Electronic Supplementary Material (ESI) for MedChemComm.

Cyclic analogue of tambjamine YP1 alkaloid isolated from marine bacterium *Pseudoalteromonas citrea*

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Supplementary Information

Table S1. Proteins in the *tam* pathway, their putative functions, and the percent identity between *P. tunicata* and *P. citrea* proteins[1–4].

Protein	Putative function	Identity (%)
TamA	Adenylation and acyl-carrier protein	70
TamB	Peptidyl-carrier protein	69
TamC	Rieske oxygenase	83
TamD	Aminotransferase	78
TamE	L-prolyl-AMP ligase	56
TamF	β-ketoacyl synthase	49
TamG	L-prolyl-PCP dehydrogenase	74
TamH	Thioester reductase and aminotransferase	71
TamJ	Oxidase/dehydrogenase	53
TamK	Outer membrane lipoprotein sorting protein	74
TamL	Permease	75
TamM	Permease	75
TamN	ATP-transporter, ATP-binding protein	78
TamO	Hypothetical protein	56
TamP	SAM dependent *O*-methyl transferase	69
TamQ	Condensation enzyme	65
TamR	No assigned function	66
TamS	Phosphopantetheinyl transferase	42
TamT	Dehydrogenase	62

Tambjamine MYP1 structural data

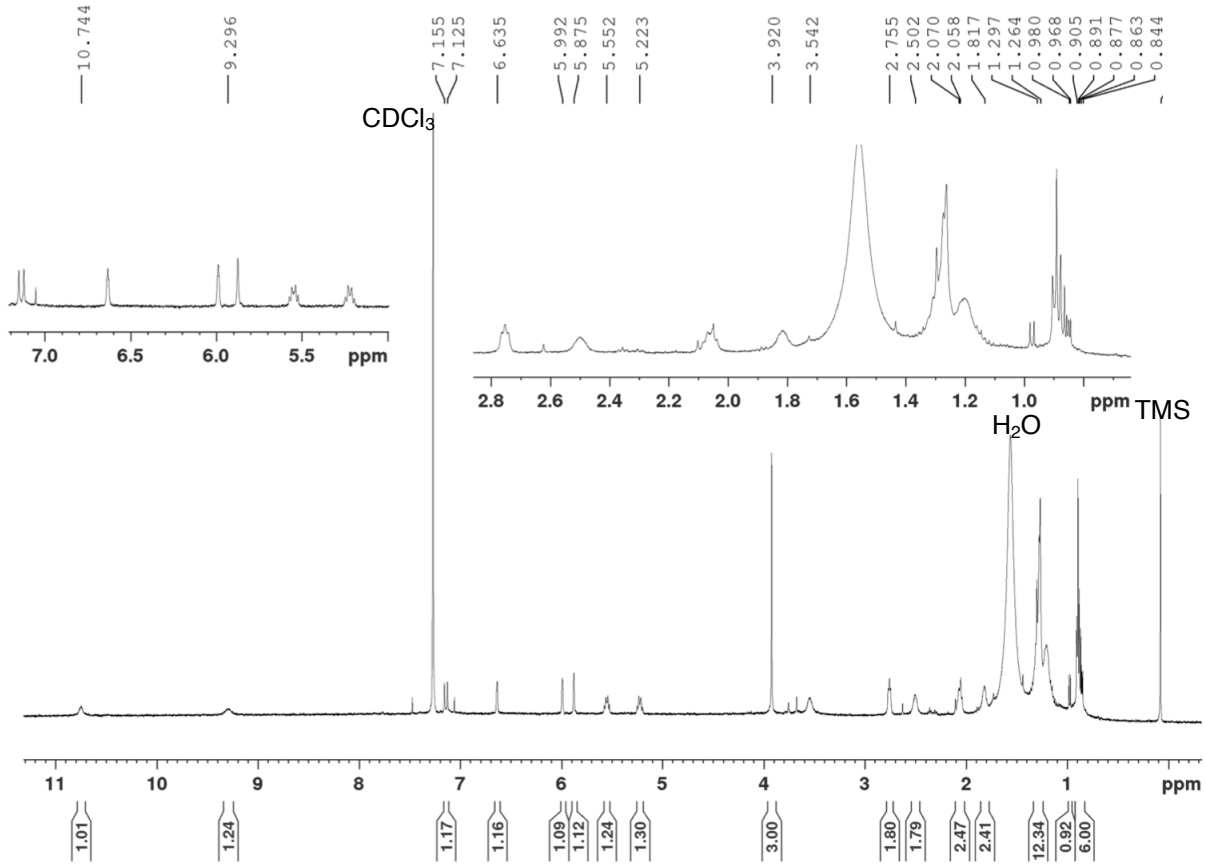


Figure S1. ^{1}H NMR spectrum of tambjamine MYP1 collected in $CDCl_3$in a 500 MHz field. Solvents and internal standard trimethylsilane (TMS) are labelled.

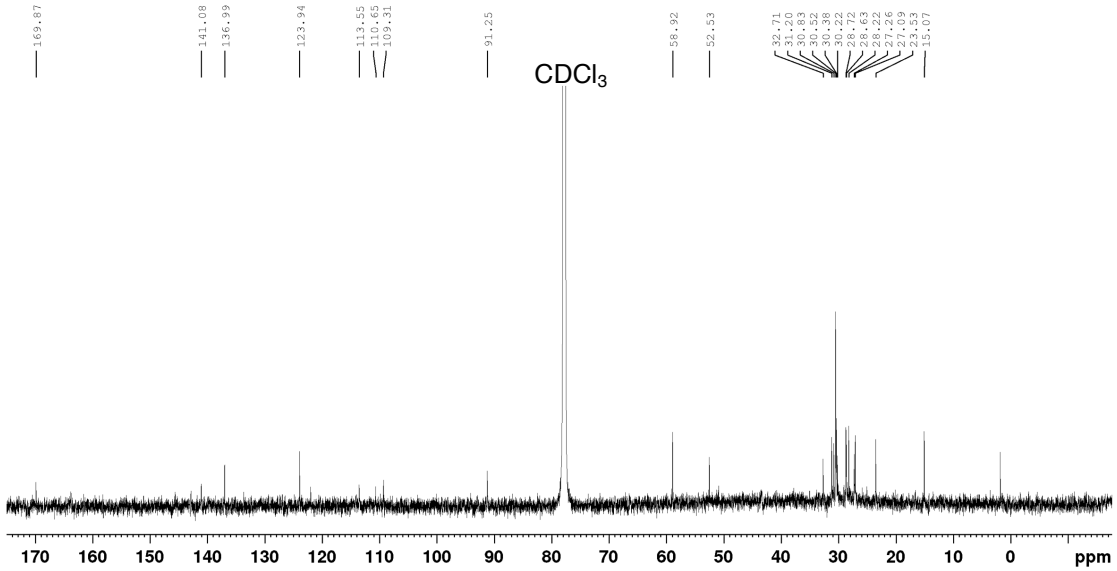


Figure S2. ^{13}C NMR spectrum of tambjamine MYP1 collected in $CDCl_3$ in a 700 MHz field.

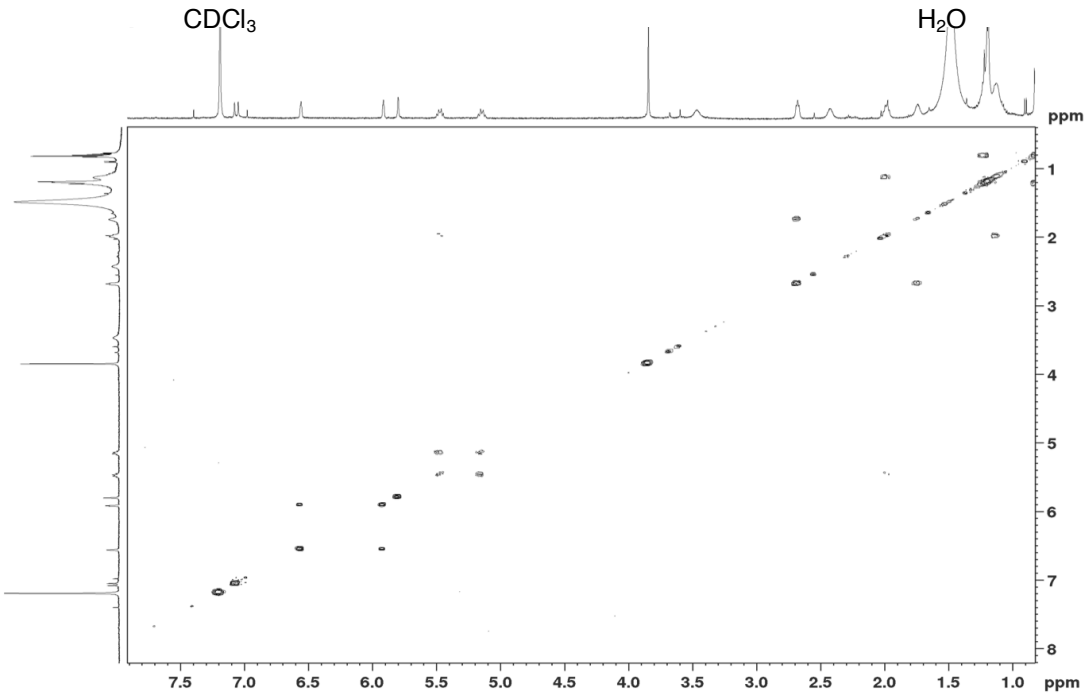


Figure S3. ^{1}H-^{1}H COSY NMR spectrum of tambjamine MYP1. Collected in $CDCl_3$in a 500 MHz field.

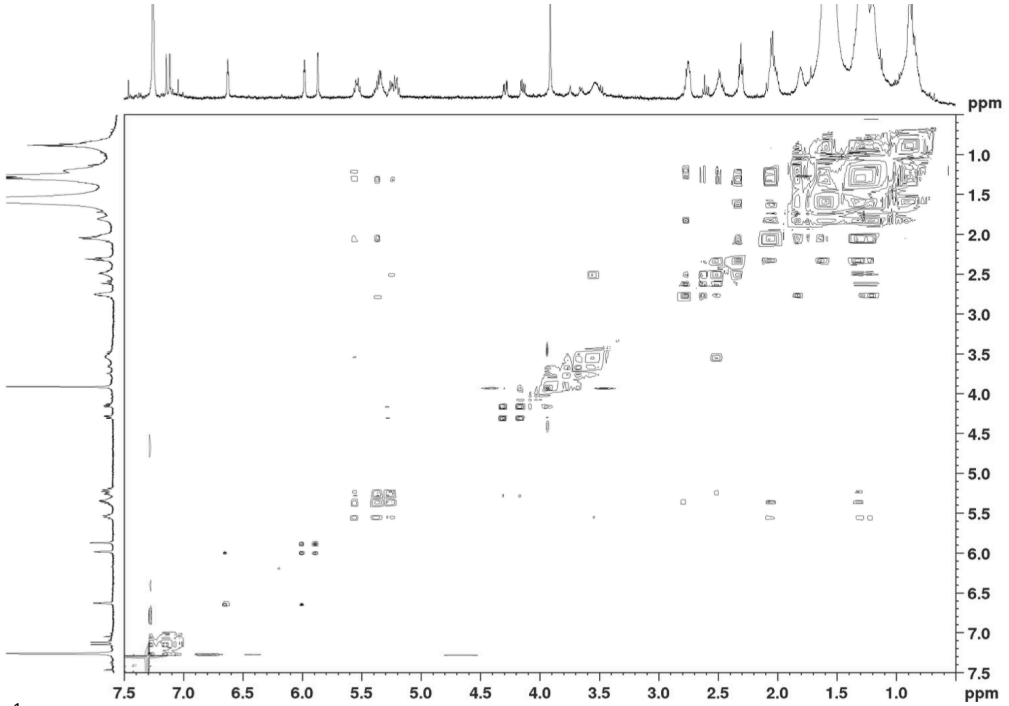


Figure S4. ^{1}H-^{1}H TOCSY NMR spectrum of tambjamine MYP1 with unknown impurity, collected in $CDCl_3$ in a 500 MHz field.

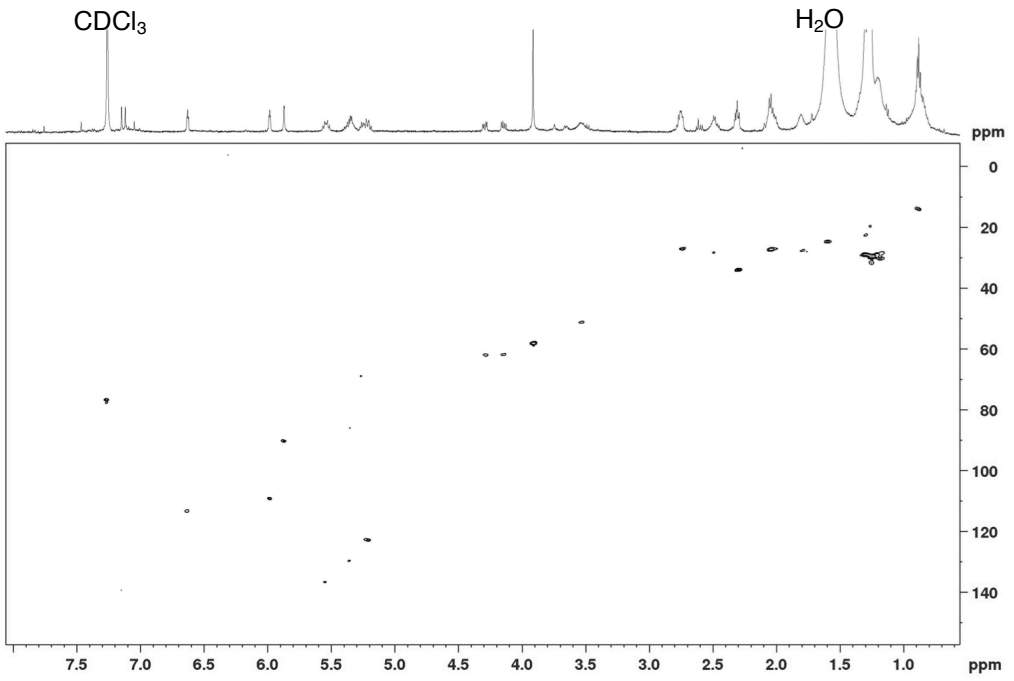


Figure S5. ^{1}H-^{13}C HSQC NMR spectrum of tambjamine MYP1 with unknown impurity, collected in $CDCl_3$ in a 500 MHz field.

Table S2. Crystal data and structure refinement for tambjamine MYP1[5,6].

Crystal Data	
Empirical formula	$C_{24}H_{35}N_3O_5$
Formula weight	445.55
Crystal Color, Habit	yellow, plate-like
Crystal dimensions (mm)	0.186 × 0.128 × 0.090
Crystal system	triclinic
Space group	$P\bar{1}$ [2]
Unit cell parameters	
a (Å)	9.8155(5)
b (Å)	11.1719(5)
c (Å)	11.1821(5)
α (°)	91.5571(16)
β (°)	95.2218(16)
γ (°)	101.2158(17)
V (Å^3)	1196.53(10)
Z^b	2
F(000)	480
Density (ρ_{calcd})	1.237 Mg/m^3
Absorption coefficient (μ)	0.087 mm^{-1}
Data Collection and Refinement Conditions	

Diffractometer	Bruker AXS D8 Venture Duo diffractometer
Radiation	monochromated Mo K$_\alpha$ (λ = 0.71073 Å)
Temperature	-93(2) °C [180(2) K]
Scan type	φ- and ω-scans (1.5º/frame, 15 s exposure/frame, 9 sets)
Theta range for data collection	2.533 to 26.396°
Completeness to theta = 25.242°	99.9%
Reflections collected	38405
Index ranges	$-12 \le h \le 12$, $-13 \le k \le 13$, $-13 \le l \le 13$
Independent reflections [$F_o^2 \ge -3\sigma(F_o^2)$]	4891 [R_{int} = 0.0736]
Observed reflections [$F_o^2 > 2\sigma(F_o^2)$]	3437
Absorption correction method	multi-scan [SADABS]
Anomalous Dispersion	For all non-hydrogen atoms
Structure solution method	Direct methods (SHELXT-2014)
Refinement method	Full-matrix least-squares on F^2 (SHELXL-2017/1)[i]
Function Minimized	$\Sigma w(\lvert F_o\rvert^2 - \lvert kF_c\rvert^2)^2$ (k: overall scale factor)
Weighing scheme, w	$w = [\sigma(F_o^2) + (0.0723\,P)^2 + 1.2456\,P]^{-1}$
$w = [\sigma(F_o^2) + (a\,P)^2 + (b\,P)]^{-1}$	
P-factor	$[\mathrm{Max}(F_o^2,0) + 2\,F_c^2]/3$
Data / restraints / parameters	4891 [$F_o^2 \ge -3\sigma(F_o^2)$] / 5 / 305
Reflection (observed)/parameter ratio	11:1
Reflection (data)/parameter ratio	16:1
Goodness-of-fit on F^2 $GooF = \{\Sigma[w(F_o^2-F_c^2)^2]/(n-p)\}^{1/2}$ n: number of reflections, p: number of parameters	1.018
Final R indices	
$R_1 = [\Sigma\lvert\lvert F_o\rvert-\lvert F_c\rvert\rvert]/[\Sigma\lvert F_o\rvert]$ for [$F_o^2 > 2\sigma(F_o^2)$]	0.0641
$wR_2 = \{[\Sigma w(F_o^2-F_c^2)^2]/[\Sigma w(F_o^2)^2]\}^{1/2}$ [all data]	0.1795
Max. Shift/Error in Final Cycle	0.000
Largest difference peak and hole	0.833 and -0.603 e$^-$/Å^3
Transmission factor (min)	0.7071 [SADABS]
Transmission factor (max)	0.7454 [SADABS]

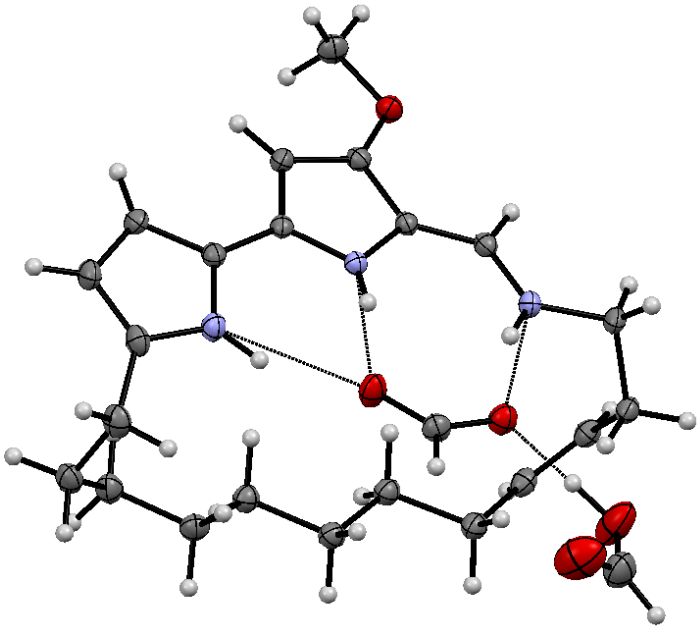


Figure S6. Full asymmetric unit of tambjamine MYP1 crystal structure, thermal ellipsoids are drawn to 30% probability.

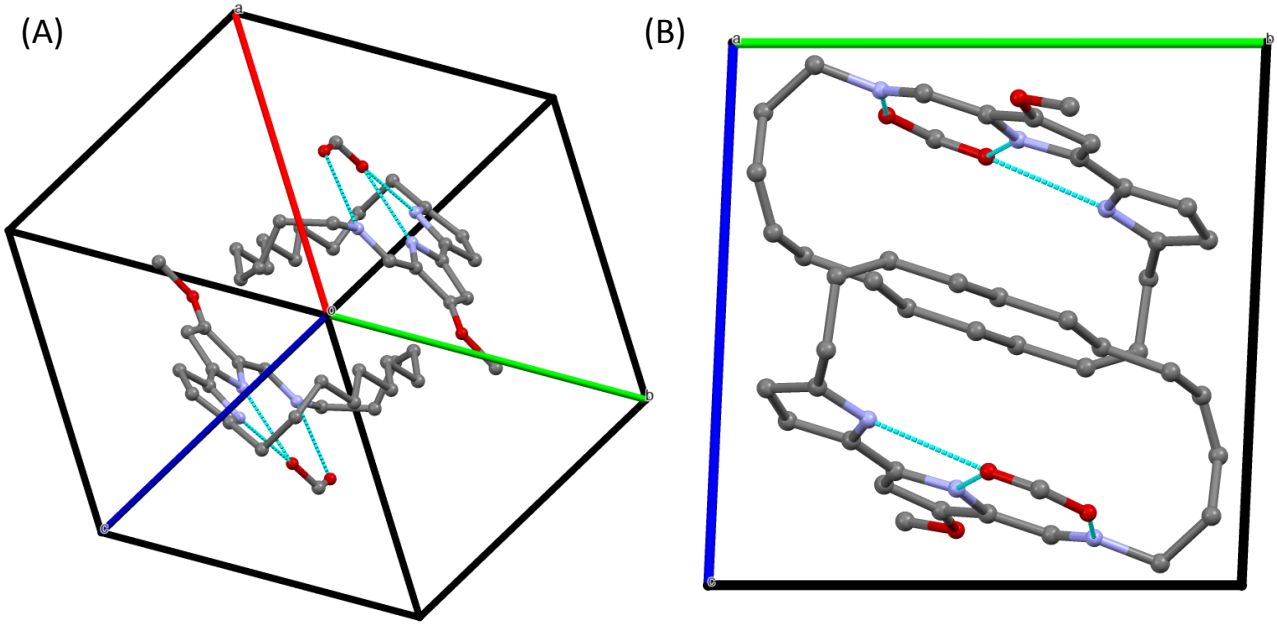


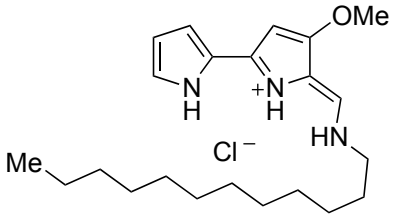
Figure S7. Unit cell of tambjamine MYP1 X-ray structure. (A) View at origin of unit cell, (B) view on *ab* face of unit cell. Hydrogen atoms and formic acid molecule omitted for clarity. The edge colours refer to the *a* (blue), *b* (green), and *c* (red) coordinates.

General synthesis information

Commercially available reagents were used throughout without further purification. Reactions were carried out under an argon atmosphere using oven-dried glassware. ^{1}H NMR spectra were recorded using a Bruker Avance-400 spectrometer operating at 400 MHz. Anhydrous DCE (Sure/Seal™) was obtained from Sigma-Aldrich and used as received.

Synthesis of Tambjamine BE-18591·HCl

(*Z*)-*N*-((4'-methoxy-1*H*,5'*H*-[2,2'-bipyrrol]-5'-ylidene)methyl)dodecan-1-amine hydrochloride



Tambjamine BE-18591 was synthesized by modification of the method of Saggiomo *et al*[7]. To a solution of 4-methoxy-2,2'-bipyrrole-5-carboxaldehyde (10 mg, 0.053 mmol) and dodecylamine (13 mg, 0.068 mmol) in DCE (1 mL) was added 2 drops AcOH (cat.). The reaction mixture was heated at 60 °C for 3 h, then cooled to rt, diluted with CH_2Cl_2 (5 mL), and washed with 1 M HCl (3 × 10 mL). The organic fraction was dried over $MgSO_4$, subjected to filtration, and concentrated *in vacuo* to deliver the title compound as a yellow oil (18 mg, 89%).

^{1}H NMR (400 MHz; $CDCl_3$): δ 13.70 (br s, 1H), 10.62 (br s, 1H), 9.52-9.40 (m, 1H), 7.33 (d, *J* = 14.9 Hz, 1H), 7.06 (dd, *J* = 1.4 and 2.7 Hz, 1H), 6.73 (dd, *J* = 1.4 and 3.7 Hz, 1H), 6.28 (2.6 and 3.8 Hz), 5.94 (d, *J* = 2.2 Hz, 1H), 3.92 (s, 3H), 3.51-3.45 (m, 2H), 1.75 (p, *J* = 7.3 Hz, 2H), 1.34-1.25 (m, 18H), 0.87 (t, *J* = 6.7 Hz, 3H).

Physical and spectral data were found to be consistent with those reported[7].

pK_a determination information

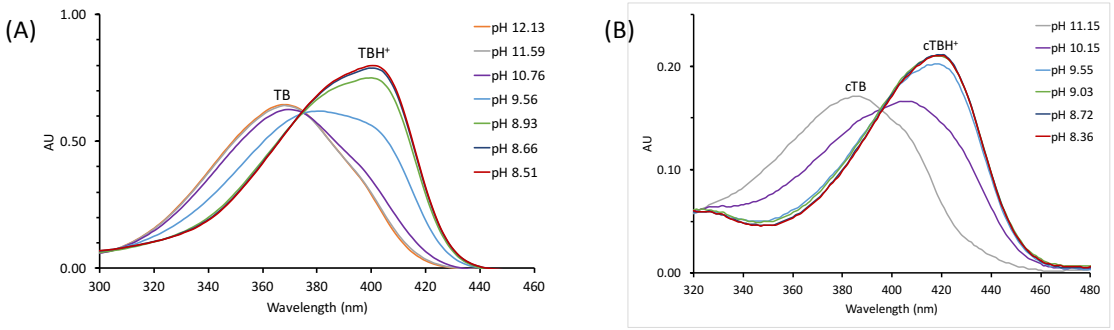


Figure S8. Absorbance spectra at varying pH of (A) the linear tambjamine BE-19591 (TB = base form, TBH^+ = acid form) and (B) the tambjamine MYP1 (cTB = base form, $cTBH^+$ = acid form). Spectra taken in 0.1 M NaCl in 1:1 (v/v) MeCN/H_2O, pH adjusted with 0.1-0.01 M HCl.

Table S3. The absorbance maxima of each compound in their basic and acidic forms, and the calculated pK_a.

Compound	**Base λ_{max} (nm)**	**Acid λ_{max} (nm)**	**pK_a**
Tambjamine BE-18591	368	400	9.9 ± 0.2
Tambjamine MYP1	385	420	10.4 ± 0.3

The pK_a was calculated using Equation S1 from previous literature[8], this was done with absorbance measurements at several pH values using both λ_{max} (basic and acidic) for calculations, these were then averaged. In the equation, A refers to the experimental absorbance at a particular wavelength, Ab^- is the absorbance of the base form at this wavelength, and AH is the absorbance of the acidic form.

Equation S1 $$pK_a = pH + \log\left(\frac{A - Ab^-}{AH - A}\right)$$

References:

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