Supplementary Material (ESI) for Soft Matter


***Supporting Information***

# Target-Selective Vesicle Fusion System with pH-Selectivity and Responsiveness

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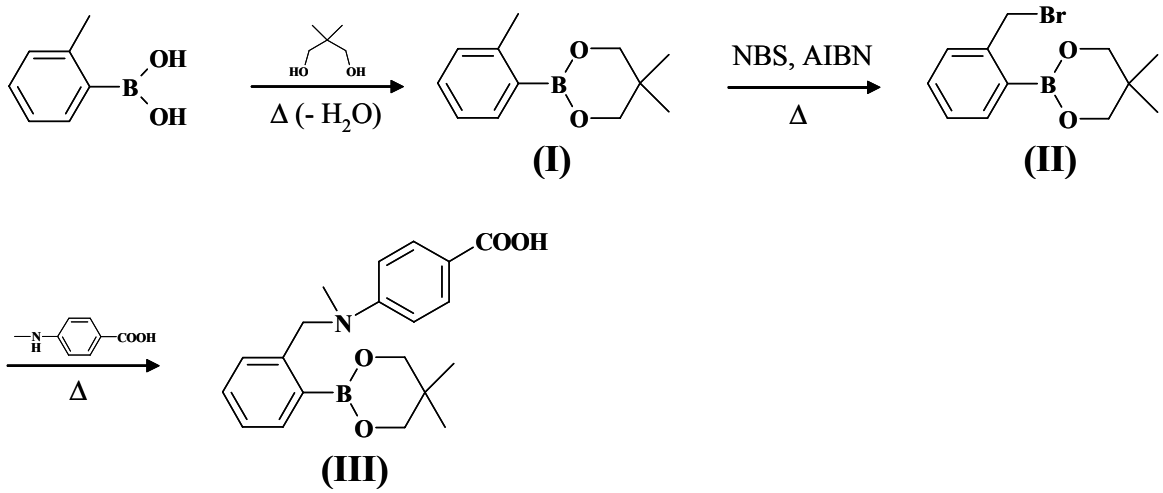
**Contents:**

# Synthesis of Compound III as the raw material for Compound 1




**2-Methylphenylboronic acid neopentylglycol ester (I)**

2-Methylphenylboronic acid (2.72 g, 20.0 mmol) and 2,2-dimethyl-1,3-propanediol (2.50 g, 24.0 mmol) were dissolved in toluene (50 $cm^3$) in a 100 $cm^3$ oven dried round bottom flask. To this solution, *p*-toluenesulfonic acid (catalytic amount) was added. The round bottom flask was connected to a Dean Stark apparatus under reflux condition to remove the water. The progress of the reaction was monitored by TLC (silica gel 60, hexane-ethyl acetate = 8:2 (v/v)). After 6 h when the spot of 2-methylphenylboronic acid ($R_f$ = 0.16) disappeared, the reaction was finished. After cooling the reaction mixture was washed rapidly with water (50 $cm^3$). The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated to dryness. The residue being further purified through column chromatography (silica gel 60, hexane-ethyl acetate = 8:2 (v/v)) to obtain the pure title compound **I** as a pale yellow oil (4.03 g, 97% yield).

FAB-MS spectroscopy for $MH^+$: 205.18 (calcd. 205.08). $^1$H NMR (400 MHz, DMSO-$d_6$) : δ = 0.97 (s, 6H), 2.43 (s, 3H), 3.75 (s, 4H), 7.10-7.13 (br t+t, 2H), 7.26 (d, 1H), 7.60 (d, 1H).

**2-Bromomethylphenylboronic acid neopentylglycol ester (II)**

Compound **I** (4.00 g, 19.6 mmol) and *N*-bromosuccinimide (NBS) (3.69 g, 20.7 mmol) were dissolved in $CCl_4$ (50 $cm^3$) in a 100 $cm^3$ oven dried round bottom flask. To this solution,

α,α'-azobisisobutyronitrile (AIBN) (0.37 g, 10 wt% of NBS) was added. The solution was held at reflux for 3 h. The progress of the reaction was monitored by TLC (silica gel 60, hexane-ethyl acetate = 7:3 (v/v)). After cooling, insoluble materials were removed by filtration and then the filtrate was washed rapidly with water (50 $cm^3$). The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated to dryness. The residue being further purified through column chromatography (silica gel 60, hexane-ethyl acetate = 7:3 (v/v)) to obtain the pure title compound **II** as a brown oil (4.81 g, 86% yield from **I**).

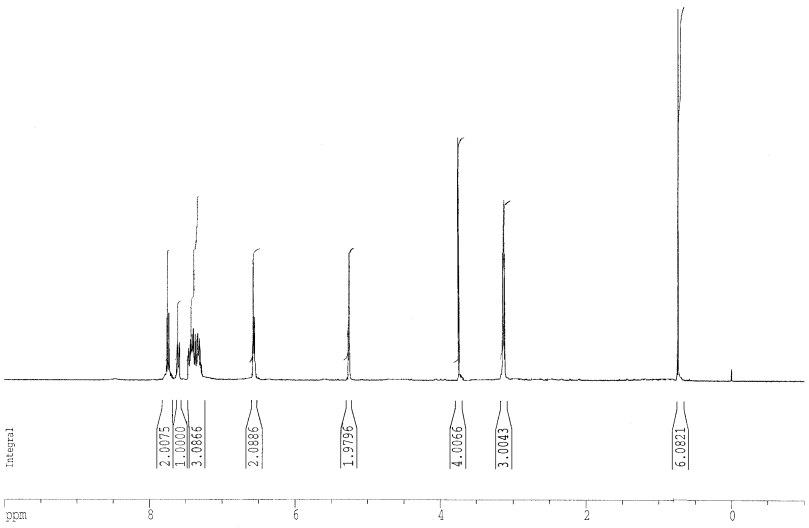
FAB-MS spectroscopy for $MH^+$: 286.12 (calcd. 283.98). $^1$H NMR (400 MHz, DMSO-$d_6$) : δ = 0.98 (s, 6H), 3.75 (s, 4H), 4.95 (s, 2H), 7.29 (d, 1H), 7.39-7.42 (br t+t, 2H), 7.69 (d, 1H).

**2-[*N*-Methyl-*N*-(*p*-carboxyphenyl)]aminomethylphenylboronic acid neopentylglycol ester (III)**

Compound **II** (4.81 g, 16.9 mmol) and 4-(methylamino)benzoic acid (2.80 g, 18.5 mmol) were dissolved in *N*,*N*-dimethylformamide (20 $cm^3$) in a 100 $cm^3$ oven dried round bottom flask. The solution was held at reflux for 3 h in the presence of potassium carbonate (3.50 g, 25.4 mmol). After cooling, insoluble materials were removed by filtration and then the filtrate was concentrated to dryness. The residue was taken with a mixture of chloroform (20 $cm^3$) and aqueous 5% sodium hydrogen carbonate solution (20 $cm^3$). This heterogeneous mixture was stirred for 30 min at room temperature. The organic layer was separated, washed with water (50 $cm^3$), dried over anhydrous sodium sulfate, and concentrated to dryness. The residue being further purified through column chromatography (silica gel 60, hexane-ethyl acetate = 7:3 (v/v)) to obtain the pure title compound **III** as a brown oil (2.95 g, 49% yield from **II**).

FAB-MS spectroscopy for $MH^+$: 354.30 (calcd. 354.23). $^1$H NMR (400 MHz, DMSO-$d_6$) : δ = 0.75 (s, 6H), 3.11 (s, 3H), 3.76 (s, 4H), 5.25 (s, 2H), 6.57 (d, 2H), 7.30-7.40 (br d+t+t, 3H), 7.60 (d, 1H), 7.74 (d, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) : δ = 22.1, 37.7, 65.6, 67.4, 110.8, 115.8, 127.2, 128.2, 128.9, 130.9, 131.6, 137.4, 138.1, 139.0, 166.3 ppm.

# $^{1}H$ and $^{13}C$ NMR charts of **Compound III**

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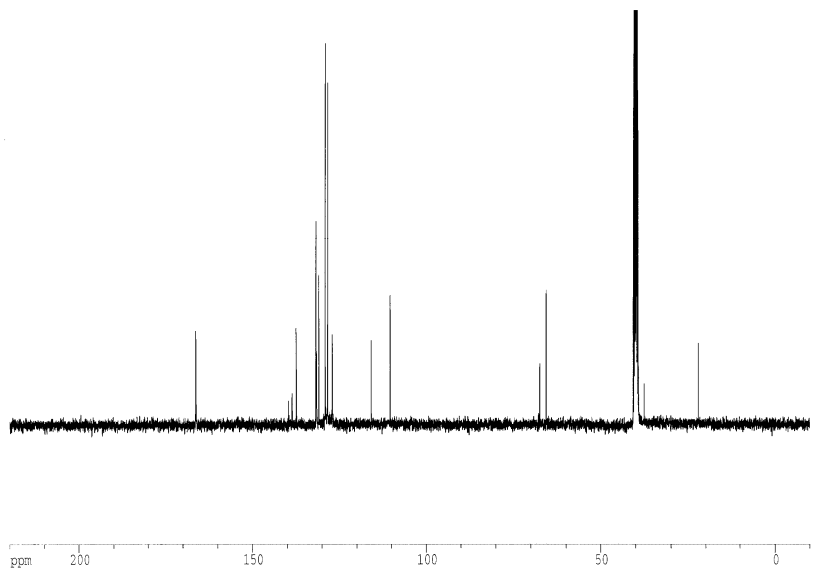


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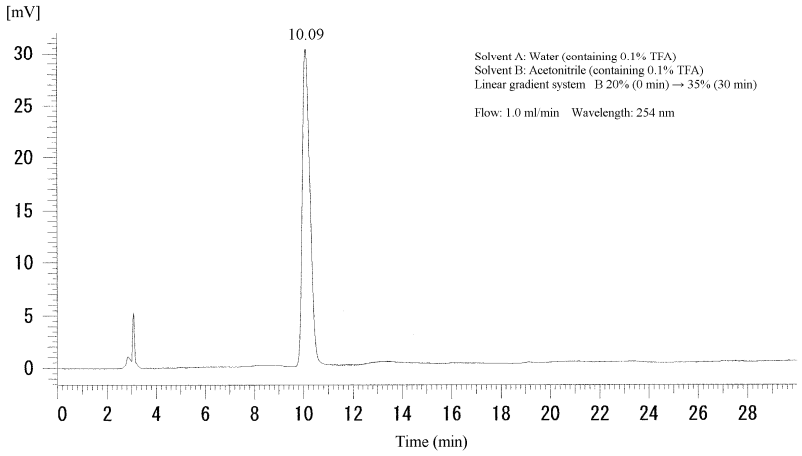
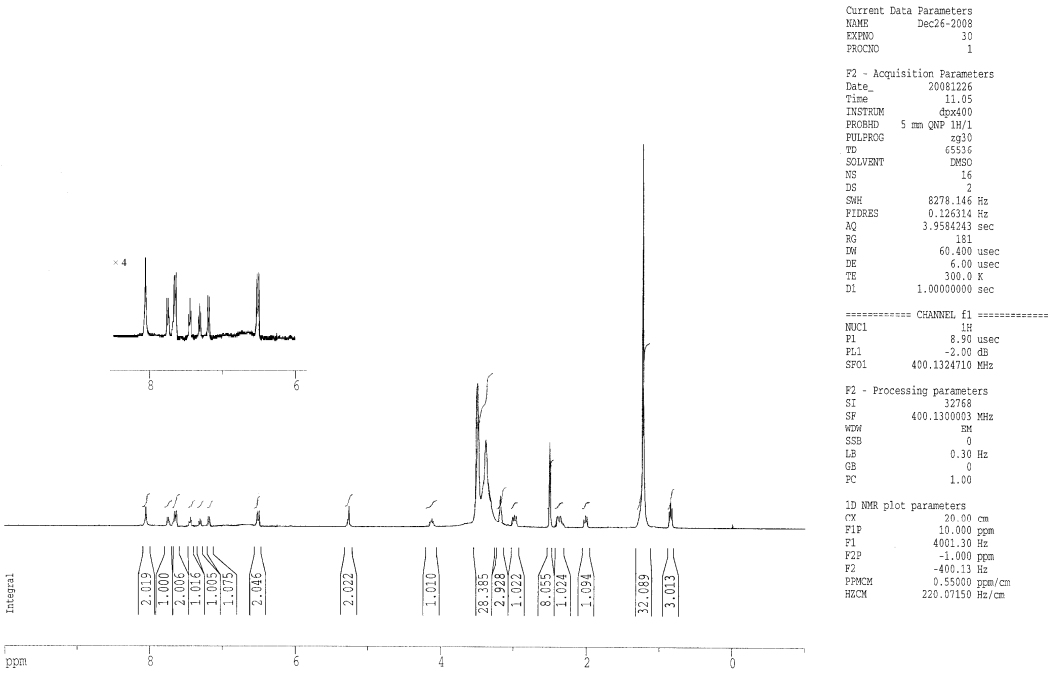
# Spectral data of Compound 1

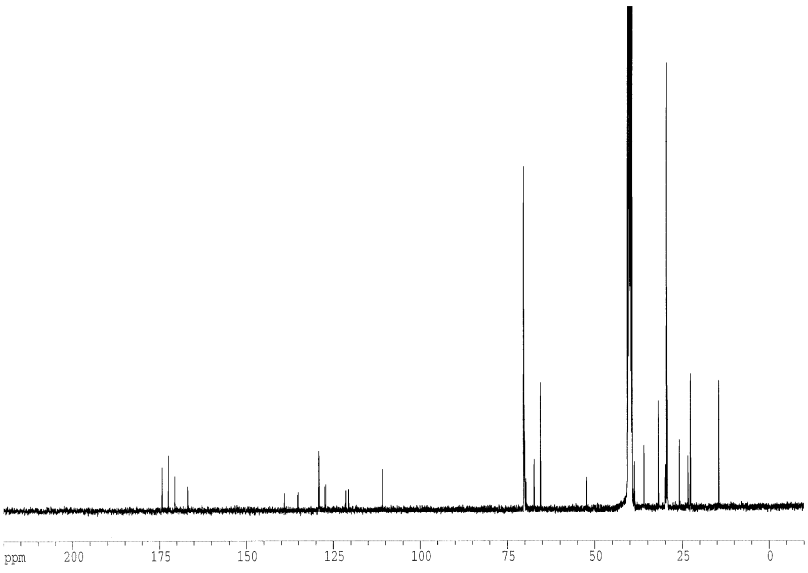
## HPLC trace of Compound 1 (after purification)




## $^1$H NMR chart of **Compound 1**



# $^{13}$C NMR chart of **Compound 1**

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1D NMR plot parameters
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F1              22134.80 Hz
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F2              -1006.13 Hz
PPMCM           11.50000 ppm/cm
HZCM         1157.04675 Hz/cm
```

## Supporting figures

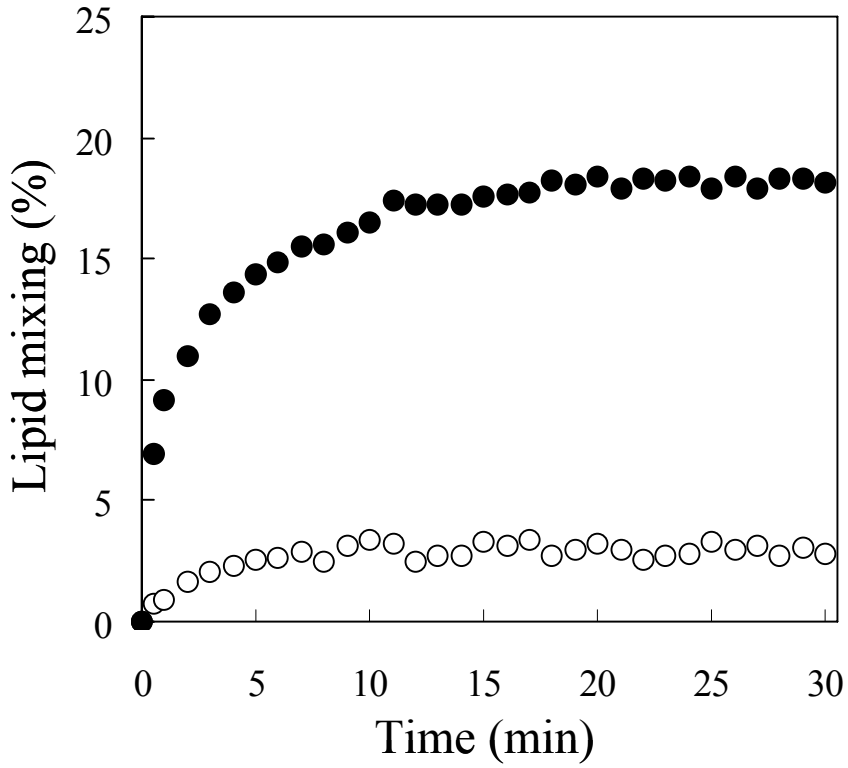


**Fig. S1** The lipid mixing experiment by the use of pre-incubated pilot vesicles (EggPC/DPGS/Compound 1) with 10 mM of free *myo*-inositol (open circle). The measurements were performed in 10 mM acetic acid/sodium acetate buffer (containing 100 mM NaCl, pH 5.0) at 30 °C.

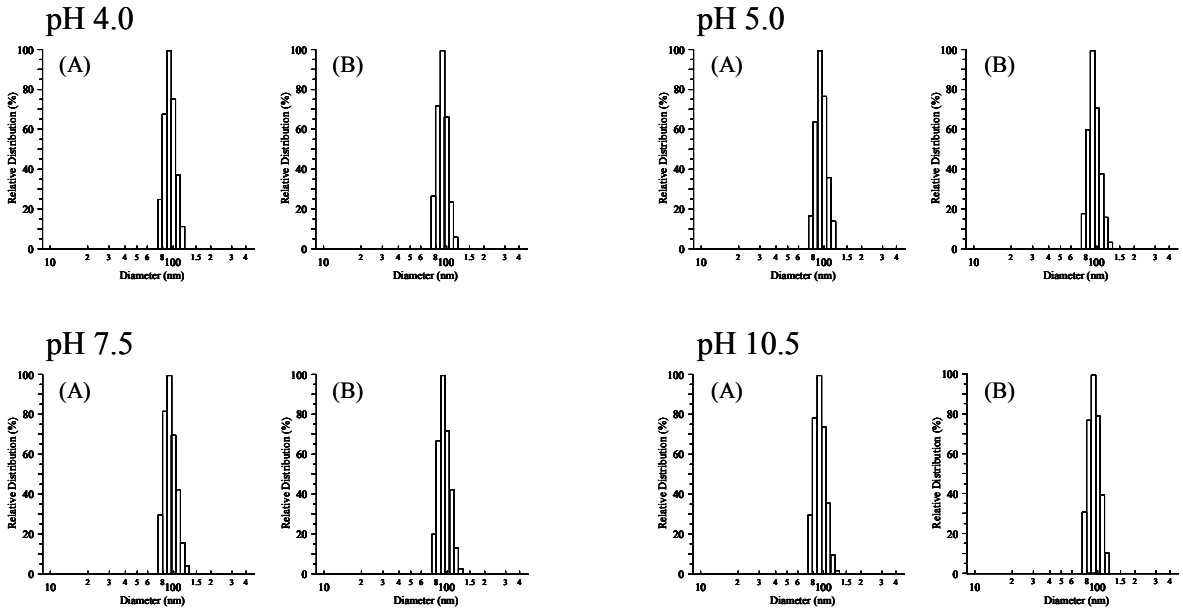


**Fig. S2** DLS size distribution profiles of target vesicles (EggPC/PI/NBD-PE/Rh-PE) before (A) and after (B) gel filtrations for inner leaflet mixing assays.

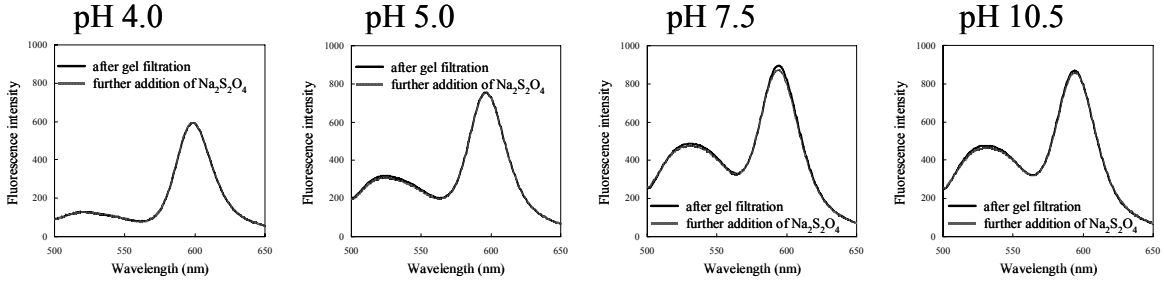


**Fig. S3** Fluorescence spectra of gel filtrated target vesicles and further sodium dithionite added vesicles.