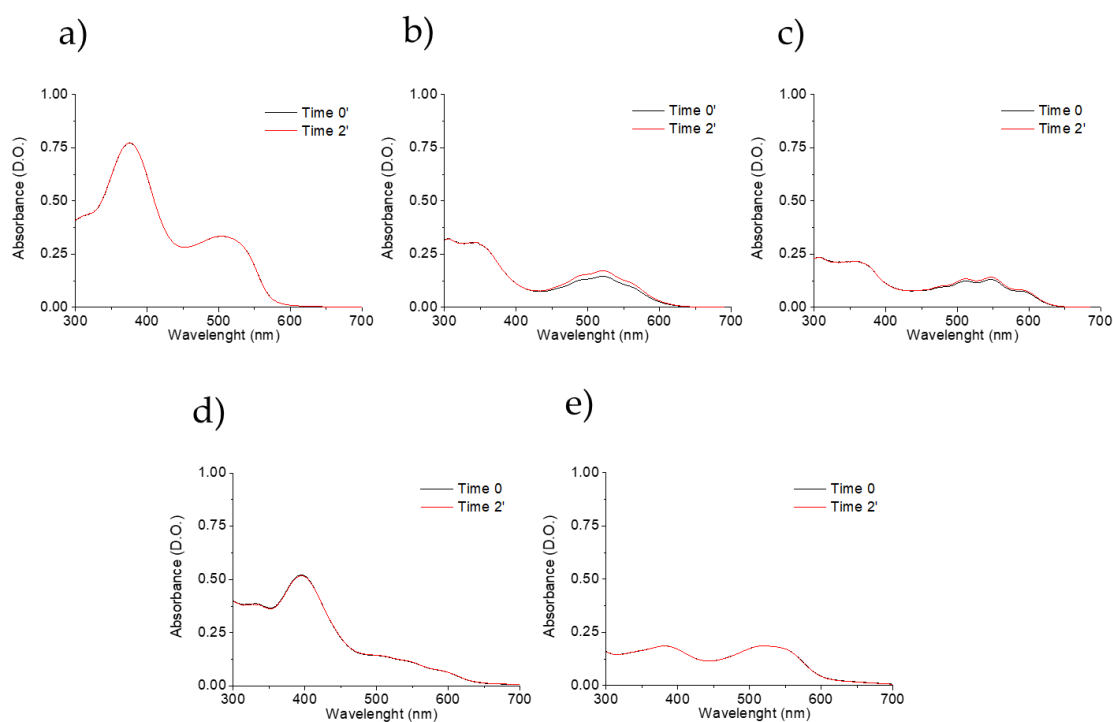
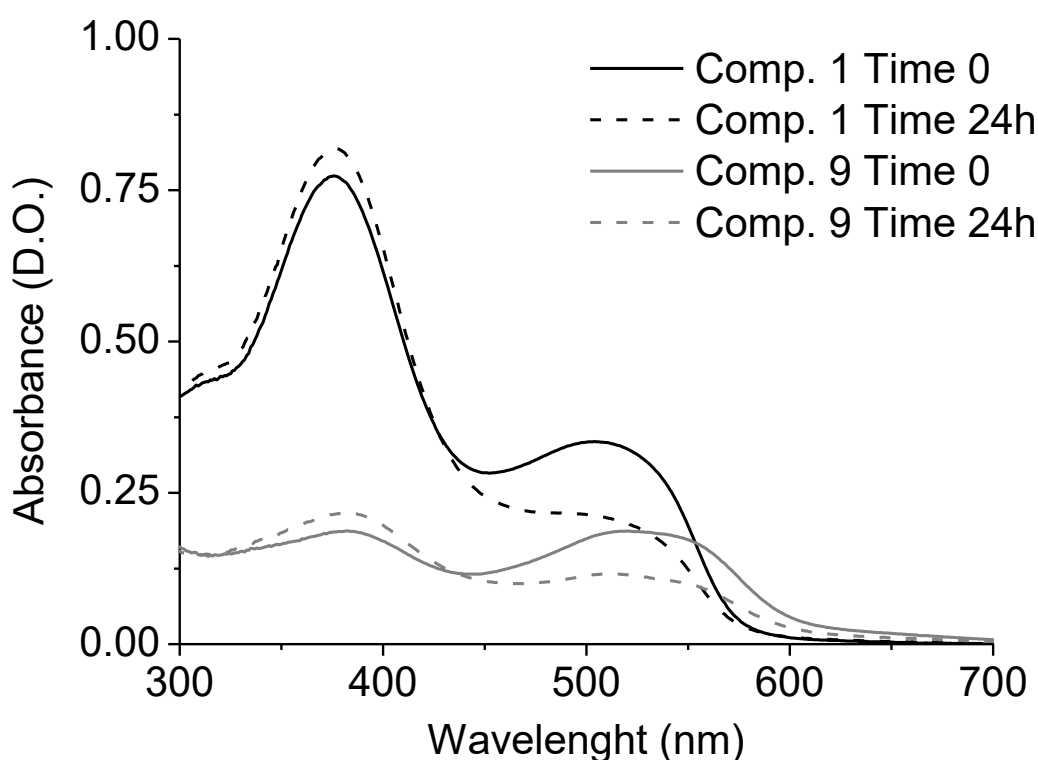


Supplementary Information



- Figure S1. Absorbance spectra of the flavylium salts (50 μM) were immediately measured after addition to potassium phosphate buffer 20mM, EDTA 1mM, pH 7.0, and after incubation for 2 minutes in these conditions. The absorbance spectra of compounds 1, 2, 3, 4, 5 measured in phosphate buffer, EDTA 1mM pH 7.0 are shown in panel a, b, c, d, e, respectively, after addition to the buffer (black line) and after 2 minutes incubation (red line).



- Figure S2. The UV-vis spectra of the non-equilibrated form of compounds 1 and 5 were obtained after instant measurement of the spectra of the acidified solution of each compound (DMSO+ 0.1M HCl) upon addition to 100mM of potassium phosphate pH 7.0 (non-equilibrated conditions) or by incubation in this buffer for 24h (equilibrated conditions), confirmed that the composition of the tested aliquots was correct (Panel c).

Q6BCY4	1	MNSRRREPIT	LQDPEAKYPL	PLIEKEKISH	NTRRRFRGLP	40
1I7P	27	. . MHHHMIT	LENPDIKYPL	RLIDKEILSH	DTRRRFRFALP	64
Q6BCY4	41	SPDHVLGLPV	GNVYQLLAKI	DNELVVRAYT	PVSSDDDRGF	80
1I7P	65	SPQHILGLPI	GQHIYLISTRI	DGNLVIRPYT	PVSSDDDKGF	104
Q6BCY4	81	VDLI IKIYFK	NVHPQYPEGG	KMTQYLENMK	IGETIFFRGP	120
1I7P	105	VDLVVKVYFK	ETHPKFPAGG	KMSQYLENMN	IGDTIEFRGP	144
Q6BCY4	121	RGRLFYHGPG	NLGIRPDQTS	EPKKTADHL	GMIAGGTGIT	160
1I7P	145	NGLLVYQGKG	KFAIRADKKS	NPVVRTVKSV	GMIAGGTGIT	184
Q6BCY4	161	PMLQLIRHIT	KDPSDRTRMS	LIFANQTEED	ILVRKELEEI	200
1I7P	185	PMLQVIRAVL	KDPNDHTVCY	LLFANQSEKD	ILLRPELEEL	224
Q6BCY4	201	ARTHPDQFNL	WYTLDRPPIG	WKYSSGFVTA	DMIKEHLPPP	240
1I7P	225	RNEHSSRFKL	WYTVDKAPDA	WDYSQGFVNE	EMIRDHLPPP	264
Q6BCY4	241	AKSTLILVCG	PPPLIQTAAH	PNLEKLGYTQ	DMIFTY	276
1I7P	265	GEETLILMCG	PPPMIQFACL	PNLERVGHPK	ERCFTF	300

- Figure S3. Alignment of the rat Cb5R sequence of the PDB used in this study (PDB file:1I7P) and the sequence of human soluble Cb5R (Unitpro code: Q6BCY4). Cb5R's residues that were found common for the interaction with inhibitors are labeled in orange. As shown in the alignment, those residues are the same in the sequence of human Cb5R.

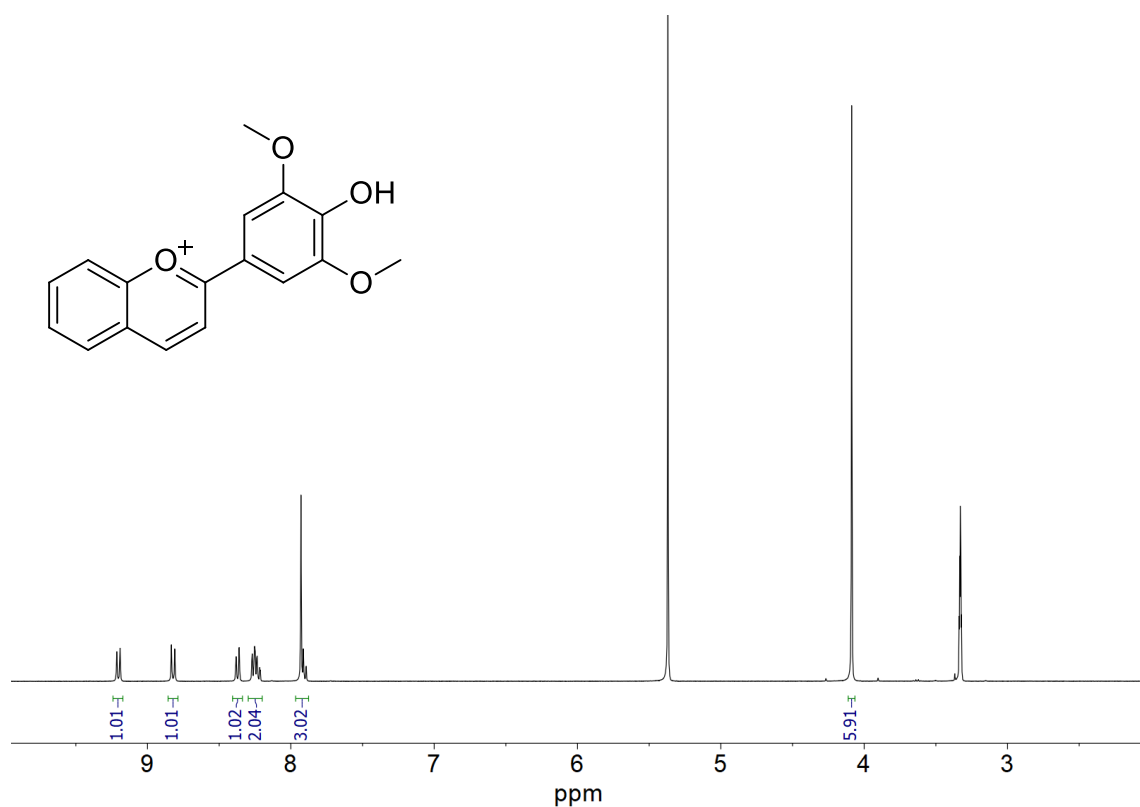


Figure S4. ¹H NMR spectrum (400 MHz) of compound **3** in 99:1 (v:v) CD₃OD:DCl 20% in D₂O.

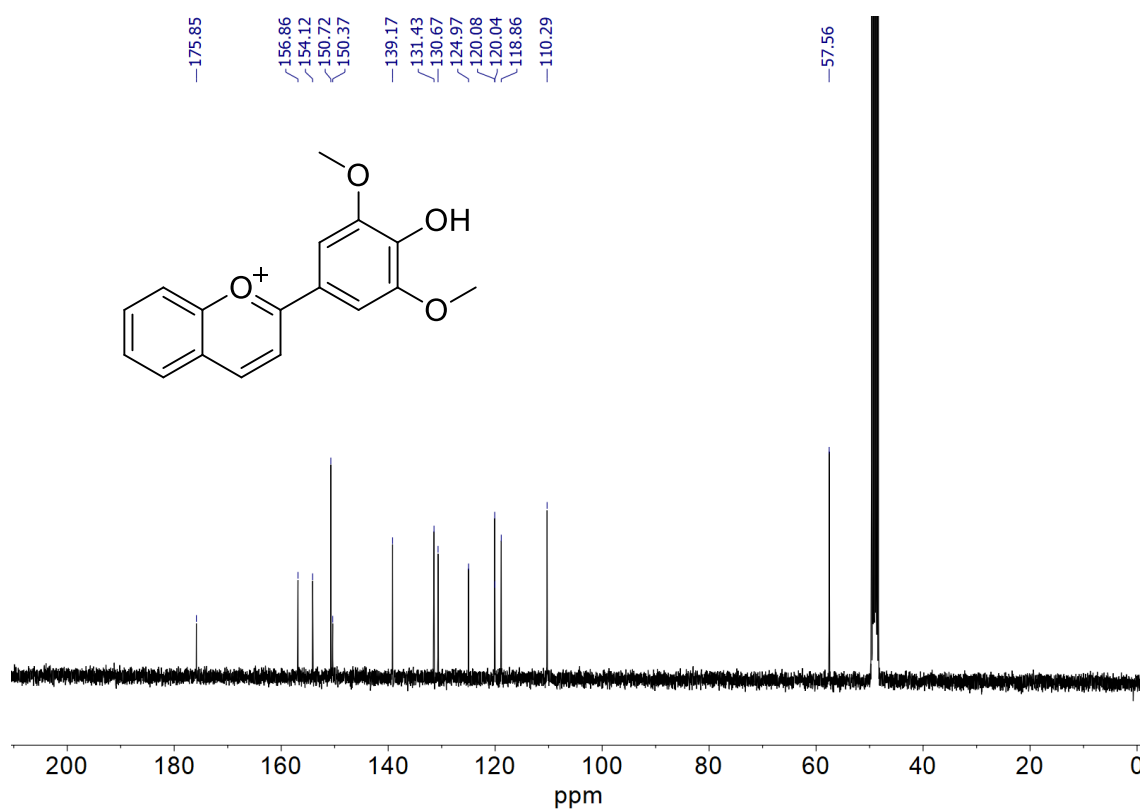


Figure S5. ¹³C{¹H} NMR spectrum (101 MHz) of compound **3** in 99:1 (v:v) CD₃OD:DCl 20% in D₂O.

Nunoc_221016115028 #99 RT: 4.28 AV: 1 NL: 3.88E5
T: FTMS + p ESI Full ms [50.00-500.00]

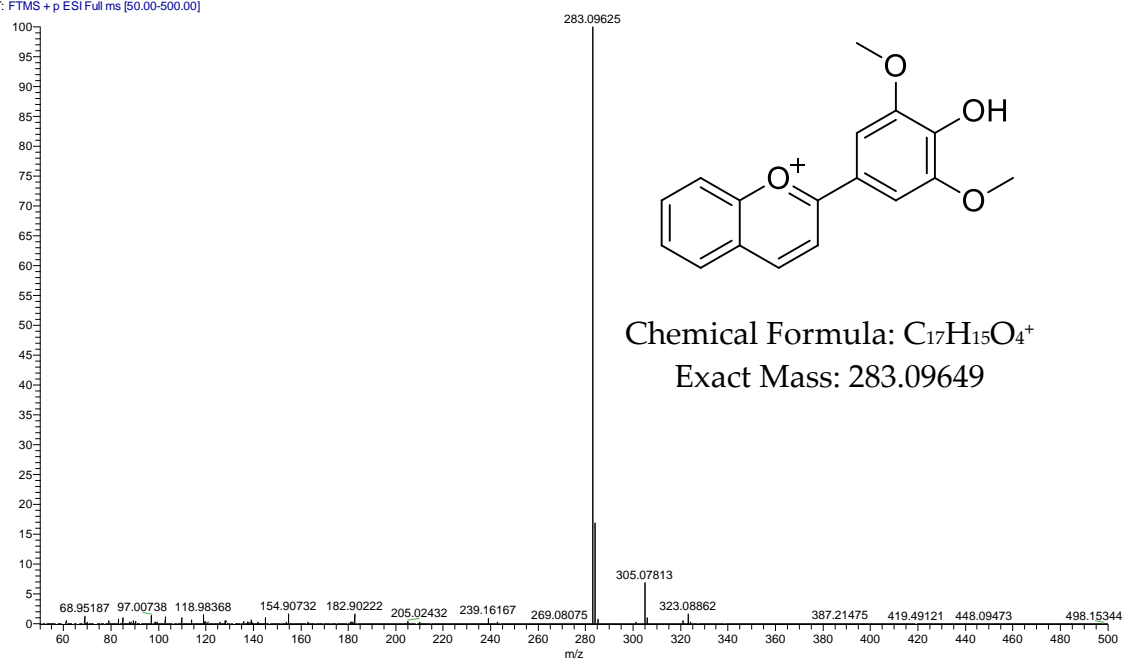


Figure S6. HRMS spectrum of compound **3**.