Electronic Supplementary Material (ESI) for ChemComm.

SUPPORTING INFORMATION

Highly Specific Detection of Aβ Oligomers in Early Alzheimer's Disease by Near-infrared Fluorescent Probe with a "V-shaped" Spatial Conformation

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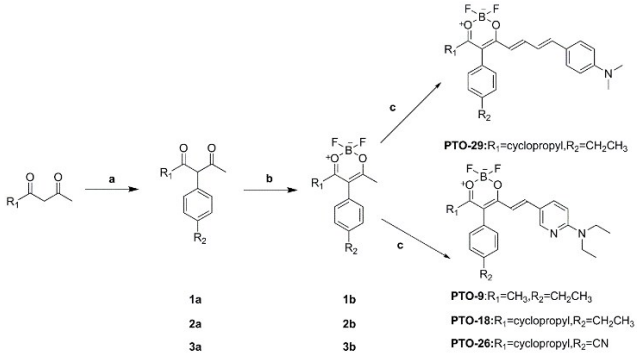
Materials and Methods:

All chemicals for the synthesis were purchased from commercial suppliers and used without further purification. Column chromatography was performed on silica gel slurry packed into glass columns. Synthetic Aβ peptide (1-42) is from DgPeptides Co, Ltd., HangZhou City, China. PTO-29 was dissolved in DMSO to prepare a 25.0 μM stock solution. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 125 MHz respectively, and reported in ppm downfield from tetramethylsilane. HPLC was run on a Shimadzu LC-20A machine; mobile phase: 20% water in CH_3CN, UV detection at 320 nm. Fluorescence measurements were carried out using an FL-4600 Fluorescence Spectrophotometer (Hitachi). Mass spectra were obtained at the Department of Pharmaceutical Analysis of China Pharmaceutical University. The synthetic trifluoroacetic acid salt forms of amyloid-β (1−42) peptides were obtained from Osaka PEPTIDE INSTITUTE, Inc. (Osaka, Japan). The human neuronal cell line (SH-SY5Y) were purchased from Cell Bank of the Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences (Shanghai, China). Transgenic female APP-PS1 mice and age-matched wild type female mice were purchased from the Cavens Animal Technology Co. Ltd., Changzhou, China. Procedures related to animal experiments were implemented in accordance with our institutional guidelines and approved by the China Pharmaceutical University Animal Care Committee.

Chemistry.

Scheme S1: Synthetic route for PTO-9, 18, 26 and 29.



Reagents and conditions: (a) 1-ethyl-4-iodobenzene, K_2CO_3, CuI, L-Pro, DMSO, 90°C; (b) $BF_3 \cdot Et_2O$, tributyl borate, r.t.; (c) tetrahydroisoquinoline, acetic acid, toluene, 65°C.

The synthesis of 3-(4-ethylphenyl)pentane-2,4-dione**(1a)**: 2,4-Pentanedione(3.6 ml, 38.8 mmol) and 1-ethyl-4-iodobenzene (0.937 ml, 6.47 mmol) were dissolved in DMSO (15 mL), and then K_2CO_3 (3.75 g, 18 mmol), CuI (c.a.) and L-Proline (316 mg, 1.38 mmol) were added to the mixture, which were stirred at 90 °C for 20 h. The reaction mixture was dissolved in water, and then extracted with ethyl acetate (3*15 mL), washed with saturated NaCl, and dried over Na_2SO_4. Flash column chromatography (70:1 Petroleum ether : ethyl acetate) afforded 1a (352 mg, 24.6%) as pale-yellow oily liquid.^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 16.64 (s, 1H), 7.28 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 2.67 (q, J = 7.5 Hz, 2H), 2.04 (s, 6H), 1.23 (t, J = 7.6 Hz, 3H).

The synthesis of 5-(4-ethylphenyl)-2,2-difluoro-4,6-dimethyl-dioxaborinine **(1b)**: $BF_3 \cdot Et_2O$ (0.930 ml, 3.45 mmol) was added to 1a (352mg, 1.72mmol) in tributyl borate (0.930 ml, 3.45 mmol) slowly under the protection of nitrogen. The reaction mixture was then stirred at r.t. for 4 h. A brownish yellow residue (350 mg, yield 80.1%) was obtained after removing the solvent. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 7.34 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 2.73 (q, J = 7.5 Hz, 2H), 2.06 (s, 6H), 1.25 (t, J = 7.6 Hz, 3H).

The synthesis of (E)-N,N-diethyl-5-(2-(5-(4-ethylphenyl)-2,2-difluoro-6-methyl-2H-dioxaborinin-4yl)vinyl)pyridin-2-amine**(PTO-9)**: 6-(diethylamino)nicotinaldehyde (64

mg, 0.36 mmol) and 1b (100 mg, 0.40mmol) were dissolved in toluene (2.0 mL), followed by the additions of acetic acid (15.5 μL, 0.092 mmoL), tetrahydroisoquinoline (11.5 μL, 0.276 mmoL). The resulting solution was stirred at r.t. for 6.5 h. The mixture was extracted with CH_2Cl_2 (3 × 40 mL), and the organic phase was dried over Na_2SO_4. After the solvent was removed in vacuum, the residue was purified by flash column chromatography (CH_2Cl_2) to give PTO-9 as an orange solid (40 mg, 27.0%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 8.24 (d, J = 2.4 Hz, 1H), 7.98 (d, J = 15.3 Hz, 1H), 7.37 (dd, J = 9.2, 2.4 Hz, 1H), 7.23 (d, J = 1.7 Hz, 2H), 7.14 – 7.03 (m, 2H), 6.39 (d, J = 9.1 Hz, 1H), 6.14 (d, J = 15.2 Hz, 1H), 3.52 (q, J = 7.1 Hz, 4H), 2. 70 (q, J = 7.6 Hz, 2H), 2.06 (s, 3H), 1.28 (t, J = 7.6 Hz, 3H), 1.16 (t, J = 7.1 Hz, 6H). HRMS(ESI) $C_{23}H_{27}BF_2N_2O_2$, $[M+H]^+$ calculated=413.2206; found=413.2220

The synthesis of 1-cyclopropyl-2-(4-ethylphenyl)butane-1,3-dione **(2a)**: 1-cyclopropylbutane-1,3-dione (0.59 ml, 5 mmol) and 1-ethyl-4-iodobenzene (0.724 ml, 5 mmol) were dissolved in DMSO (20 mL), and then K_2CO_3 (2.76 g, 20 mmol), CuI (c.a.) and L-Proline (230 mg, 2 mmol) were added to the mixture, which were stirred at 90 °C for 18 h. The reaction mixture was dissolved in water, and then extracted with ethyl acetate (3*15 mL), washed with saturated NaCl, and dried over Na_2SO_4. Flash column chromatography (70:1 Petroleum ether : ethyl acetate) afforded 1a (320 mg, 28.0%) as pale-yellow oily liquid.^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 17.03 (s, 1H), 7.28 – 7.19 (m, 4H), 2.71 (t, J = 7.6 Hz, 2H), 1.92 (s, 3H), 1.57 (tt, J = 7.9, 4.6 Hz, 1H), 1.30 (d, J = 7.6 Hz, 3H), 1.16 (dt, J = 4.4, 3.2 Hz, 2H), 0.84 – 0.77 (m, 2H). HRMS(ESI) $C_{15}H_{18}O_2$, $[M+H]^+$ calculated=231.1307; found=231.1393.

The synthesis of 4-cyclopropyl-5-(4-ethylphenyl)-2,2-difluoro-6-methyl-2H-dioxaborinine**(2b)**: $BF_3{\cdot}Et_2O$ (0.47 ml, 1.57 mmol) was added to 2a (160mg, 0.78 mmol) in tributyl borate (0.47 ml, 1.57 mmol) slowly under the protection of nitrogen. The reaction mixture was then stirred at r.t. for 6 h. A brownish yellow residue (153 mg, yield 78.0%) was obtained after removing the solvent. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33

(m, J = 8.1 Hz, 2H), 7.23 – 7.17 (m, 2H), 2.75 (q, J = 7.6 Hz, 2H), 2.12 (s, 3H), 1.70 (tt, J = 8.0, 4.5 Hz, 1H), 1.55 (q, J = 3.7 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H), 1.16 (dq, J = 7.7, 4.1 Hz, 2H).

The synthesis of (E)-5-(2-(6-cyclopropyl-5-(4-ethylphenyl)-2,2-difluorodioxaborinin-4-yl)vinyl)-N,N-diethylpyridin-2-amine **(PTO-18)**: 6-(diethylamino)nicotinaldehyde (64 mg, 0.36 mmol) and 2b (100 mg, 0.36mmol) were dissolved in toluene (2.0 mL), followed by the additions of acetic acid (15.5 μL, 0.092 mmoL), tetrahydroisoquinoline (11.5 μL, 0.276 mmoL). The resulting solution was stirred at r.t. for 7 h. The mixture was extracted with CH_2Cl_2 (3 × 40 mL), and the organic phase was dried over Na_2SO_4. After the solvent was removed in vacuum, the residue was purified by flash column chromatography (CH_2Cl_2) to give PTO-18 as an orange solid (77 mg, 48.8%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 8.25 (d, J = 2.4 Hz, 1H), 7.94 (d, J = 15.3 Hz, 1H), 7.39 (dd, J = 9.1, 2.5 Hz, 1H), 7.34 – 7.16 (m, 4H), 6.42 (d, J = 9.1 Hz, 1H), 6.19 (d, J = 15.3 Hz, 1H), 3.55 (q, J = 7.1 Hz, 4H), 2.74 (q, J = 7.6 Hz, 2H), 1.68 (tt, J = 8.1, 4.5 Hz, 1H), 1.47 (q, J = 3.9 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H), 1.19 (t, J = 7.1 Hz, 6H), 1.03 (dq, J = 7.6, 3.8 Hz, 2H). HRMS(ESI) $C_{23}H_{29}BF_2N_2O_2$, $[M+H]^+$ calculated= 439.2363; found= 439.2379.

The synthesis of 4-(1-cyclopropyl-1,3-dioxobutan-2-yl)benzonitrile **(3a)**: 1-cyclopropylbutane-1,3-dione (0.900 ml, 7.9 mmol) and 4-Iodobenzonitrile (1000 mg, 4.36 mmol) were dissolved in DMSO (20 mL), and then K_2CO_3 (2.40 g, 17.4 mmol), CuI (c.a.) and L-Proline (200 mg, 1.77 mmol) were added to the mixture, which were stirred at 90 °C for 18 h. The reaction mixture was dissolved in water, and then extracted with ethyl acetate (3*15 mL), washed with saturated NaCl, and dried over Na_2SO_4. Flash column chromatography (70:1 Petroleum ether : ethyl acetate) afforded 3a (205 mg, 20.6%) as pale-yellow oily liquid. ^{1}H NMR (300 MHz, CDCl3) δ (ppm): δ 16.58 (s, 1H), 7.27 – 7.09 (m, 4H), 1.88 (s, 3H), 1.69 (tt, J = 8.0, 4.5 Hz, 1H), 1.48 (q, J = 3.9 Hz, 2H), 1.04 (dq, J = 7.6, 3.9 Hz, 2H)

The synthesis of 4-(4-cyclopropyl-2,2-difluoro-6-methyl--dioxaborinin-5yl)

benzonitrile **(3b)**: $BF_3 \cdot Et_2O$ (0.485 ml,1.80 mmol) was added to 3a (205mg, 0.9 mmol) in tributyl borate (0.485ml, 1.80 mmol) slowly under the protection of nitrogen. The reaction mixture was then stirred at r.t. for 5 h. A brownish yellow residue (200 mg, yield 81.0%) was obtained after removing the solvent. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.16 (m, 4H), 1.70 (tt, J = 8.0, 4.5 Hz, 1H), 1.47 – 1.32 (m, 6H), 1.49 (q, J = 3.9 Hz, 2H), 1.05 (dq, J = 7.6, 3.9 Hz, 2H).

The synthesis of (E)-4-(4-cyclopropyl-6-(2-(6-(diethylamino)pyridin-3-yl)vinyl)-2,2-difluoro-dioxaborinin-5-yl)benzonitrile **(PTO-26)**: 6-(diethylamino)nicotinaldehyde (72 mg, 0.41 mmol) and 3b (113 mg, 0.41mmol) were dissolved in toluene (2.0 mL), followed by the additions of acetic acid (14 μL, 0.246 mmoL), tetrahydroisoquinoline (10.5 μL, 0.082 mmoL). The resulting solution was stirred at r.t. for 6 h. The mixture was extracted with CH_2Cl_2 (3 × 40 mL), and the organic phase was dried over Na_2SO_4. After the solvent was removed in vacuum, the residue was purified by flash column chromatography (CH_2Cl_2) to give PTO-26 as an orange solid (80mg, 44.0%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 8.26 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 15.1 Hz, 1H), 7.81 (d, J = 7.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.39 (dd, J = 9.2, 2.4 Hz, 1H), 6.46 (d, J = 9.2 Hz, 1H), 5.97 (d, J = 15.1 Hz, 1H), 3.57 (q, J = 7.2 Hz, 4H), 1.51 (dd, J = 11.0, 5.6 Hz, 3H), 1.21 (t, J = 7.1 Hz, 6H), 1.09 (t, J = 5.8 Hz, 2H). HRMS(ESI) $C_{23}H_{27}BF_2N_2O_2$, $[M+H]^+$ calculated=436.1930; found=436.2061.

The synthesis of 4-((1E,3E)-4-(6-cyclopropyl-5-(4-ethylphenyl)-2,2-difluoro-2H-dioxaborinin-4-yl)buta-1,3-dien-1-yl)-N,N-dimethylaniline **(PTO-29):** 4-(Dimethylamino) cinnamaldehyde (82 mg, 0.46 mmol) , 2b (100 mg, 0.32 mmol) was dissolved in methylbenzene (2.0 mL), followed by the additions of acetic acid (15.5 μL, 0.276 mmoL), tetrahydroisoquinoline (11.5 μL, 0.092 mmoL). The resulting solution was stirred at r.t. for 6.5 h. The mixture was extracted with CH_2Cl_2 (3 × 40 mL), and the organic phase was dried over Na_2SO_4. After the solvent was removed in vacuum, the residue was purified by flash column chromatography (CH_2Cl_2) to give PTO-29 as a

black green solid (128 mg, 64.0%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 7.88 (dd, J = 14.4, 11.6 Hz, 1H), 7.38 (d, J = 9.4 Hz, 4H), 7.25 (d, J = 7.7 Hz, 2H), 7.02 (d, J = 15.1 Hz, 1H), 6.69 (t, J = 10.3 Hz, 3H), 5.90 (d, J = 14.5 Hz, 1H), 3.07 (s, 6H), 2.79 (q, J = 7.6 Hz, 2H), 1.79 – 1.64 (m, 1H), 1.52 (t, J = 3.9 Hz, 2H), 1.37 (t, J = 7.7 Hz, 3H), 1.07 (dq, J = 7.7, 3.8 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ (ppm): δ 190.51, 175.96, 151.77, 149.85, 146.44, 144.48, 131.86, 130.58, 129.98, 128.62, 123.77, 122.50, 119.17, 114.45, 111.97, 40.21, 28.71, 16.86, 15.48, 13.78. ESI-MS (M+H) m/z: 436.62; HRMS calculated for 435.2289, m/z, [$(M + H)^+$]; 436.2267 found.

Molecular modelling study. PTO-29 docking search with Aβ oligomer were executed by using AutoDock 4.0 software package. The docking simulations were carried out with a box centered on the Aβ oligomer and employing 50 × 50 × 50 grid points. For the Aβ oligomer structure, we served X-ray RCSB database (PDB ID: 4NTR) determined Aβ trimmers derived from the β-amyloid peptide as a working model for toxic Aβ oligomers[1,2].

Preparation of the Aβ42 oligomers. The preparation was performed according to Kayed's reported procedure[3].

Preparation of the Aβ42 aggregates. Aβ42 peptide (1.0 mg) was resuspended in 1% hydroxylamine solution (1.0 mL). One hundred microliters of the resulting solution were diluted 10-fold with PBS buffer (pH 7.4) and stirred at room temperature[4,5].

Log P measurement. PTO-29 (250 μM) in octanol (1.5 mL) was subjected to partition with octanol saturated water (1.5 mL). The resulting mixture was stirred vigorously for 5 min and centrifuged at 3000 × g for 5 min. The octanol layer was separated, and its fluorescence spectrum was recorded (Ex = 560 nm). The above water layer was partitioned with water-saturated octanol (1.5 mL); the octanol layer was separated after 5 min of vigorous stirring and 5 min of centrifugation at 3000 × g, and its spectrum was recorded. The log P value was calculated using the F.I. ratio at 680 nm

for the above two octanol extractions.

Fluorescence spectral testing of PTO-29 with Aβs and BSA. To test the interactions of PTO-29 with Aβs and BSA, the solution tests were conducted by following the previously re-ported procedures[5].

BBB penetration test. C57BL/6 mice were I.V. injected with PTO-29 (4.0 mg/kg). After 30 min, mice were per-fused with saline solution, and the brains were excised. The brain samples were homogenized in 2.0 mL water followed by the addition of ethyl acetate (2.0 mL). The resulting homogenate was stirred for 2 h and centrifuged for 5 min at 3750 × g. The extractions were subjected to fluorescence spectral recording[5].

The quantitative determination of the brain pharmacokinetics. The test was conducted following previously established procedures[6].

Brain phantom imaging. A 5-month old wild-type (C57BL/6) mouse was sacrificed. The brain was dissected, then homogenized with 2.0 mL of PBS. 0.1 mL of homogenate was added to 15 wells of a 96-well plate, followed by the addition of PTO-29 (25 μM, 6.6 μL) and the Aβ monomer, oligomers and aggregates (25 μM, 19.8 μL). The resulting brain homogenates were recorded using an IVIS®Spectrum imaging system the parameter is Ex/Em = 570 nm/660 nm. The P values were calculated using Student's t-test[5,7].

Stability of PTO-29 in serum. The experiment of stability of the probe in serum was performed by following the previously reported methods[5,8].

Cell cytotoxicity test of PTO-29. A human neuronal cell line (SH-SY5Y) were planted in 96-well plates at a concentration of 5000 per well. After around 12 h, the cells were treated with different concentrations of PTO-29 or 0.1% DMSO for 24 h. And then the cells were incubated with 20 μL 5 mg/mL MTT solution for 4h. After incubation, the media were discarded and 100 μL of DMSO was added into each well. Subsequently, the plates were read at 570 nm by using a microplate reader. The experiments were

repeated three times independently[5,8].

***In vivo* NIRF imaging.** Four-month female transgenic APP-PS1 and age-matched wild type mice (n = 3-4) were shaved in the brain region, then background signals were recorded. A solution of PTO-29 (4 mg/kg) was freshly prepared in the mixture solvents (15% DMSO, 15% cremorphor and 70% PBS). Before injection, the solution was stabilized for 20 min. 100 µL of PTO-29 was injected intravenously to the mouse. Fluorescence signals from the brain were recorded prior to and 30, 60, 120, 240 and 360 min after I.V. injection of the probe. To evaluate the imaging results, an ROI was drawn around the brain region. *In vivo* study was performed using an IVIS®Spectrum animal imaging system (Caliper Life-Sciences, Perkin Elmer). The images were acquired with the parameter of 570 nm excitation and 660 nm emission filter. Data analysis was calculated with LivingImage® 4.2.1 software[5,8].

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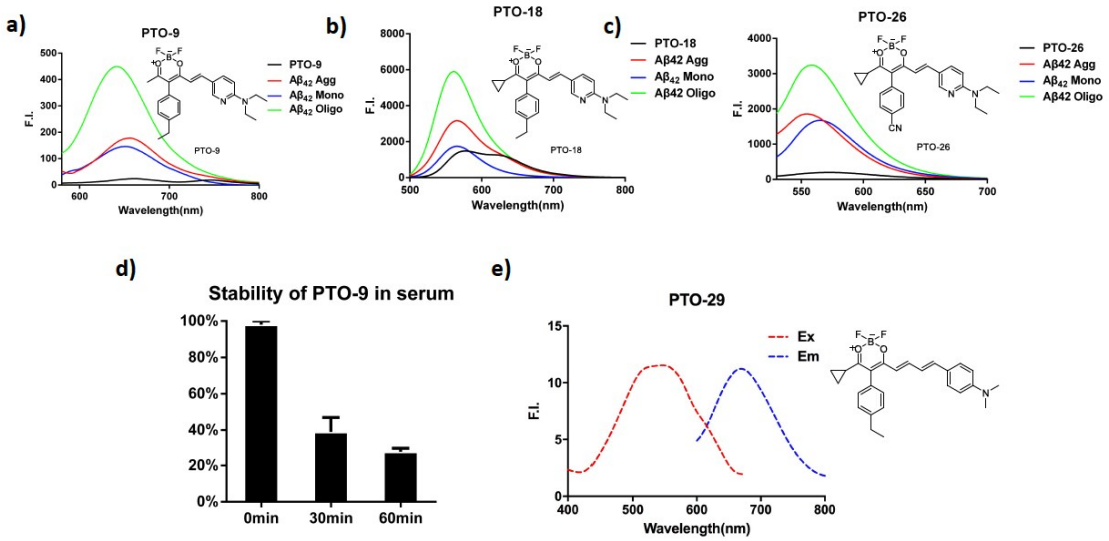
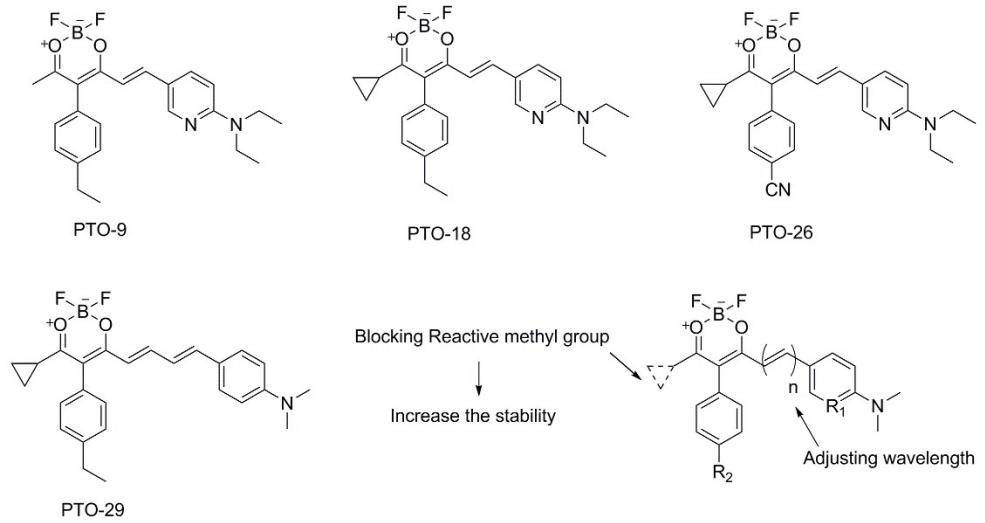
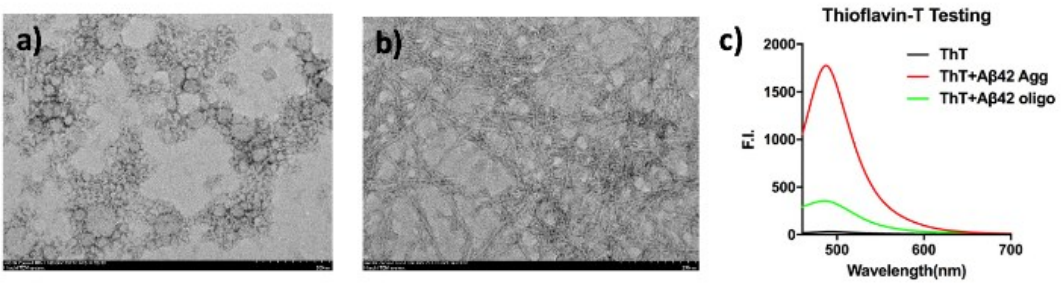
Figures



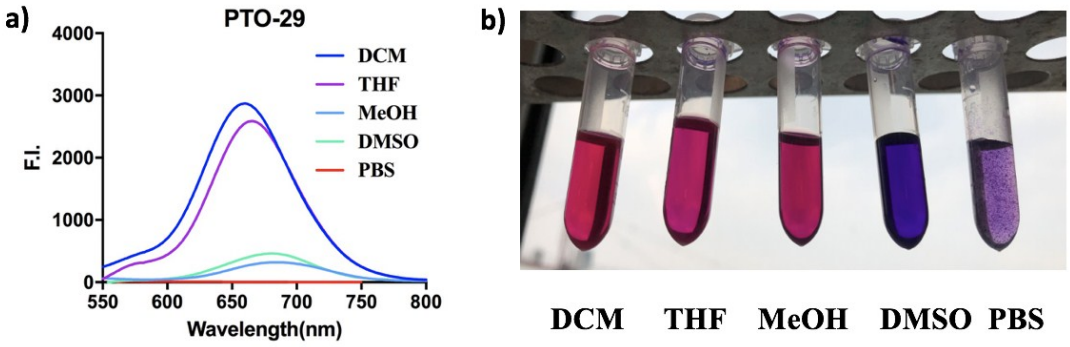
SI Fig.1 The four "V-shape" probes. a-c) The response of **PTO-9**, **18** and **16** to Aβs (monomers, oligomers and aggregates); d) Stability of PTO-9 in the serum; e) Fluorescence excitation/emission spectra of **PTO-29** in PBS.



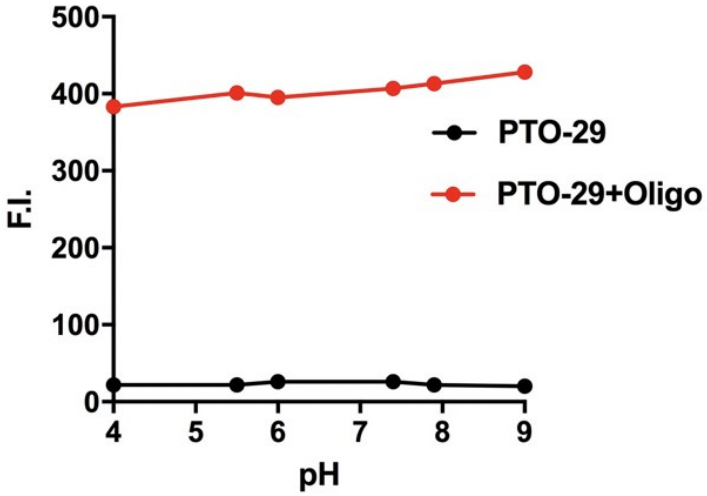
SI Fig.2 The structure of PTO-9, PTO-18, PTO-26 and PTO-29



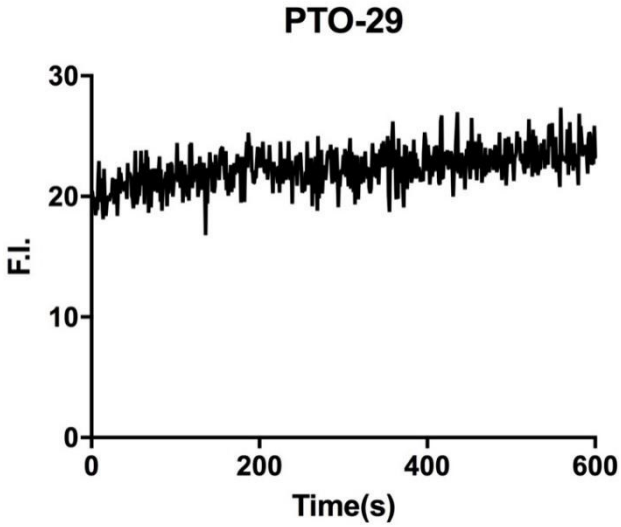
SI Fig.3 TEM images and the curves of ThT test. (a-b) TEM images of Aβ42 oligomers and aggregates, scale bar 200 nm; (c) The fluorescence curves of ThT to oligomers and aggregates.



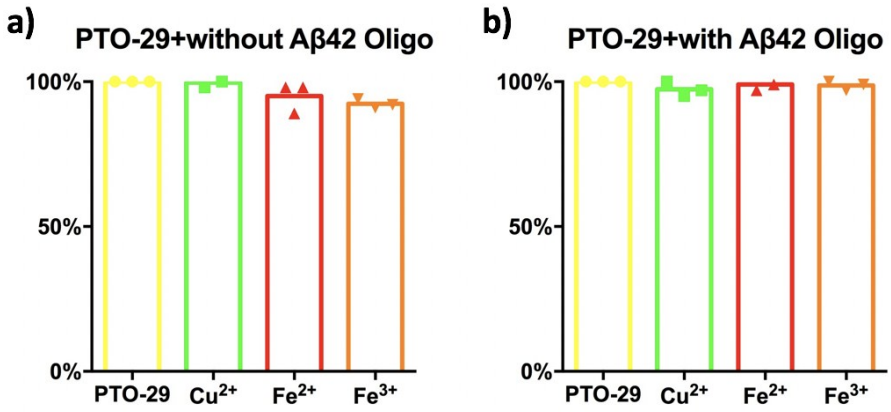
SI Fig.4 a) Emission fluorescence spectra of **PTO-29** in various solvents (DCM, THF, methanol, DMSO and PBS), the final concentration is 500nM; b) The color of **PTO-29** in different solvents.



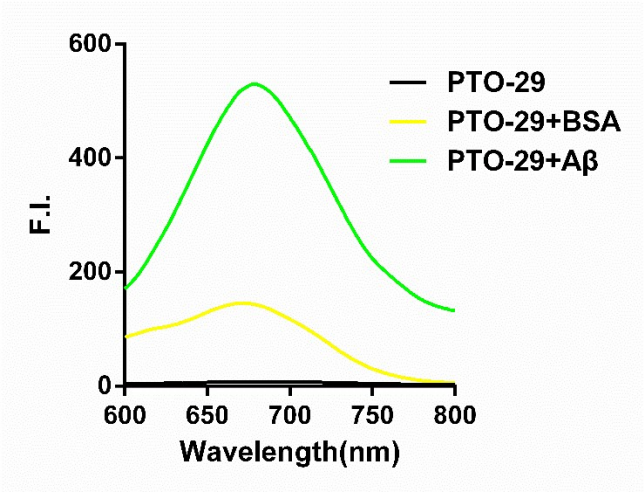
SI Fig.5 Stability of **PTO-29** and incubated with oligomers in different pH values.



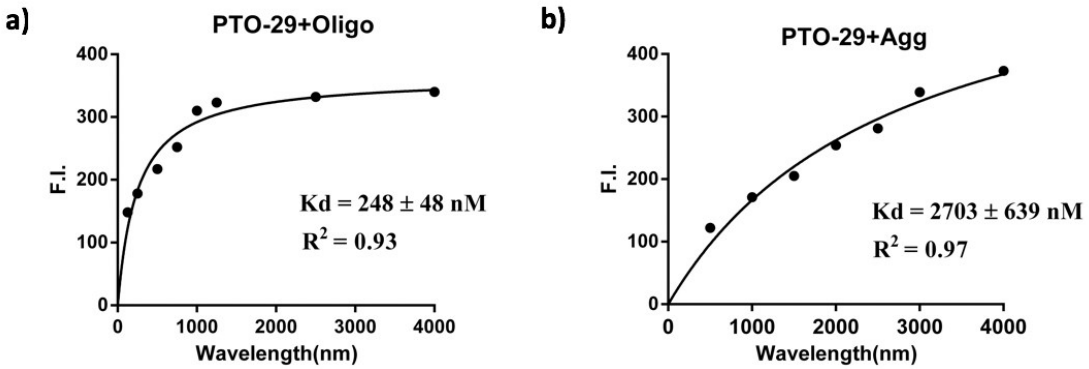
SI Fig.6 Photostability of **PTO-29** for 10min.



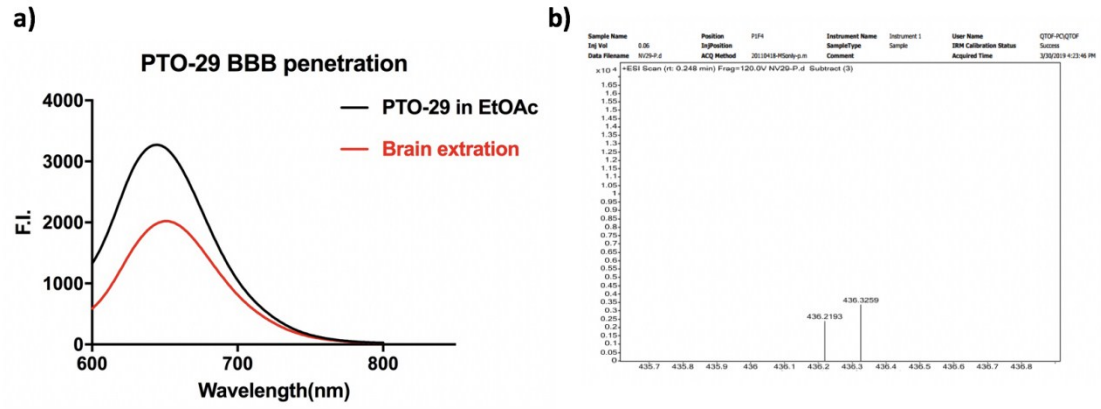
SI Fig.7 Quenching effects of metal ions (Cu^{2+}, Fe^{2+} and Fe^{3+}) on the fluorescence of alone and with Aβ42 oligomers.



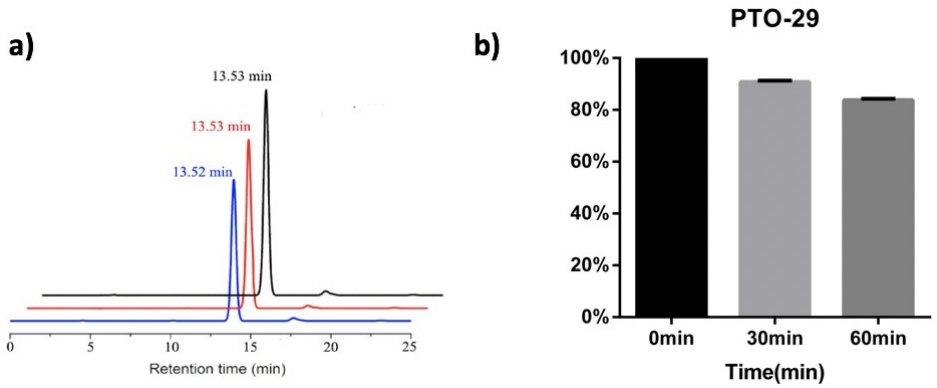
SI Fig.8 Emission fluorescence spectra of PTO-29 upon interaction with Aβ42 oligomers and BSA.



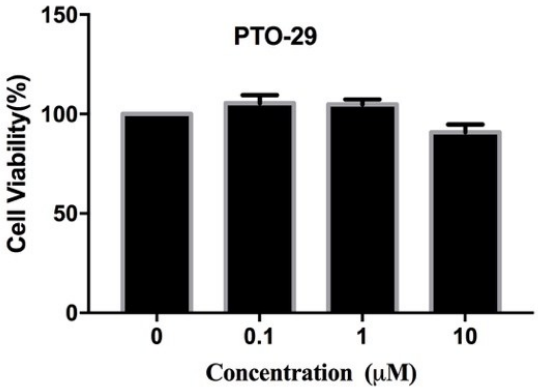
SI Fig.9 K_d of **PTO-29** to oligomers and aggregates.



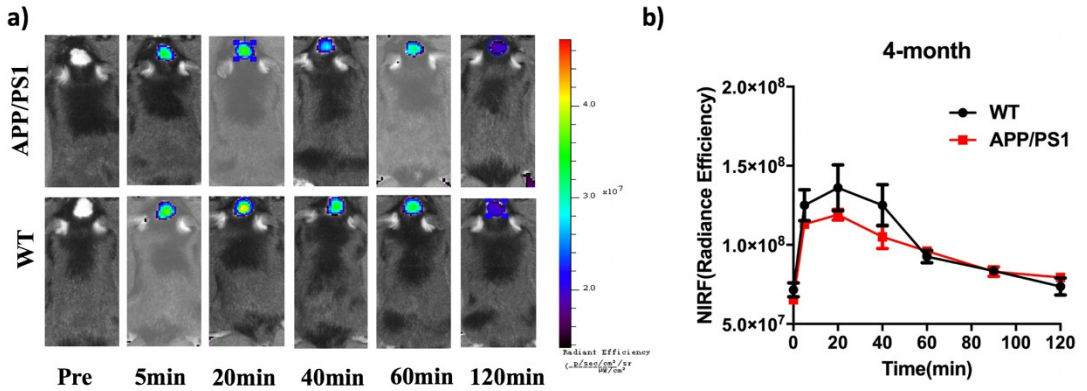
SI Fig.10 BBB penetration studies of **PTO-29**. a) Emission fluorescence spectra of **PTO-29** in Ethyl Acetate (EtOAc) (standard) and brain extraction with EtOAc after **PTO-29** was I.V. injected; b) HRMS of **PTO-29** in brain extraction.



SI Fig.11 *In vitro* stability of **PTO-29** in mouse serum at 37℃. (a) HPLC profiles of **PTO-29** after incubation with mice serum for 0-, 30- and 60-min; (b) Quantification of HPLC peaks, and nearly 85% of **PTO-29** was remained after incubating in mouse serum for 60-min.



SI Fig.12 Cell viability after incubation of PTO-29 at different concentrations with SH-SY5Y by MTT assay at 37°C for 24 h (each sample was tested using three replicates, and the results are reported as the mean ± standard deviation).



SI Fig.13 *In vivo* NIRF imaging with **CRANAD-2**. a) Representative images of APP/PS1 and WT mice after I.V. injection with **CRANAD-2** at 5-, 20-, 40-, 60- and 120-min; b) Time-course curves of NIRF from **CRANAD-2** in APP/PS1 and WT mice.

Table S1 Spectroscopic data for PTO-29.

Probe	λ_{ex} (nm)	[a]λ_{em1} (nm)	[a]λ_{em1} (nm)	[b]Φ (%)	[c]K_d(nM)	[d]K_d(nM)
PTO-29	550	675	656	15	248±48	2703±639

[a] Determined in PBS (λ_{em1}) and upon binding with $A\beta_{42}$ oligomers (λ_{em1}).

[b] QYs were measured in DCM

[c] For $A\beta_{42}$ aggregates

[d] For $A\beta_{42}$ oligomers

[c d] Measured in triplicate with results given as the mean ± SD

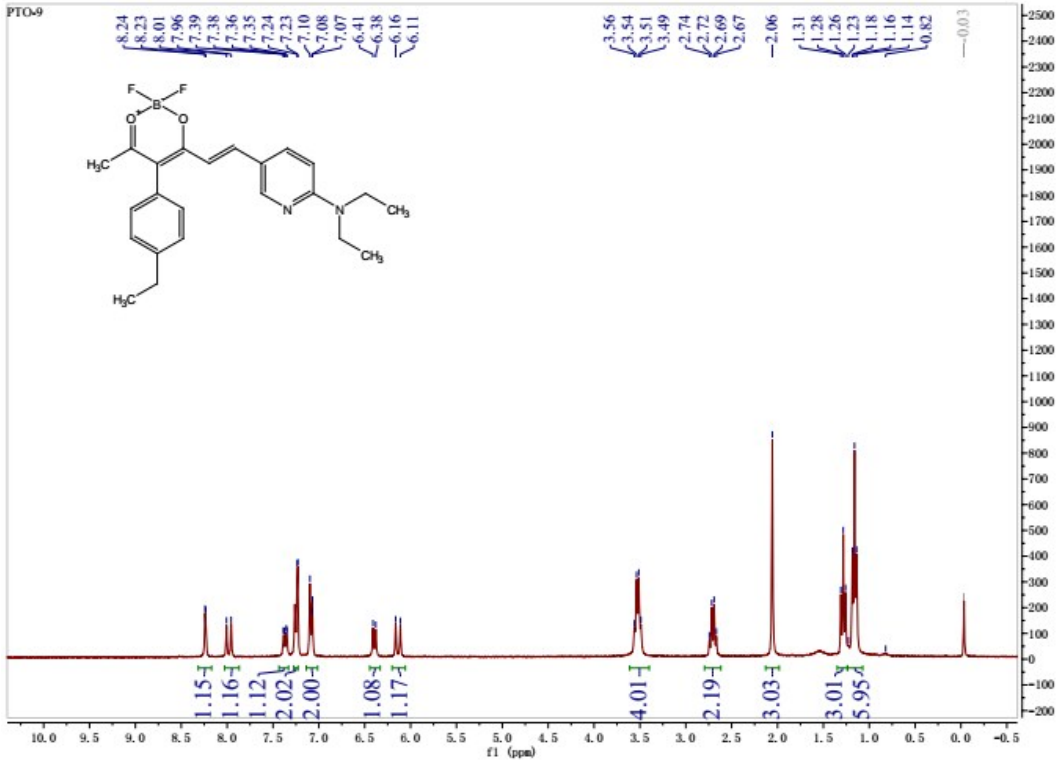
Table S2 The conditions used in HPLC analyses.

Table S3 Biodistribution of PTO-29 in brains of ICR mice

Probe	log P	Time after injection（% ID/g）				$Brain_{2\ min}/brain_{60\ min}$
		2	10	30	60	
PTO-29	3.13 ± 0.019	6.99 ± 0.40	5.05 ± 0.61	3.28 ± 0.10	1.77 ± 0.20	3.9

Probe	HPLC analyses			
	Eluent	Retention time	UV detector	Recovery rate
	H_2O:CH_3CN	min	nm	
PTO-29	20:80	14.13	320	0.96 ± 0.012

Appendixes: ^{1}H NMR, ^{13}C NMR and HRMS



Sample Name		**Position**	P2A4	**Instrument Name**	Instrument 1
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Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	PTO-9
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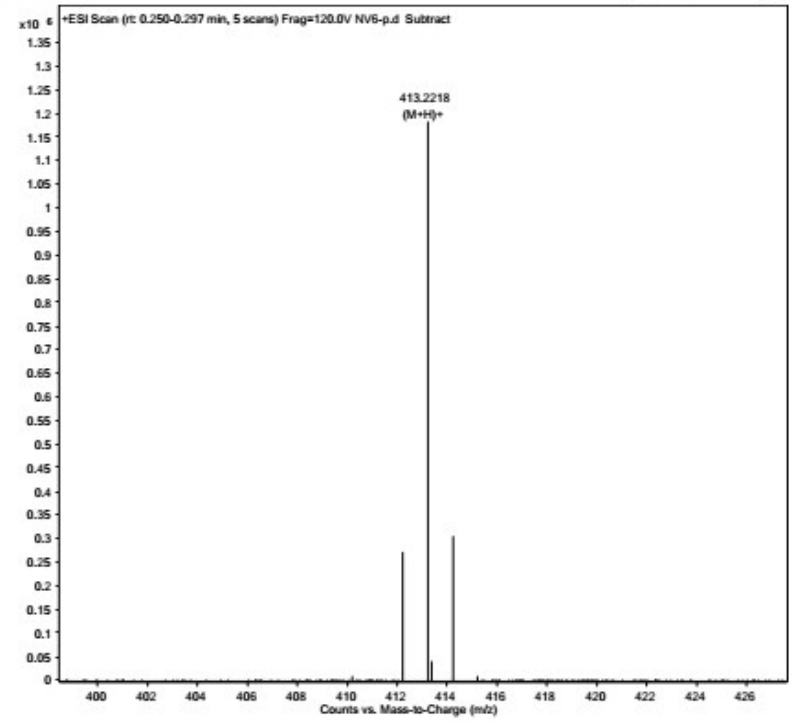

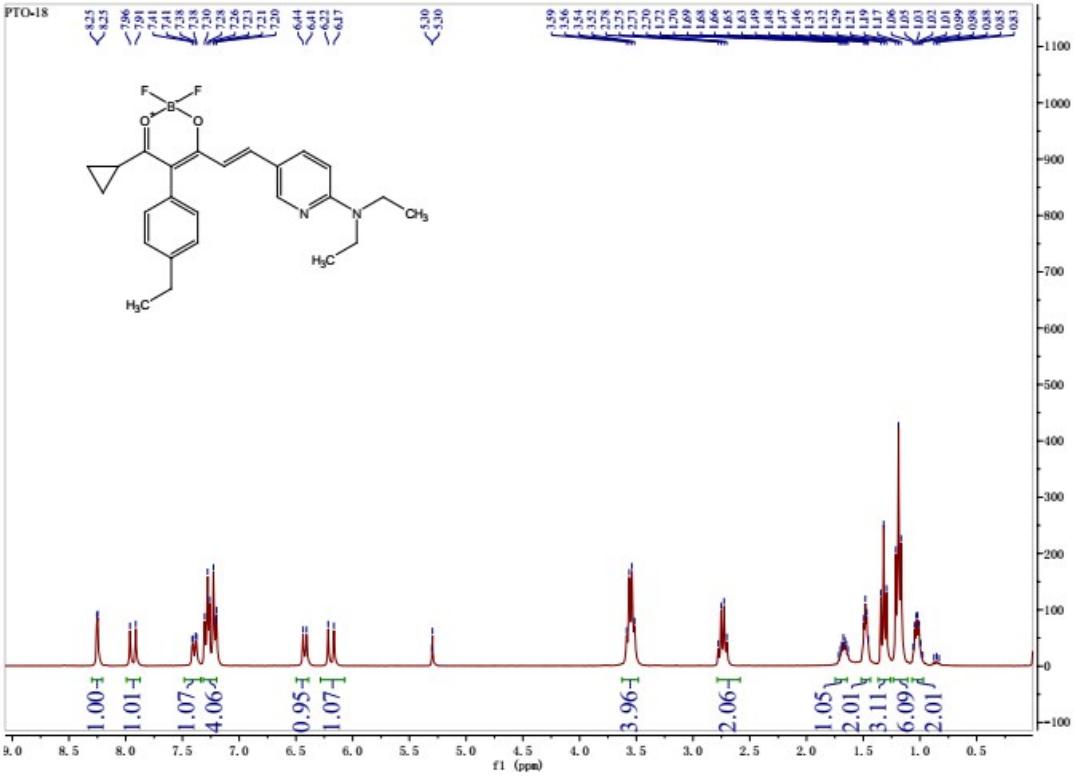

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Sample Type	Sample	IRM Calibration Status	Success	Data Filename	PTO-18
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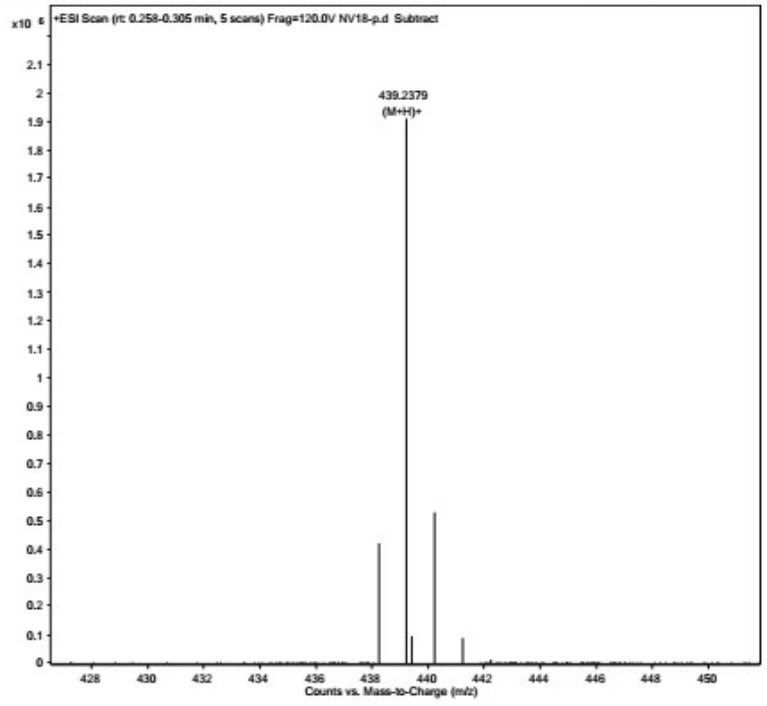

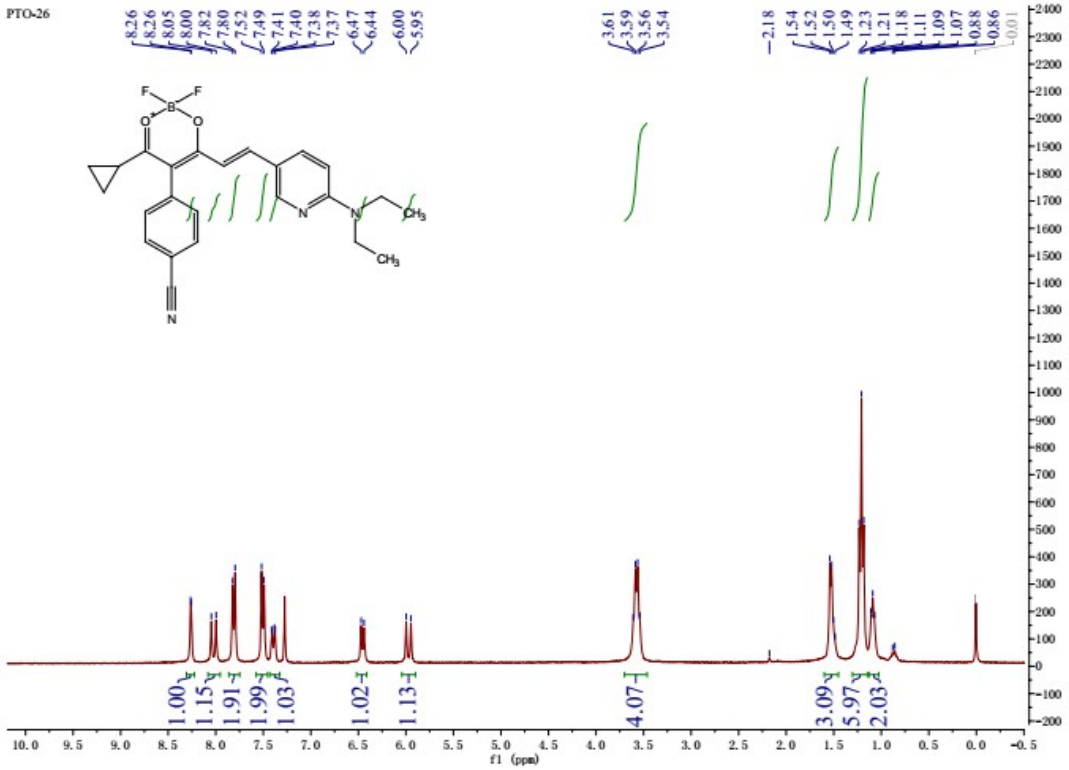

Sample Name		**Position**	p1e3	**Instrument Name**	Instrument 1	**User Name**	G6520B-PC\Admin
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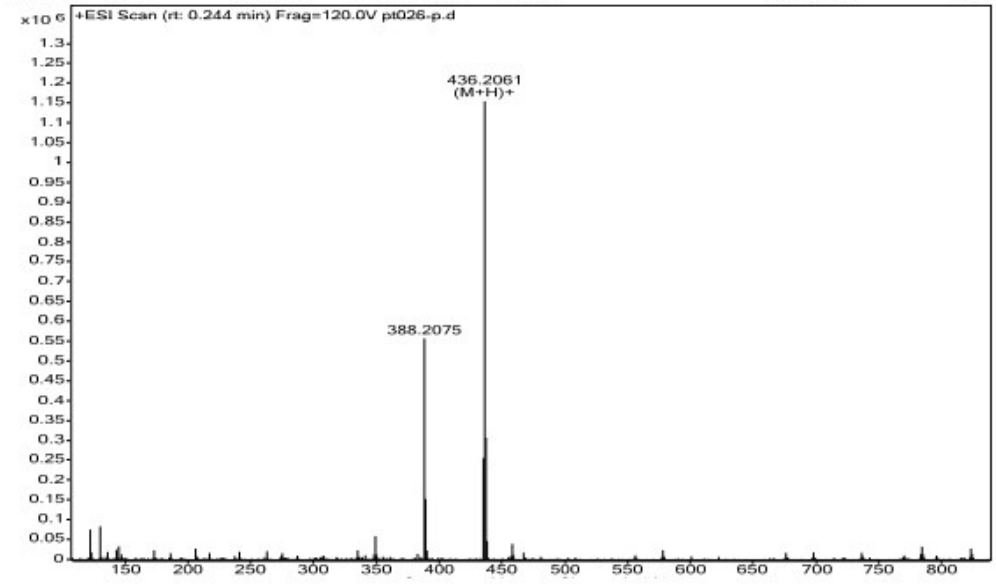

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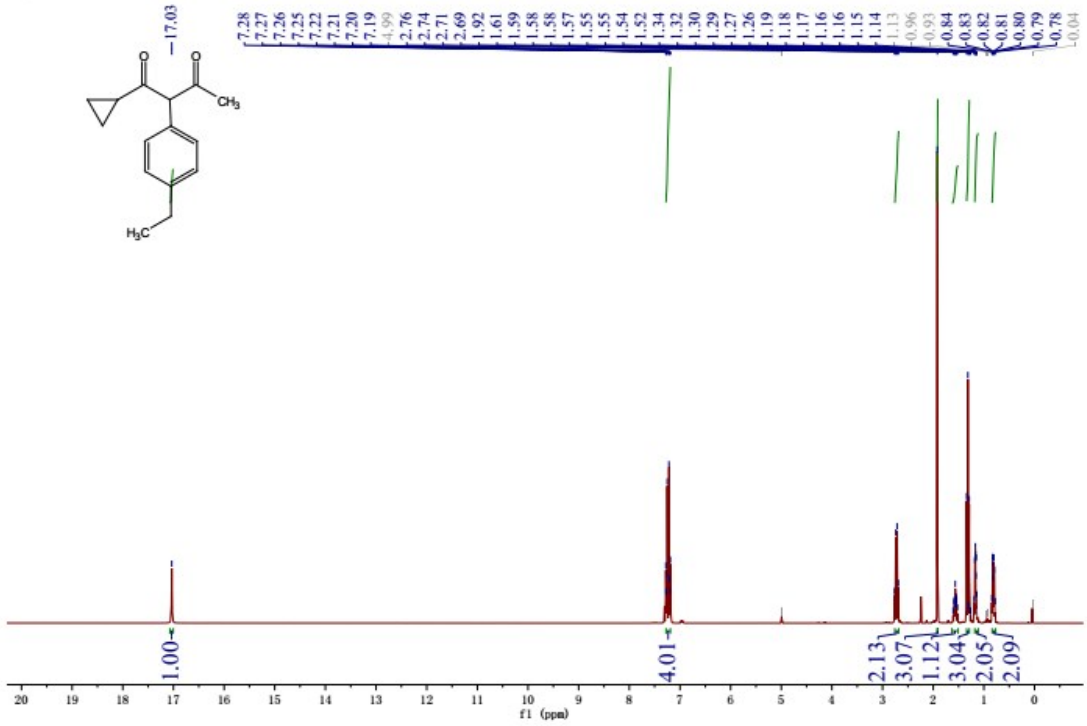

Sample Name		**Position**	p1e4	**Instrument Name**	Instrument 1	**User Name**	G6520B-PC\Admin
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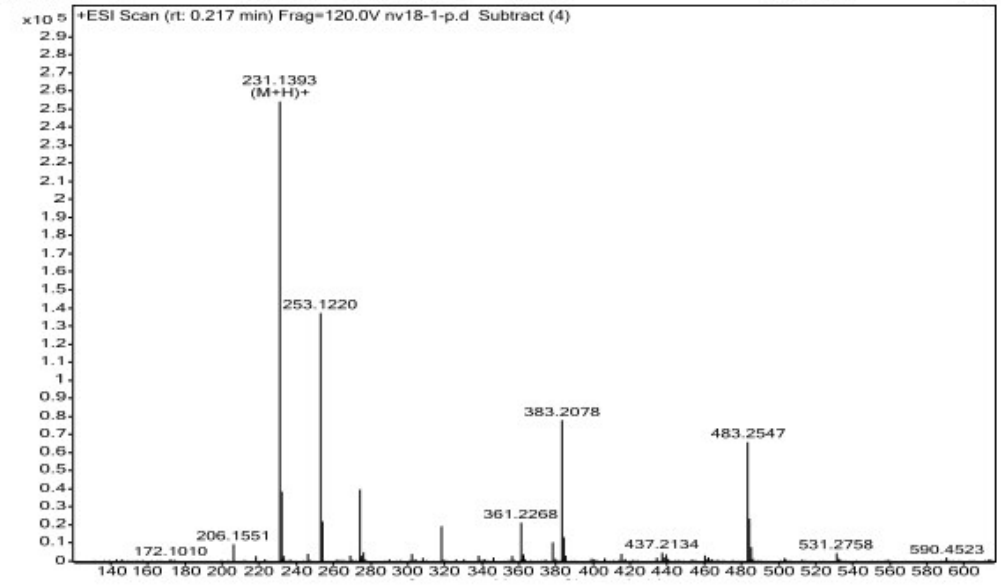
Data Filename	2a	**ACQ Method**	20110418-MSonly-p.m	**Comment**		**Acquired Time**	11/29/2019 5:05:38 PM



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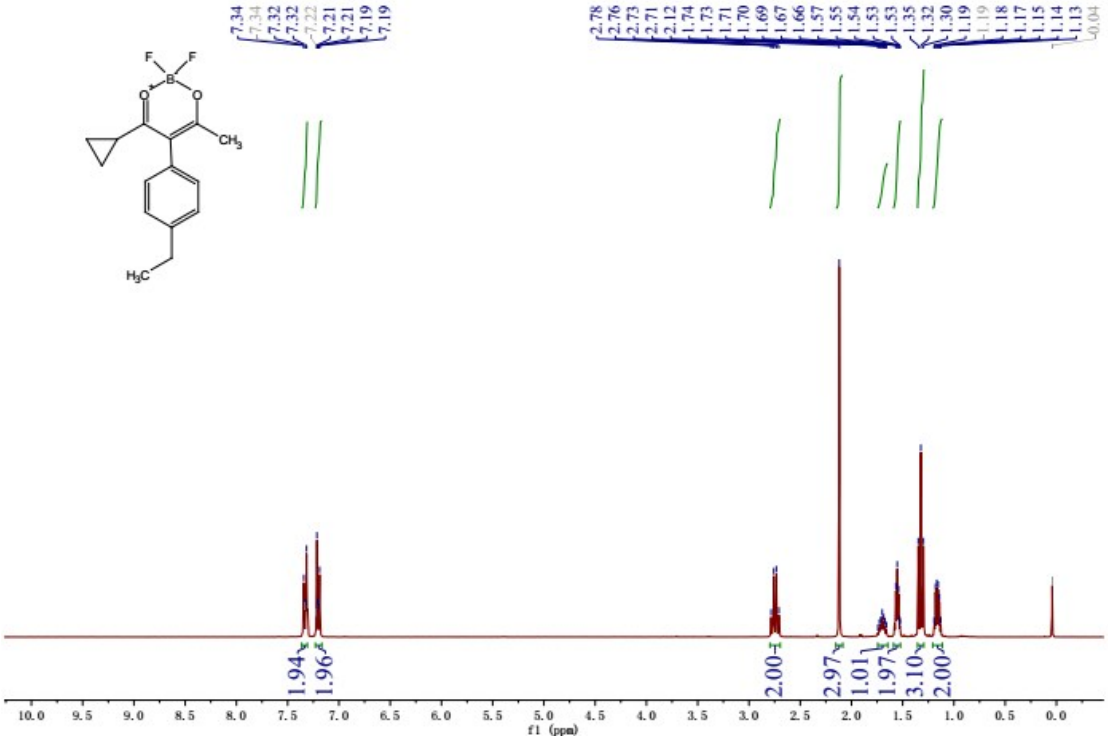
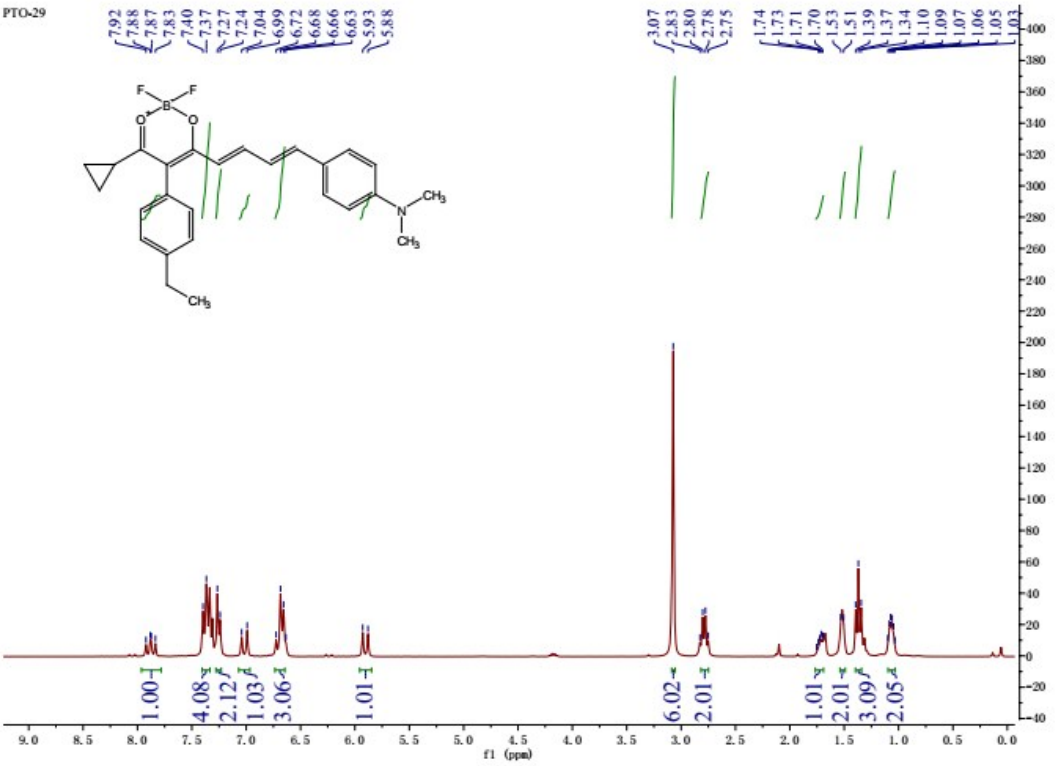
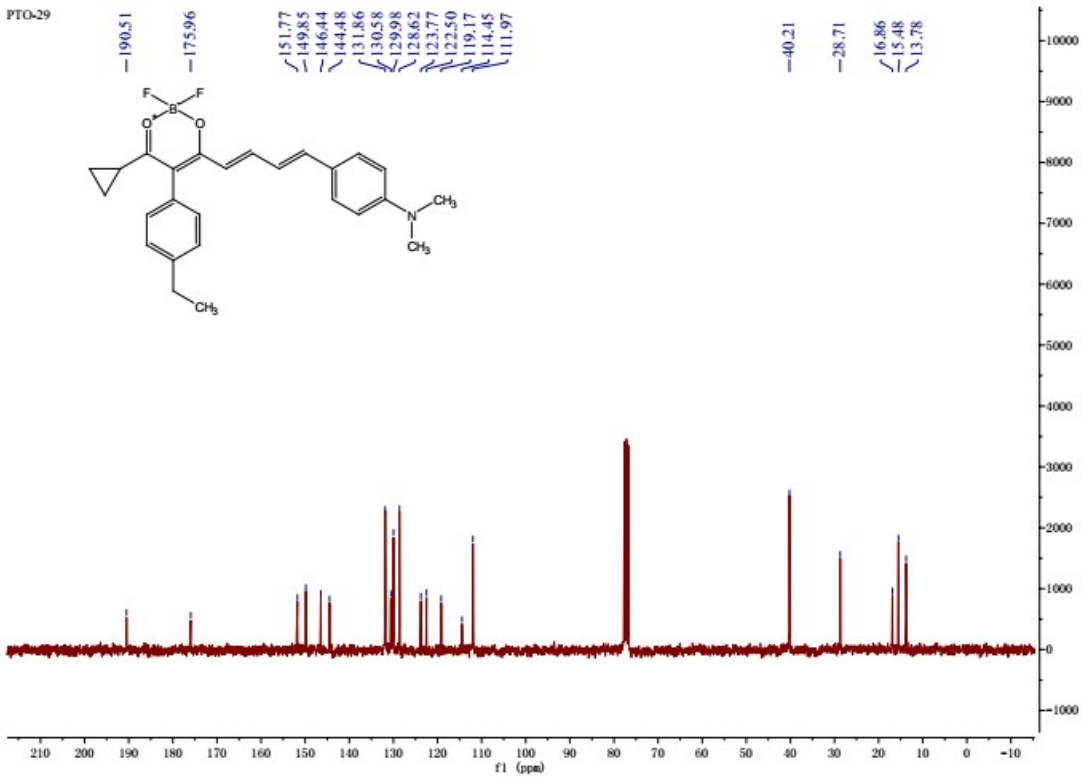


PTO-29





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