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Supporting Information

A novel amphiphilic fluorescent probe BODIPY—O-CMC—cRGD as nanoparticle vector

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Experiment:

Synthesis

Compound 1: ethyl 6-(4-formylphenoxy) hexanoate

A mixture of 4-hybroxybenzaldehyde derivative (2.440 g, 20 mmol) and ethyl 6-bromohexanoate (4.906 g, 22 mmol) was refluxed in dry acetone for 12 h in the presence of potassium carbonate. The crude mixture was filtered to remove remaining K_2CO_3.And the resulting solution was concentrated in vacuo and purified by silica gel column chromatography by using CH_2Cl_2/hexane. ^{1}H NMR (400MHZ, $CDCl_3$ δ inppm):δ=9.87(s,1H),7.82(d,J=8.8,2H),6.98(d,J=8.6,2H),4.13(q,J=7.1 Hz,2H),4.05(t,J=6.4Hz,2H),2.32(t,J=7.5,2H),1.84(m,2H),1.72(m,2H), 1.52(m,2H),1.27(t, J=7.0,3H).MALDI-TOF MS calcd for $C_{15}H_{20}O_4$ 264.32,found 264.7892.

Compound 2: ethyl 6-(4-(3,7-dibromo-5,5-difluoro-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenoxy)hexanoate

This compound was prepared in a sequence of steps in one pot reaction. Compound 1 (2.640 g, 10 mmol) and 2.5 equivalent of pyrrole (1.68 g,25 mmol) was dissolved in dry CH_2Cl_2 under nitrogen over 0.5 h, then one drop of CF_3COOH was added and the solution was stirred for 1.5 h at room temperature. A simple base wash followed by removal of the solvent and vacuum desiccation gave dipyrromethene. The intermediate in dry THF was added dropwise with 2.2 equivalent of N-bromosuccinimide (3.89 g,22 mmol) in dry THF under nitrogen in an ice bath over 1 h and stirred for another 1 h .When the reaction mixture was warmed to room temperature, 2.3-Dichloro-5,6-dicyno-1,4-benzoquinone (DDQ)(2.50 g, 11 mmol) in dry THF was added dropwise over 10 min. The reaction was monitored by TLC. The organic solvent was removed on a rotary evaporator under vacuum. The crude intermediate product was purified by flash column chromatography using CH_2Cl_2 to collect the red intermediate product. A solution of collected intermediate product and triethylamine(2 ml) in dried toluene were stirred about 5 min, then 6 mL of $BF_3{\cdot}Et_2O$ was added dropwise. The mixed solution was refluxed for an 1 h. The reaction mixture was washed with 0.1 M NaOH solution and methylene dichloride successively. The organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude compound was filtered by flash column. The residue was purified by silica gel column chromatography by using dichloromethane/petroleum ether and the required red powder compound.^{1}H NMR (400 MHz,DMSO-d6 , δ in ppm) δ=7.73(d, J=8.8Hz, 2H), 7.68(d, J=8.8Hz, 2H), 7.28(d, J=4.4, 2H), 6.72(d, J=4.4, 2H), 4.09(d, J=2.6Hz,2H), 4.03(d, J=2.8,3H), 2.00(d, J=7.7Hz, 2H),1.34(d, J=7.4Hz, 2H）1.06(t, J=7.0Hz,3H), 1.41(d, J=7.2Hz,2H). MALDI-TOF MS calcd for $C_{23}H_{23}BBr_2F_2N_2O_3$ 582.01, found 583.2376.

Compound 3: ethyl 6-(4-(5,5-difluoro-3,7-bis(4-methoxyphenyl)-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenoxy)hexanoate

Compound 2, 4-methoxyphenylboronic acid(2.9 g, 5 mmol), and K_2CO_3(1.38 g, 10 mmol) was dissolved in the solvent pair(toluene/water) in a 100 ml round-bottomed flask fitted with a reflux condenser. After bubbling with nitrogen for half an hour, a catalytic amount of $Pd(PPh_3)Cl_2$ (3.5 mg) was added and the reaction mixture was refluxed at 80 ℃ for 8 h.The system was cooled to room temperature and then extracted with CH_2Cl_2/H_2O twice. The organic layer was then dried with $MgSO_4$ and evaporated in vacuum. The residue was subjected to chromatography on a silica gel by using dichloromethane/hexane. ^{1}H NMR (400MHZ, $CDCl_3$ δ in ppm): δ=7.90 (d,J=8.7Hz,4H),7.46(d,J=2.4Hz,2H),6.88(d,J=8.7Hz,4H),6.78(d,J=4.0H z,2H),6.62(d,J=4.4Hz,2H) ,6.53(d,J=4.3Hz,2H),4.10(q,J=7.5Hz,2H),4.04(t,J=7.4,2H),3.81(s,6H),1.6 2(m,2H),1.53(m,2H), 1.30(m,2H). MALDI-TOF MS calcd for $C_{37}H_{37}BF_2N_2O_5$ 638.28, found 638.2170.

Compound 4: ethyl 6-(4-(5,5-difluoro-3,7-bis(4-methoxyphenyl)-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenoxy)hexanoate

The compound 3 (1.276 g,2 mmol) and KOH(4.704 g, 84 mmol) were dissolved in EtOH (59 ml) and the mixture solution was refluxed at 85℃ for 1h.After cooling to the room temperature, the mixture product was neutralized with dilute HCl, extracted with CH_2Cl_2 and dried with Na_2SO_4. The crude compound was purification by chromatography on a silica gel by using ethyl acetate/ methylene dichloride.^{1}H NMR (400MHZ, $CDCl_3$ δ in ppm):δ=7.87 (d, J = 8.9 Hz, 4H), 7.51 (d, J = 4.1 Hz, 2H), 7.04 (d, J = 7.1 Hz, 1H), 6.83 (d, J = 2.1 Hz, 1H), 6.61 (d, J = 4.4 Hz, 2H),6.95 (d, J = 8.9 Hz, 4H), 4.07 (t, J = 6.2 Hz, 1H), 3.85 (s, 6H),2.26(t,J=7,2H),1.80-1.20(m,6H). MALDI-TOF MS calcd for $C_{35}H_{33}BF_2N_2O_5$ 610.25, found 611.7846.

BODIPY dye: 2,5-dioxopyrrolidin-1-yl 6-(4-(5,5-difluoro-3,7-bis(4-methoxyphenyl)-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenoxy)hexanoate

The compound 4 (0.61 g, 1 mmol), N-hydroxysuccinimide(0.23 g, 2 mmlo), dimethylaminopyridine(DMAP) (0.244 g,2 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (0.382 g, 2 mmol) were dissolved in dry dichloromethane at 35℃ for 2 h. After that, the mixture was washed with 2 × 10 mL of water, the organic phase was dried with $MgSO_4$ and evaporated in vacuum. The crude product was purified by chromatography on silica gel by using dichloromethane/hexane.^{1}H NMR (400MHz, $CDCl_3$, δ in ppm) : 7.87(d,J=5.2Hz,4H)7.07(d,J=2.4,2H),7.52(d,J=2.4,2H),6.97(d,J=8Hz,4 H;Ar), 6.6(d, J=4.4，2H), 4.10(t, J=3.85), 6.88(d, J=4.6, 2H), 3.80 (s,6H), 4.10(t, J=9.2,2H), 3.98(t, J=2.5,2H), 2.68(S,2H), 2.58(S,2H) , 2.33(s, 2H),1.78-1.55（m, 6H）.MALDI-TOF MS calcd for $C_{39}H_{36}BF_2N_3O_7$ 707.54, found 707.8739.