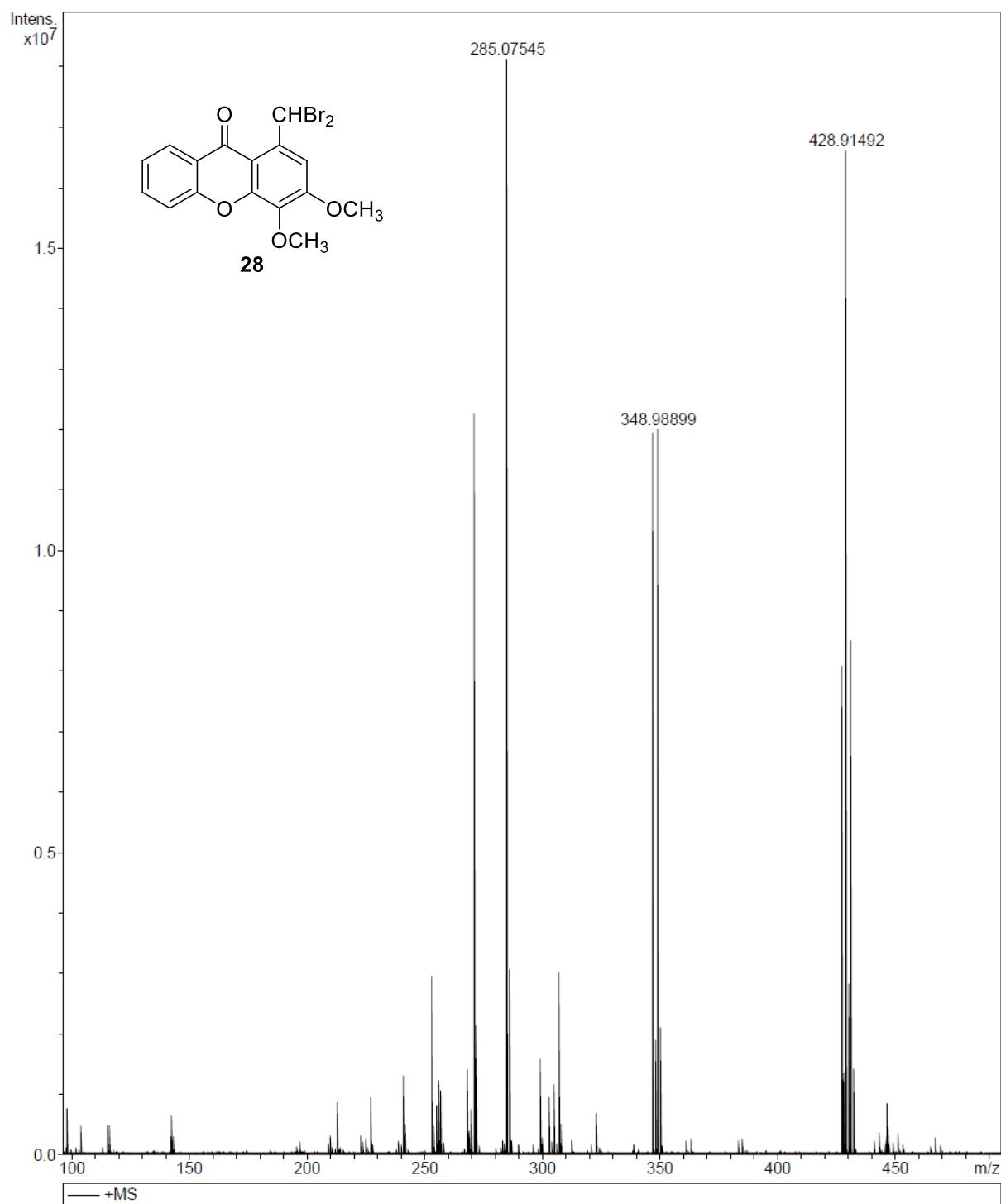


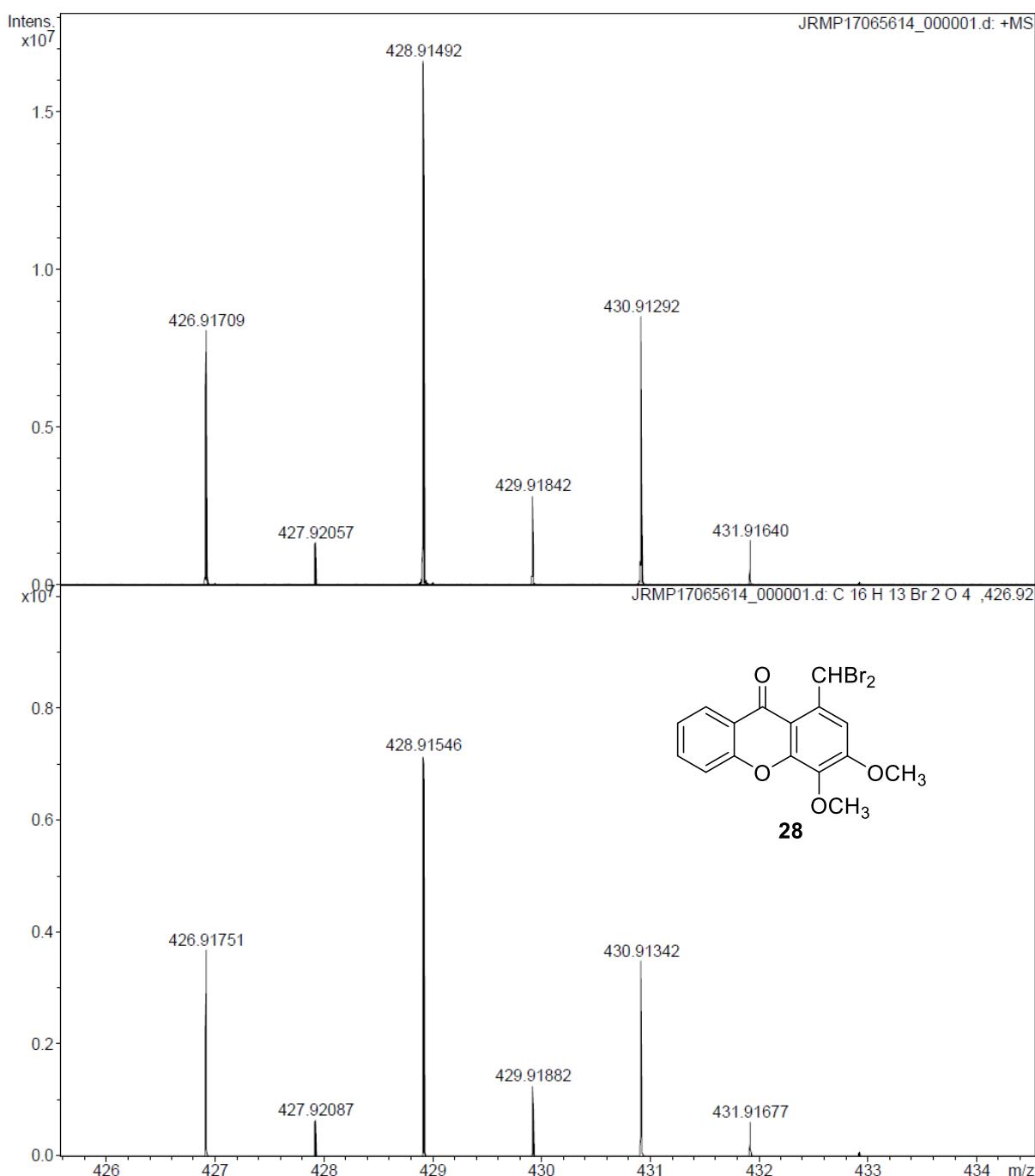
**Figure S1.** HRMS spectrum of 3,4-dimethoxy-9-oxo-9*H*-xanthene-1-carbaldehyde (**5**).



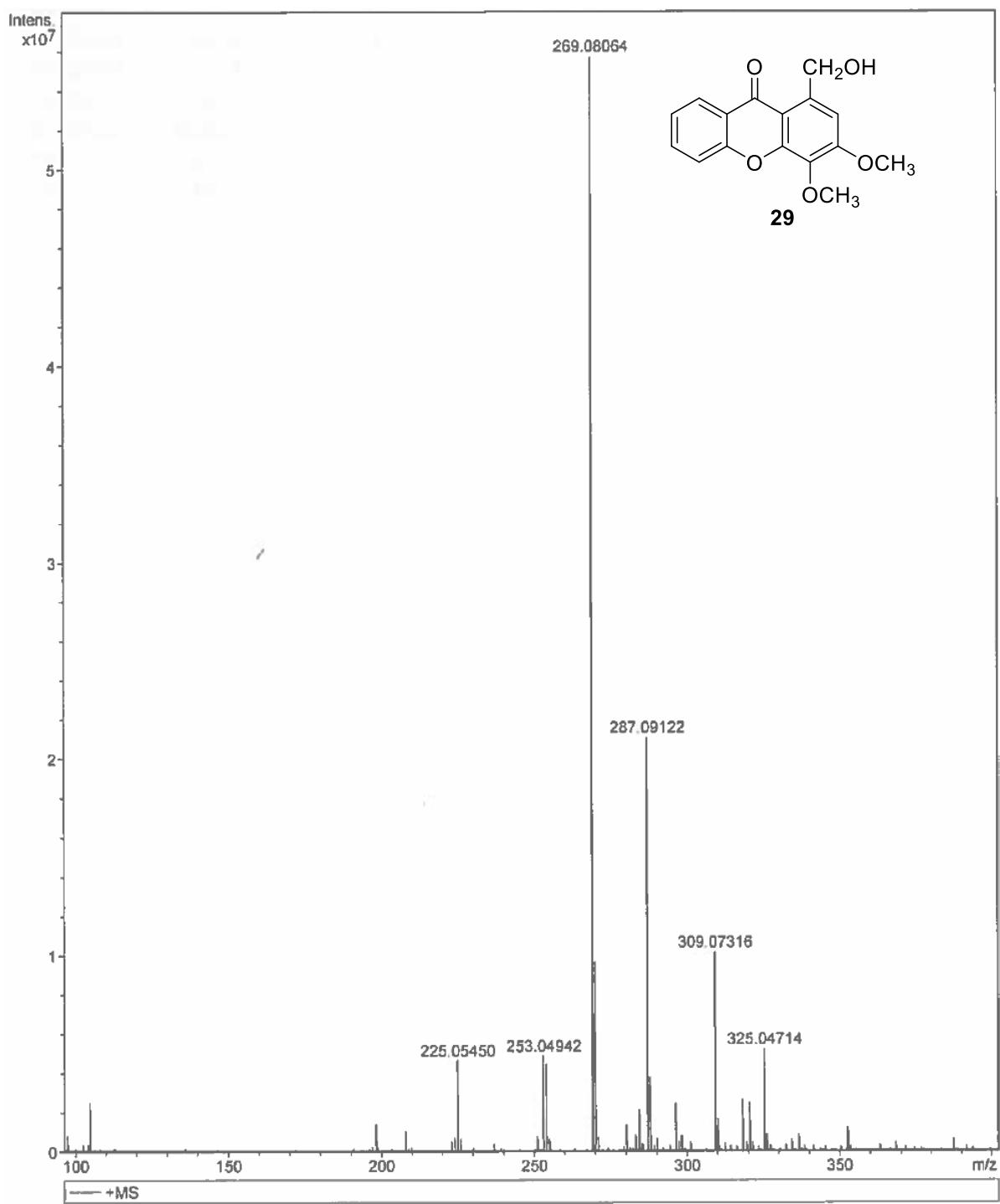


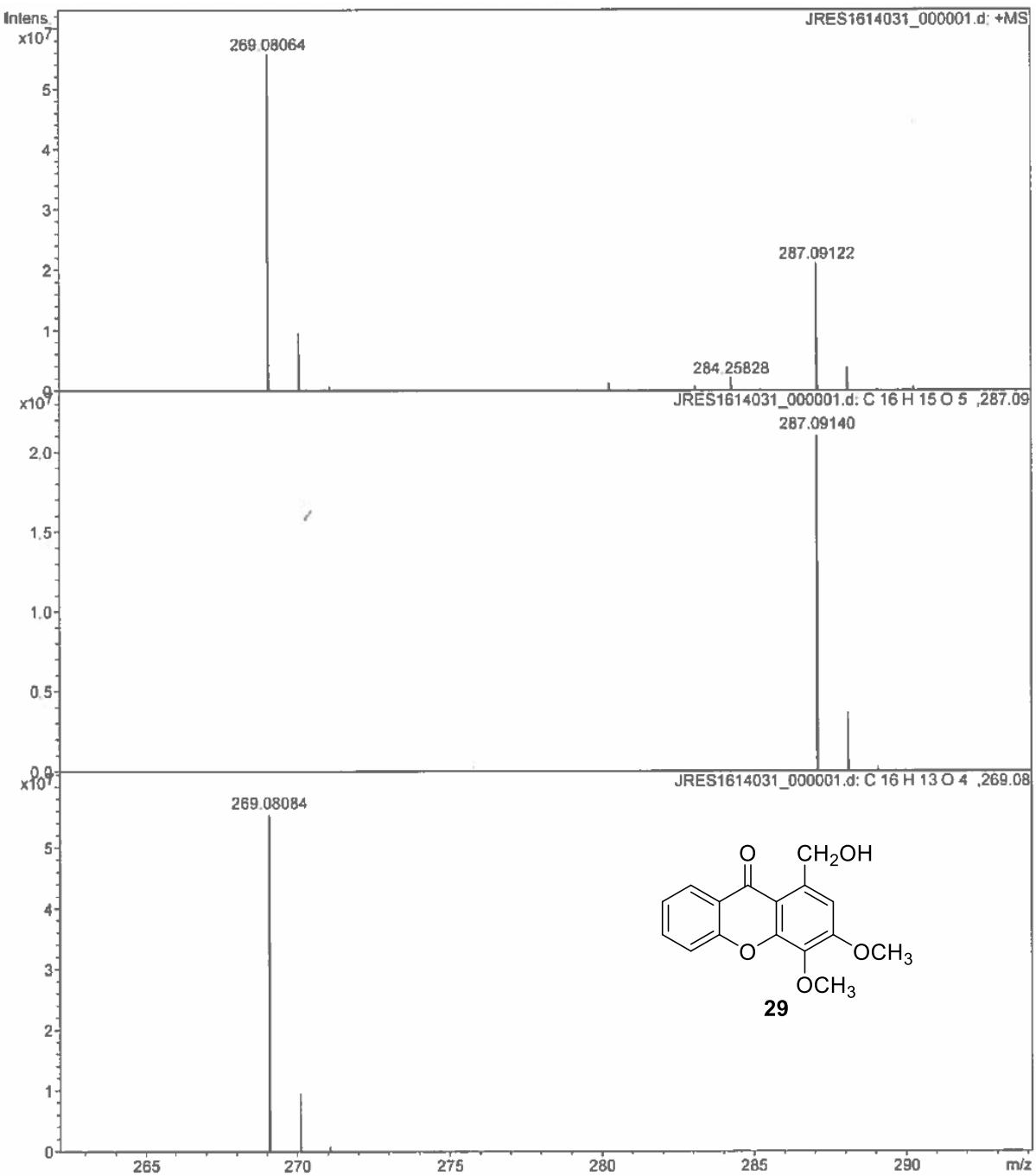
**Figure S2.** HRMS spectrum of 3,4-dimethoxy-1-methyl-9*H*-xanthen-9-one (**27**).



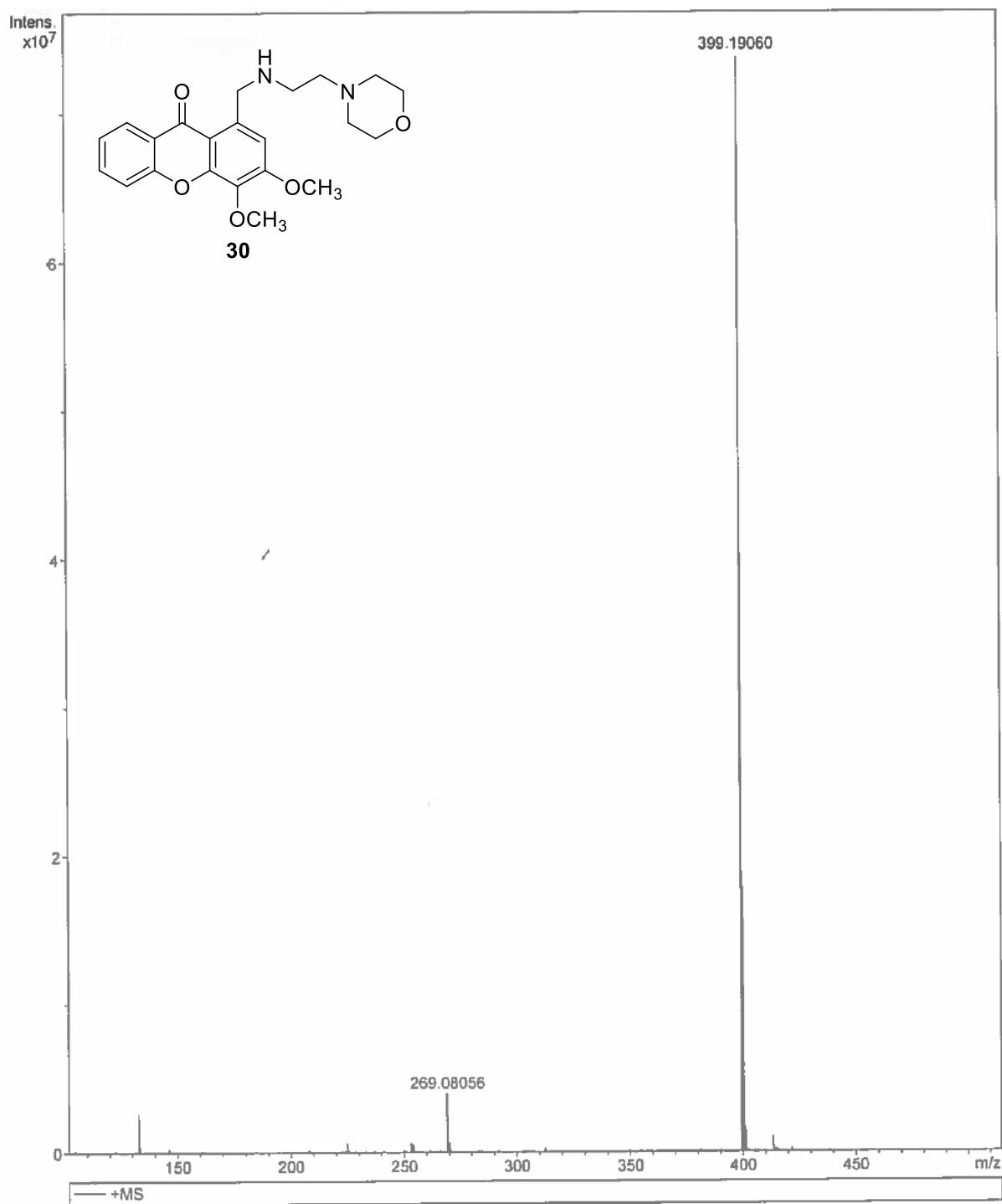


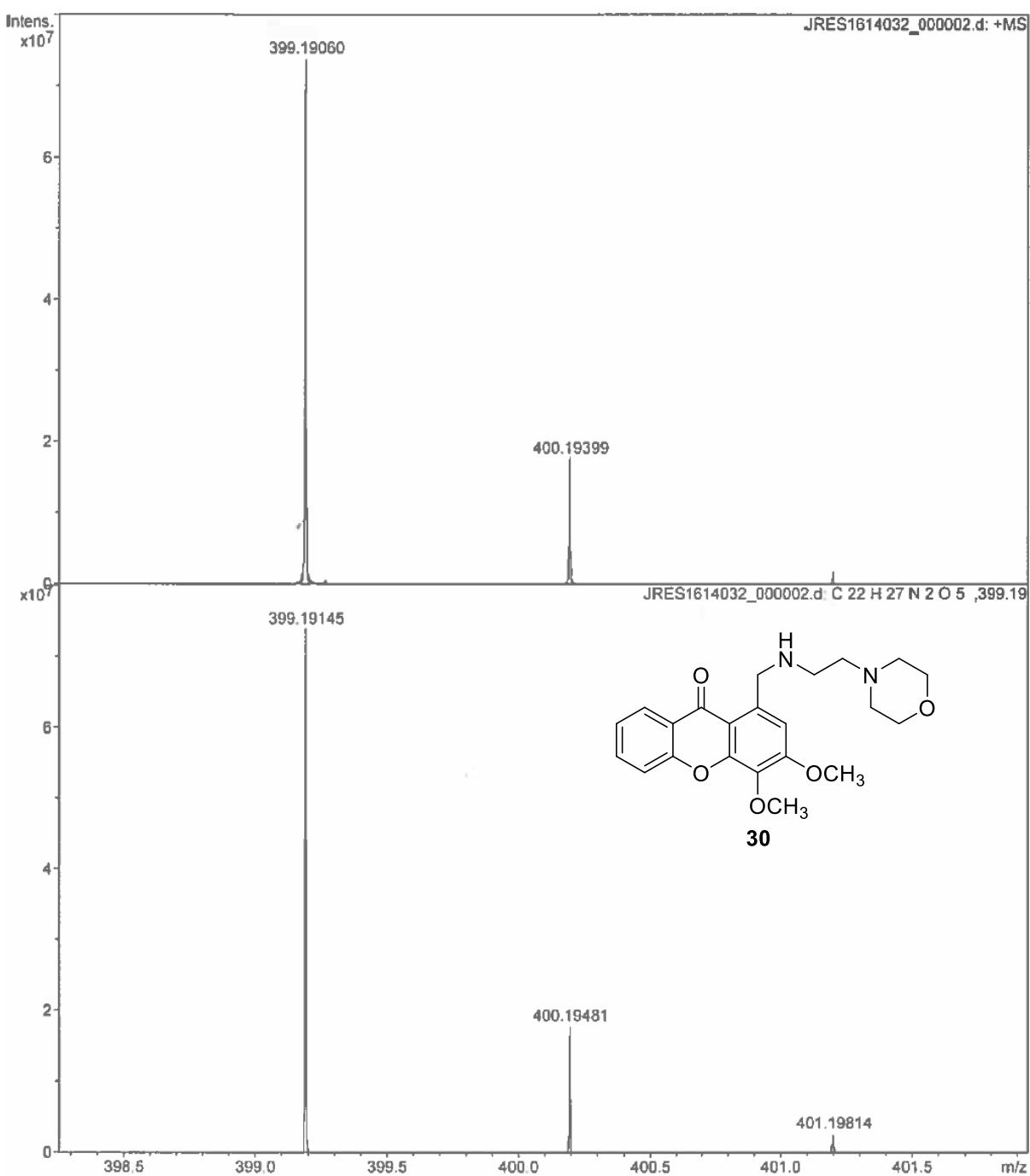
**Figure S3.** HRMS spectrum of 1-(dibromomethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**28**).



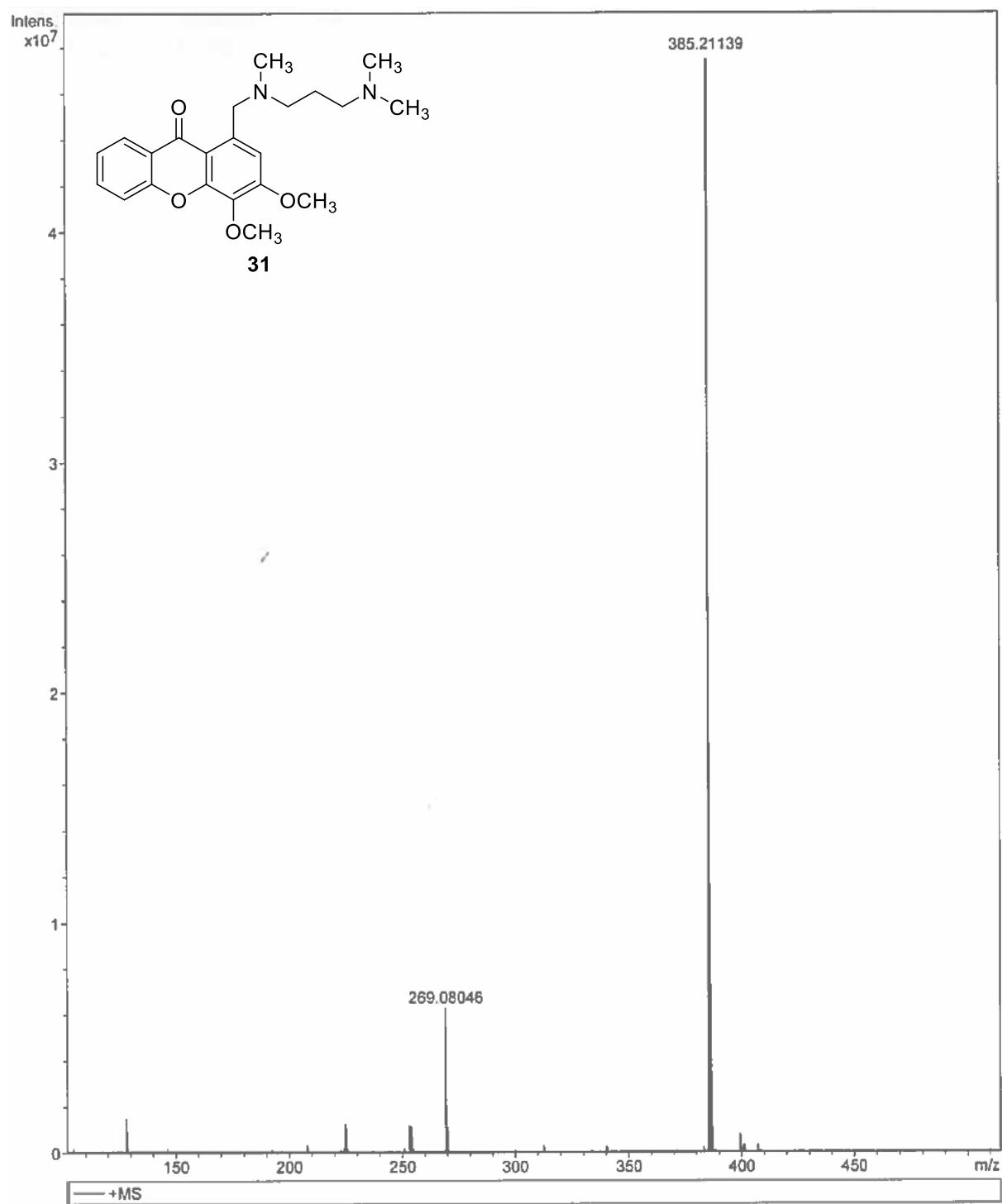


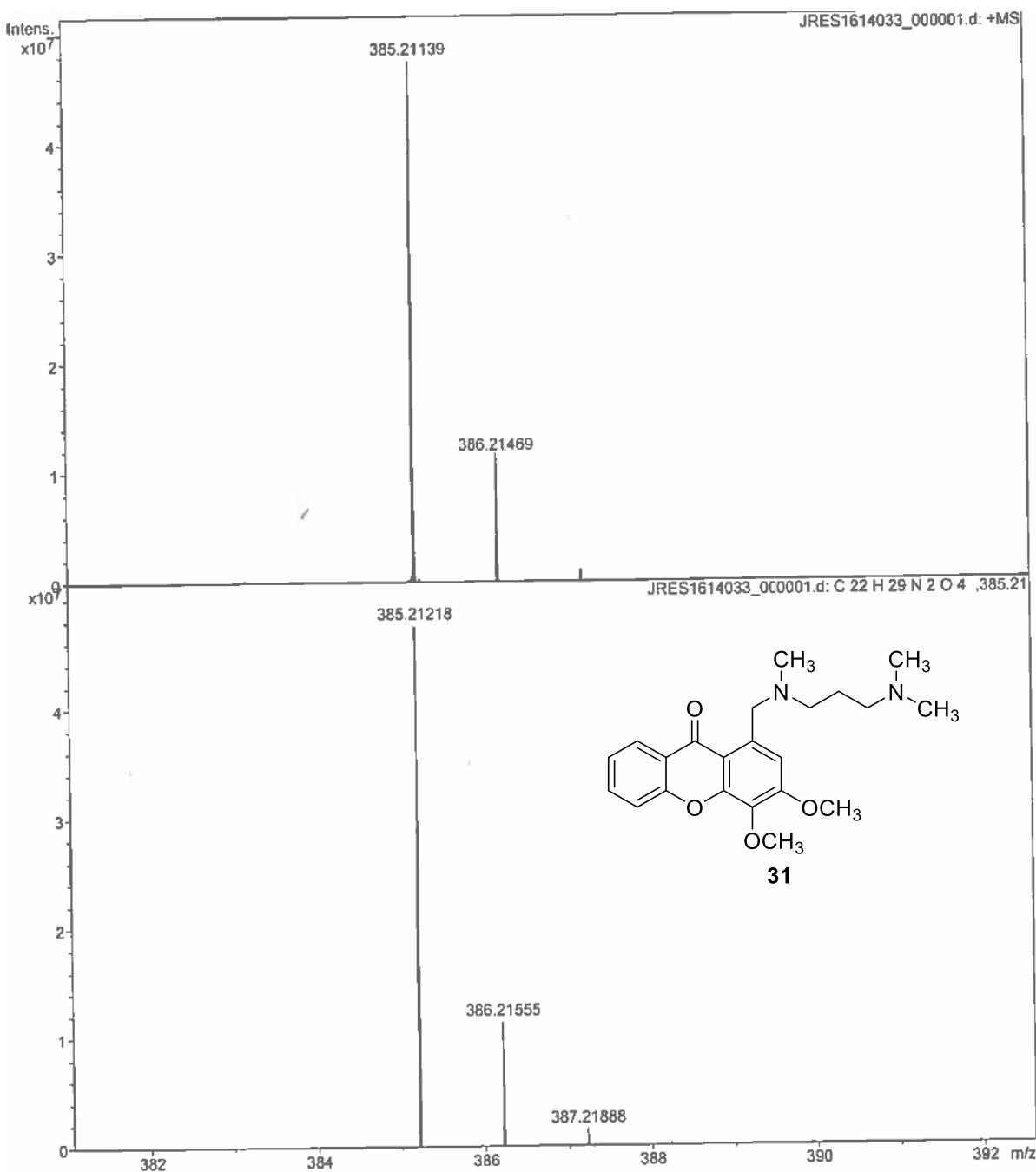
**Figure S4.** HRMS spectrum of 1-(hydroxymethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**29**).



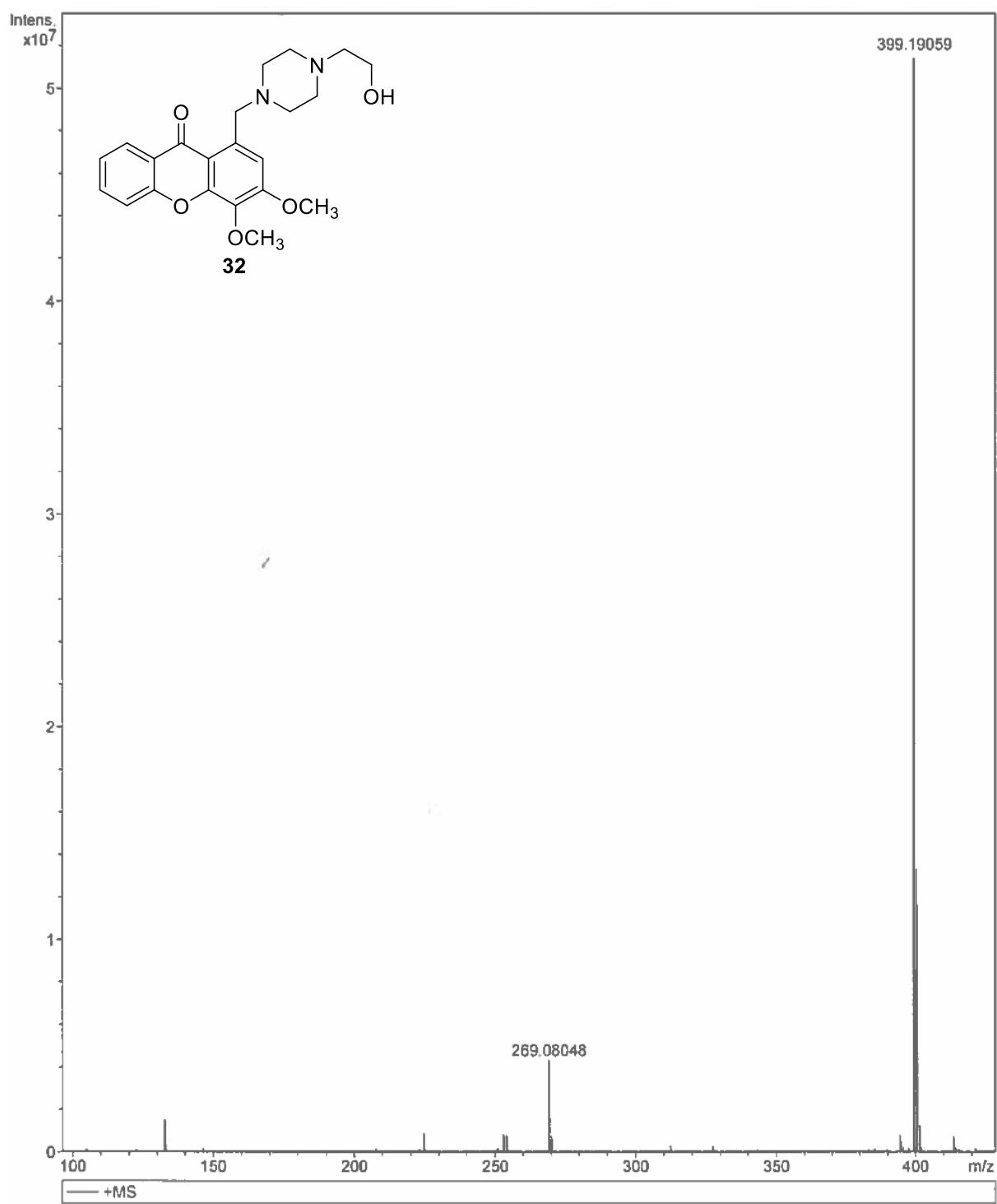


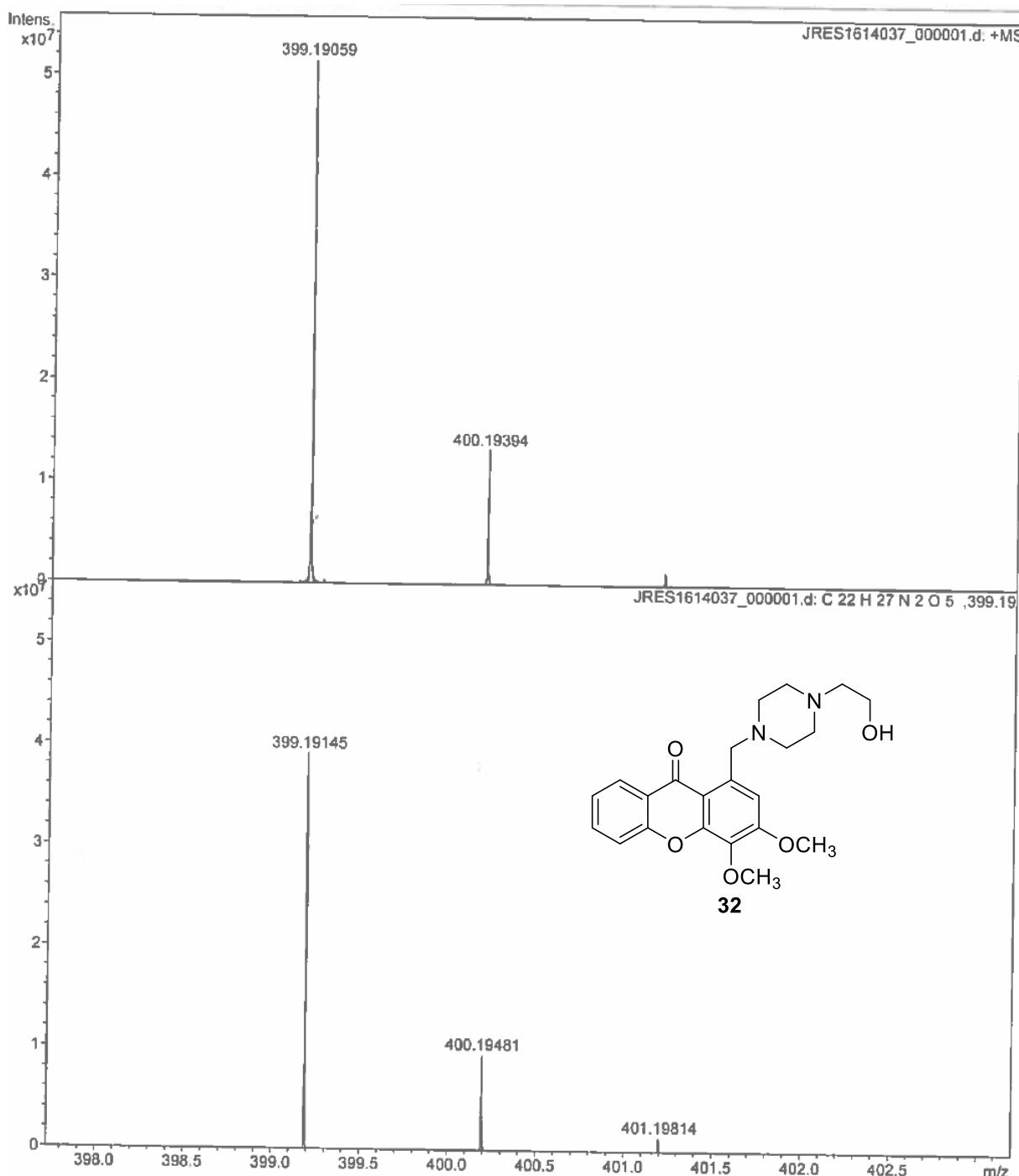
**Figure S5.** HRMS spectrum of 3,4-dimethoxy-1-((2-morpholinoethyl)amino)methyl)-9*H*-xanthen-9-one (**30**).



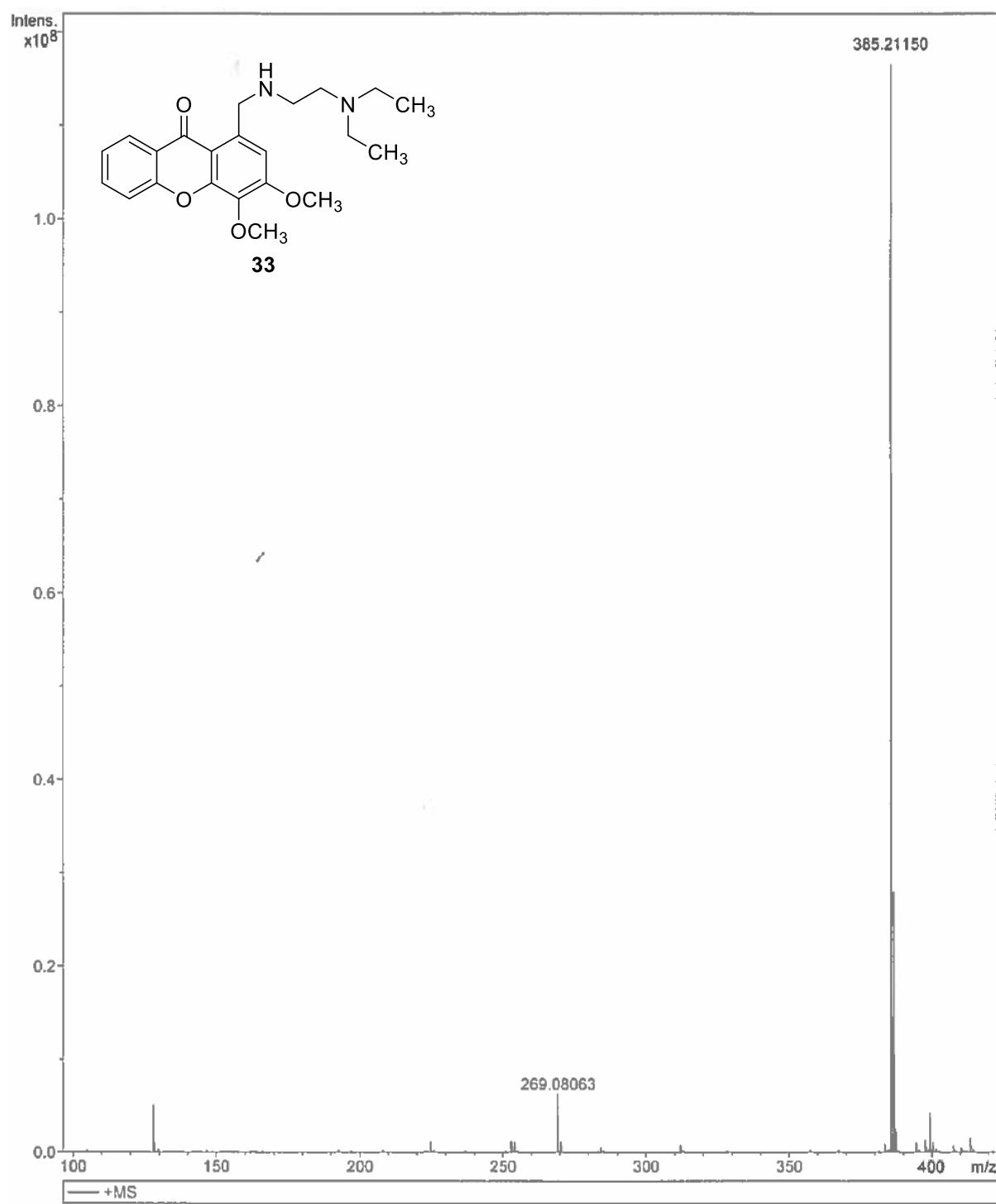


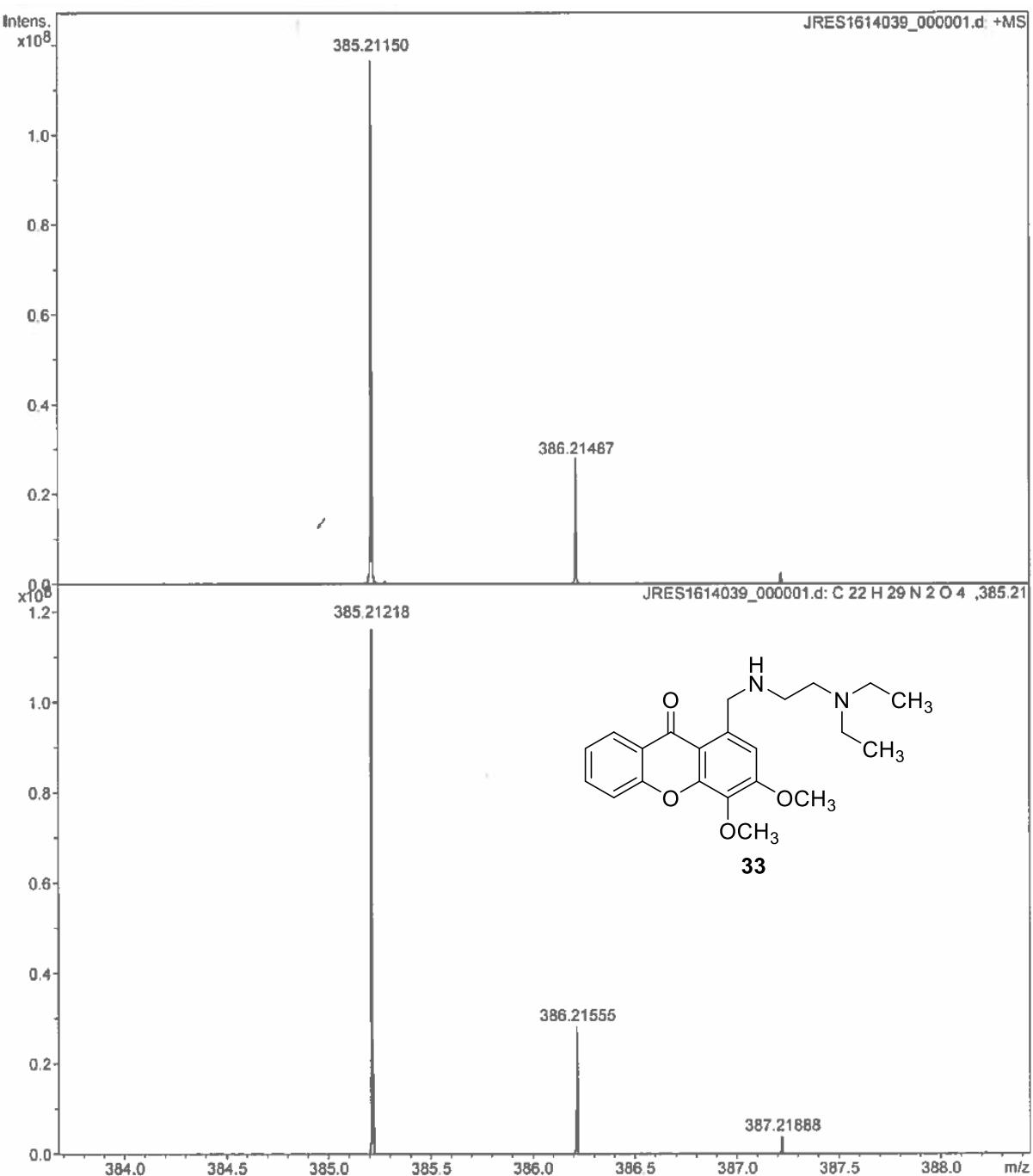
**Figure S6.** HRMS spectrum of 1-((3-(dimethylamino)propyl)(methyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (**31**).



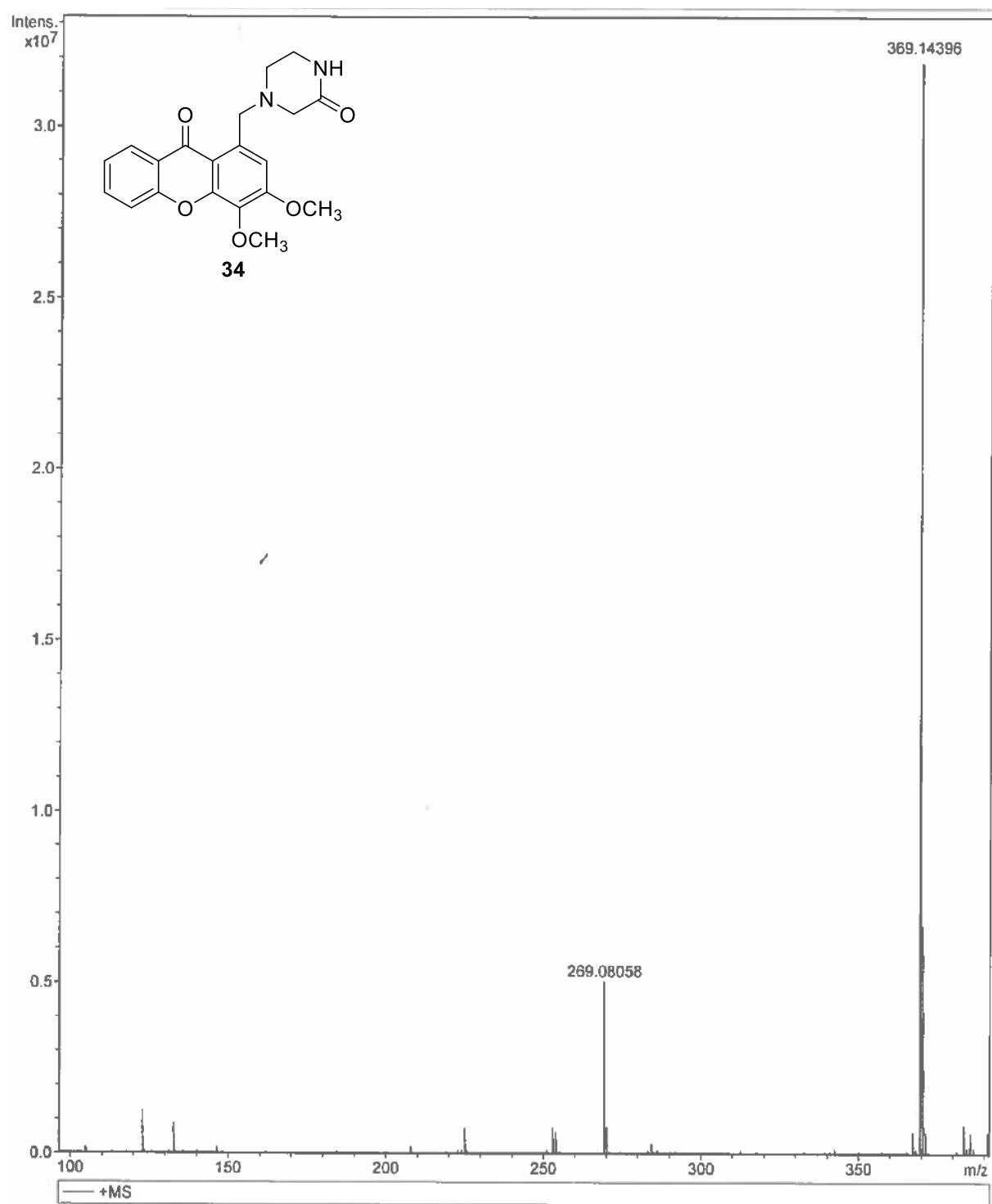


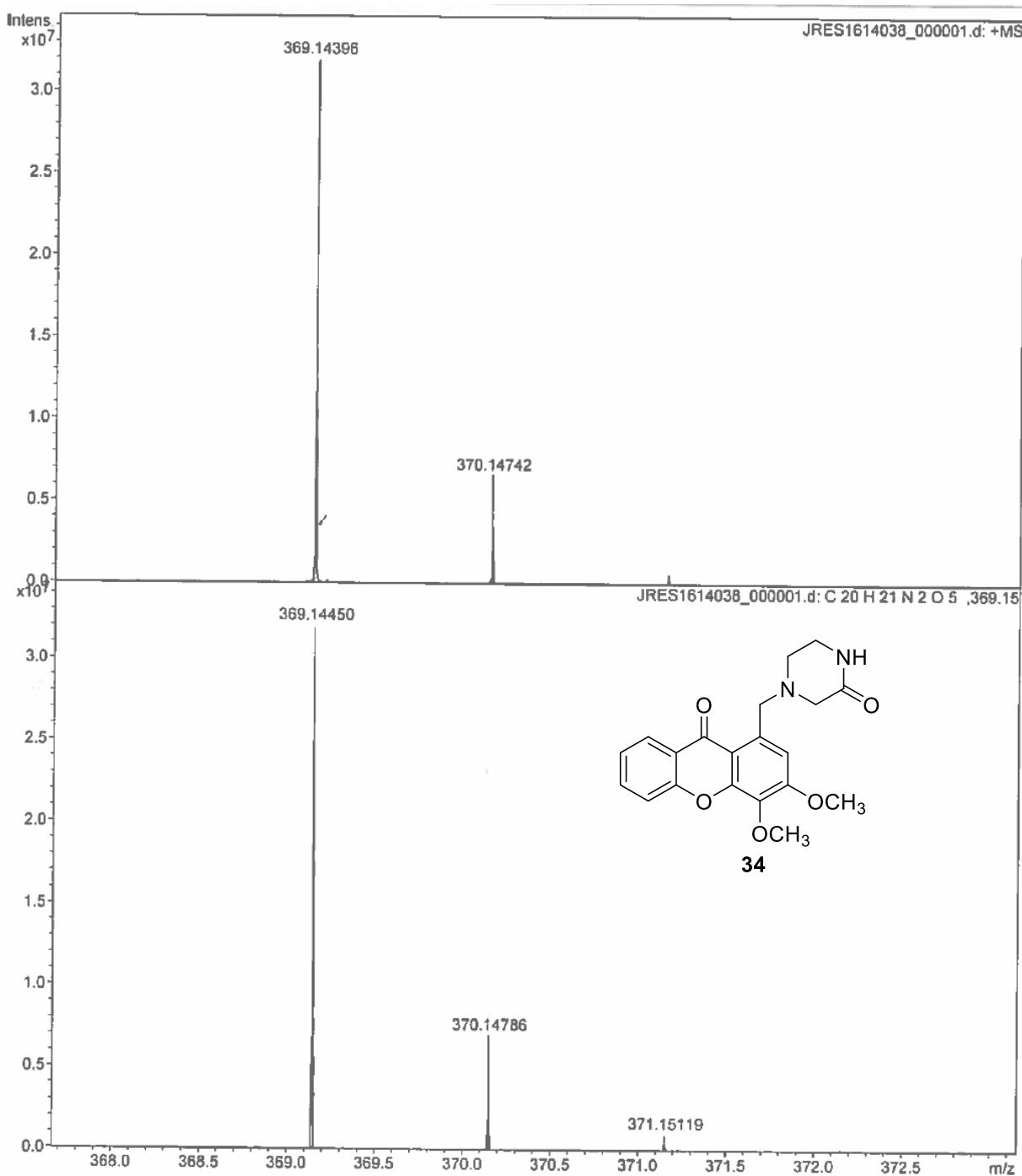
**Figure S7.** HRMS spectrum of 1-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**32**).



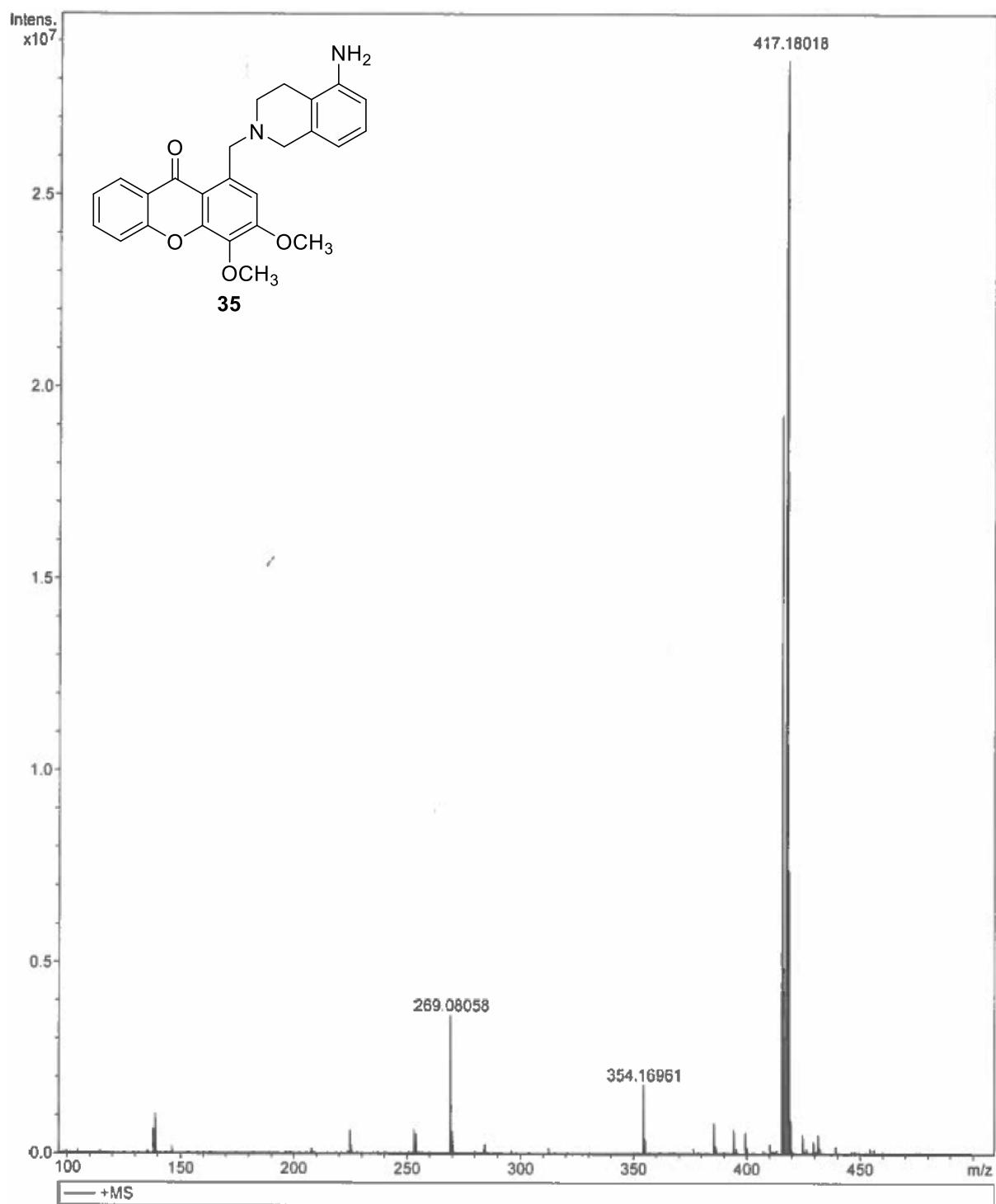


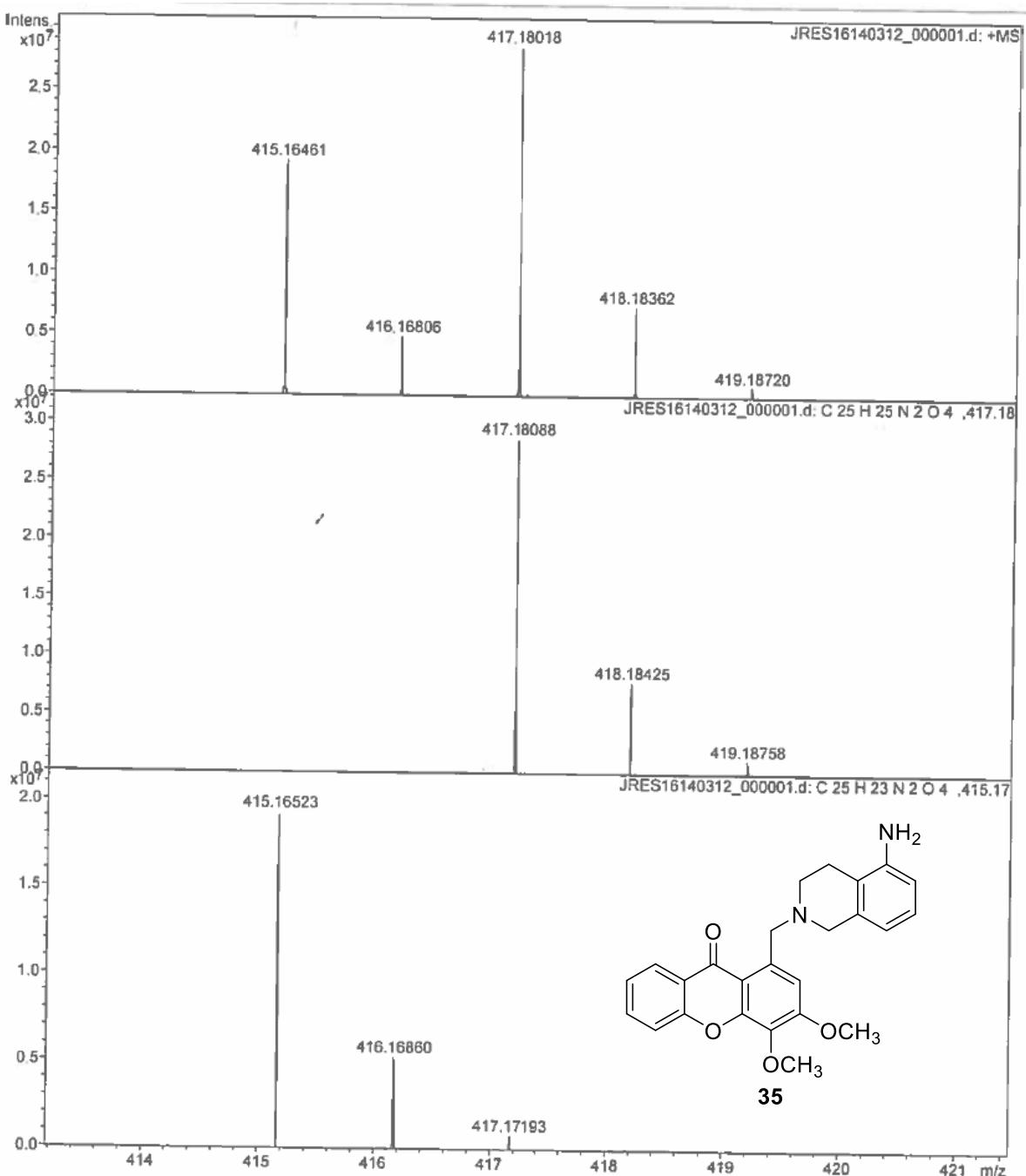
**Figure S8.** HRMS spectrum of 1-(((2-(diethylamino)ethyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (33).



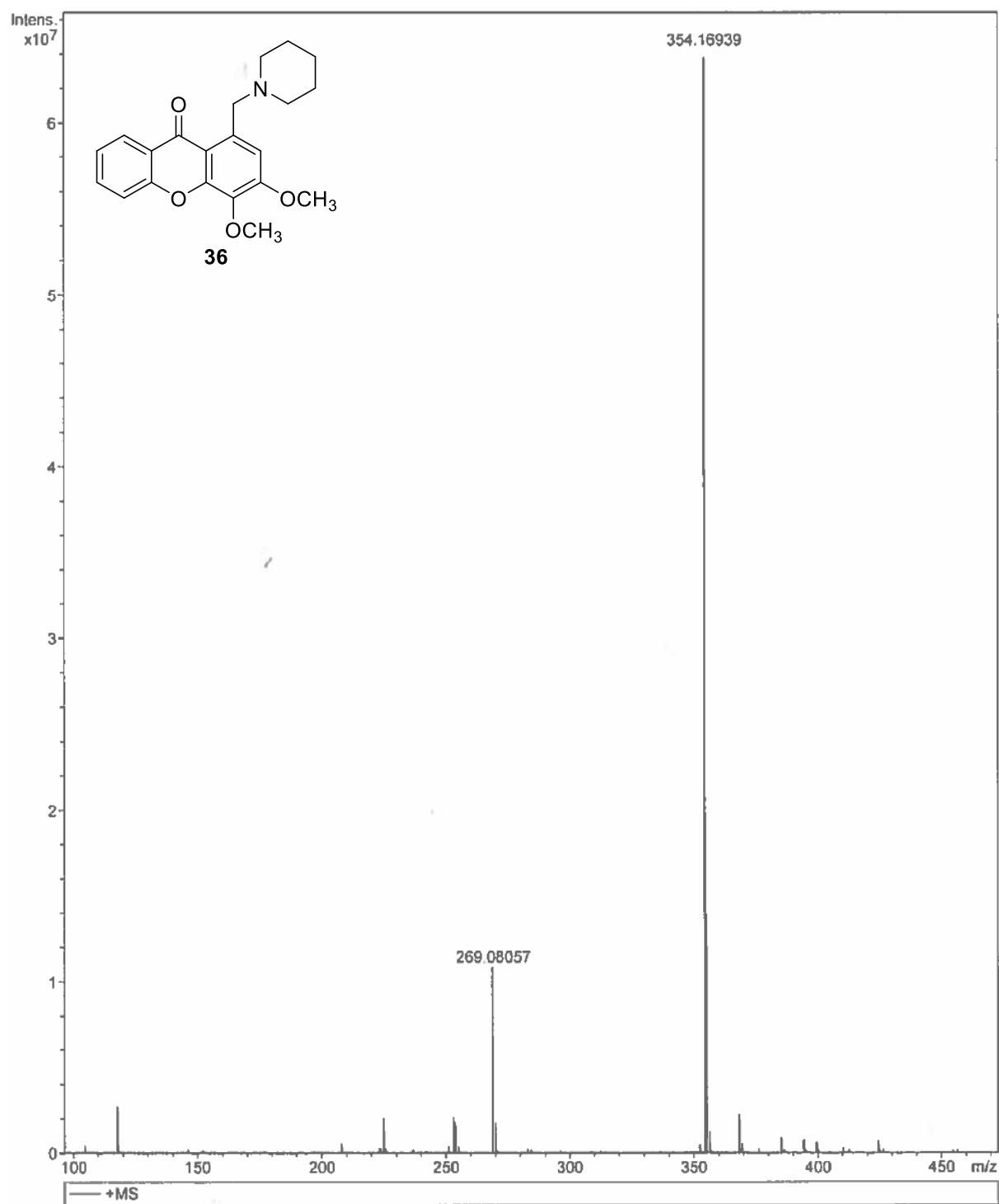


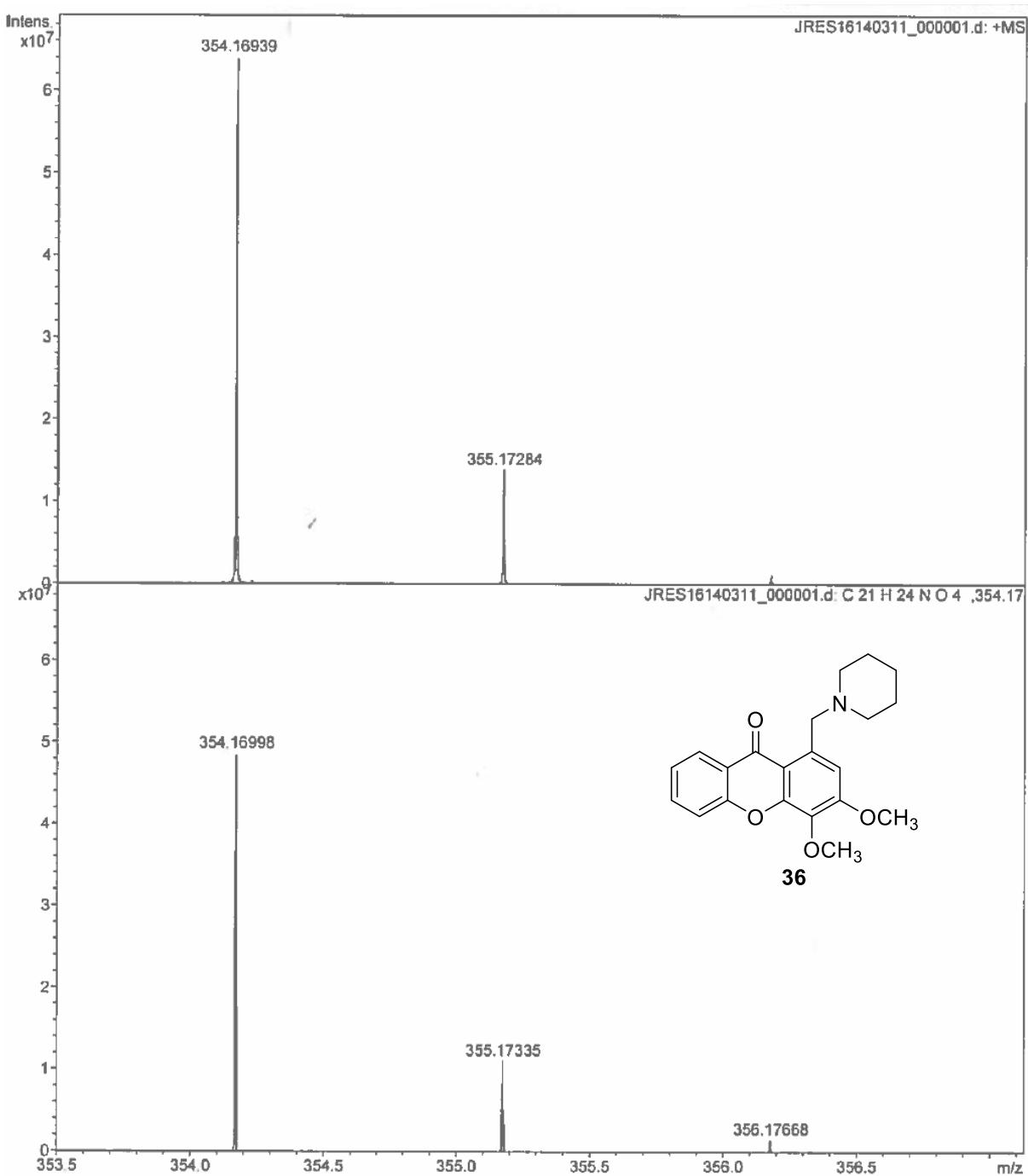
**Figure S9.** HRMS spectrum of 4-((3,4-dimethoxy-9-oxo-9*H*-xanthen-1-yl)methyl)piperazin-2-one (**34**).



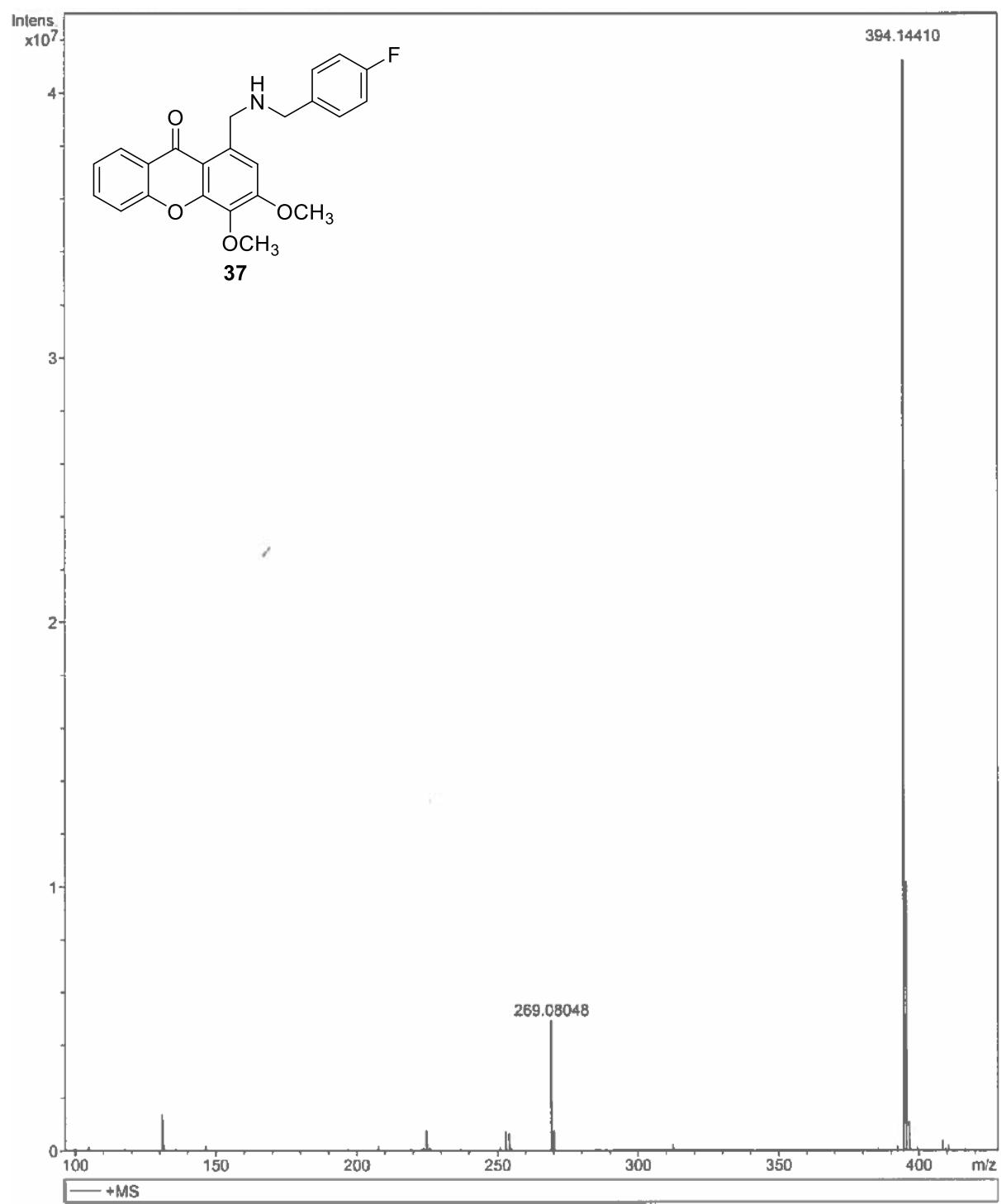


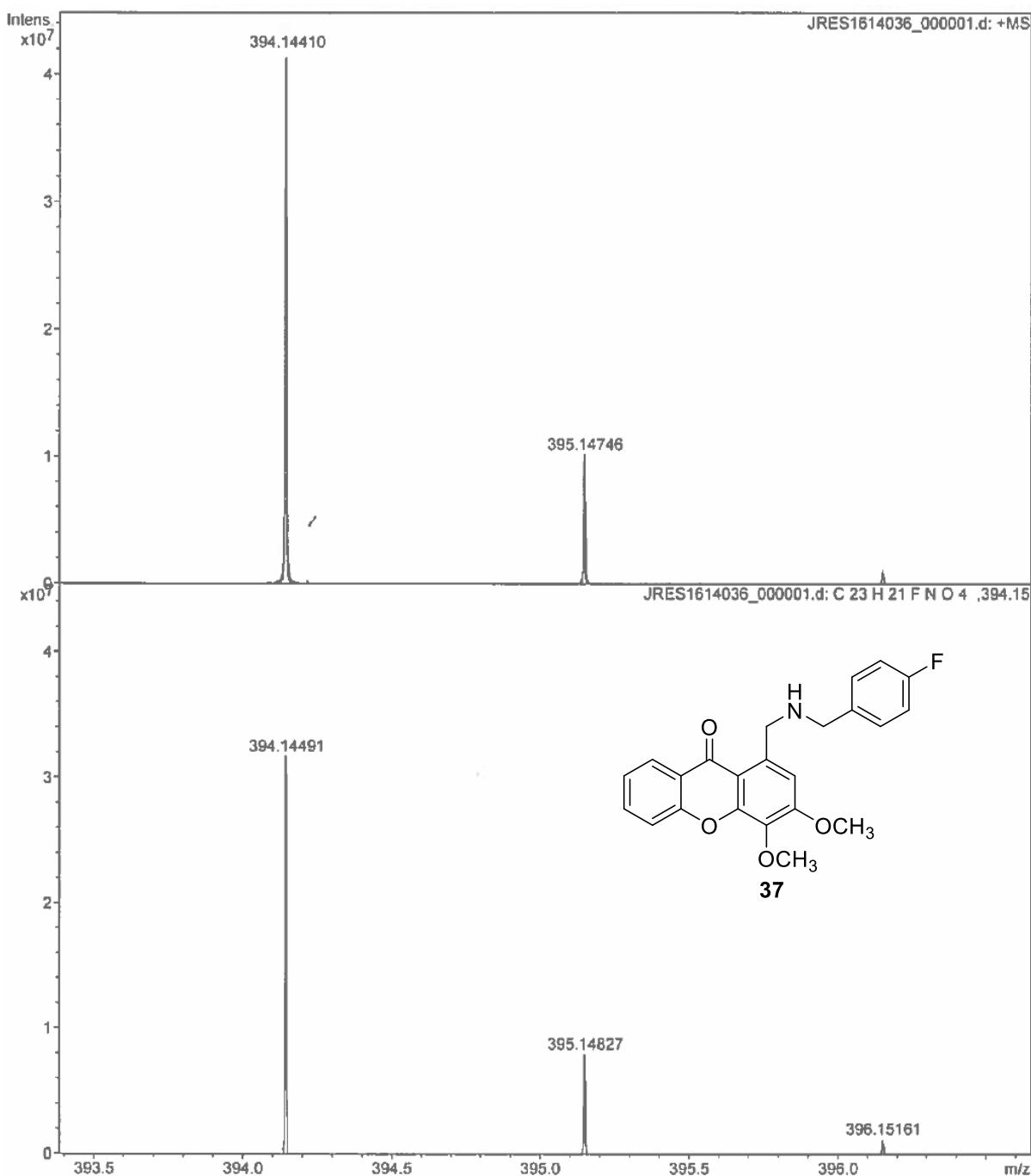
**Figure S10.** HRMS spectrum of 1-((5-amino-3,4-dihydroisoquinolin-2(1H)-yl)methyl)-3,4-dimethoxy-9H-xanthen-9-one (**35**).



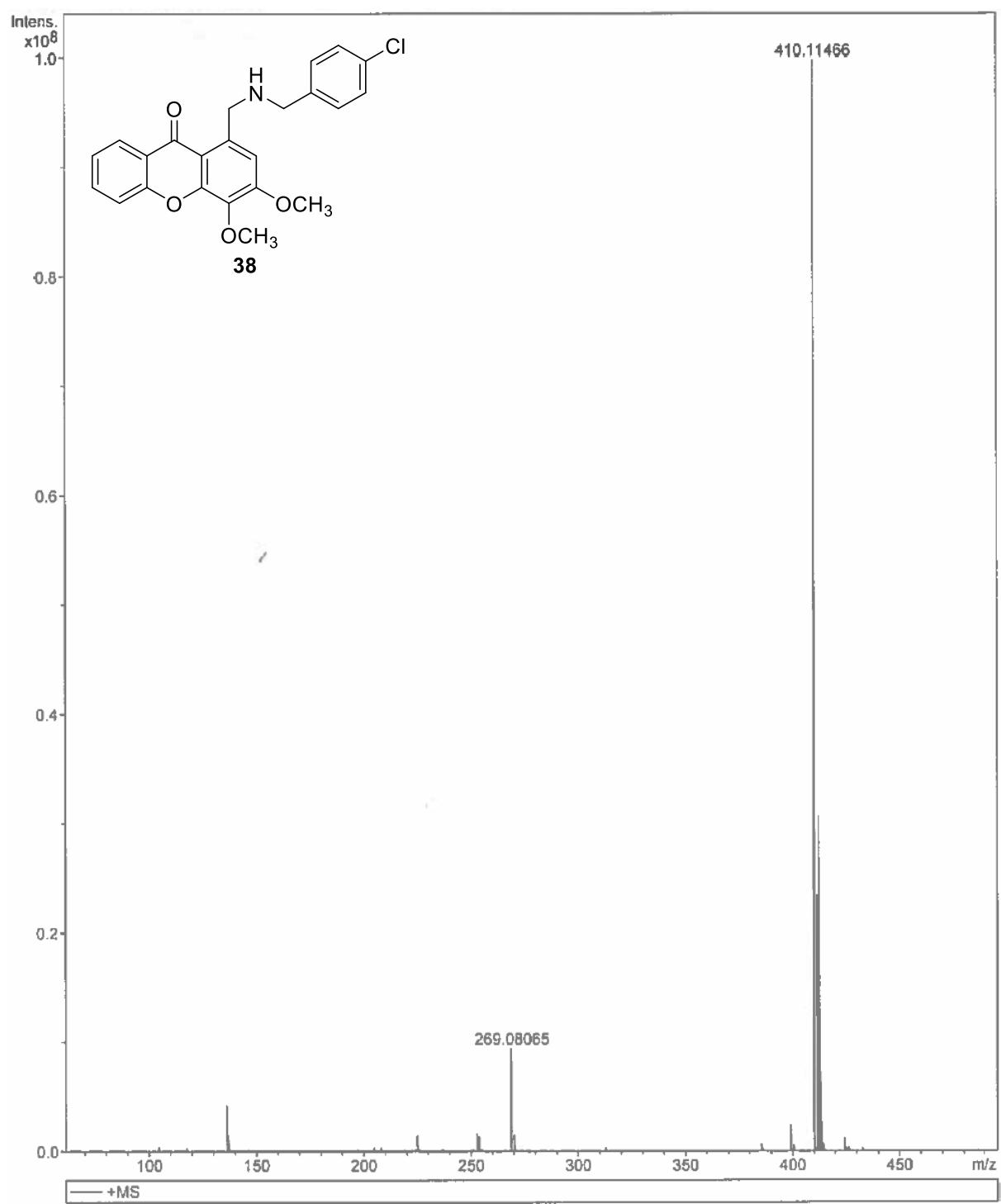


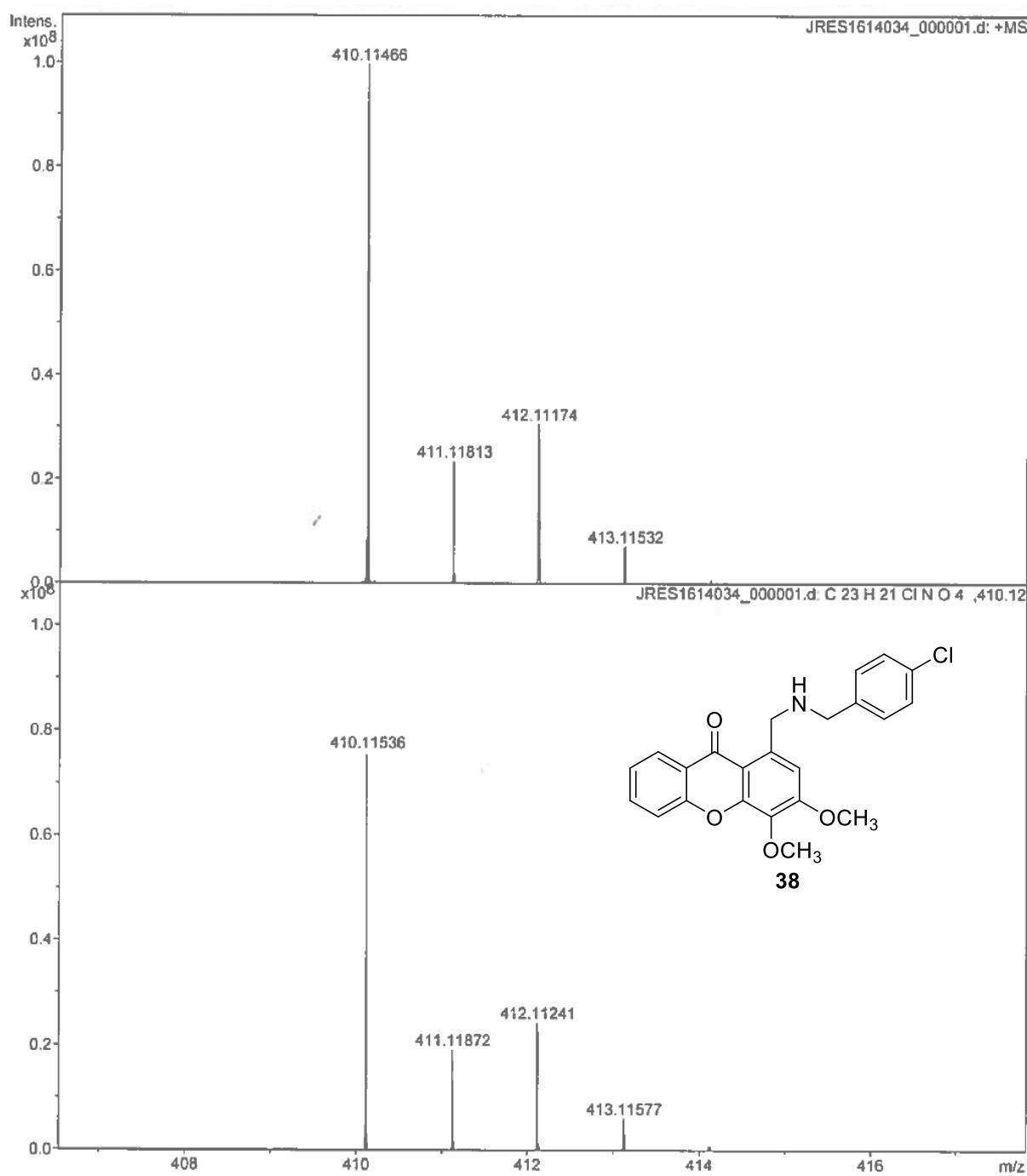
**Figure S11.** HRMS spectrum of 3,4-dimethoxy-1-(piperidin-1-ylmethyl)-9*H*-xanthen-9-one (**36**).



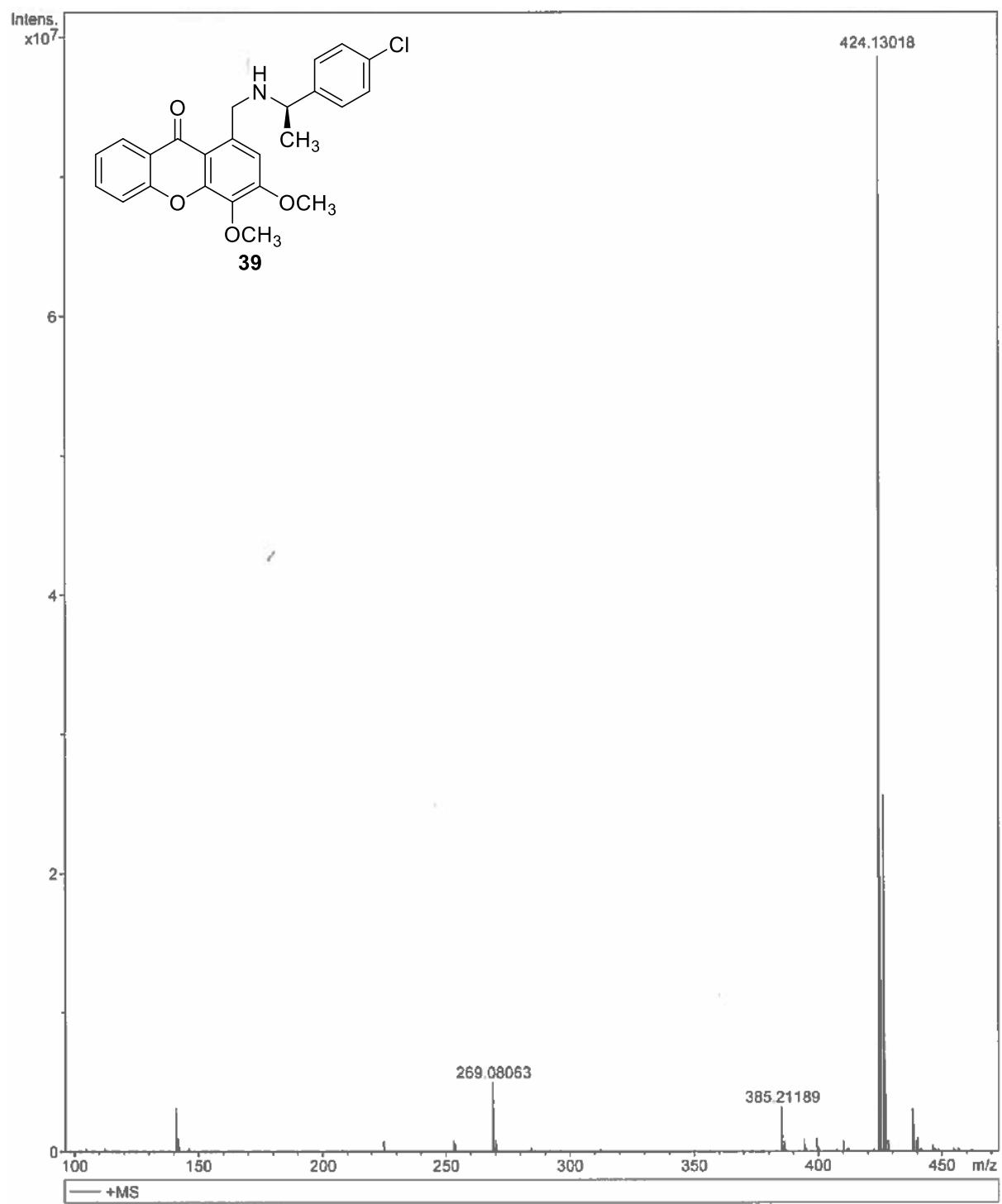


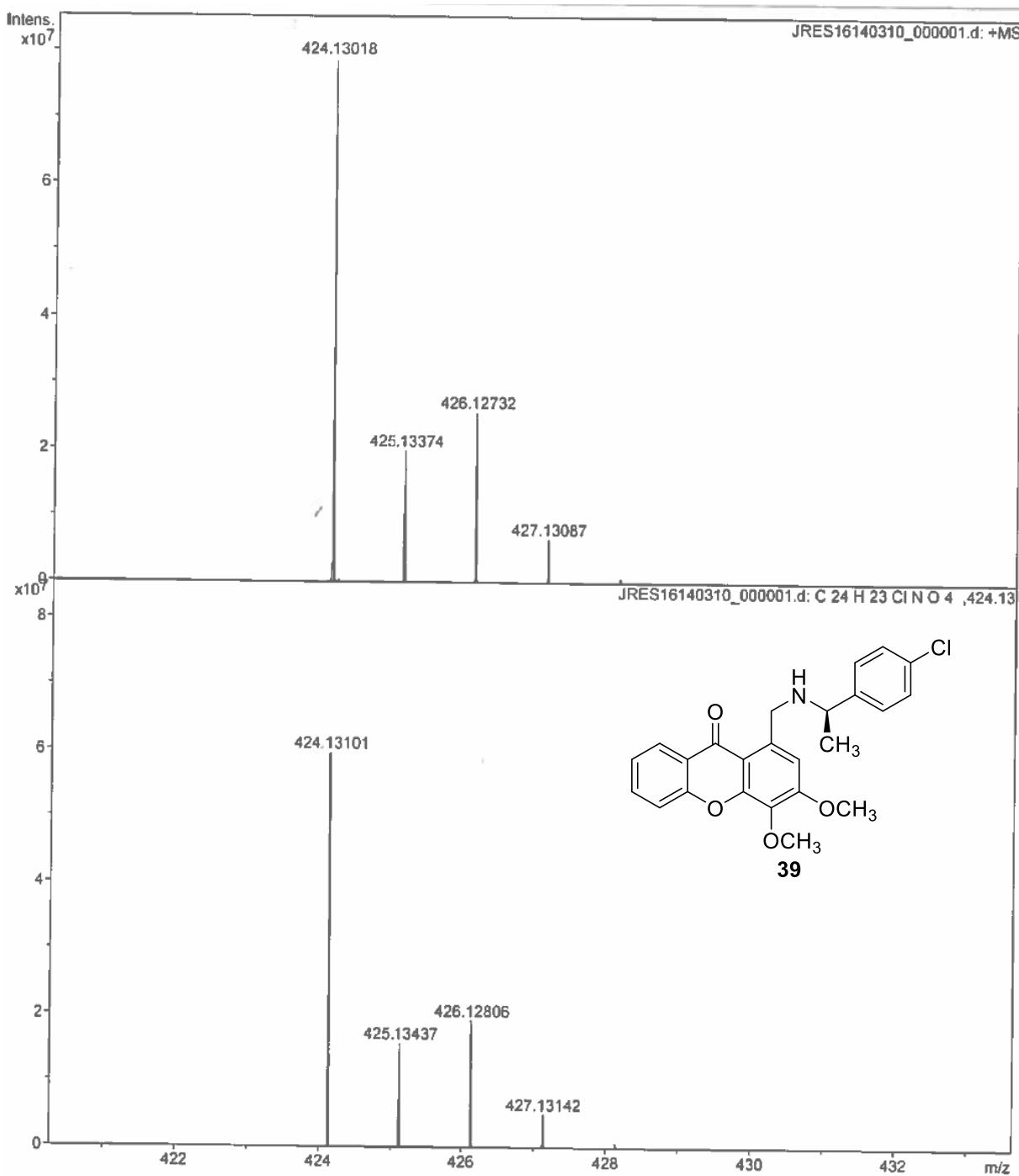
**Figure S12.** HRMS spectrum of 1-((4-fluorobenzyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (**37**).



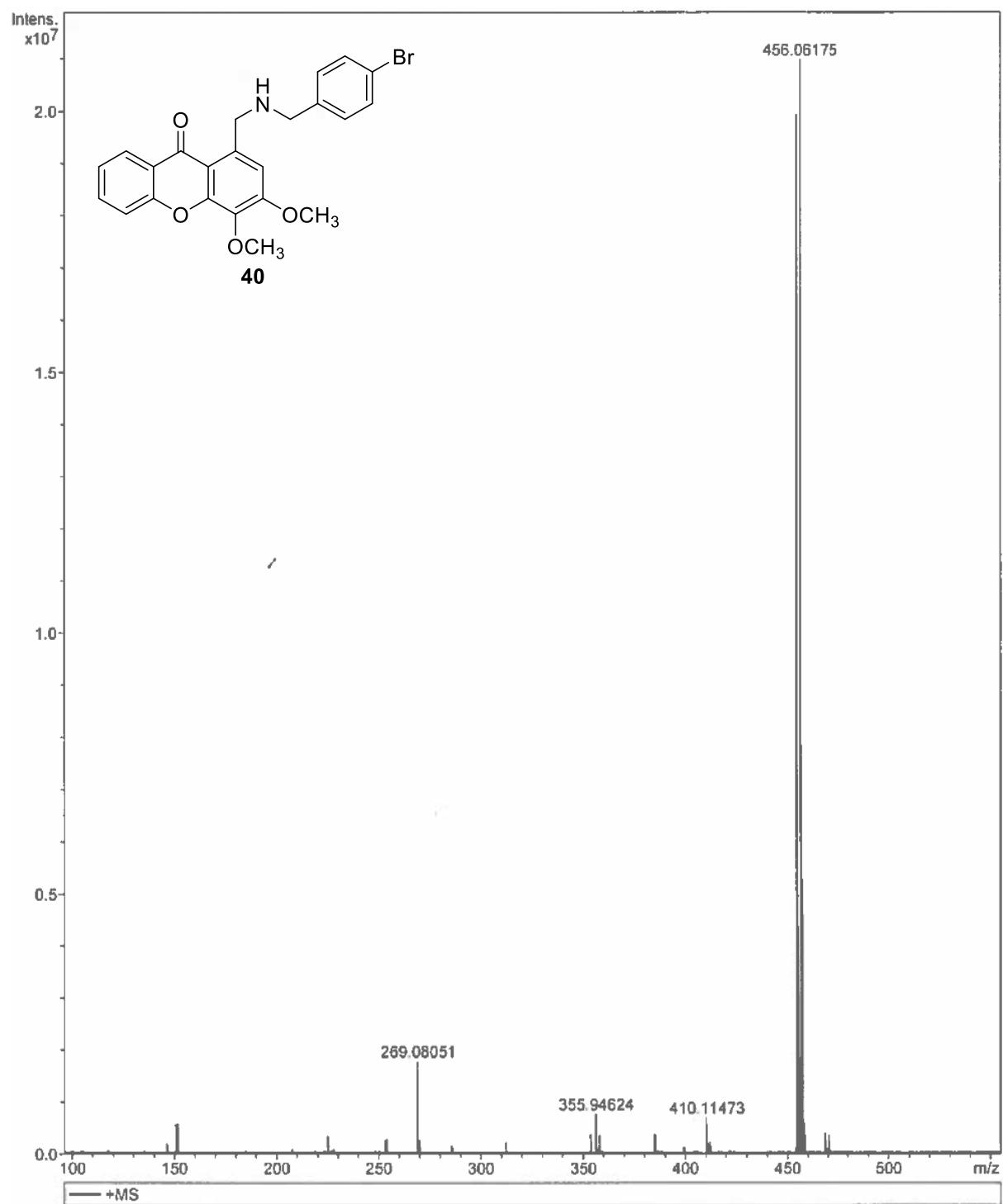


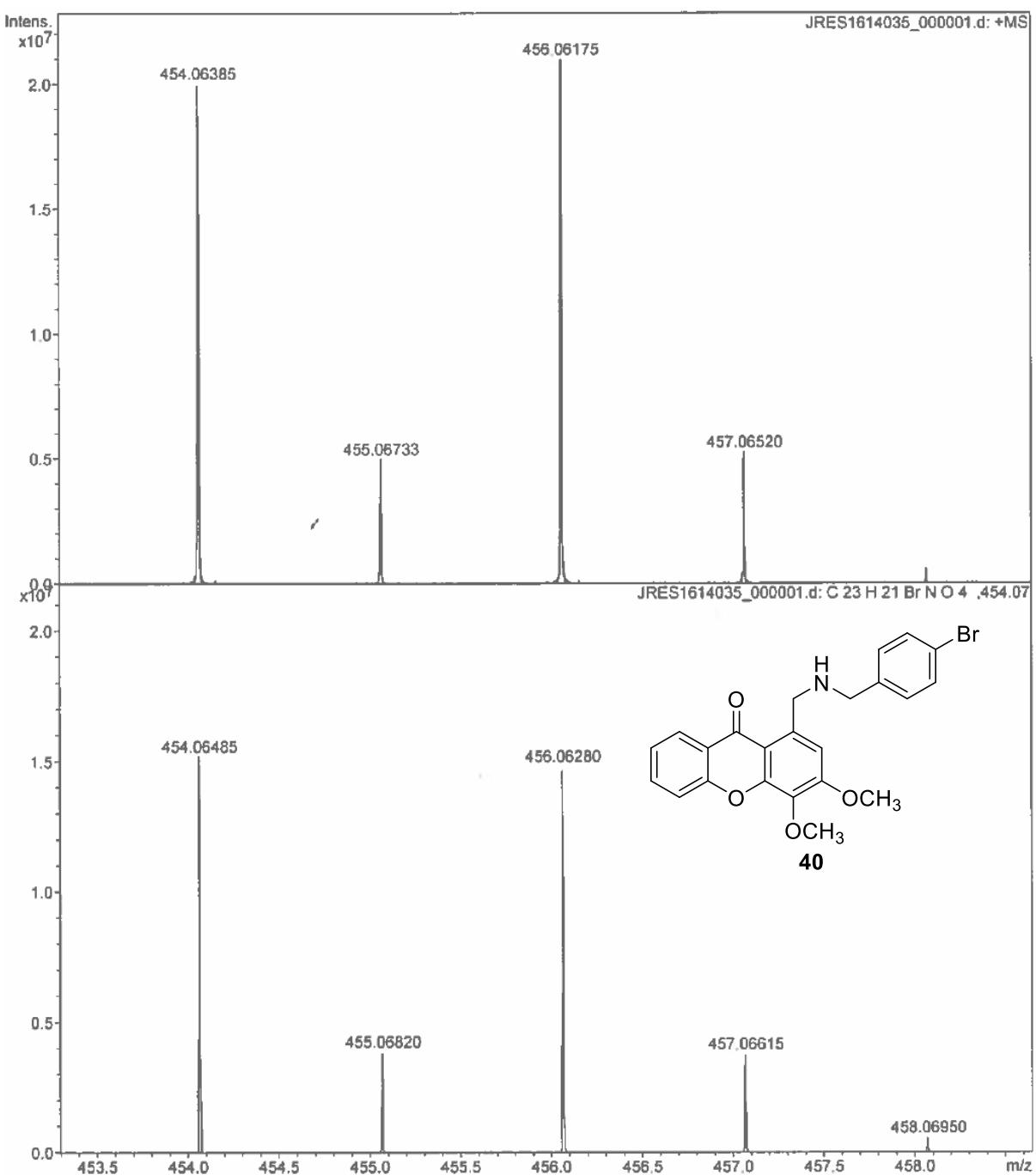
**Figure S13.** HRMS spectrum of 1-((4-chlorobenzyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**38**).





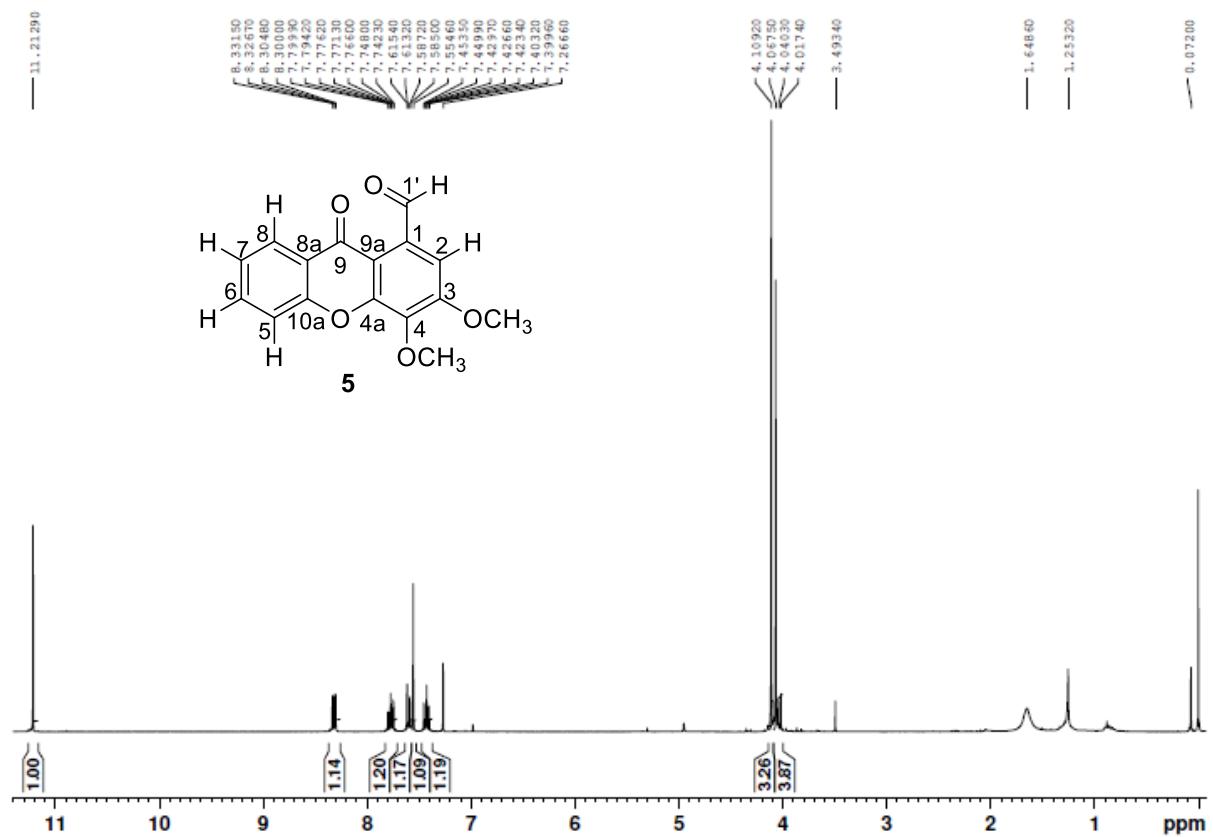
**Figure S14.** HRMS spectrum of (*R*)-1-(((1-(4-chlorophenyl)ethyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (39).



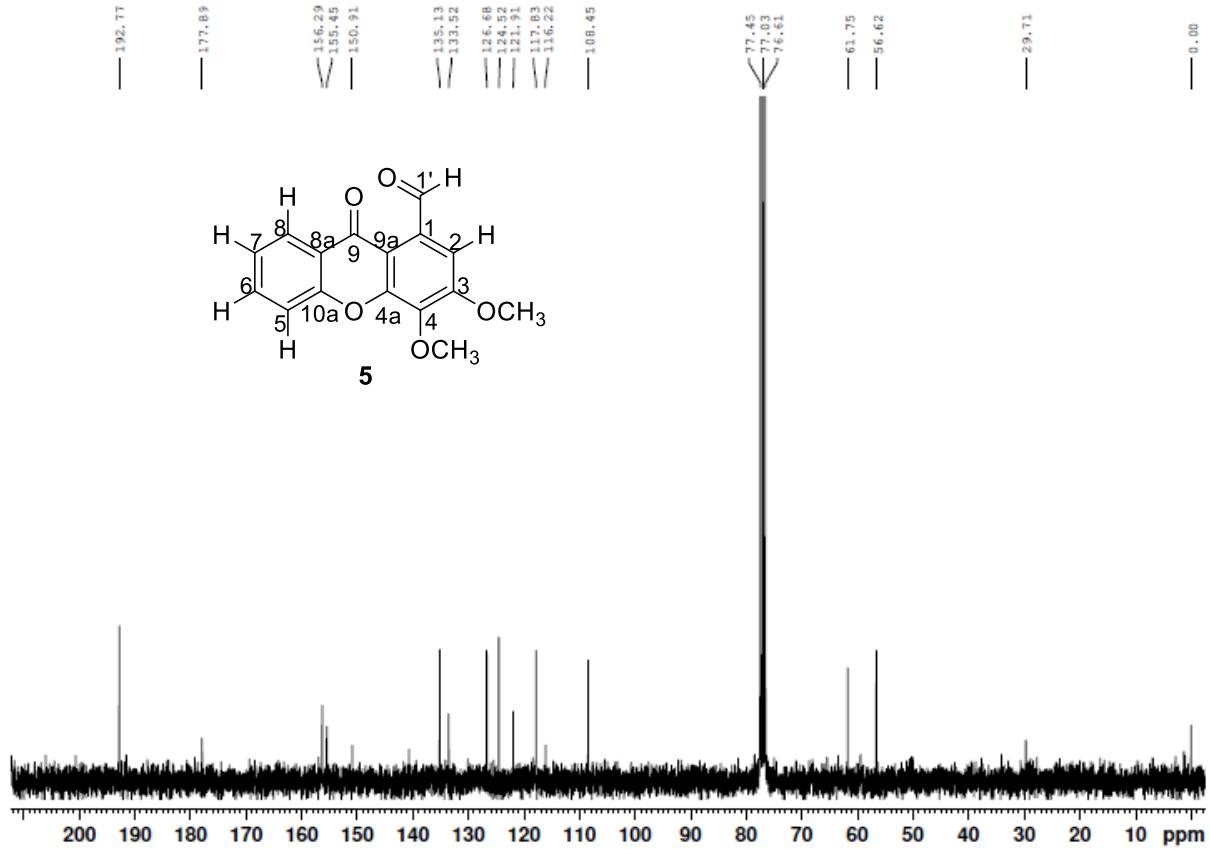


**Figure S15.** HRMS spectrum of 1-((4-bromobenzyl)amino)methyl-3,4-dimethoxy-9*H*-xanthen-9-one (**40**).

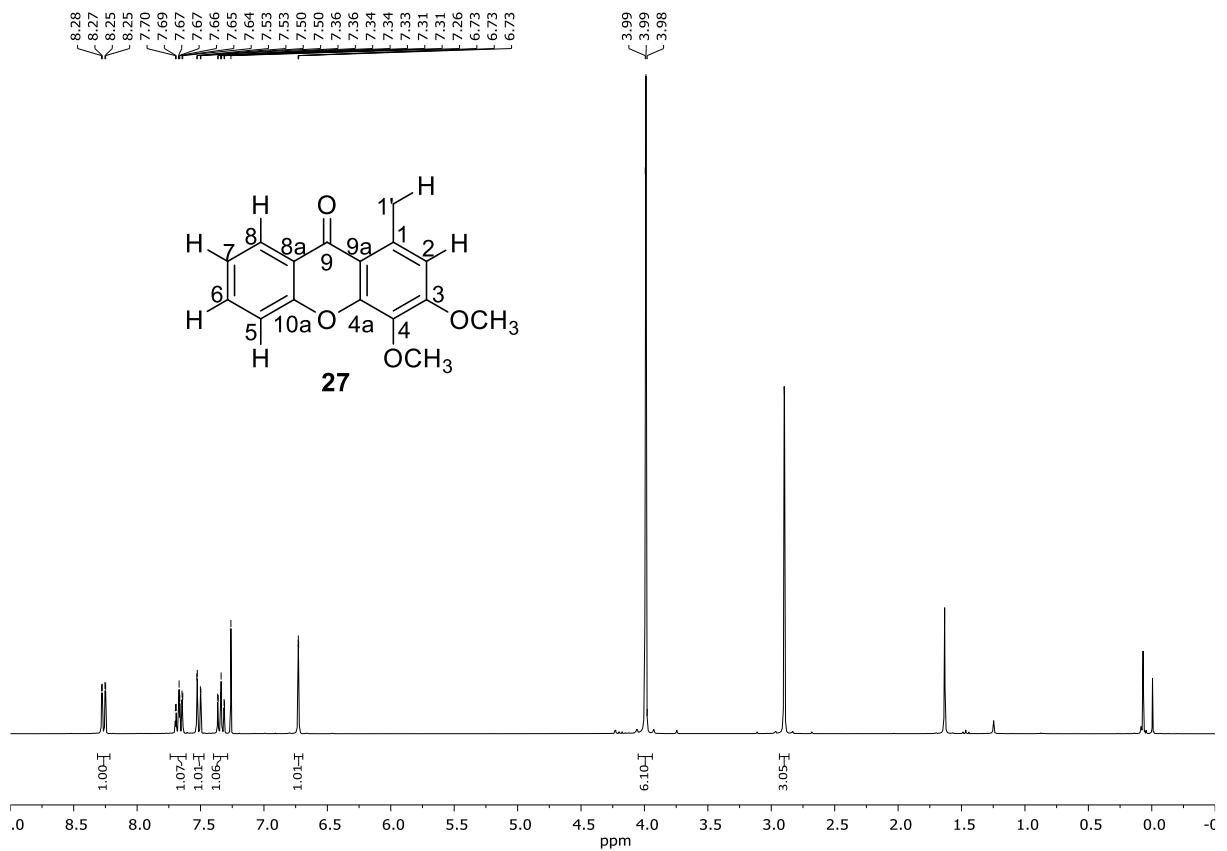
2.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of the described xanthone derivatives



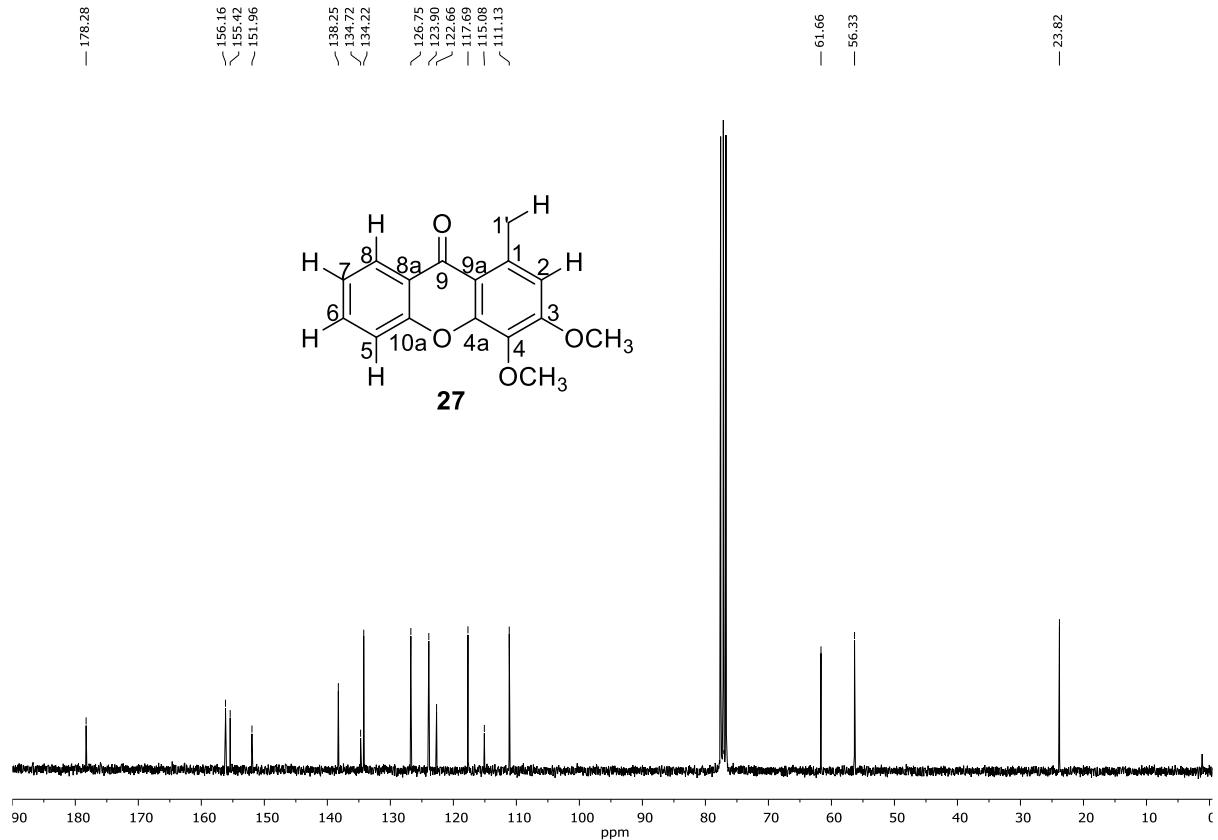
**Figure S16.**  $^1\text{H}$ -NMR spectrum of 3,4-dimethoxy-9-oxo-9*H*-xanthene-1-carbaldehyde (**5**).



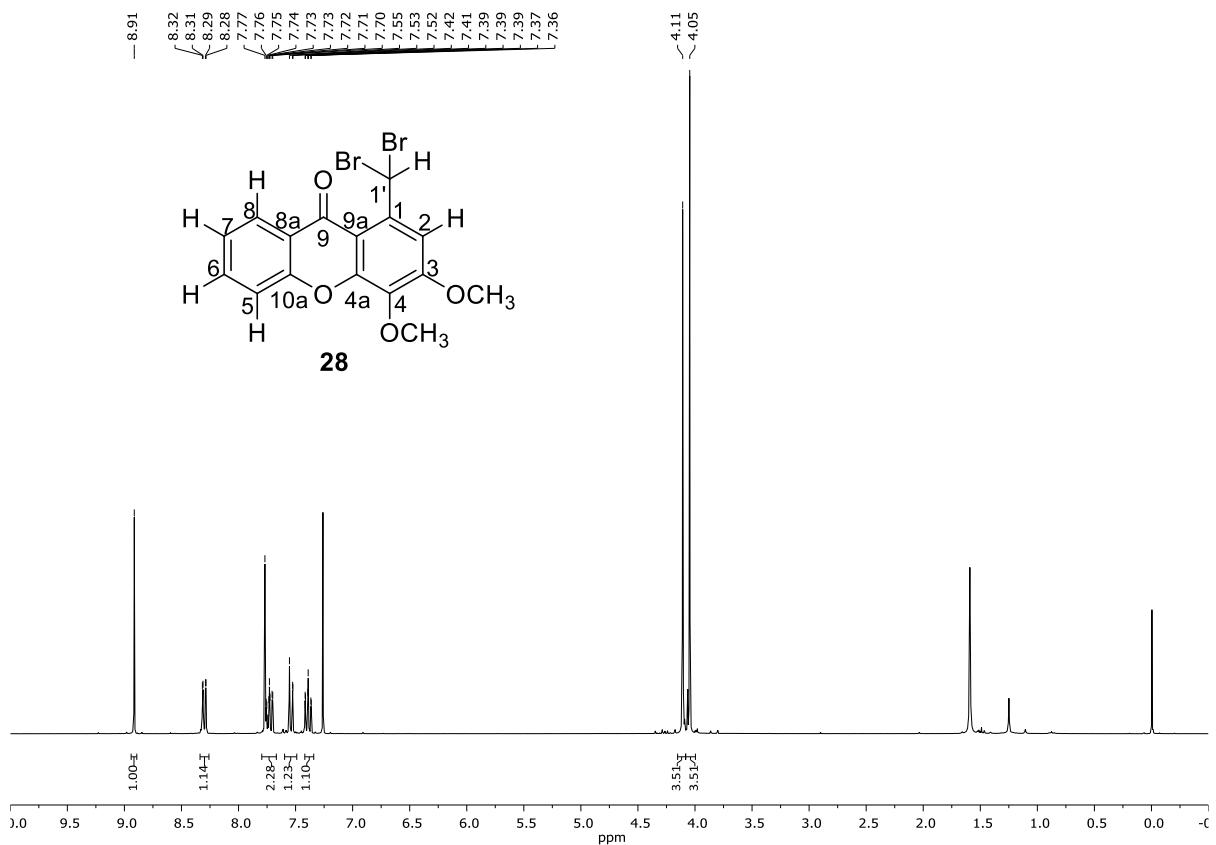
**Figure S17.**  $^{13}\text{C}$ -NMR spectrum of 3,4-dimethoxy-9-oxo-9*H*-xanthene-1-carbaldehyde (**5**).



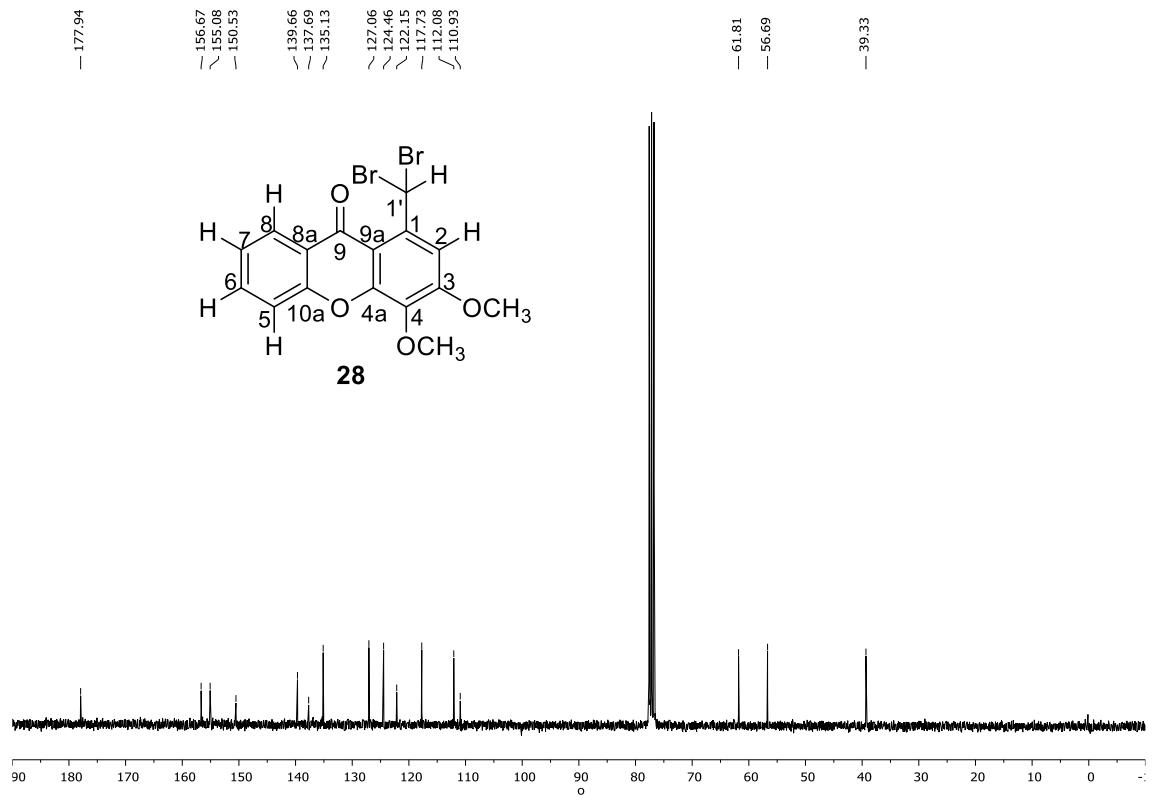
**Figure S18.** <sup>1</sup>H-NMR spectrum of 3,4-dimethoxy-1-methyl-9*H*-xanthen-9-one (**27**).



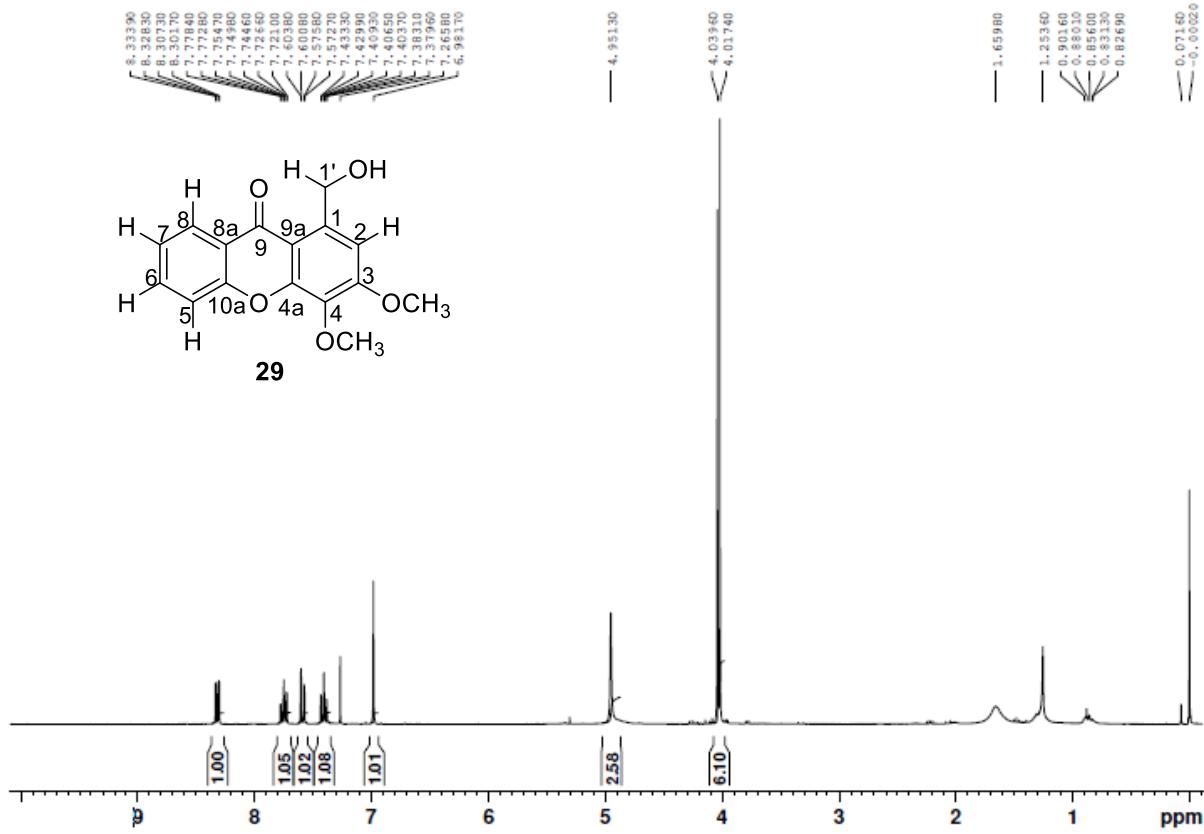
**Figure S19.** <sup>13</sup>C-NMR spectrum of 3,4-dimethoxy-1-methyl-9H-xanthen-9-one (27).



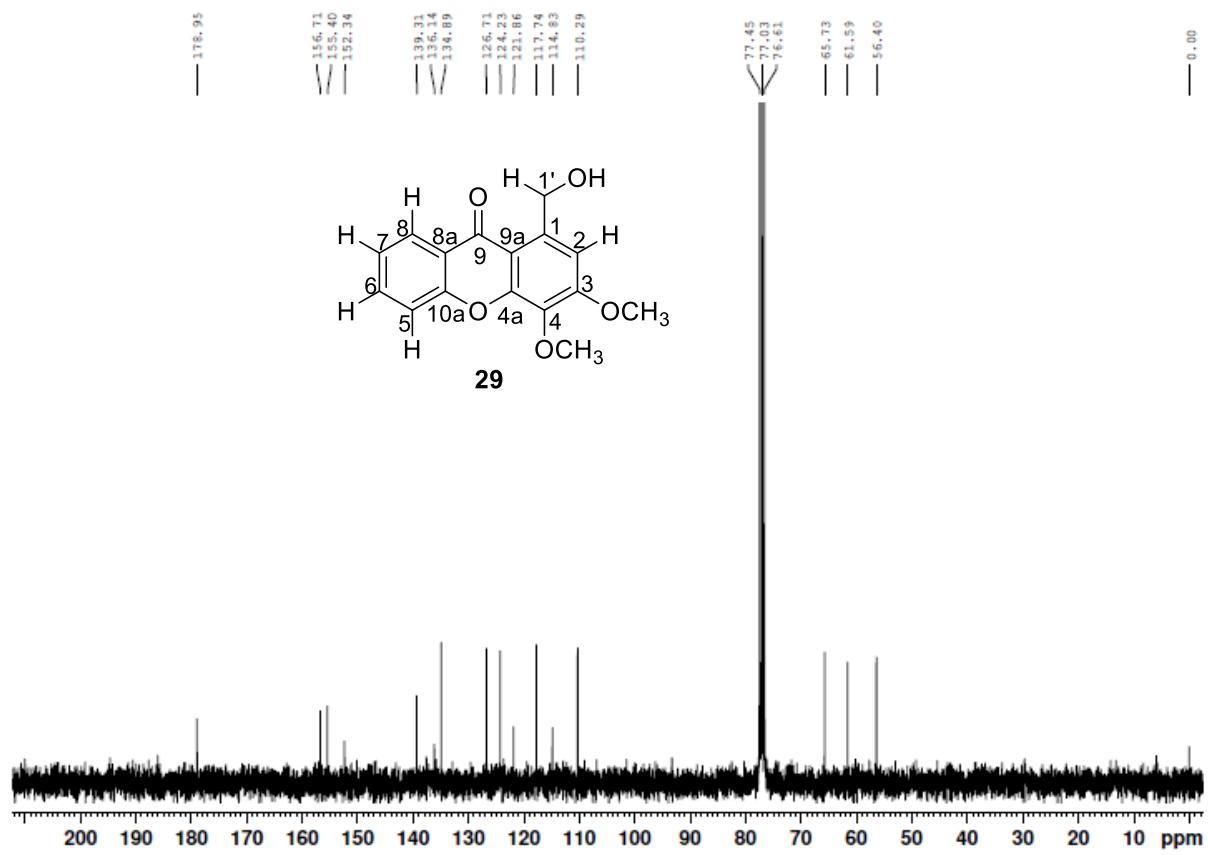
**Figure S20.**  $^1\text{H}$ -NMR spectrum of 1-(dibromomethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**28**).



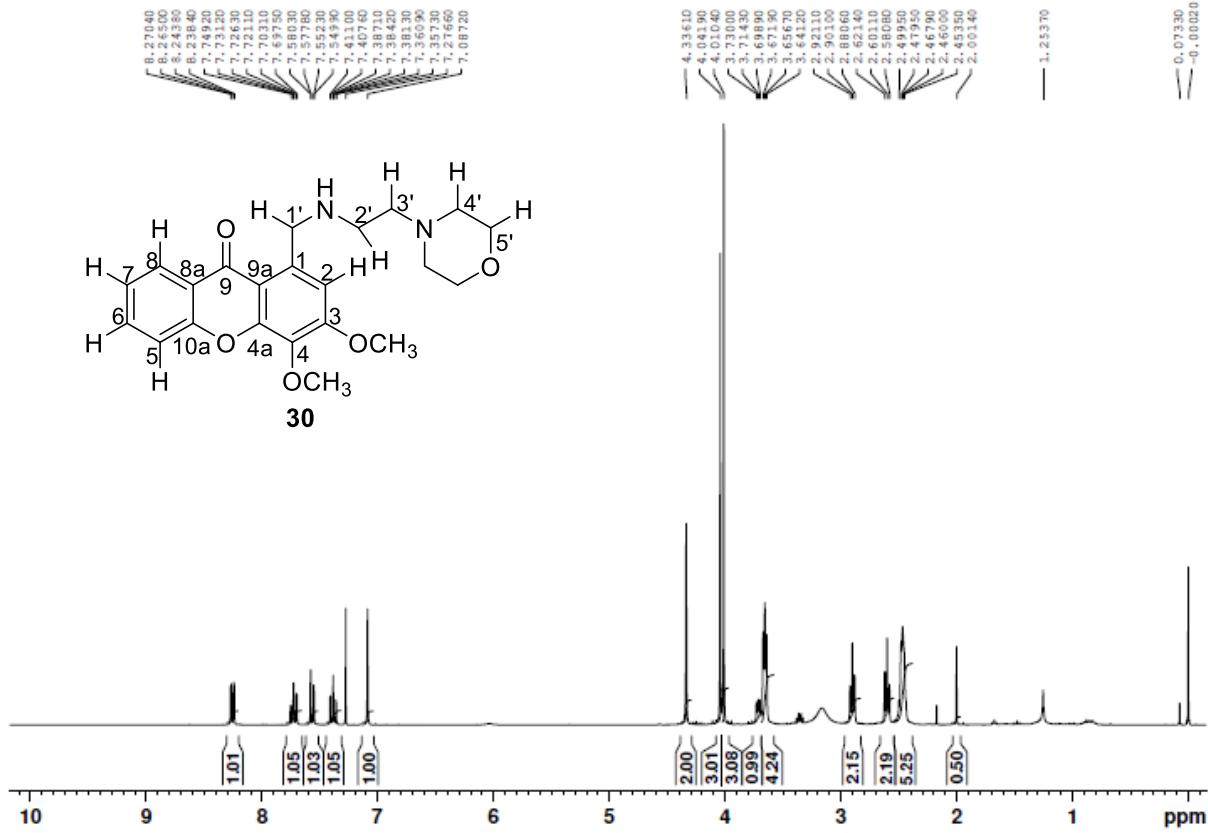
**Figure S21.**  $^{13}\text{C}$ -NMR spectrum of 1-(dibromomethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**28**).



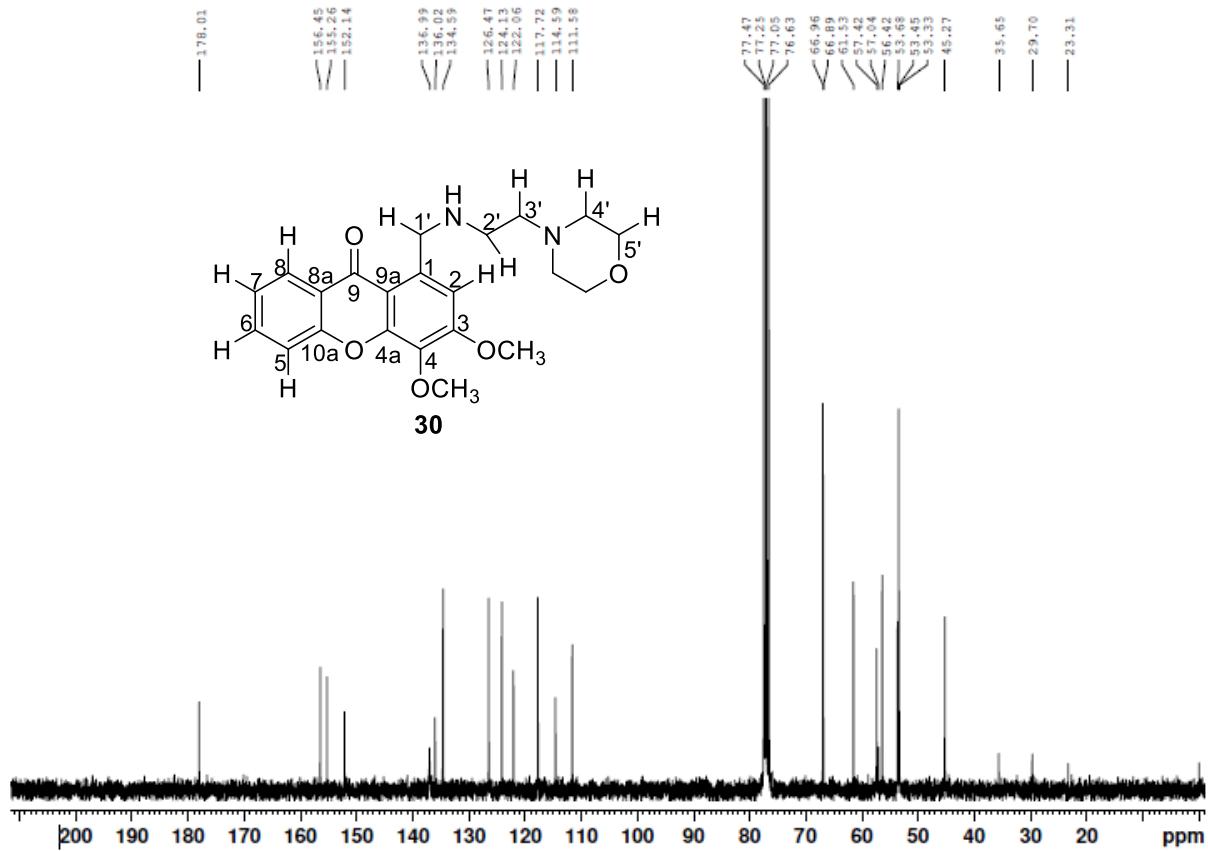
**Figure S22.**  $^1\text{H}$ -NMR spectrum of 1-(hydroxymethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**29**).



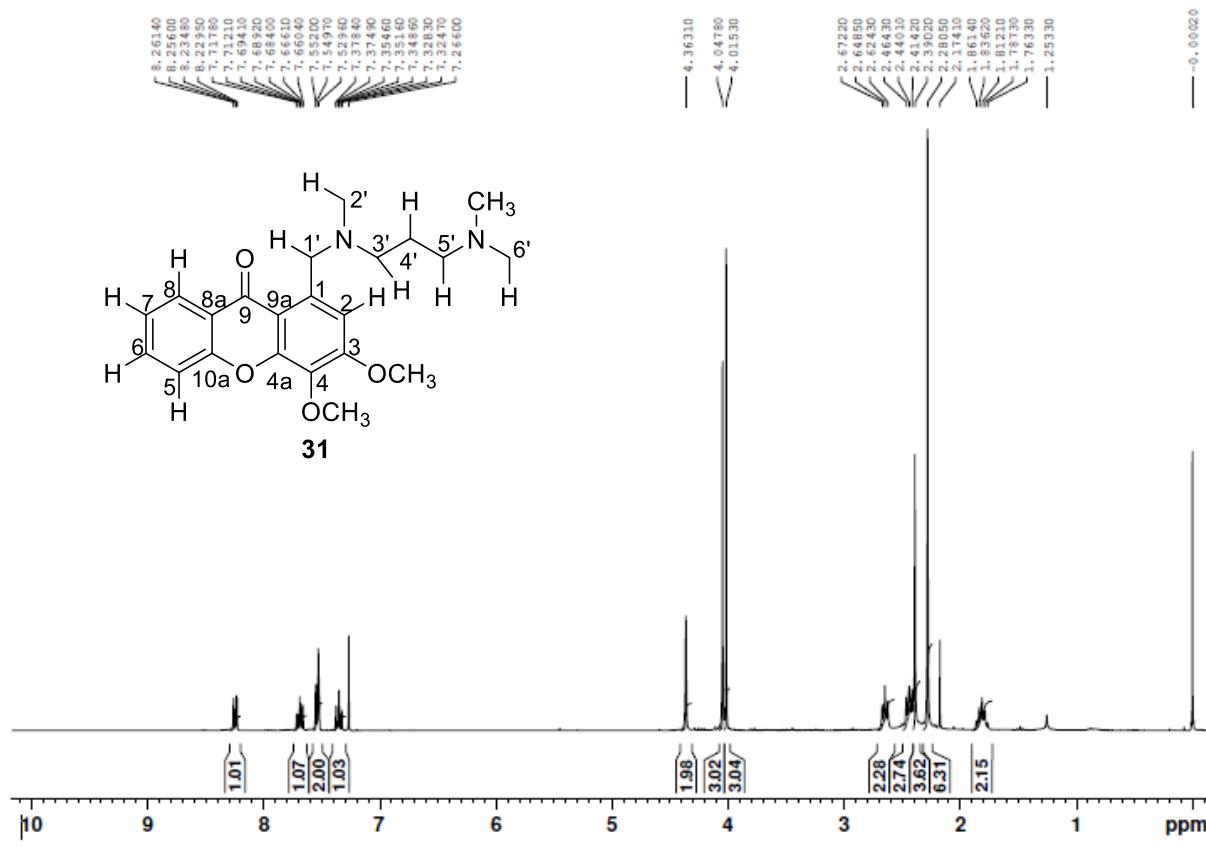
**Figure S23.**  $^{13}\text{C}$ -NMR spectrum of 1-(hydroxymethyl)-3,4-dimethoxy-9*H*-xanthen-9-one (29).



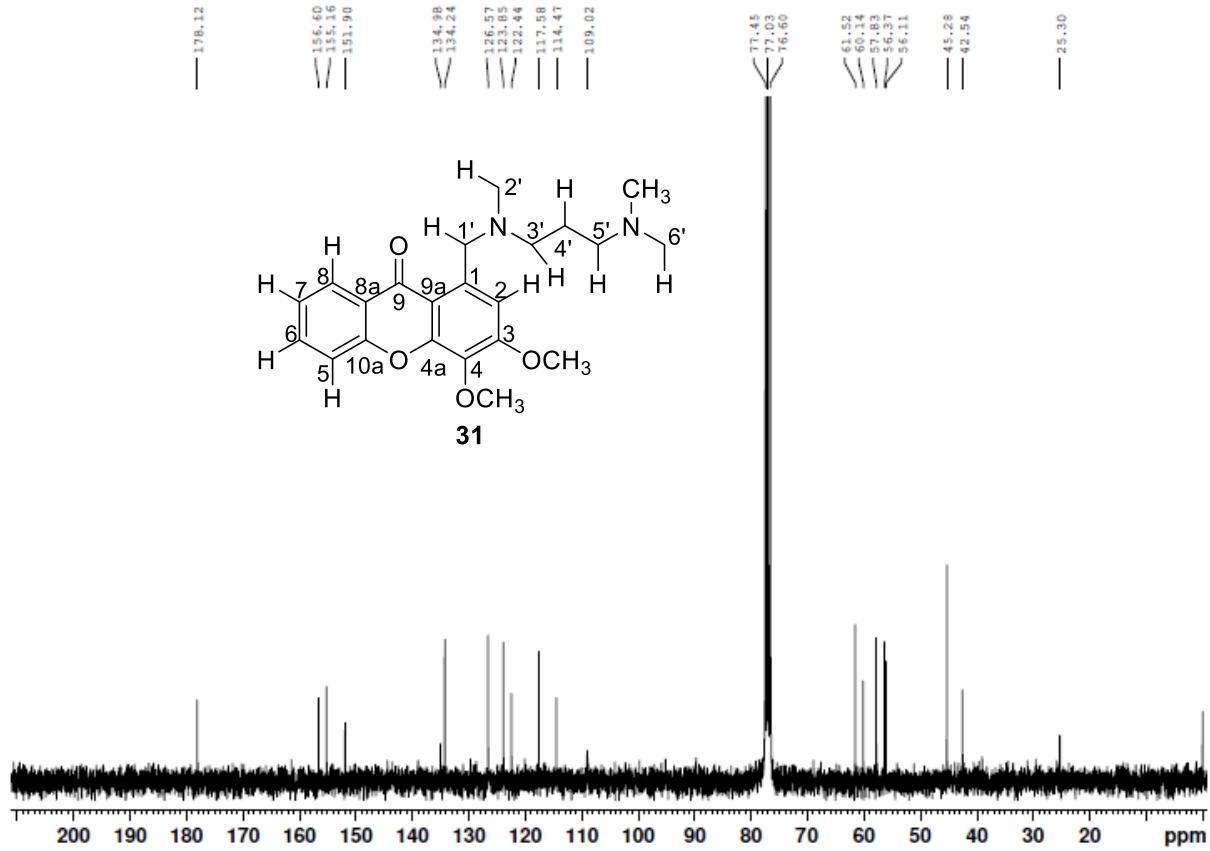
**Figure S24.** <sup>1</sup>H-NMR spectrum of 3,4-dimethoxy-1-((2-morpholinoethyl)amino)methyl)-9*H*-xanthen-9-one (30).



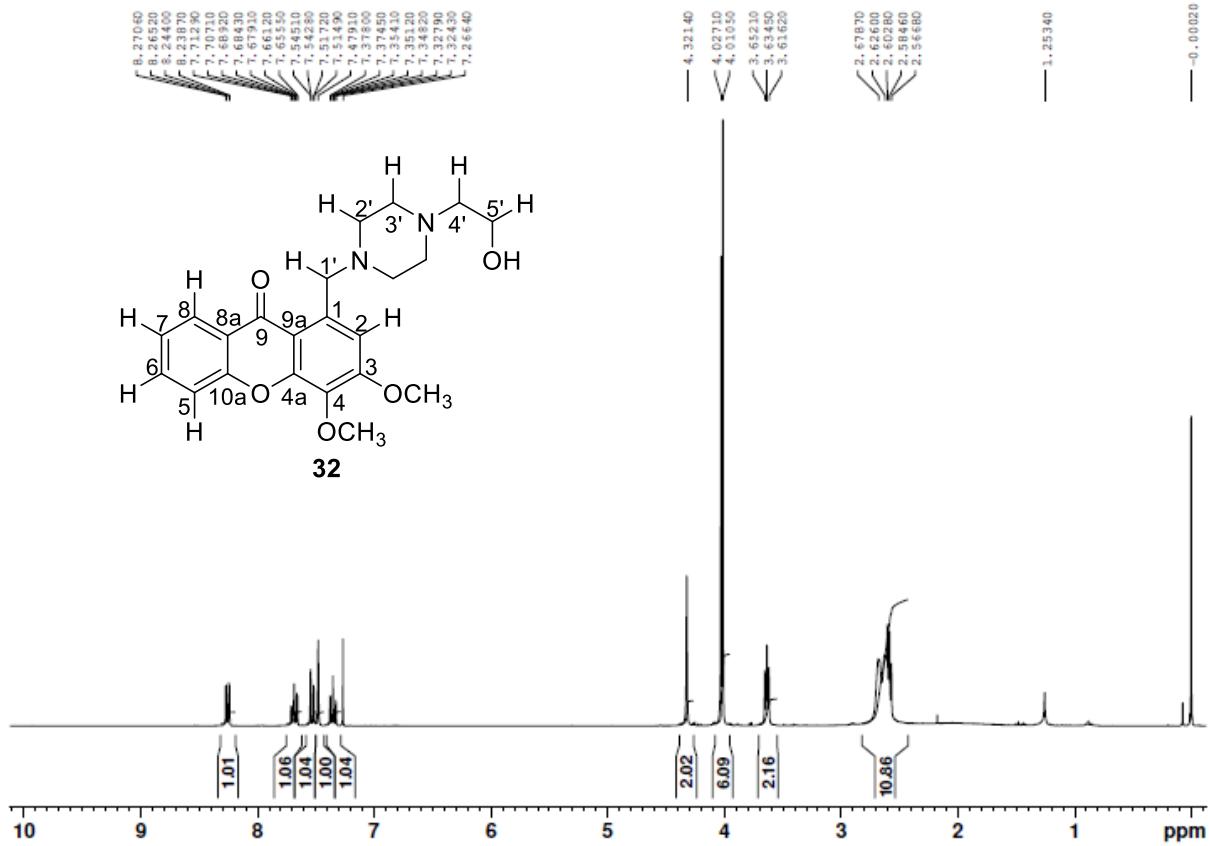
**Figure S25.**  $^{13}\text{C}$ -NMR spectrum of 3,4-dimethoxy-1-((2-morpholinoethyl)amino)methyl-9*H*-xanthen-9-one (30).



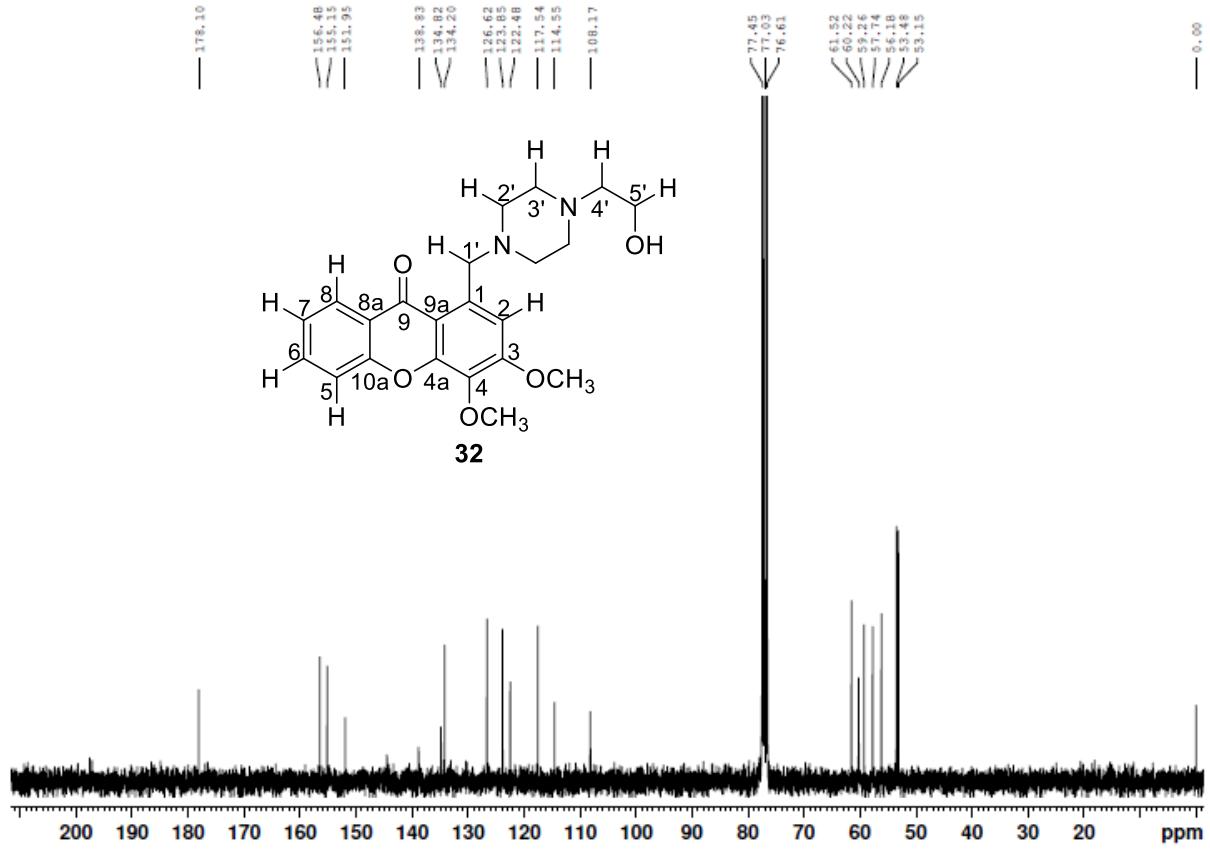
**Figure S26.**  $^1\text{H}$ -NMR spectrum of 1-((3-(dimethylamino)propyl)(methyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**31**).



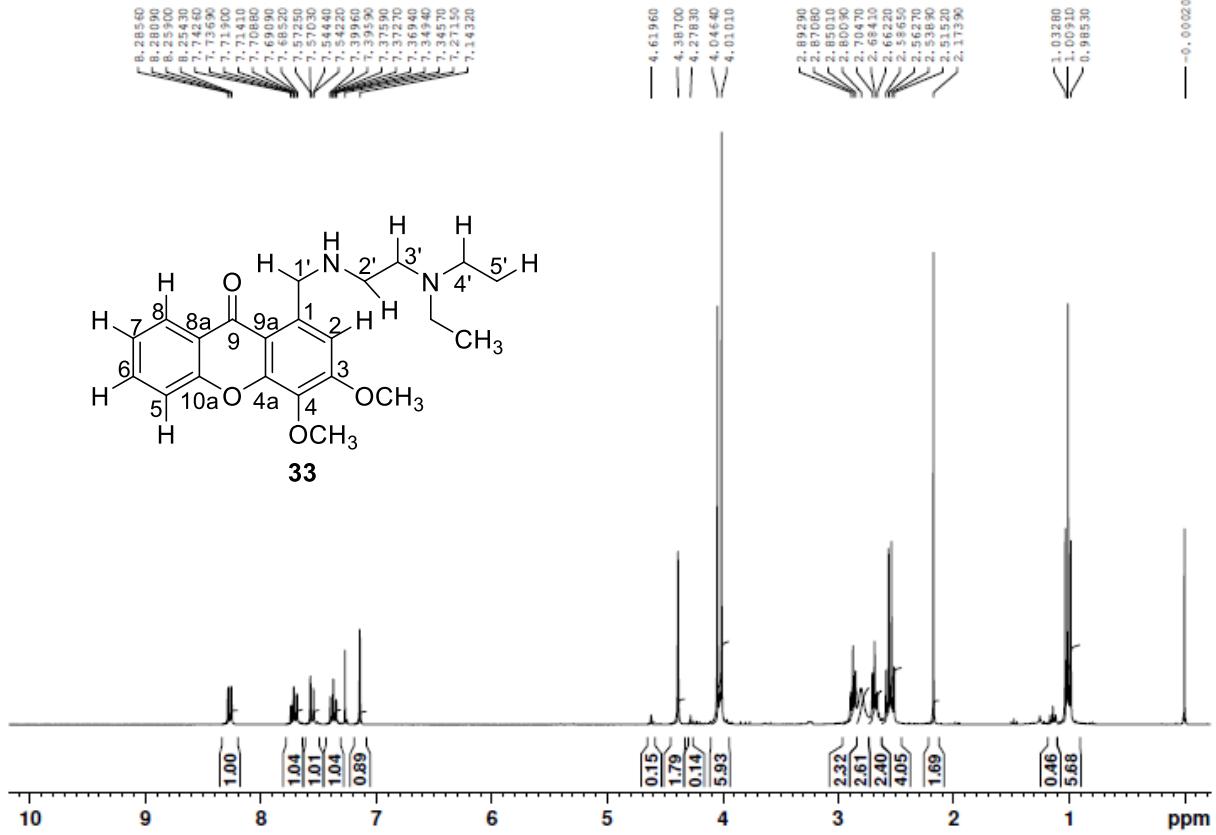
**Figure S27.** <sup>13</sup>C-NMR spectrum of 1-((3-(dimethylamino)propyl)(methyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (31).



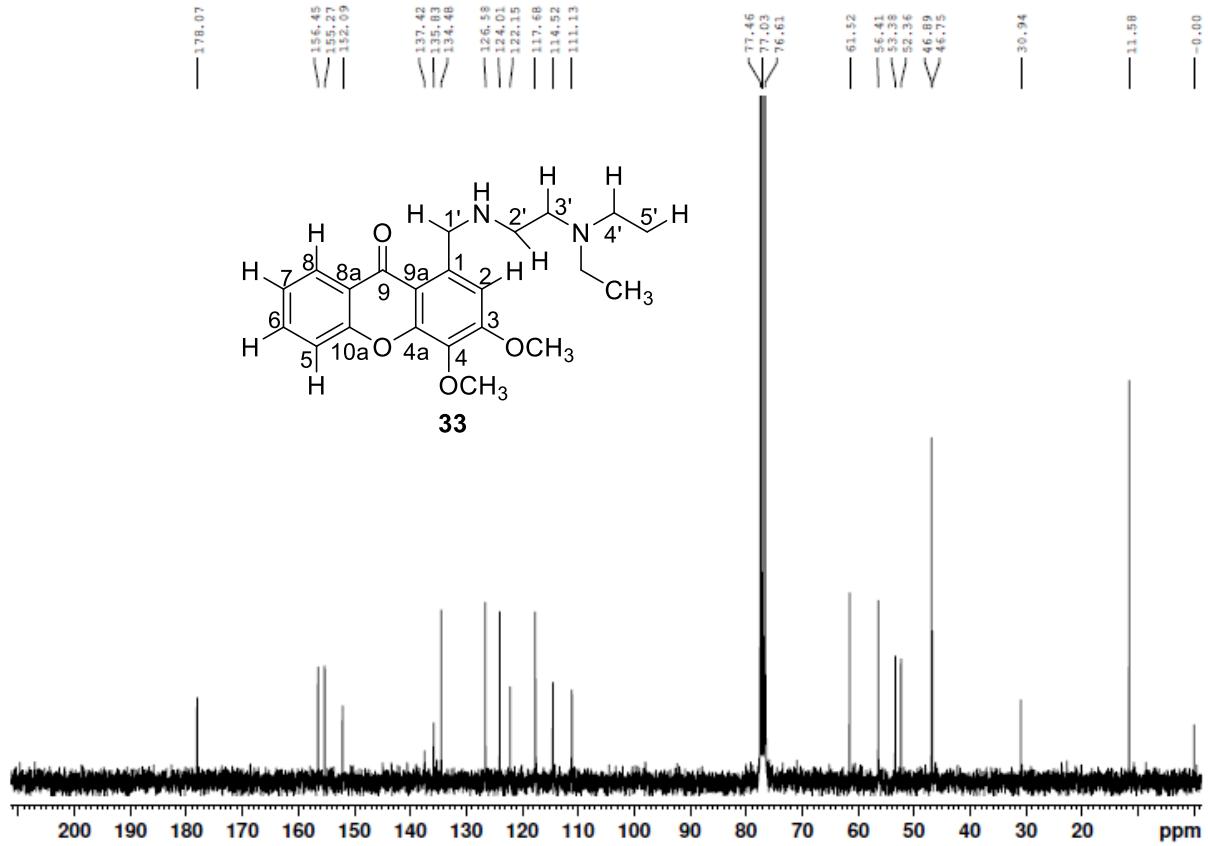
**Figure S28.** <sup>1</sup>H-NMR spectrum of 1-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)-3,4-dimethoxy-9H-xanthen-9-one (32).



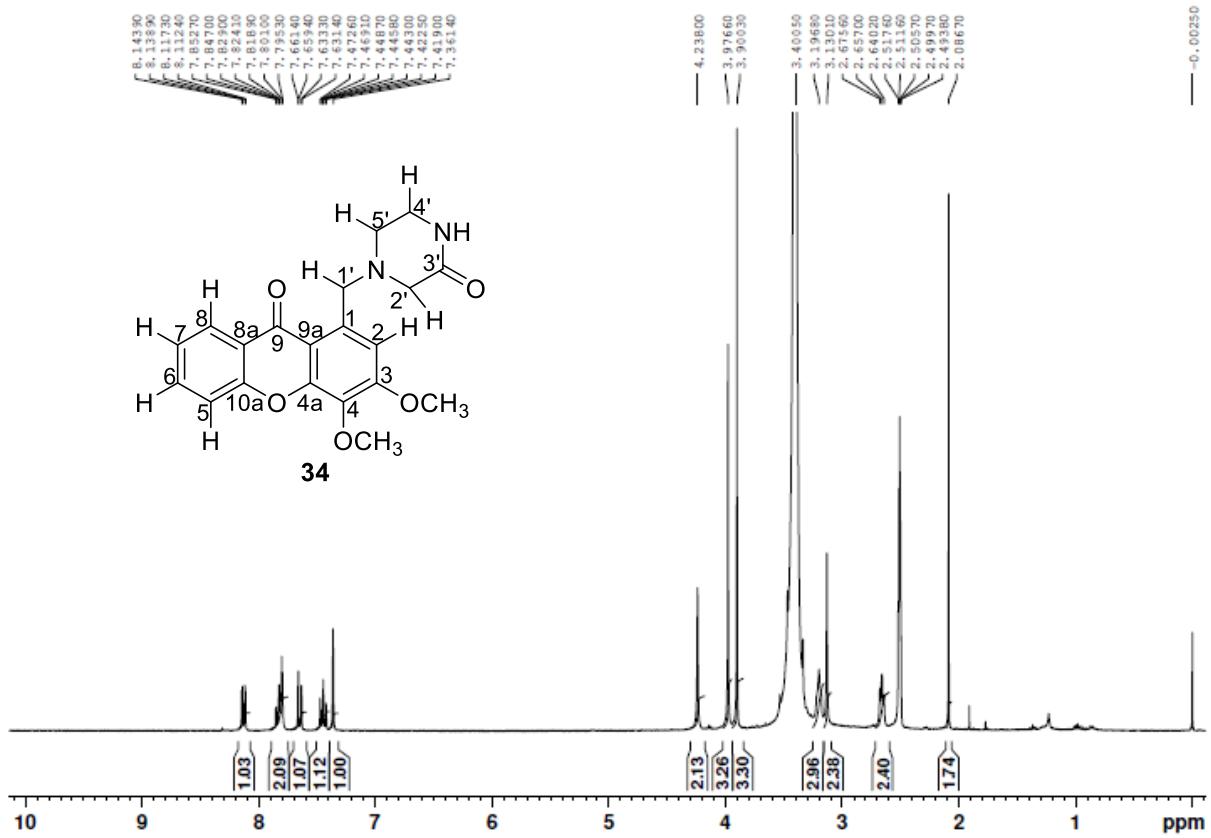
**Figure S29.**  $^{13}\text{C}$ -NMR spectrum of 1-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (32).



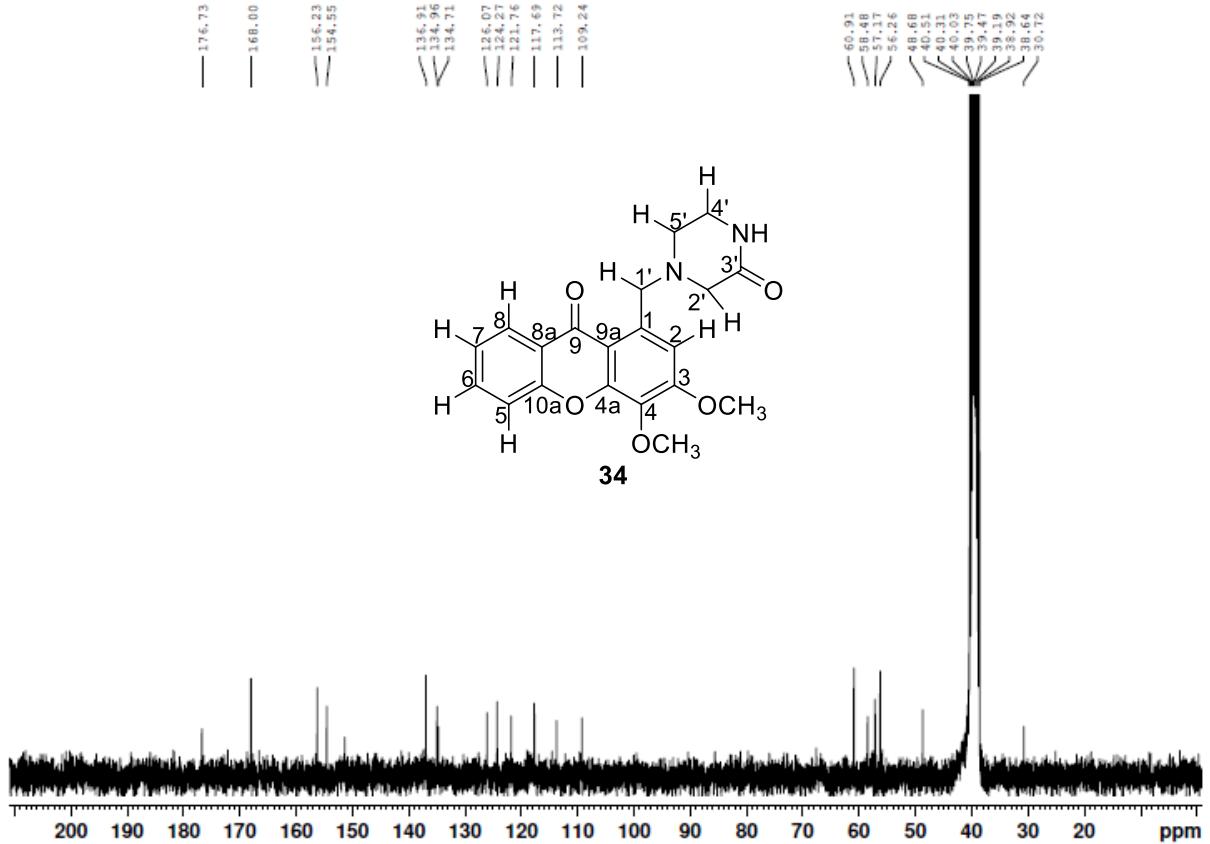
**Figure S30.**  $^1\text{H}$ -NMR spectrum of 1-((2-(diethylamino)ethyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (**33**).



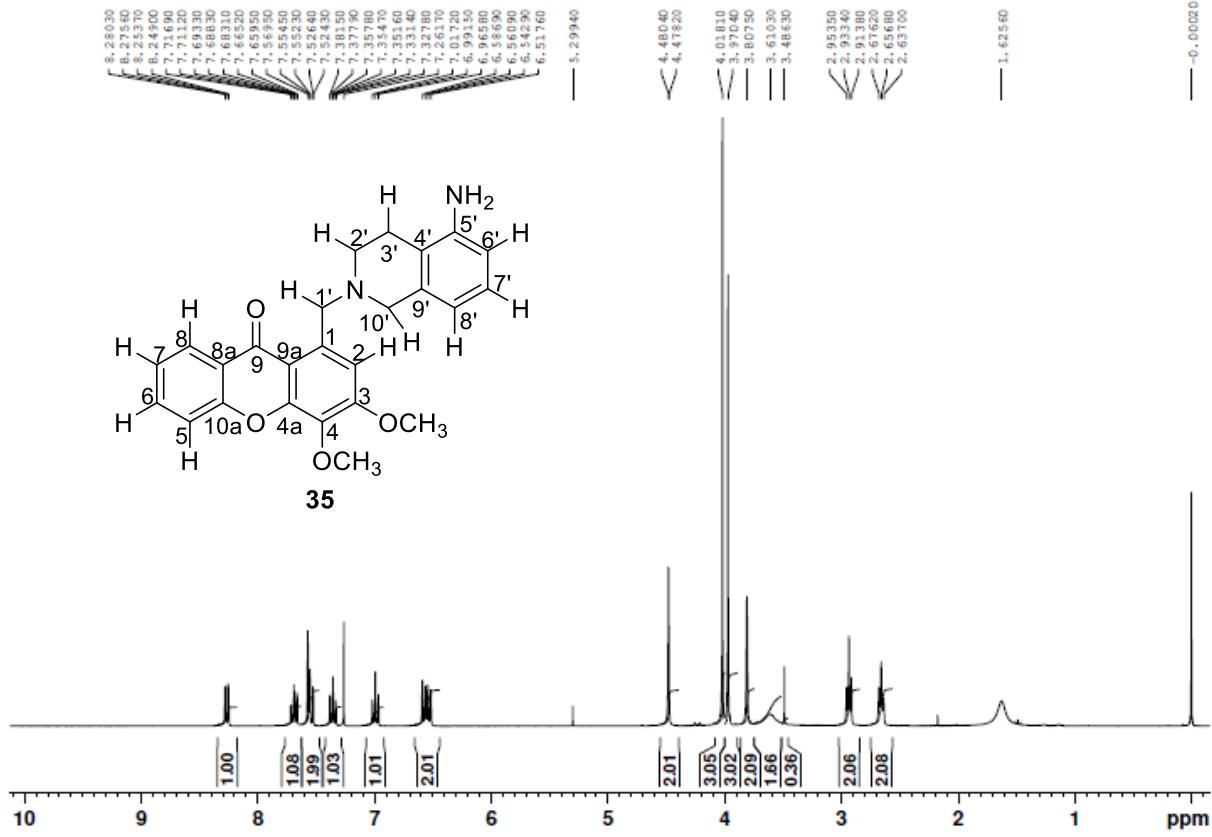
**Figure S31.**  $^{13}\text{C}$ -NMR spectrum of 1-(((2-(diethylamino)ethyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (33).



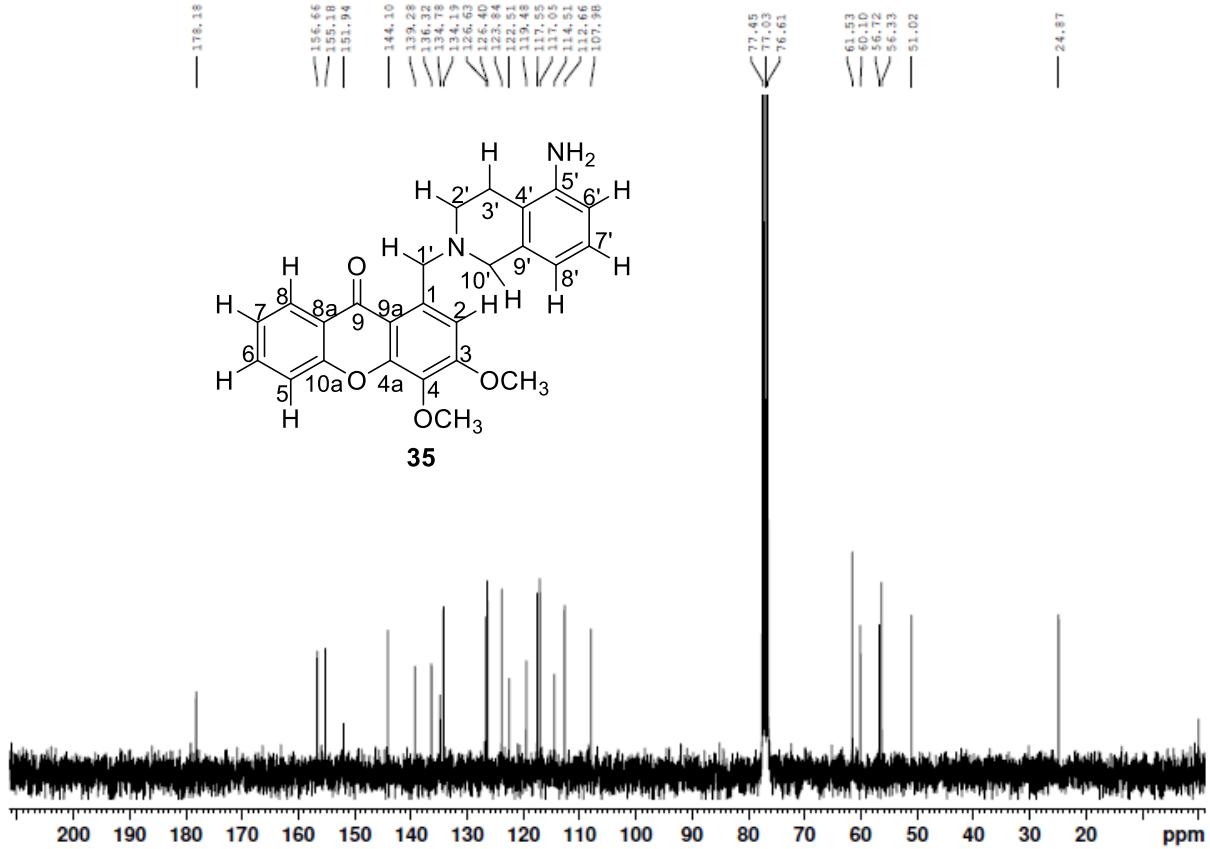
**Figure S32.** <sup>1</sup>H-NMR spectrum of 4-((3,4-dimethoxy-9-oxo-9*H*-xanthen-1-yl)methyl)piperazin-2-one (34).



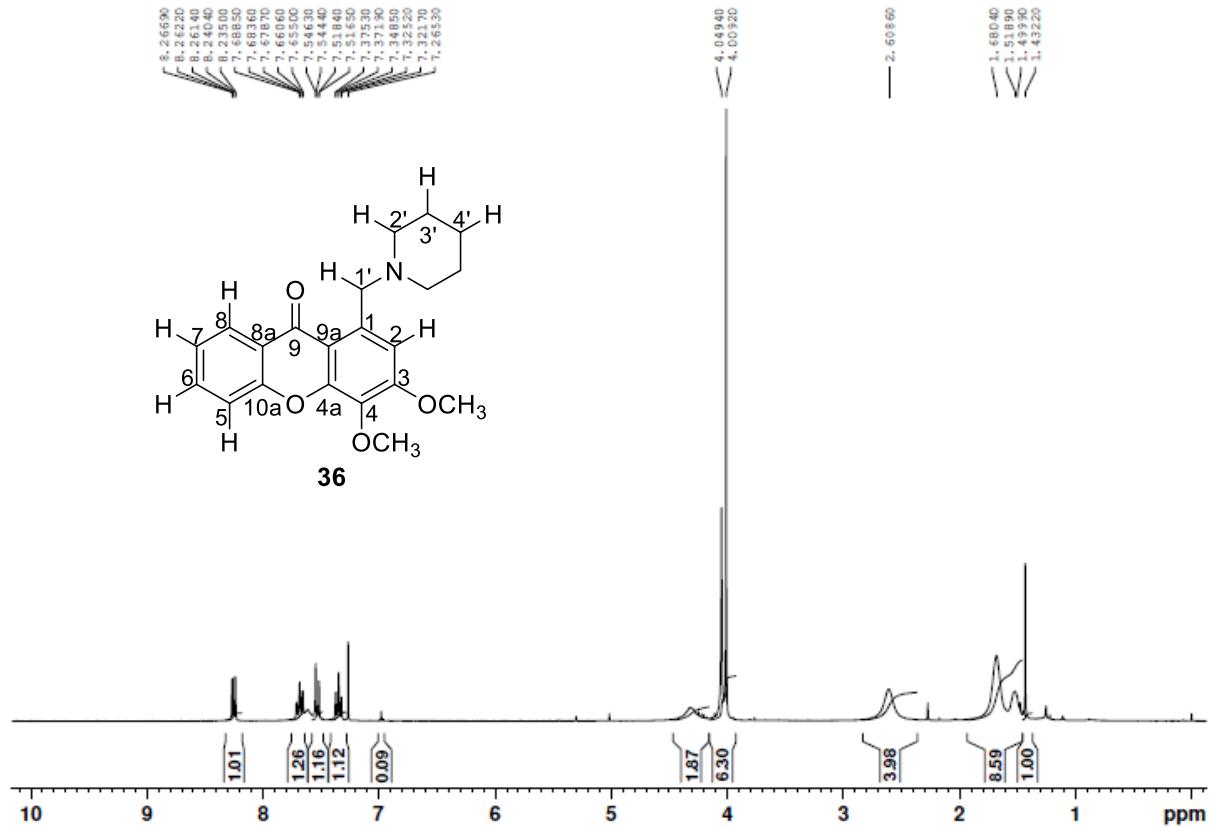
**Figure S33.**  $^{13}\text{C}$ -NMR spectrum of 4-((3,4-dimethoxy-9-oxo-9*H*-xanthen-1-yl)methyl)piperazin-2-one (34).



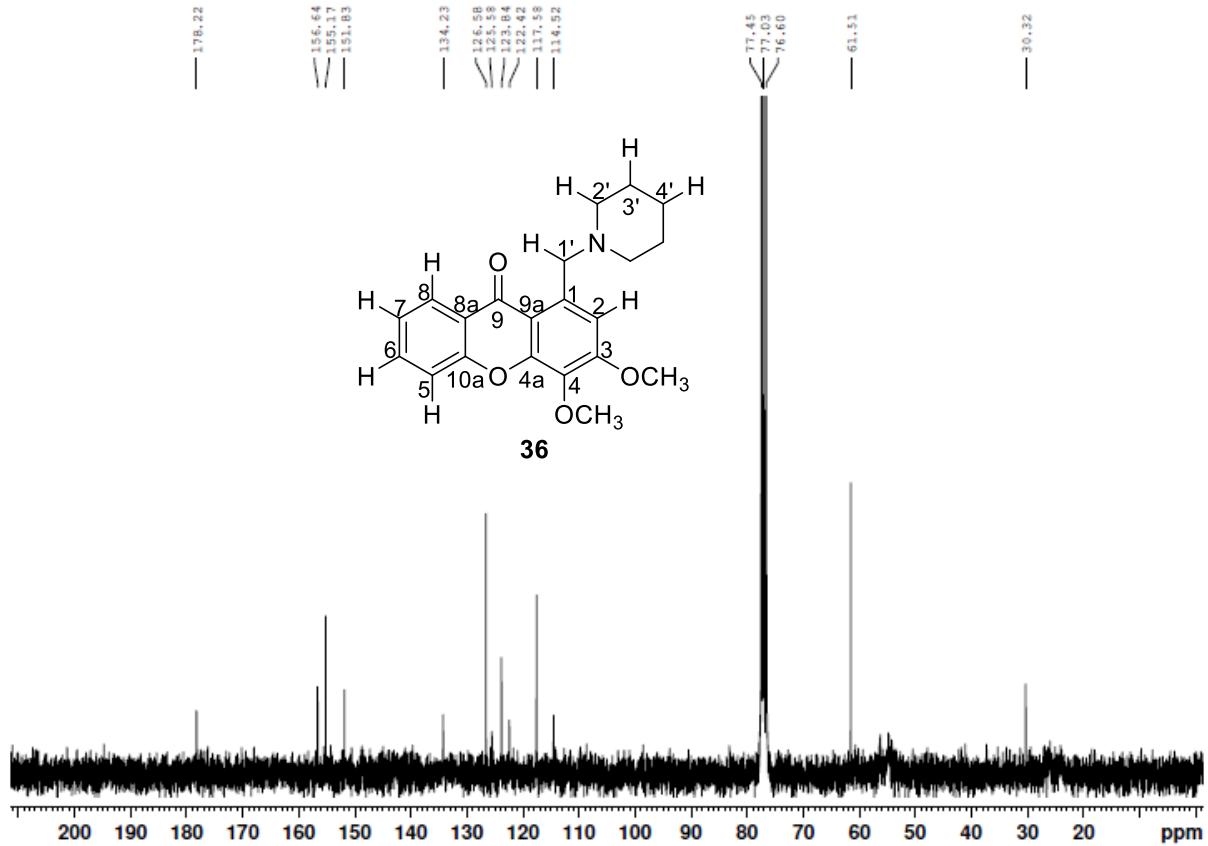
**Figure S34.** <sup>1</sup>H-NMR spectrum of 1-((5-amino-3,4-dihydroisoquinolin-2(1*H*)-yl)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (35).



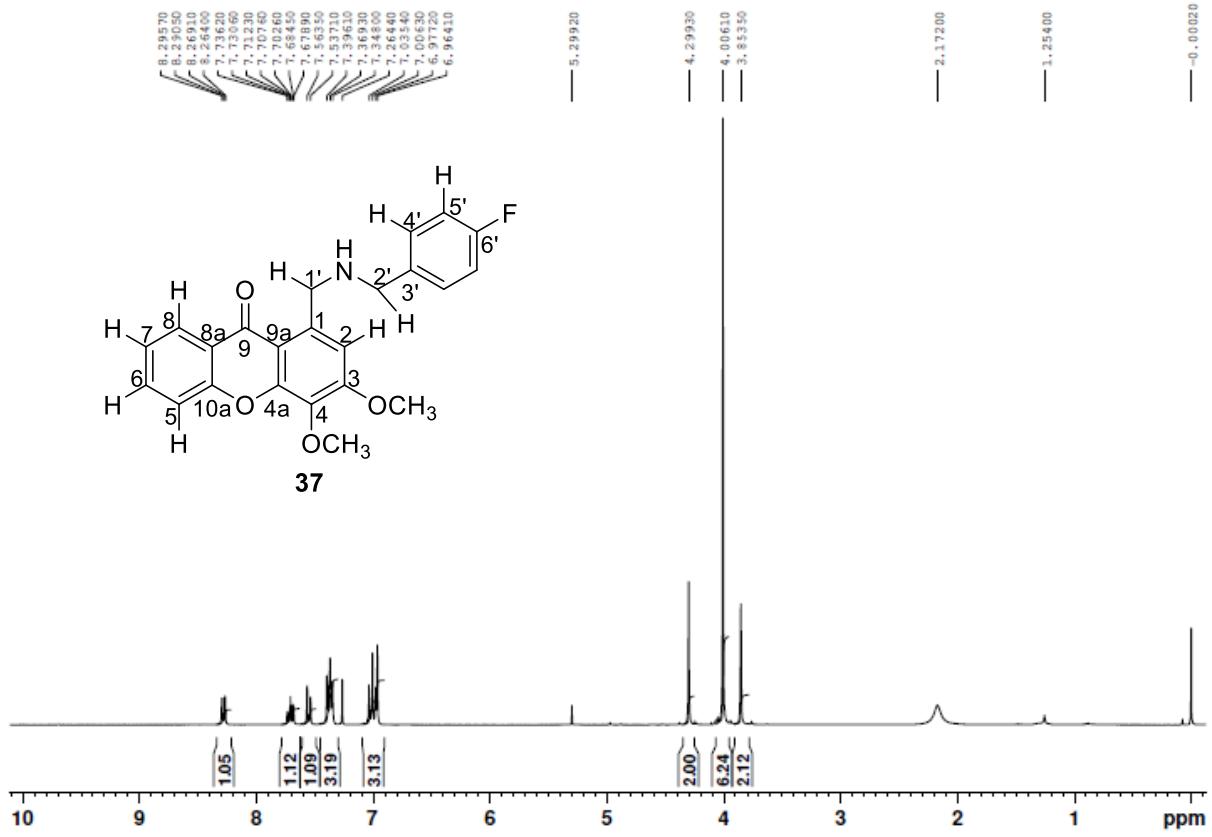
**Figure S35.**  $^{13}\text{C}$ -NMR spectrum of 1-((5-amino-3,4-dihydroisoquinolin-2(1*H*)-yl)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (35).



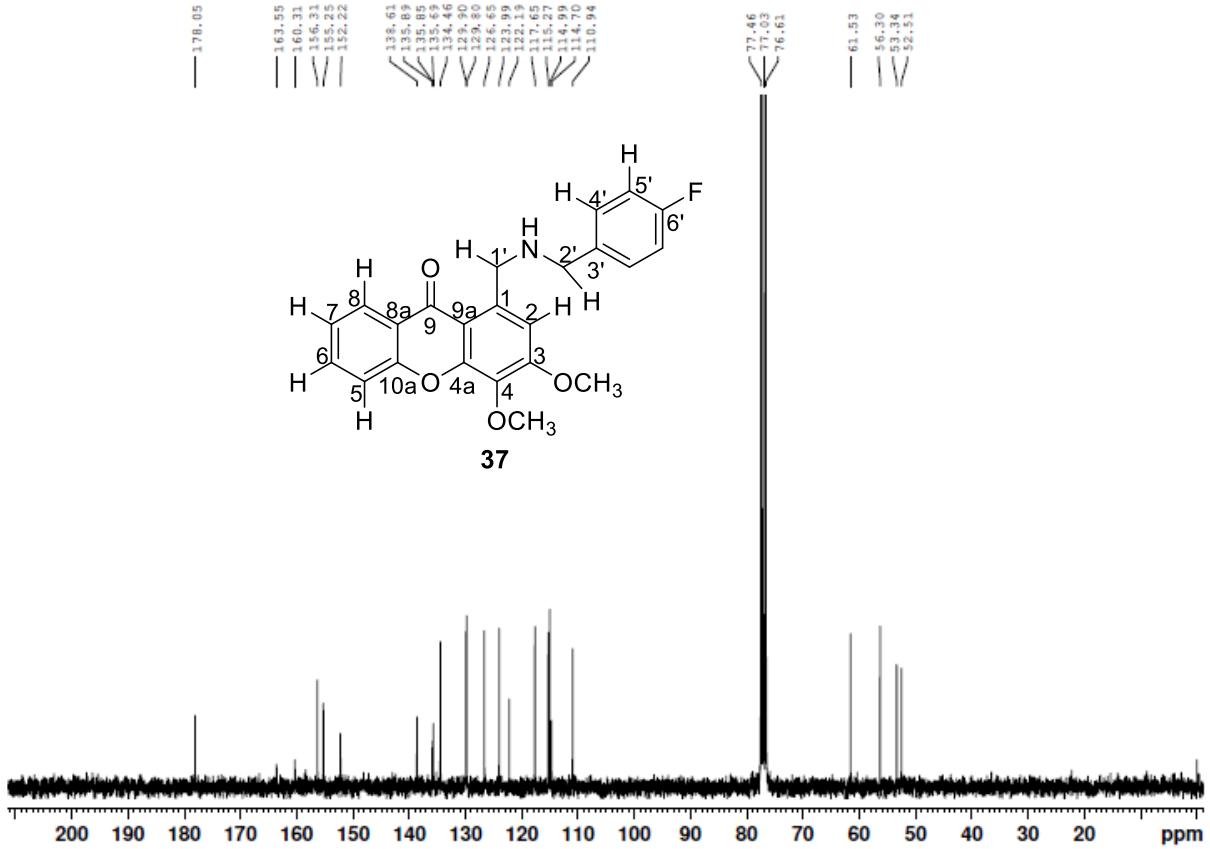
**Figure S36.**  $^1\text{H}$ -NMR spectrum of 3,4-dimethoxy-1-(piperidin-1-ylmethyl)-9*H*-xanthen-9-one (**36**).



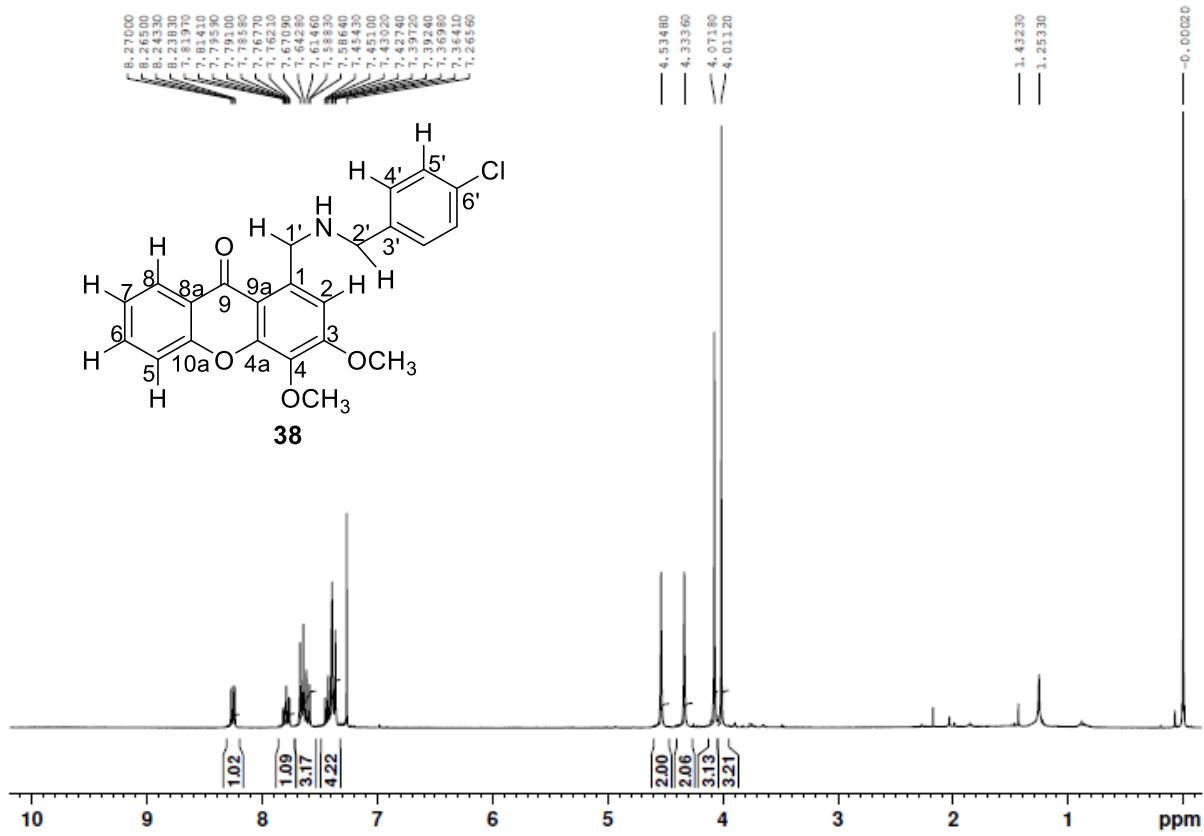
**Figure S37.**  $^{13}\text{C}$ -NMR spectrum of 3,4-dimethoxy-1-(piperidin-1-ylmethyl)-9H-xanthen-9-one (**36**).



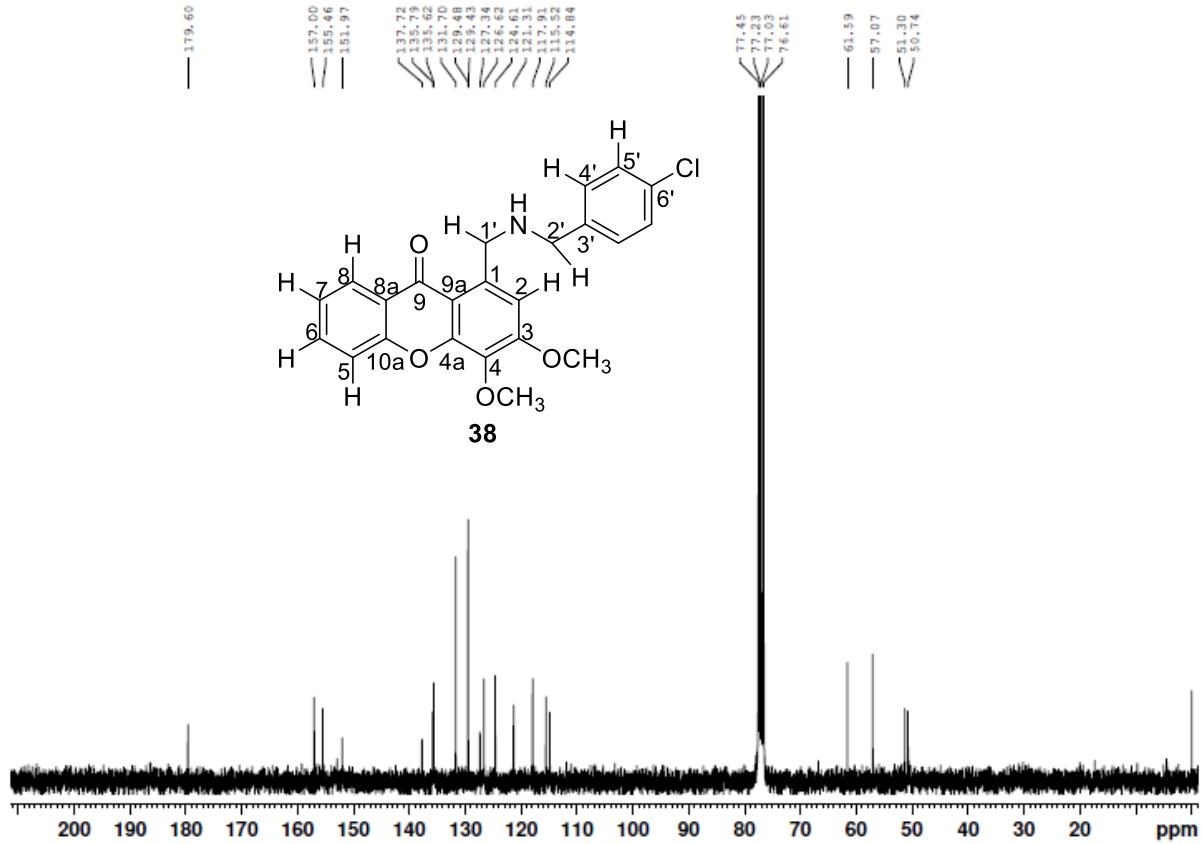
**Figure S38.**  $^1\text{H}$ -NMR spectrum of 1-((4-fluorobenzyl)amino)methyl-3,4-dimethoxy-9*H*-xanthen-9-one (**37**).



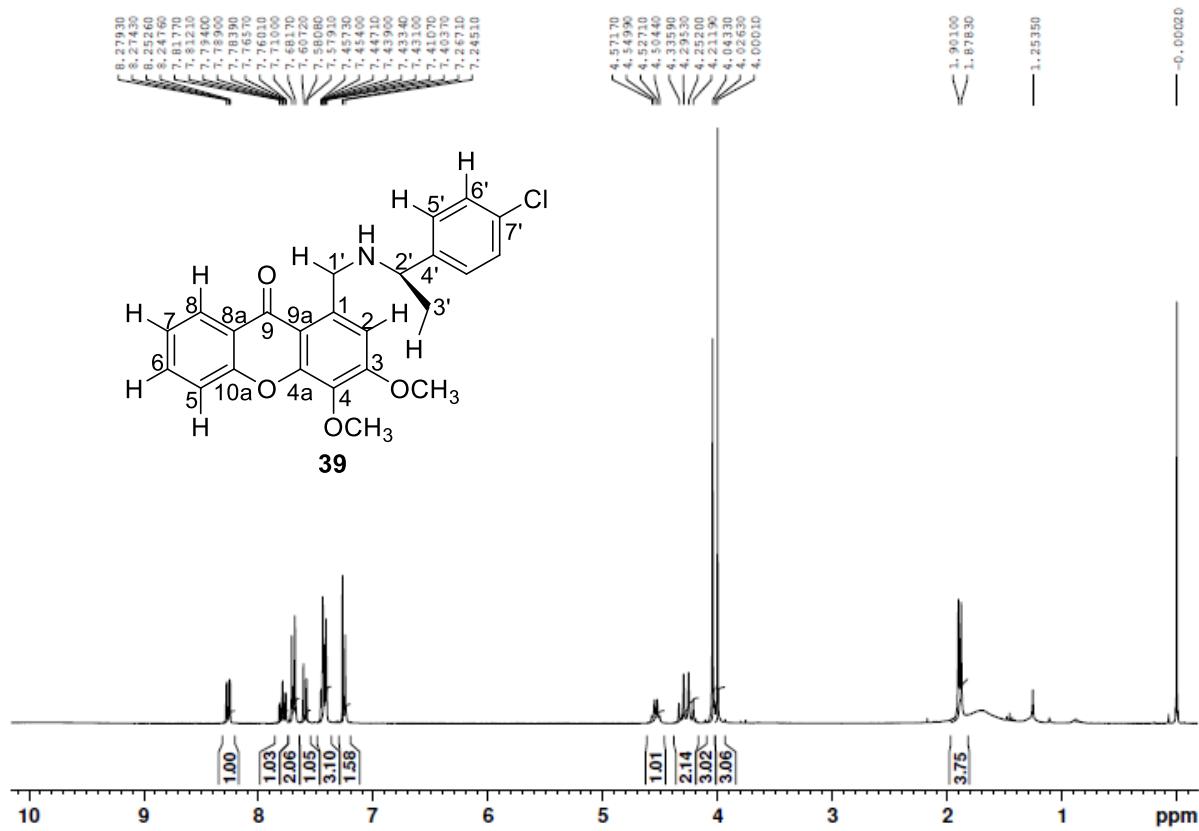
**Figure S39.**  $^{13}\text{C}$ -NMR spectrum of 1-((4-fluorobenzyl)amino)methyl)-3,4-dimethoxy-9H-xanthen-9-one (37).



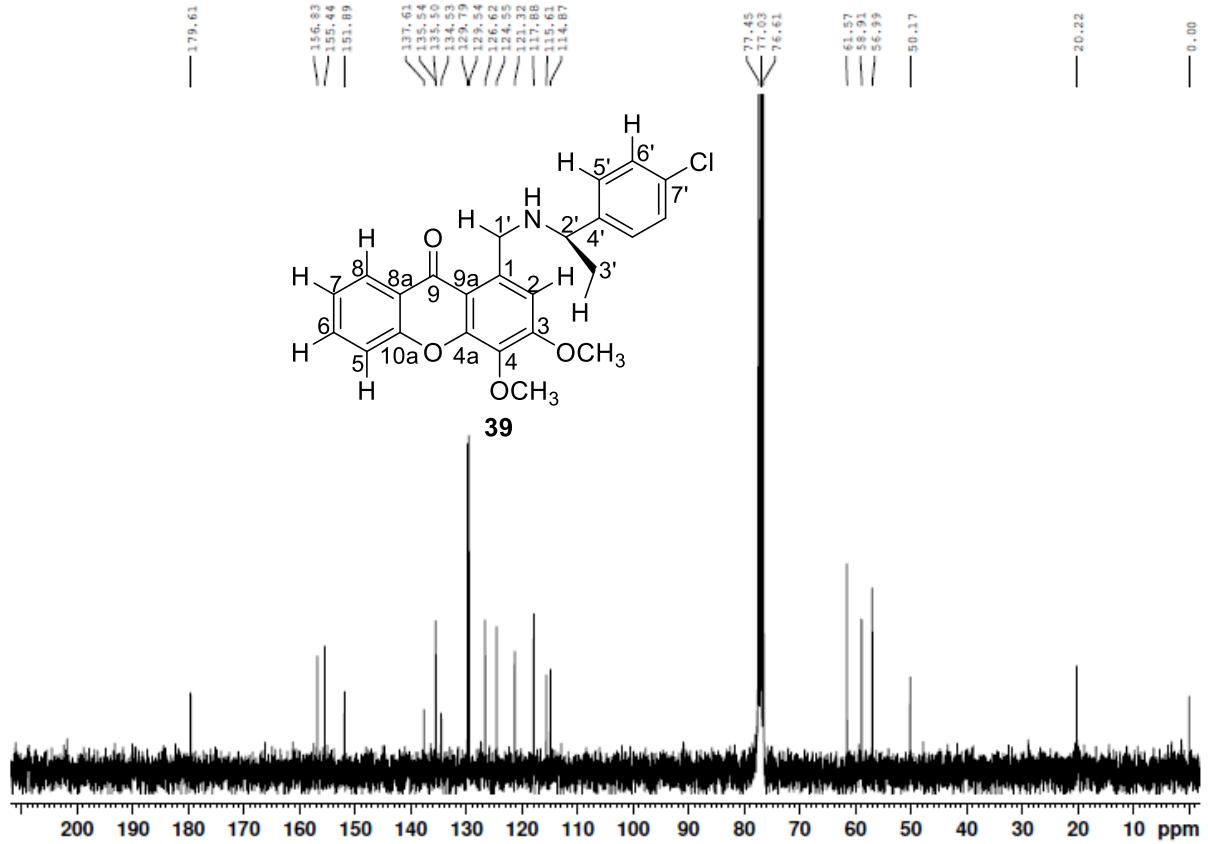
**Figure S40.**  $^1\text{H}$ -NMR spectrum of 1-(((4-chlorobenzyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**38**).



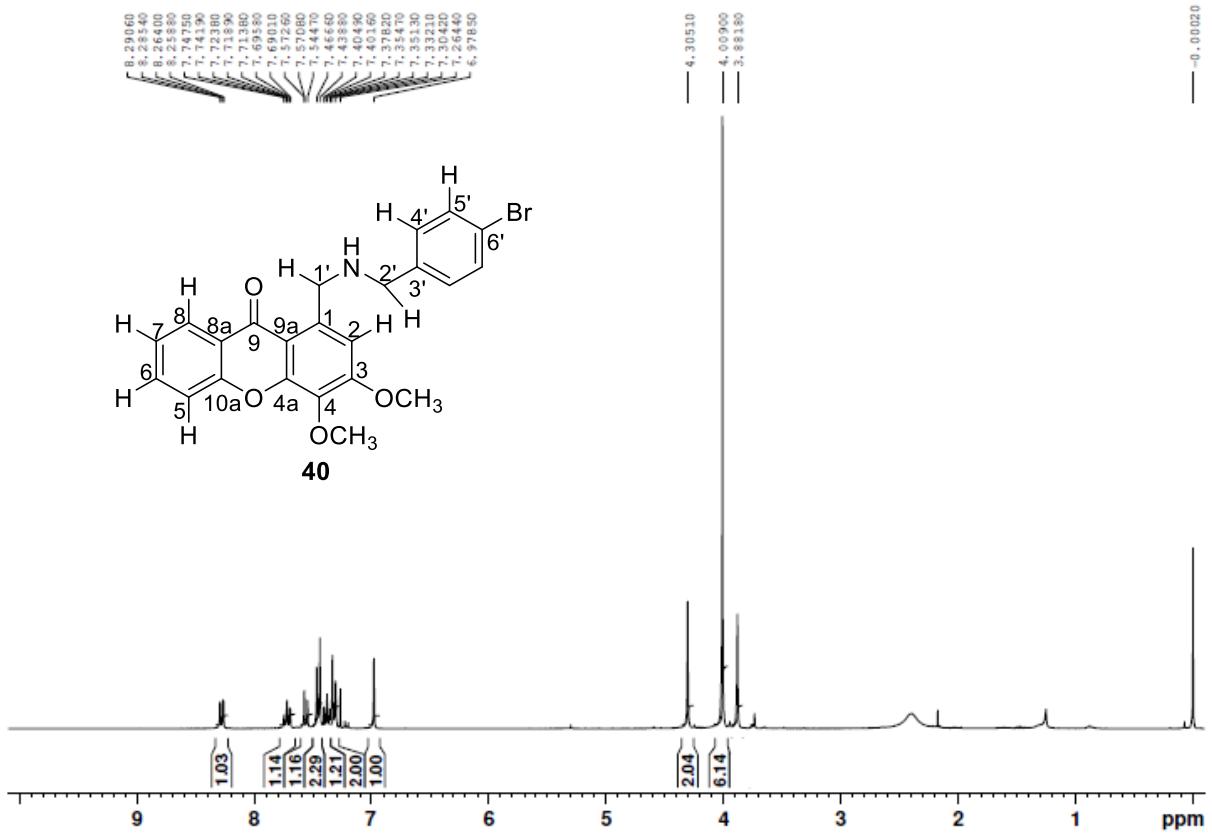
**Figure S41.**  $^{13}\text{C}$ -NMR spectrum of 1-(((4-chlorobenzyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**38**).



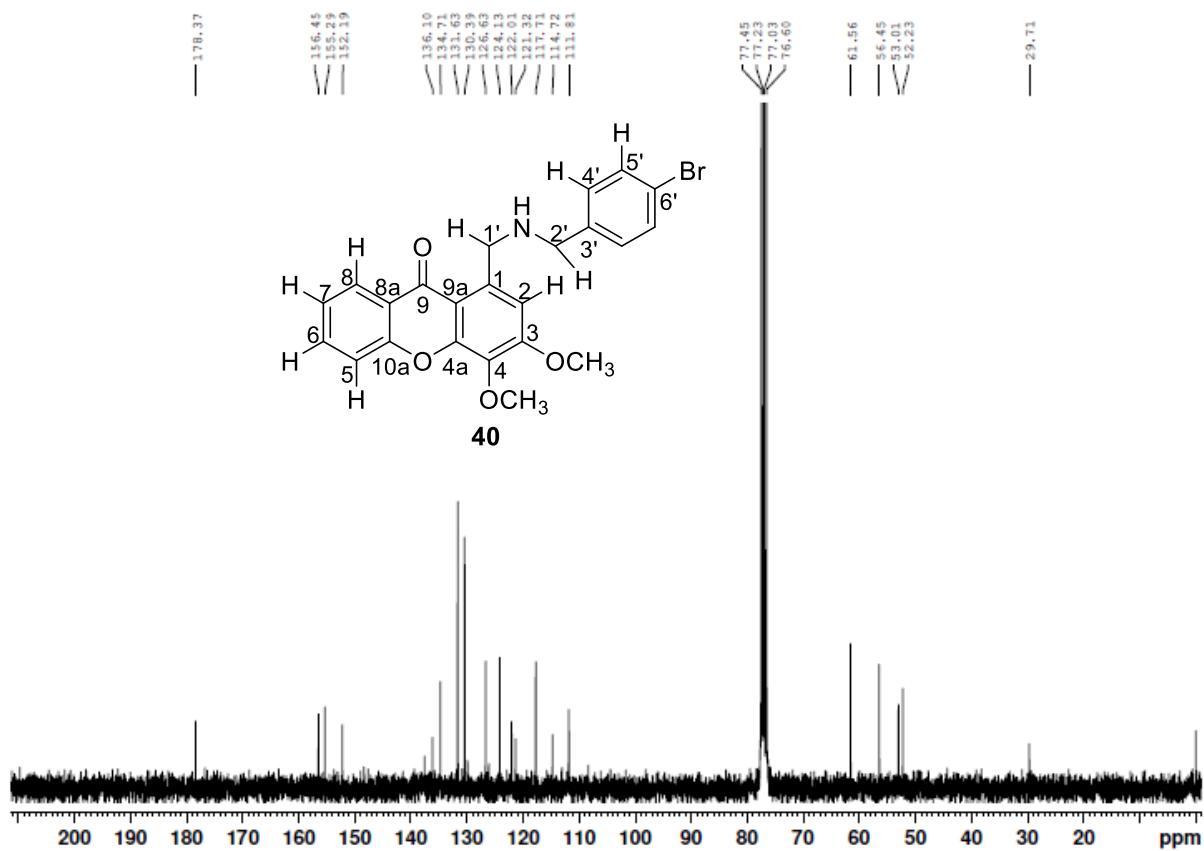
**Figure S42.**  $^1\text{H}$ -NMR spectrum of (*R*)-1-(((1-(4-chlorophenyl)ethyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (39).



**Figure S43.**  $^{13}\text{C}$ -NMR spectrum of (*R*)-1-(((1-(4-chlorophenyl)ethyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (39).



**Figure S44.** <sup>1</sup>H-NMR spectrum of 1-((4-bromobenzyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**40**).



**Figure S45.**  $^{13}\text{C}$ -NMR spectrum of 1-(((4-bromobenzyl)amino)methyl)-3,4-dimethoxy-9*H*-xanthen-9-one (**40**).