# Chiral Self-assembled (*β*, D)-RIB-TPE Micron vesicle with AIE Characteristics Used as Targeting-drug Carriers

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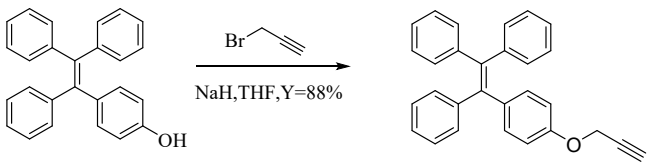
## Contents



## Synthesis

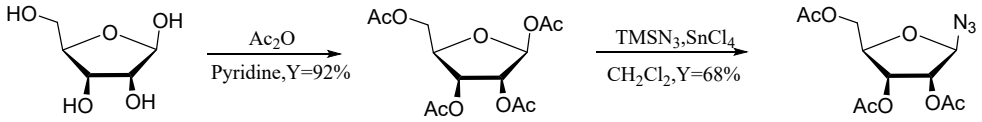
### Synthesis of the (2-(4-(prop-2-yn-1-yloxy)phenyl)ethene-1,1,2-triyl)tribenzene




TPE-OH 4

Accurately weighed TPE-OH 4-(1,2,2-triphenylvinyl)phenol (1.0 g, 2.87 mmol) and K2CO3 (0.7932 g, 5.74 mmol) were added to 100 ml three-necked flask, 30 ml of acetone was added to make it dissolved, and then 3-bromopropargyl (0.5 ml, 5.17 mmol) was added slowly to the system, stirred at room temperature for 10 min, then warmed up to 55 ℃ reflux, the reaction was 12h, after TLC detection of the reaction was complete (EA:PE=1:4), and then added distilled water quenched reaction, and then ethyl acetate was detected by TLC. After stirring for 10 min at room temperature, the reaction was refluxed at 55 ℃ for 12 h. The reaction was completely detected by TLC (EA:PE=1:4), the reaction was quenched by adding distilled water, and then extracted by ethyl acetate for three times, and the organic phases were combined, the organic phase was washed by saturated sodium chloride solution, and the organic phase was dried with anhydrous magnesium sulfate, filtered, spun-dried, and chromatographed by column chromatography (EA:PE=1:5), and a yellow color product was obtained **4** (2-(4-(prop-2-yn-1-yloxy)phenyl)ethene-1,1,2-triyl)tribenzen (0.9792 g) in the following yields 88%. 1H NMR (400 MHz, DMSO-d6) δ 7.08 (s, 9H), 6.94 (d, J = 8.0 Hz, 6H), 6.84 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.3 Hz, 2H), 4.68 (s, 2H), 3.53 (s, 1H).

**Synthesis of the 2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl azide**



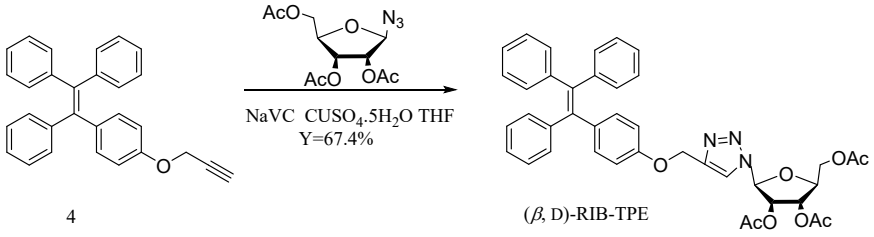

*R*-1 *R*-2 *R*-3

Accurately weigh *R*-**1** (2*S*,5*R*)-5-(hydroxymethyl)tetrahydrofuran-2,3,4-triol) (1.0g,6.66mmol) in a round-bottomed flask, add acetic anhydride(6.26ml,6.8mol) to dissolve it, stir for a few minutes, then add pyridine(1.61ml,1.58mol) and react for 12 h. After the reaction was completely detected by TLC, the reaction solution was diluted with ethyl acetate, and the organic phase was extracted several times by adding saturated sodium bicarbonate solution, followed by washing of the organic phase with saturated sodium chloride solution, drying with anhydrous magnesium sulfate, filtration, spin drying, and anhydrous ethanol recrystallization, which can be used to obtain the fully *R*-**2** (1,2,3,5-Tetra-O-acetyl-*b*-D-ribofuranose) (1.76g). Yield 83%. $^{1}$H NMR (400 MHz, Chloroform-d) δ 5.71 (d, J = 6.8 Hz, 1H), 5.20 (t, J = 8.3 Hz, 1H),

5.07 – 4.88 (m, 2H), 4.14 (dd, J = 12.0, 5.0 Hz, 1H), 3.52 (dd, J = 12.0, 8.4 Hz, 1H), 2.17 – 1.97 (m, 12H). 13C NMR (101 MHz, Chloroform-d)δ169.6,169.2, 168.5, 90.6, 67.0, 65.9, 62.4, 20.6, 20.4.

Accurately weighed whole *R*-**2** (1 g, 3.14 mmol) in 100 ml round bottom flask, under the protection of nitrogen, add dry dichloromethane, wait for the solid to be dissolved, $TMSN_3$(1.07 ml, 0.94 mol) and $SnCl_4$ (0.44 ml, 0.98 mol)were slowly added dropwise to the solution, stirred at room temperature for 1h, TLC detection of the reaction was complete, dichloromethane was added to dilute the reaction solution, saturated sodium bicarbonate solution was extracted for several times, the organic phases were combined, the organic phases were washed by saturated sodium chloride solution, dried with anhydrous magnesium sulfate, pumped filtration, spun-dried, column chromatography was performed to obtain *R*-**3** (2,3,5-tri-O-acetyl-*b*-D-ribofuranosyl azide) 0.68 g. Yield 72%. $^1$H NMR(400 MHz, Chloroform-d) δ 5.48 (t, J = 2.9 Hz, 1H), 5.09 (dd, J = 6.9, 3.3 Hz, 2H), 4.87 (dd, J = 6.2, 3.2 Hz, 1H), 4.06 (dd, J = 11.9, 4.0 Hz, 1H), 3.86 (dd, J = 11.9, 7.4Hz, 1H), 2.22 – 1.98 (m, 9H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 169.4, 169.1, 86.5, 84.8, 68.1, 67.2, 66.7, 66.3, 65.8, 65.3, 6.6, 20.4.

**Synthesis of (*β*, D)-RIB-TPE**




4 (*β*, D)-RIB-TPE

Accurately weigh **4** (0.34 g, 0.88 mmol) and *R*-**3** (0.32 g, 1.06 mmol) in 100 mL of Schlenk, several times evacuated and protected by argon, and then 10 mL of tetrahydrofuran was added to the system under an ice bath, while stirring and allowing the solids to be completely solved, and then accurately weighed after a few minutes to remove sodium ascorbate (0.39 g, 1.94 mmol) and copper sulfate pentahydrate (0.24 g, 0.97 mmol) were dissolved in 10 mL of water, and then added into the reaction system after they turned into earthy yellow colour.After it turned into earthy yellow, it was added into the reaction system, the colour of the system was yellow at the beginning,

and the colour of the solution changed to bright yellow and then to grass green after about 1h of reaction, and the reaction was carried out for 12 h at room temperature, and it was detected by TLC (pure EA, $R_f$=0.86). The reaction was quenched by adding 10 mL of ice water, extracted with 30 mL of ethyl acetate for three times, the organic phases were combined, washed with saturated NaCl solution, dried with anhydrous $MgSO_4$ for 30 min, filtered and spun-dried, and then separated by column chromatography (PE:EA=4:1), and 0.41 g of white solid was obtained, with the yield of 67.4%.$^1$H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 7.27 – 6.67 (m, 19H), 6.12 (d, J = 9.1 Hz, 1H), 5.67 (d, J = 17.5 Hz, 2H), 5.16 (s, 1H), 5.05 (s, 2H), 3.97 (s, 2H), 2.17 (s, 3H), 1.98 (s, 3H), 1.77 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 169.60, 169.33, 168.75, 156.72, 144.98, 143.89, 143.85, 140.35, 136.82, 132.56, 131.31, 127.70, 127.58, 126.36, 126.28, 126.25, 120.93, 113.86, 83.60, 68.37, 67.93, 65.77, 63.76, 61.81, 20.68, 20.55, 20.21.

## $^1$HNMR, {1H}$^{13}$CNMR

### $^1$HNMR,{1H}$^{13}$CNMR of (2-(4-(prop-2-yn-1-yloxy)phenyl)ethene-1,1,2-triyl)tribenzene

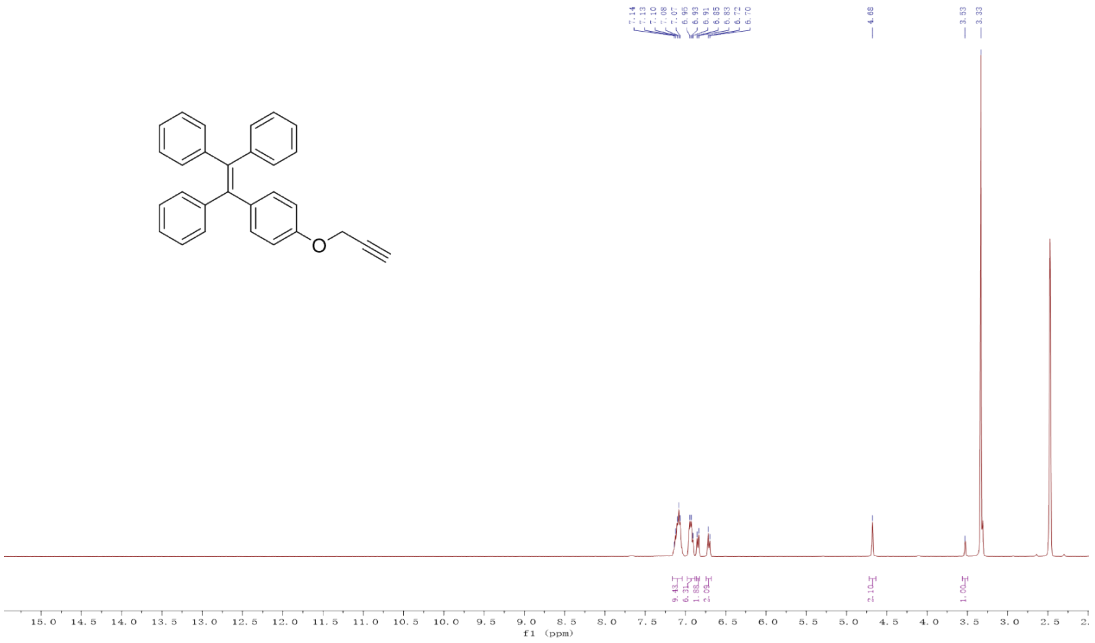


**Figure S1.** $^1$HNMR of (2-(4-(prop-2-yn-1-yloxy)phenyl)ethene-1,1,2-triyl)tribenzene (DMSO-d)

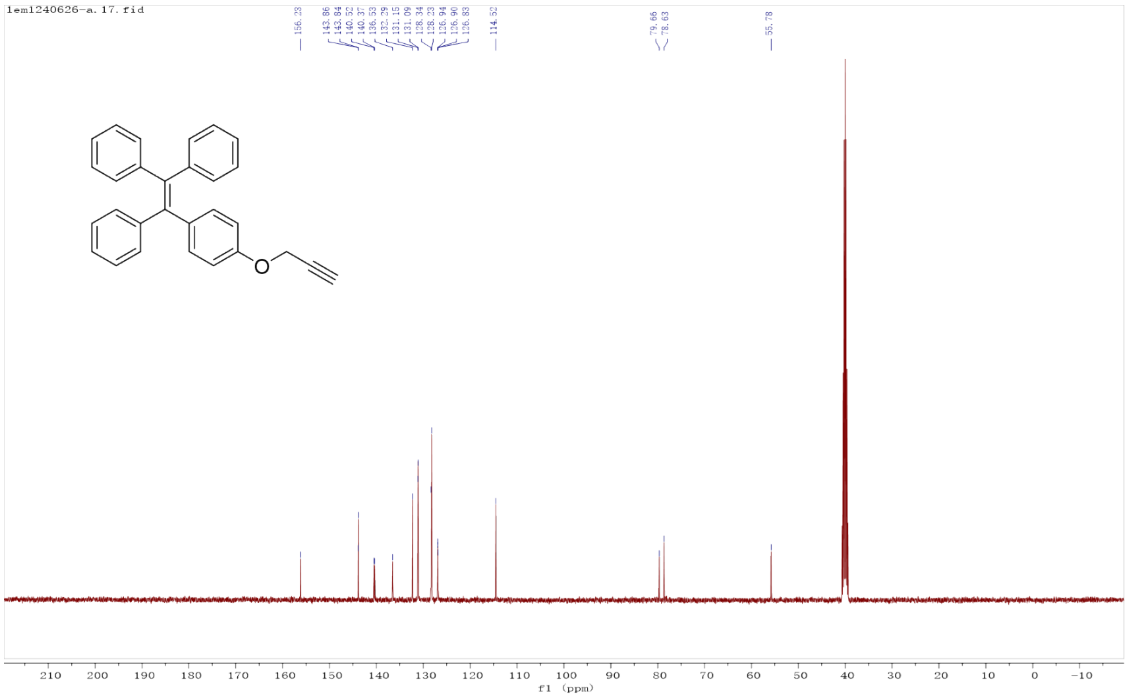



**Figure S2.** {1H}$^{13}$CNMR of (2-(4-(prop-2-yn-1-yloxy)phenyl)ethene-1,1,2-triyl)tribenzene (DMSO-d)

## $^{1}$HNMR, {1H}$^{13}$CNMR of 1,2,3,5-Tetra-O-acetyl-*β*-D-ribofuranose

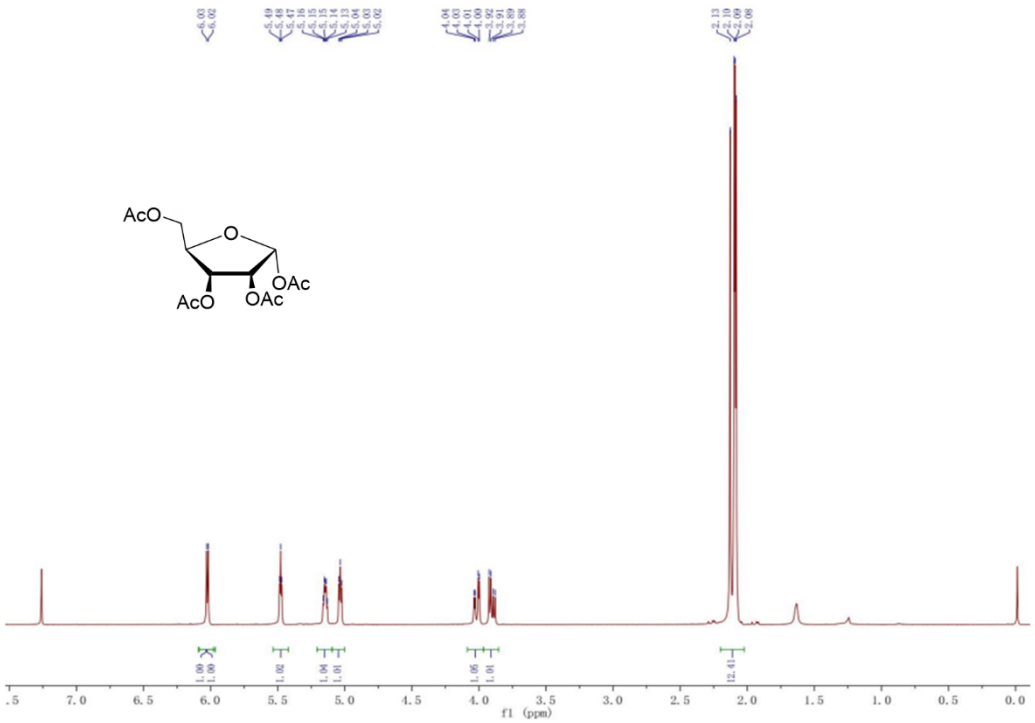



**Figure S3.** $^{1}$HNMR of 1,2,3,5-Tetra-O-acetyl-*β*-D-ribofuranose (Chloroform-d)

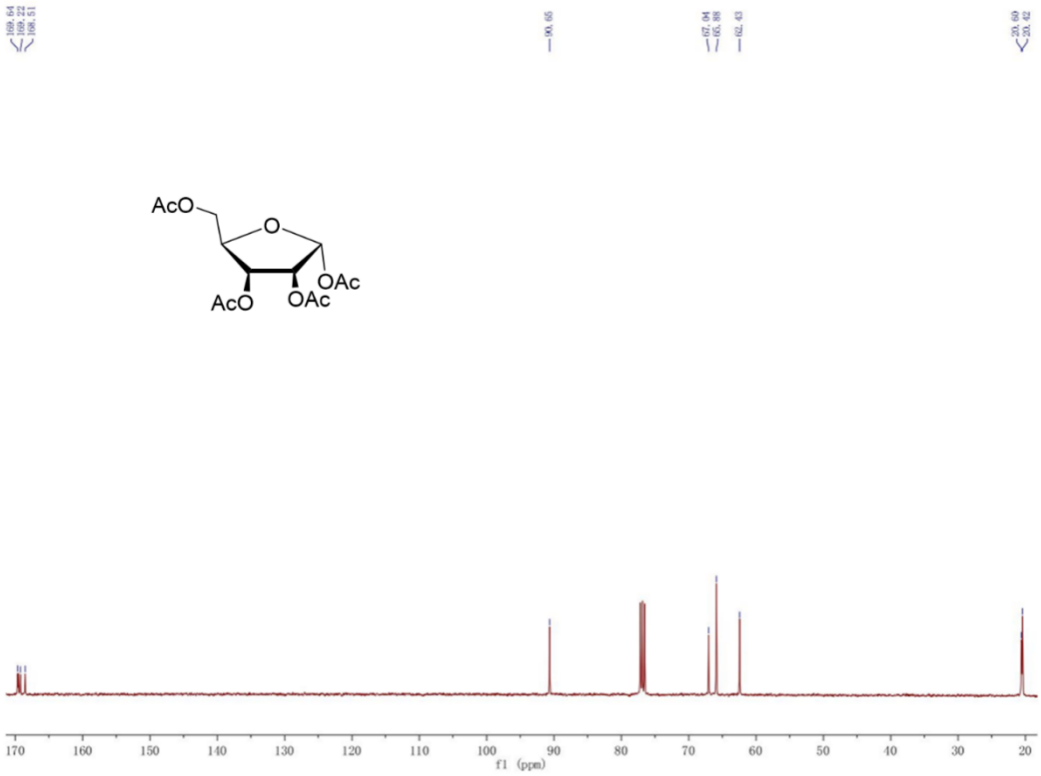



**Figure S4.** {1H}$^{13}$CNMR of 1,2,3,5-Tetra-O-acetyl-*β*-D-ribofuranose (Chloroform-d)

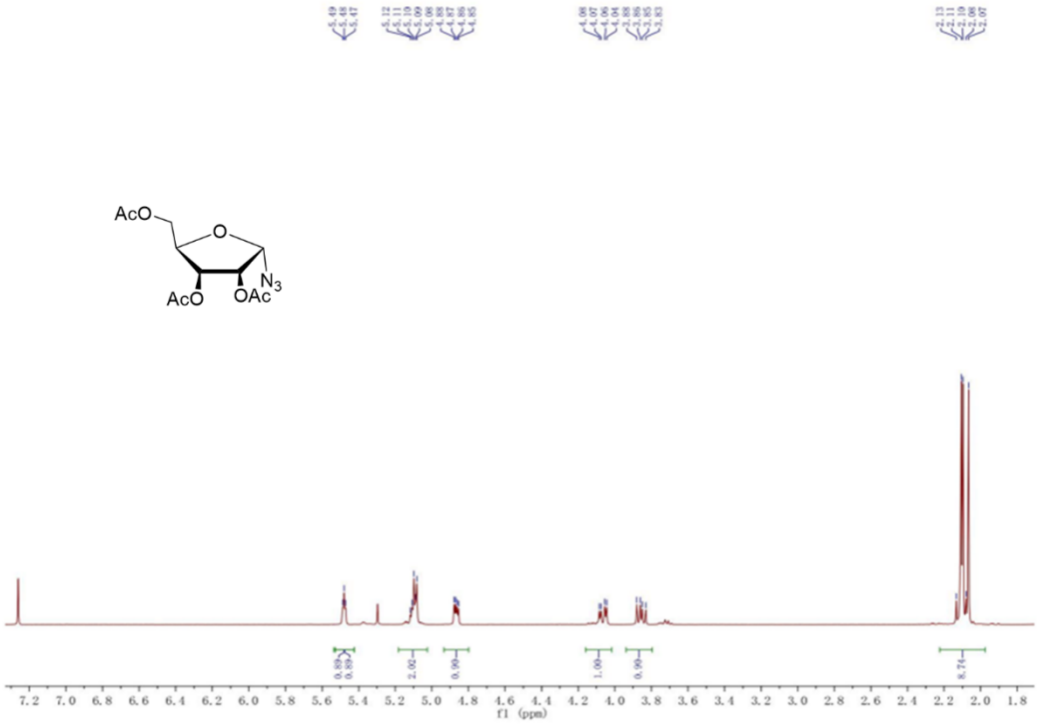



**Figure S5.** $^{1}$HNMR of 2,3,5-tri-O-acetyl-*β*-D-ribofuranosyl azide (Chloroform-d)

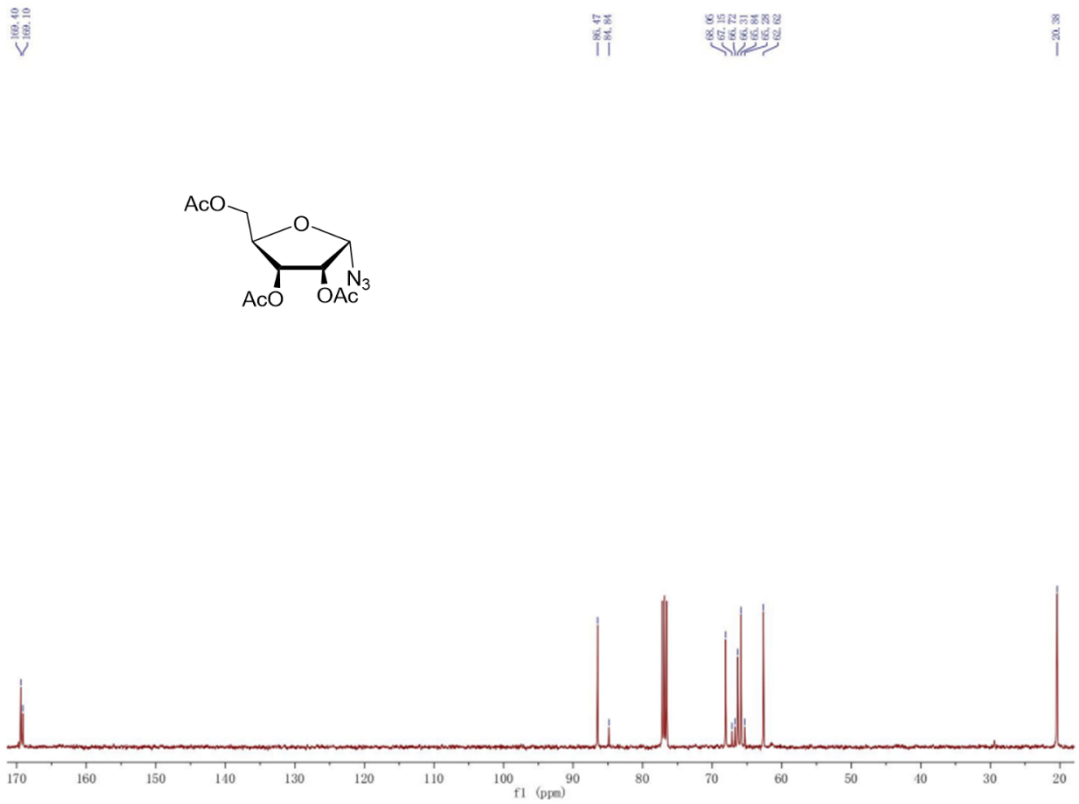



**Figure S6.** {1H}$^{13}$CNMR of 2,3,5-tri-O-acetyl-$\beta$-D-ribofuranosyl azide (Chloroform-d)

## $^{1}$HNMR, {1H}$^{13}$CNMR of ($\beta$, D)-RIB-TPE

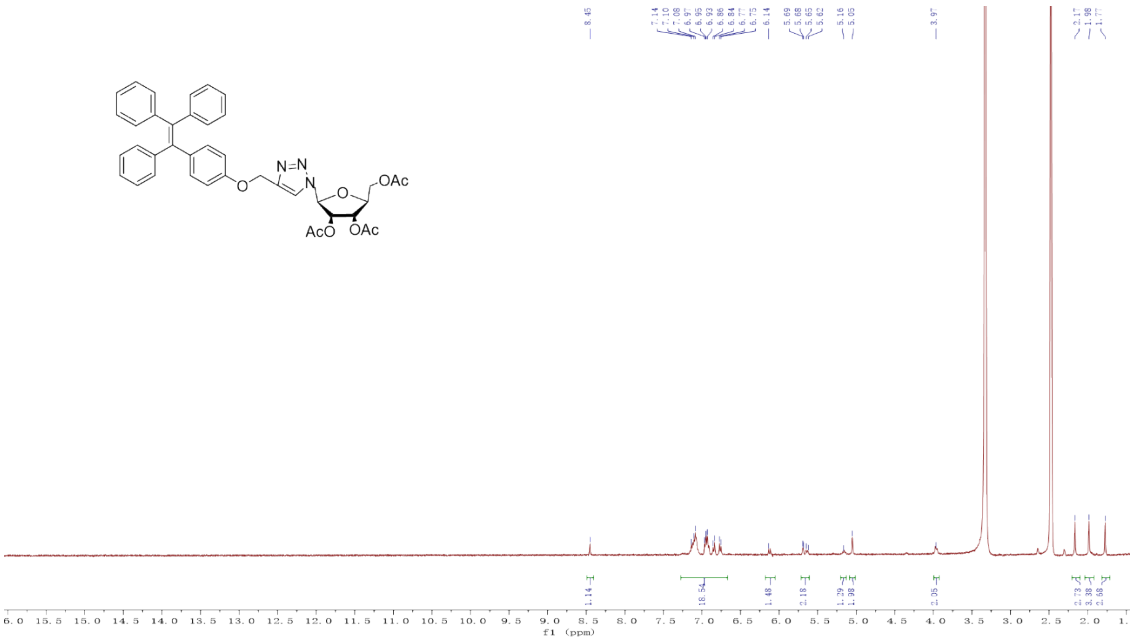



**Figure S7.** $^{1}$HNMR of ($\beta$, D)-RIB-TPE (DMSO-d)

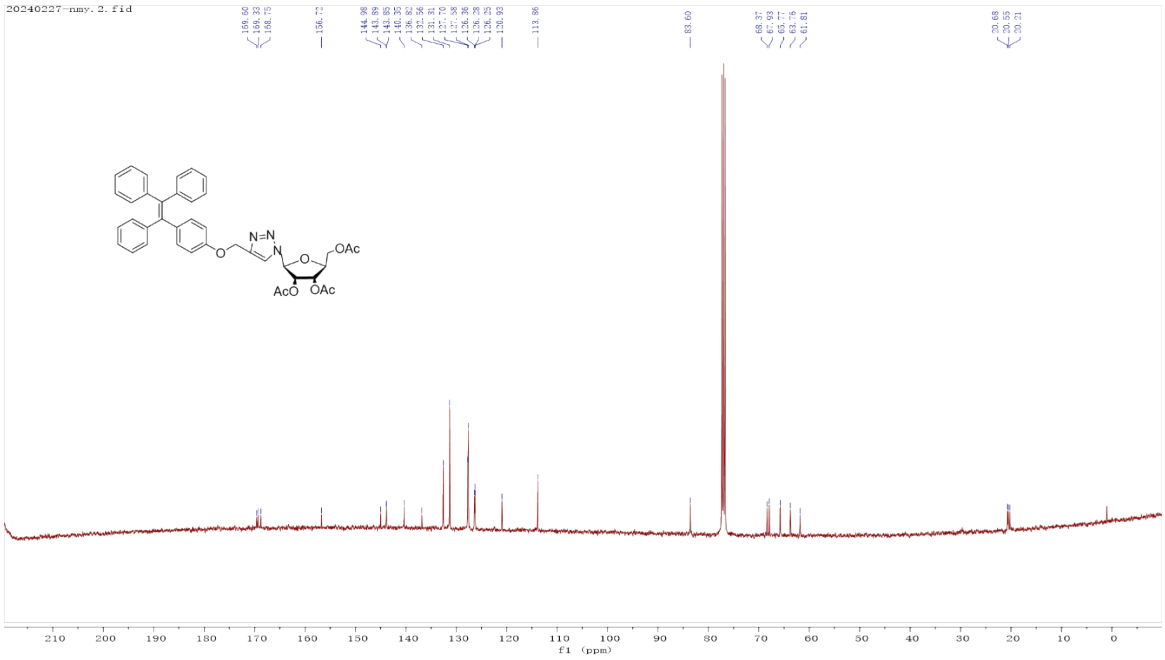



**Figure S8.** {1H}$^{13}$CNMR of (*β*, D)-RIB-TPE (DMSO-d)

## UV absorption spectra of *S*-(+)-clopidogrel sulfate and (*β*, D)-RIB-TPE

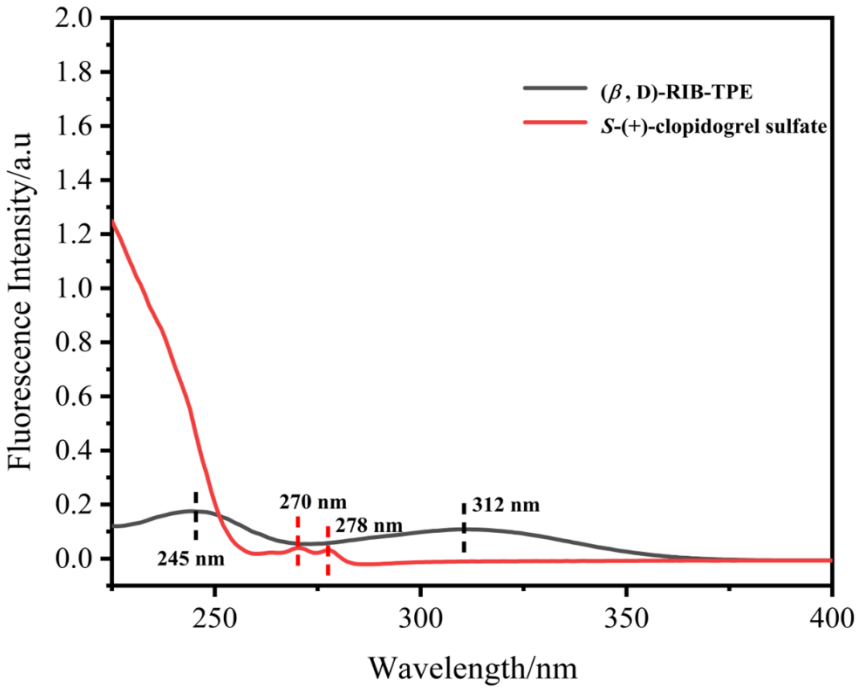



**Figure S9.** UV absorption spectra of *S*-(+)-clopidogrel sulfate($1\times10^{-5}$M,in MeOH) and (*β*, D)-RIB-TPE (0.05M,in MeOH, $\lambda_{ex}$ = 312 nm, slits = 1.0/1.0)

## Fluorescence spectra of *S*-(+)-clopidogrel sulfate

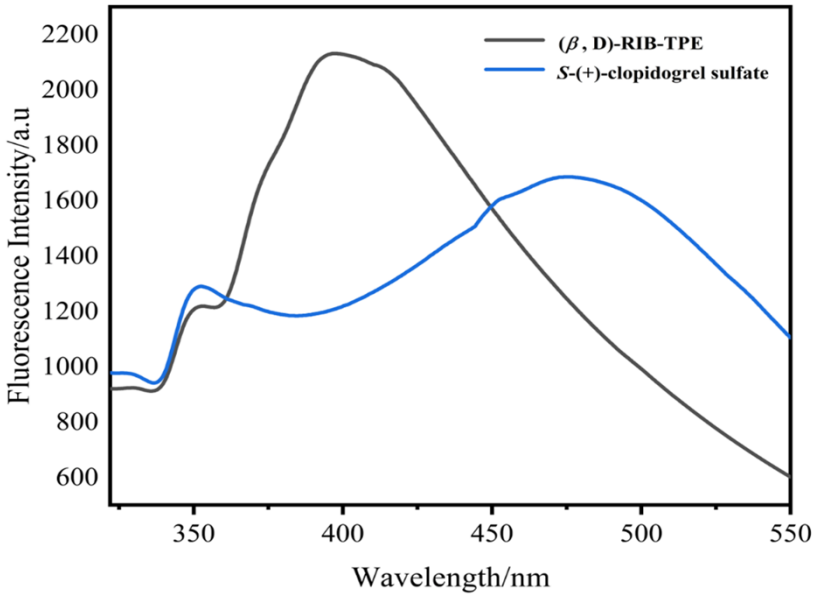



**Figure S10.** Fluorescence spectra of *S*-(+)-clopidogrel sulfate($1\times10^{-5}$M,in MeOH) and (*β*, D)-RIB-TPE (0.05M,in MeOH, $\lambda_{ex}$ = 312 nm, slits = 1.0/1.0)

## Changes in PH of (*β*, D)-RIB-TPE

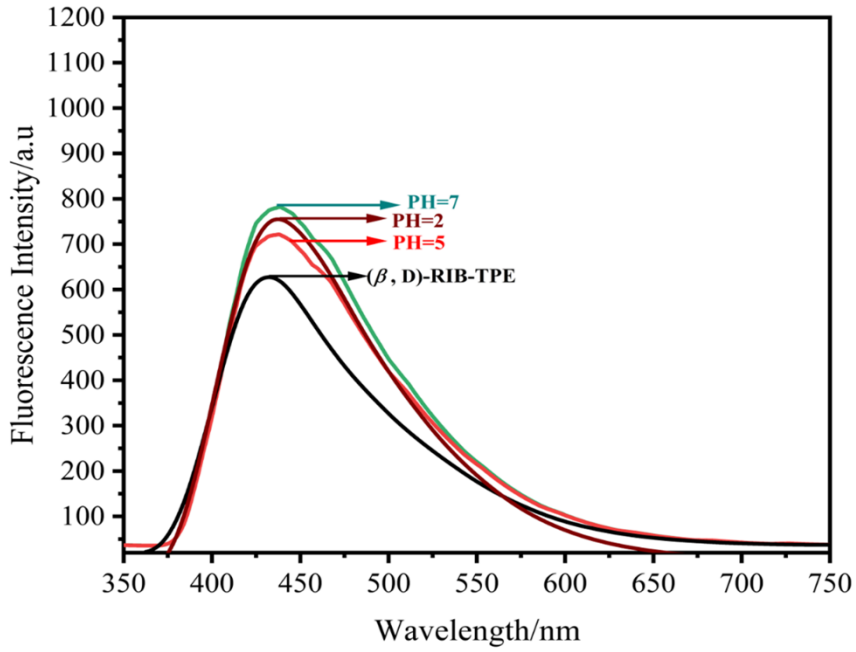



**Figure S11.** Changes in fluorescence of (*β*, D)-RIB-TPE($1\times10^{-5}$M,in MeOH, $\lambda_{ex}$ = 312 nm, slits = 1.0/1.0) in response to PH.

## (*β*, D)-RIB-TPE titration of *S*-(+)-clopidogrel sulfate when AIE works

**best**

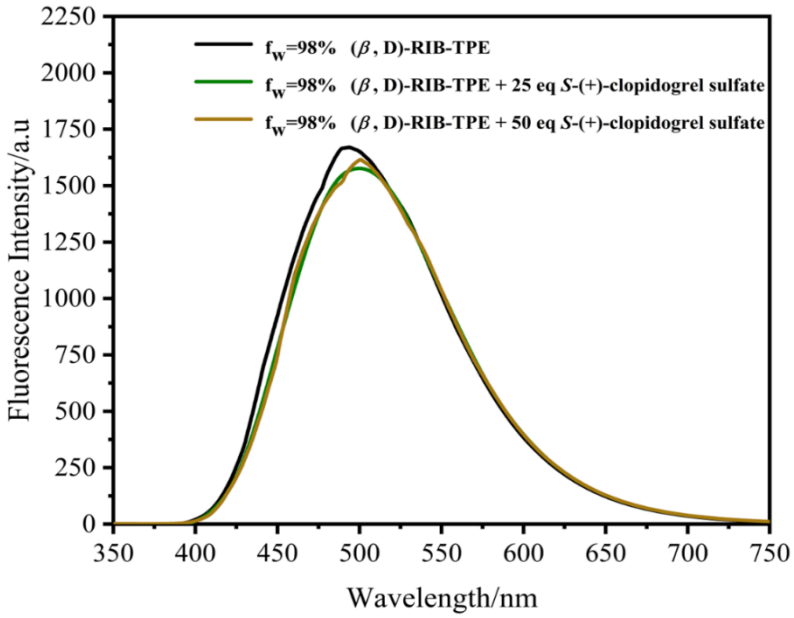



**Figure S12.** (*β*, D)-RIB-TPE titration of *S*-(+)-clopidogrel sulfate in methanol solution when AIE works best. ($2\times10^{-5}M^{-1}$, $\lambda_{ex}$ = 312 nm, slits = 1.0/1.0)

## Recognition of *S*-(+)-clopidogrel in methanol solution when (*β*, D)-RIB-TPE AIE works best

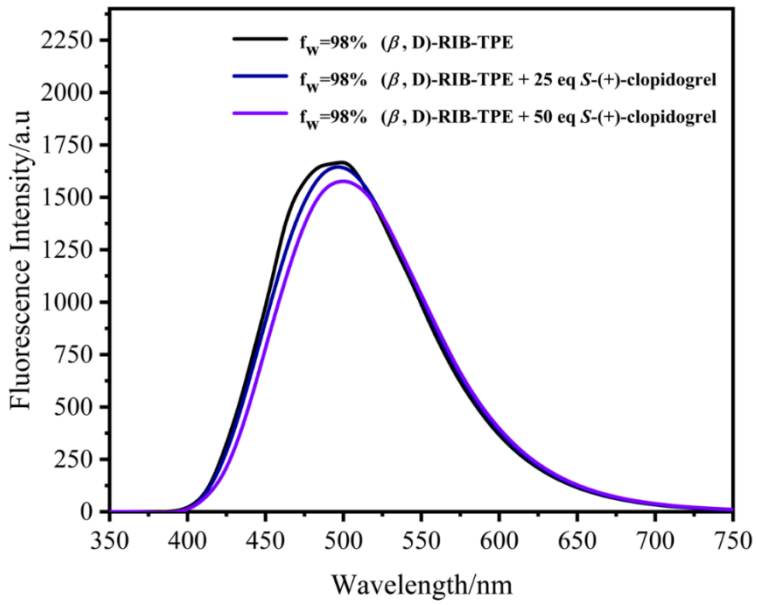



**Figure S13.** Recognition of *S*-(+)-clopidogrel in methanol solution when (*β*, D)-RIB-TPE AIE works best. ($2\times10^{-5}M^{-1}$, $\lambda_{ex}$ = 312 nm, slits = 1.0/1.0)

## Recognition of *S*-(+)-clopidogrel in DMSO solutions when (*β*, D)-RIB-

## TPE AIE works best

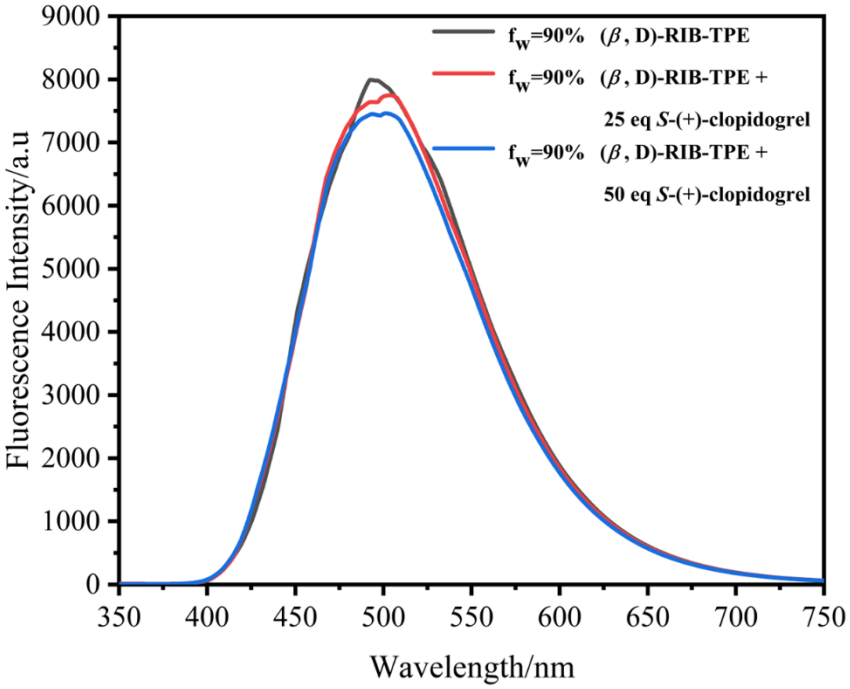



**Figure S14.** Recognition of *S*-(+)-clopidogrel in DMSO solution when (*β*, D)-RIB-TPE AIE works best. ($1\times10^{-5}M^{-1}$, $\lambda_{ex}$ = 312 nm, slits = 2.5/2.5)

## DFT calculation of (*β*, D)-RIB-TPE, *S*-(+)-clopidogrel sulfate

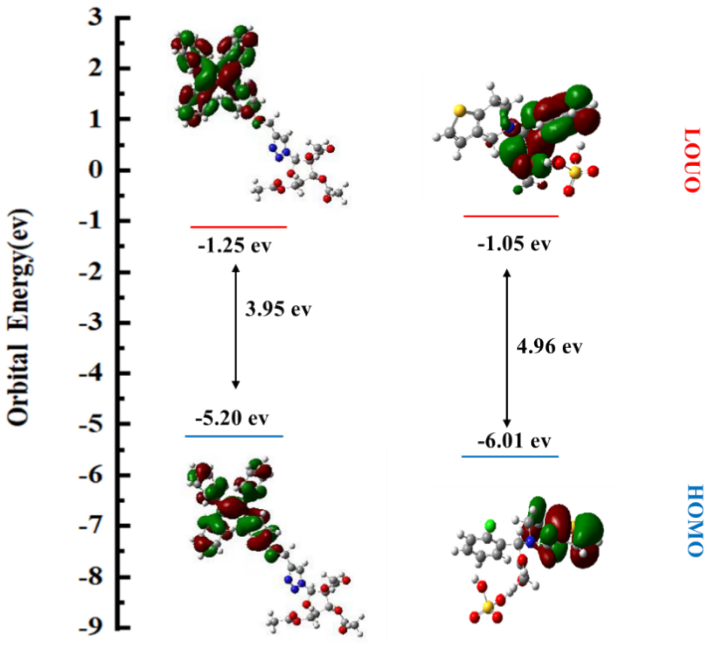
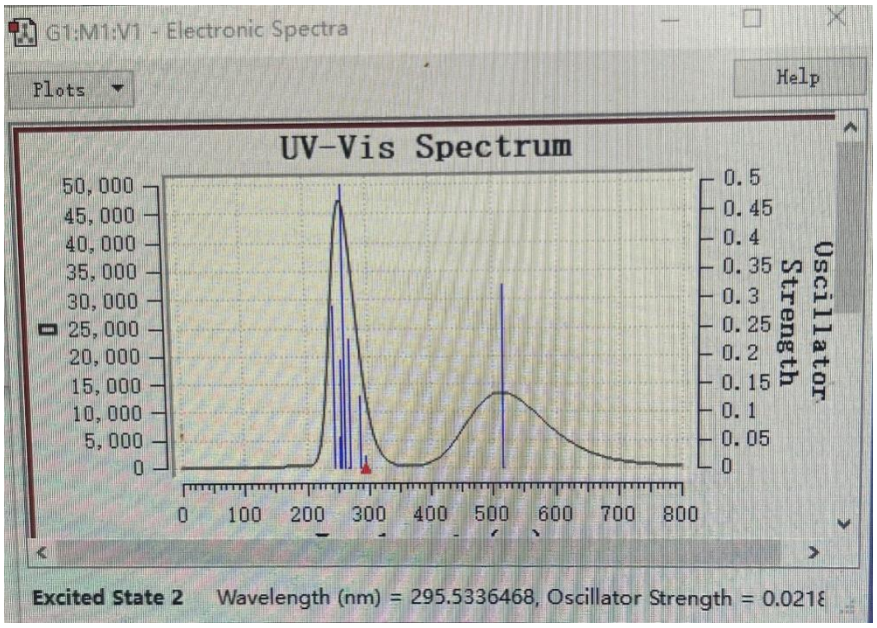



**Figure S15.** DFT calculation of (*β*, D)-RIB-TPE(right), *S*-(+)-clopidogrel sulfate(left)

## (*β*, D)-RIB-TPE - Excitation

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<S**2>=0.000
      180 ->182         0.20852
      181 ->183         0.65093
```

**Figure S16.** (*β*, D)-RIB-TPE- Excitation

## (*β*, D)-RIB-TPE - Emission

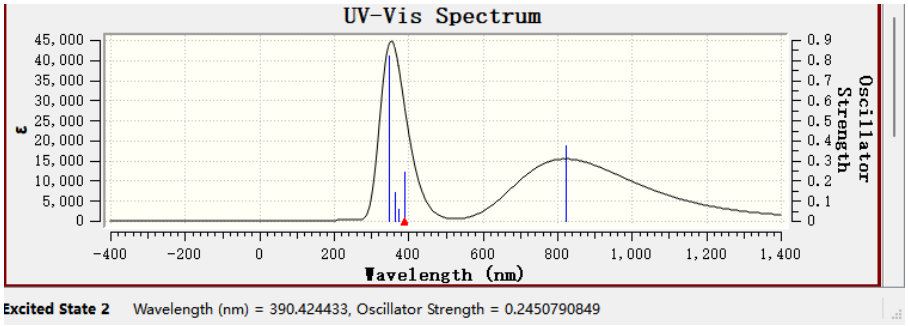


**Figure S17.** (*β*, D)-RIB-TPE- Emission

## Ions interference diagrams of (*β*, D)-RIB-TPE and (*β*, D)-RIB-TPE+

## S-(+)-clopidogrel

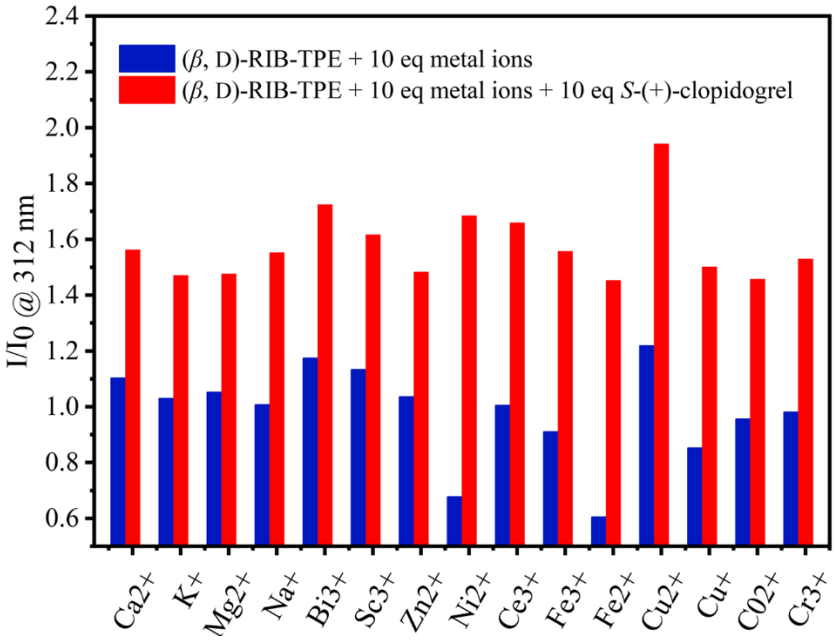


**Figure S18.** Ions(0.1M) interference diagrams of (*β*, D)-RIB-TPE($1\times10^{-5}$M) and (*β*, D)-RIB-TPE($1\times10^{-5}$M)+ *S*-(+)-clopidogrel(0.05M)

## TEM tests of (*β*, D)-RIB-TPE and (*β*, D)-RIB-TPE coated drug *S*-(+)-clopidogrel sulfate

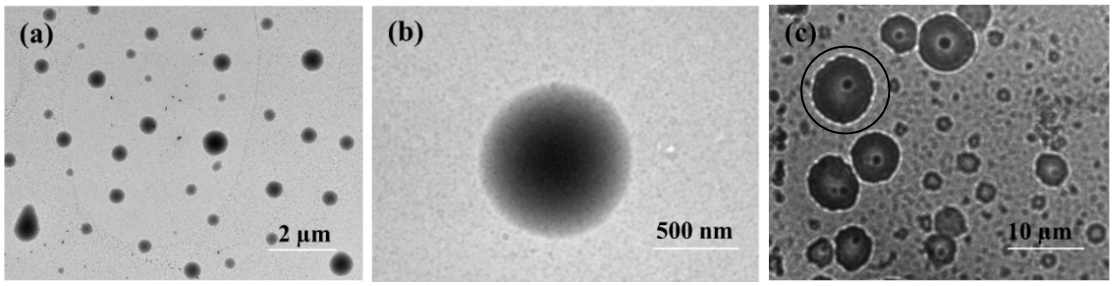


**Figure S19.** (a) (b)The TEM image of the (*β*, D)-RIB-TPE (2 mg/ml) in methanol. (c) The TEM image of the *S*-(+)-clopidogrel sulfate (2.5 mg/ml) and (*β*, D)-RIB-TPE (2 mg/ml) in methanol (Volume ratio of 3:1), (The red circle shows the embedded vesicles). Zeiss, shoot at low power

## Vesicle photobleach and stability test

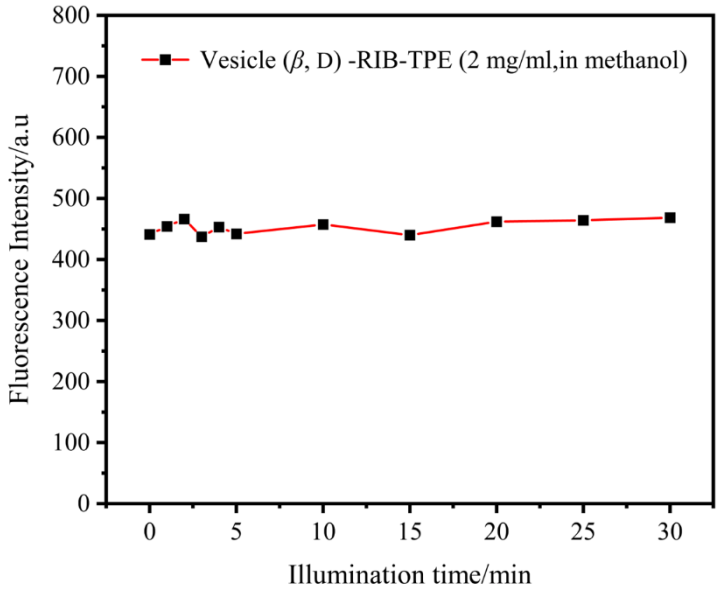


**Figure S20.** Vesicle photobleachability and stability test