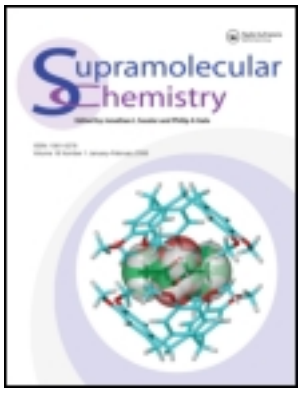

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Synthesis of tripodands with multiple hydroxyl and amide groups exhibiting fluorescent anion sensing

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Novel tripodal receptors (**T2** and **T3**) having multiple hydroxyl and amide groups with long alkyl chains (*N*-dodecylamino and *N*,*N*-didodecylamino groups, respectively) were prepared. The broadening of proton signals observed in the ^{1}H NMR spectrum of compounds **T2** and **T3** in a non-polar solvent ($CDCl_3$) was attributed to intermolecular and/or intramolecular hydrogen bonding. In the fluorescence spectrum, the addition of Bu_4NF to the solution of receptors **T2** and **T3** caused the drastic increase in fluorescence intensity compared with the addition of other anion species.

Keywords: tripodand; tandem Claisen rearrangement; anion recognition; hydrogen bonding

1. Introduction

Various anions play important roles in chemical processes and biochemical systems, where the majority of enzyme substrates and co-factors are also anionic (*1–4*). Therefore, the development of responsive and selective artificial anion receptors is of great interest and significance (*5*, *6*). So far, compounds containing multi-hydrogen bonding sites have gained considerable attention due to their ability of complexation towards ionic and/or neutral molecules. Several strategies for achieving tetrahedral anion recognition have been employed (*7*, *8*). Tripodal receptors, which are regarded to be between cyclic and dipodal ligands with regard to preorganisation, are believed to be able to make a complex with guest molecules more effectively than analogous dipodal ones (*9–11*). We have focused on the study of artificial receptors having multi-hydroxyl groups generated via tandem Claisen rearrangement (TCR) (*12*) and amide N—H groups in order to improve the recognition ability towards anions (*13–20*). Recently, we have reported the synthesis of tripodal compound having plural hydroxyl groups by TCR, which has been proved to be an excellent way to generate plural hydroxyl groups from the precursors having isobutenyl ether (*21*). More recently, the tripodal receptor (**T1**) shown in Figure 1 has been reported to exhibit the binding ability towards acetate, dihydrogen phosphate and fluoride ions with relatively strong affinity but less selectivity among them to form 1:1 complex with them in chloroform solution (*22*).

In this work, we newly designed and prepared two tripodal compounds **T2** and **T3** with three long arms besides with long alkyl end groups. Isobutenyl ether part is introduced into each arm because of the generation of plural hydroxyl groups via TCR. The introduction of long alkyl end group to tripodal compounds aims not only to improve the solubility towards organic solvents but also to assemble each arm intramolecularly (*23*). In **T2** and **T3**, we directly connected monododecyl and didodecyl groups to N-atom of each terminal amide group, respectively. For comparison of NMR spectroscopic behaviours, we used **T1**, which has been previously reported (*22*), in this study. In addition, tripodands, **T4** and **T5**, and linear compound **L1** were also prepared in order to compare the behaviours in the solution. Their binding ability with anions was investigated by ^{1}H NMR and fluorescence spectra in non-polar and polar solvents.

2. Results and discussion

2.1 Synthesis of tripodands

The synthetic procedures of tripodands **T2**–**T5** are illustrated in Scheme 1. Compound **1** was obtained in 60% yield by the reaction of 2-hydroxy-3-naphthoic acid methyl ester with NaH followed by the addition of three equimolar excess of 3-chloro-2-methyl-1-propene. Compound **2** was obtained by hydrolysis over two steps from compound **1**. Compound **4** was obtained by the reaction of 1,3,5-tris(aminomethyl)-2,4,6-triethylbenzene (*24*, *25*) in dry THF with acid chloride **3**, which was prepared by the reaction of **2** with thionyl chloride. Compound **5** was obtained by the reaction with 2-hydroxy-3-naphthoic acid methyl ester with NaH followed by the addition of

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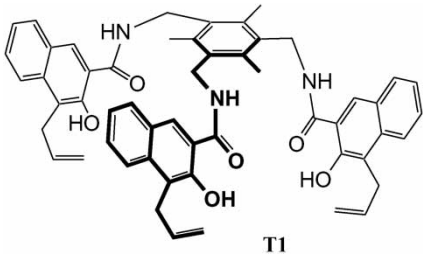


T1

Figure 1. Tripodand **T1** with three hydroxyl and three amide groups.

compound **4**. Compound **5** was converted into compound **6** by hydrolysis. Compounds **7a**, **7b** and **7c** were obtained by the dehydration reaction of **6** with *N*-dodecylamine, *N*,*N*-didodecylamine and *N*-butylamine, respectively, using 2-chloro-1-methylpyridinium iodide (CMPI). Finally, compounds **T2**–**T4** was obtained by TCR. On the other hand, **T5** was obtained by TCR of ester **5**.

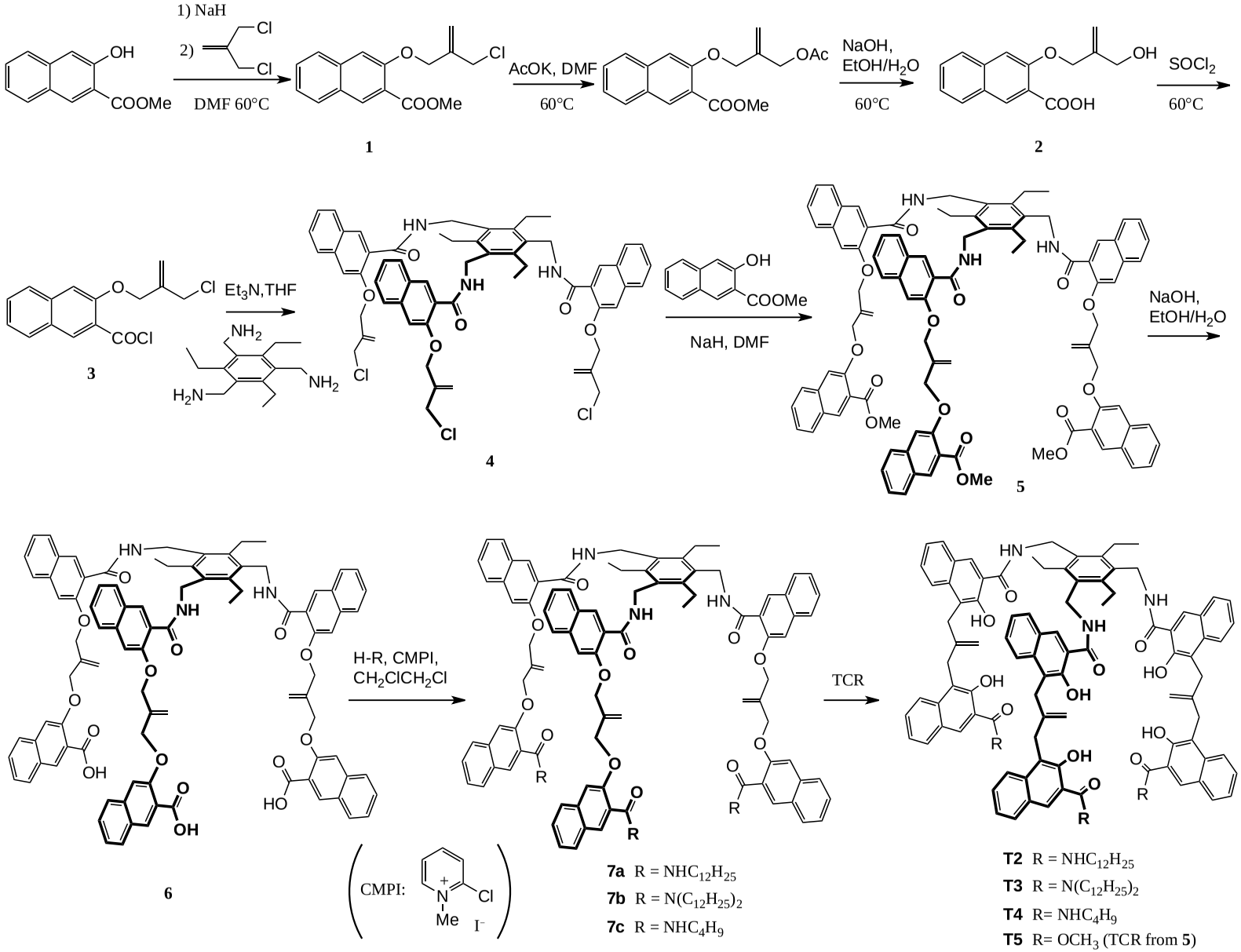
The synthetic procedure of **L1** is illustrated in Scheme 2. Compound **L1** was prepared starting from **3** according to a similar route as shown in Scheme 1. Compound **L1** has partly the same structure as **T2**. These compounds were characterised by ^{1}H NMR, FT-IR, mass spectra and elemental analysis.

2.2 *^{1}H NMR spectroscopic behaviours of tripodands*

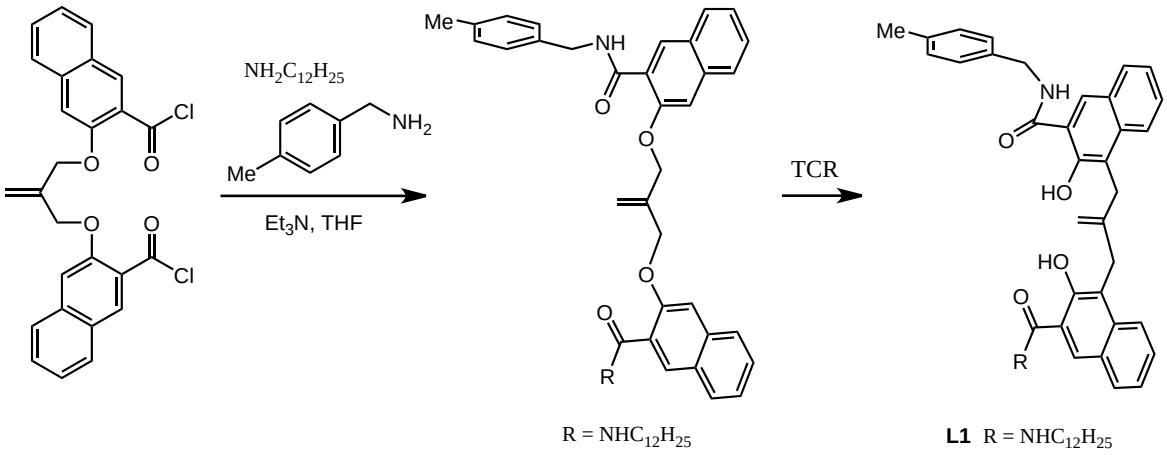
^{1}H NMR study of **T1**–**T3** was performed using $CDCl_3$ and DMSO-d_6 as solvents. The results are shown in Figure 2. In $CDCl_3$, compounds **T2** and **T3** gave broadening signals in the ^{1}H NMR spectrum at room temperature (25°C), although compound **T1** shows sharp signals under the same conditions. It is suggested that intermolecular or intramolecular hydrogen bonding is formed in the case of **T2** and **T3** because they have six phenolic OH and six amide groups in a molecule. Therefore, DMSO-d_6 was used in the measurement of ^{1}H NMR spectrum of **T2** and **T3** in order to break hydrogen bonding. Interestingly, compound **T2** was easily soluble in DMSO-d_6, whereas **T3** having totally six dodecyl terminal groups was insoluble in DMSO-d_6 at all. It means that **T3** is too hydrophobic to be soluble in a polar solvent, i.e. DMSO. When the ^{1}H NMR spectrum of **T2** was measured in DMSO-d_6, the signals of **T2** drastically became sharp compared with those in $CDCl_3$, implying that hydrogen bonding was broken by the presence of DMSO-d_6, which has the ability of H-bonding cleavage. A similar behaviour was also observed in the ^{1}H NMR spectrum of **T2** and **T3** in the mixed solvent ($CDCl_3$: DMSO-d_6 (9:1)). That is, the signals of **T2** and **T3** in the mixed solvent became sharper than those in $CDCl_3$. It is suggested that the presence of DMSO brings the cleavage of either intramolecular or intermolecular H-bonding.

The chemical shifts of OH^a, OH^b and naphthyl-H^c in $CDCl_3$, which are located at the inner hydroxyl OH^a, outer hydroxyl OH^b and the four position of outer naphthyl group of **T2** and **T3**, respectively, are shown in Figure 3(A) and (B). It should be noticed that the proton signals of OH^a and OH^b in $CDCl_3$ for phenolic-OH protons of **T2** appear around 12 ppm. On the other hand, in T3 the signal at 11.8 ppm is assigned to OH^a, whereas the chemical shift of OH^b which hardly forms intramolecular six-membered hydrogen bond structure appears around 9.5 ppm. The upfield shift of OH^b proton signal of **T3** means the decrease in the hydrogen donating ability of OH group implying the comparable decline in the acidity of OH proton (*26*). These behaviours of the two protons of OH^a and OH^b in both cases may be concerned with anion recognition properties of **T2** and **T3** discussed later.

From the above-mentioned results, it is suggested that the OH proton signals of **T2** and **T3** could be varied by the concentration of ligands in $CDCl_3$, because all of the protons signals become broadened in $CDCl_3$ implying the formation of H-bonding as shown in Figure 2, and the chemical shifts of OH protons largely depend upon the substituent on N-atom of the terminal group as shown in Figure 3. In order to elucidate such kind of behaviours, we carried out ^{1}H NMR dilution experiment of **T2** and **T3** in $CDCl_3$. The ^{1}H NMR chemical shift variation of OH^a and OH^b in **T2** and **T3** was observed as shown in Figure 4. It is easy to distinguish the signal OH^a at about 12 ppm and the signal OH^b at about 9 ppm in **T3** (Figure 4(B)). The signal at about 12 ppm is assigned to OH^a because OH proton of **T1** appears at the same region as OH^a of **T3**. The structure of **T1** is the same as the central part of **T2** and **T3**. With decreasing concentration of **T3**, the OH^a signal gradually moves upfield and the OH^b signal showed relatively little shift over a concentration range from 1.0×10^{-2} to 6.25×10^{-4} M. It is presumed that amide groups neighbouring OH^a in **T3** form six-membered hydrogen bonding structure between amide carbonyl and hydroxyl (OH^a) groups intramolecularly, because it might be sterically unfavourable for inner OH^a to form it intermolecularly. On the other hand, one of the OH signals gradually moves upfield and another one gradually moves downfield upon decreasing concentration of **T2**. Thus, it is assigned that the OH signal moving upfield is OH^a and the OH signal moving downfield is OH^b, because the same behaviour of phenolic OH^a of **T3** as that of **T2** was observed as shown in Figure 4(B). These results indicate that the mono *N*-alkyl group on each arm does not seem to disturb the formation of hydrogen bonding between amide carbonyl and OH^b proton of **T2**, because the chemical shift of OH^b appears in the same range as that of OH^a. On the contrary, *N*,*N*-disubstituted alkyl groups of **T3** disturb to make a six-membered hydrogen bonding structure between OH^b and amide groups because of the bulkiness of disubstituted alkyl groups.



Scheme 1. Synthetic route of tripodal compounds **T2**–**T5**.



Scheme 2. Synthetic route of **L1**.

The interaction through the hydrogen bonding observed in the ^{1}H NMR dilution experiment of **T2** and **T3** should be concerned with the behaviours of the guest recognition. Compounds **L1**, **T4** and **T5** (see Schemes 1 and 2) were newly synthesised for comparison with **T2** concerning the behaviours in the solution. The ^{1}H NMR dilution experiment in $CDCl_3$ using tripodands **T1**, **T4** and **T5** and a linear compound **L1** as a model of one arm of **T2** was carried out to study the behaviours of hydrogen bonding in the concentration range from 1.0×10^{-2} to 1.25×10^{-3} M. No change in the chemical shifts was observed at all in the dilution experiment of **L1**, **T1** and **T5**. These results suggest that three terminal parts of tripodands play an important role to the cooperative formation of intramolecular hydrogen bonding from the following facts: (1) **L1** has no interaction of hydrogen bonding intermolecularly in this concentration range, (2) **T1** with three short arms also has no intermolecular interaction and (3) **T5** with three methyl ester parts instead of *N*-alkyl end group also has no interaction among three arms intramolecularly and intermolecularly. In addition to these results there is no interaction among three arms, whereas the intramolecular six-membered hydrogen bonding between amide carbonyl and hydroxyl groups is surely formed in $CDCl_3$ because OH protons neighbouring the CONH group shift downfield abnormally in every case. On the other hand, the ^{1}H NMR chemical shift variation of **T4** with short *N*-substituted group (*n*-butyl) is similar to the behaviour of **T2** under the same conditions as shown in Figure 5. With decreasing concentration of **T4**, one broadening OH proton signal on each arm gradually shifts upfield and mostly disappears at a lower concentration

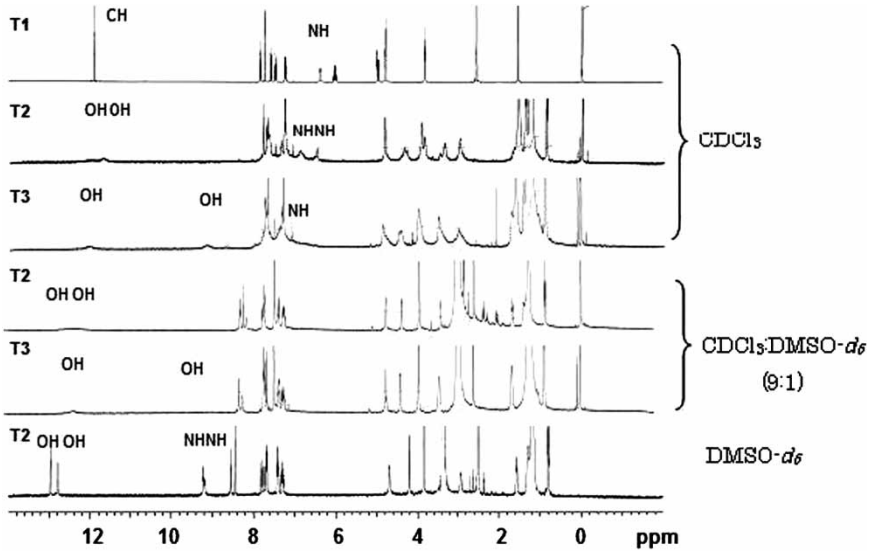


Figure 2. ^{1}H NMR spectrum of **T1**–**T3** in $CDCl_3$ and **T2**, **T3** in $CDCl_3$:DMSO-d_6 (9:1); **T2** in DMSO-d_6.

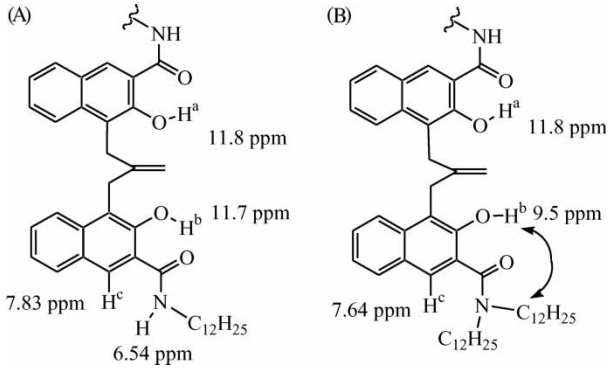


Figure 3. Intramolecular hydrogen bonding pathway proposed for the part of (A) **T2** and (B) **T3** (in $CDCl_3$, conc. = 0.01 M).

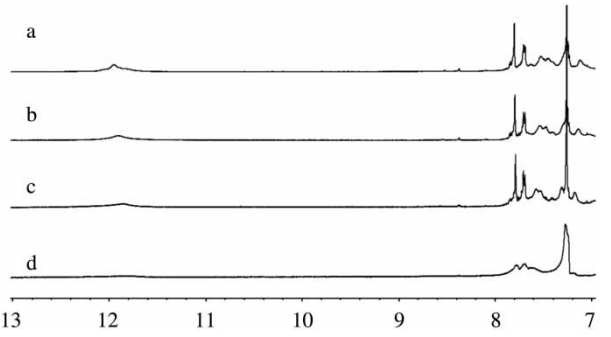


Figure 5. ^{1}H NMR dilution experiments of **T5** in $CDCl_3$: (a) conc. = 1.0×10^{-2}, (b) 5.0×10^{-3}, (c) 2.5×10^{-3}, and (d) 1.25×10^{-3} M.

(Figure 5(d)), whereas the signal of the other OH proton overlaps with the former one, and then rapidly disappears in the lower concentration range. These results imply that the intramolecular hydrogen bond among three arms of **T2** and **T4** may form in the higher concentration range in addition to the six-membered H-bonding structure in each arm in a non-polar solvent.

2.3 Complexation of T2 and T3 with anions

Both tripodands **T2** and **T3** have totally six hydroxyl and six amide groups in their three arms. Therefore, these compounds might be expected to exhibit the anion binding ability as host molecules. ^{1}H NMR spectrum of **T2** and **T3** was measured in $CDCl_3$ in the presence of anions such as F^-, AcO^- and $H_2PO_4^-$ (Figure 6). In the absence of anions, the singlet chemical shifts assigned to H^c of the naphthyl protons (see Figure 3) were observed at 7.77 and 7.64 ppm in **T2** and **T3**, respectively. Upon complexation of F^-, AcO^- and $H_2PO_4^-$, it should be noted that the singlet peak H^c of **T2** shifts downfield, whereas the singlet peak H^c of **T3** does not shift at all even after addition of fluoride ion as shown in Figure 6(B). It is inferred that there is no interaction between outer OH^b of host **T3** and any guest anion because the naphthyl proton H^c (marked in red colour) in **T3** hardly shifts as shown in Figure 4(B). This presumption might also be supported by the steric hindrance due to *N*,*N*-didodecyl end groups neighbouring OH^b. In our previous work (*22*), we found that hydroxyl and amide protons in **T1** strongly interact with F^-, $H_2PO_4^-$ and AcO^- in $CDCl_3$ to bring the drastic change in their chemical shifts in the ^{1}H NMR spectrum. This fact implies that the anion binding sites of **T3** might be OH^a and amide groups close to the central benzene ring. Thus, the anion binding ability strongly depends upon the *N*-substituted group. The *N*,*N*-didodecylamino group in **T3** surely disturbs the binding towards anion guests in $CDCl_3$. In addition, there is little change in the ^{1}H NMR spectrum in both cases of **T2** and **T3** when other anions such as Cl^-, Br^-, I^- and HSO_4^- were added into the solution of $CDCl_3$.

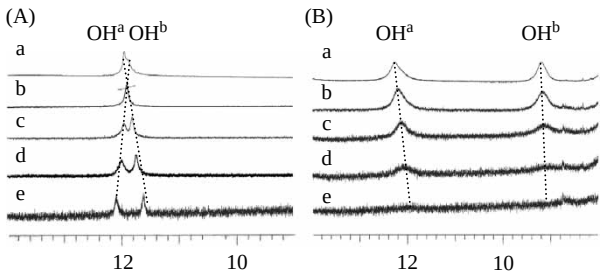


Figure 4. ^{1}H NMR dilution experiments of (A) **T2** and (B) **T3** in $CDCl_3$: (a) conc. = 1.0×10^{-2}, (b) 5.0×10^{-3}, (c) 2.5×10^{-3}, (d) 1.25×10^{-3}, (e) 6.25×10^{-4} M.

In the ^{1}H NMR titration experiment of **T2** with F^-, two OH signals showed downfield shifts due to hydrogen bond with F^- as shown in Figure 7. In the concentration (1.25×10^{-3} M) of **T2**, we can discriminate that the proton peak at lower magnetic field is due to outer OH^b and the other one at higher magnetic field is due to inner OH^a (see Figure 4(A)-d). However, it should be noticed that the signal of OH^a proton in **T2** moves downfield faster than that of OH^b when increasing the ratio of guest anion. This result suggests that inner OH^a exhibits stronger ability for complexation with F^- than outer OH^b in **T2**.

Fluorescent spectrum of receptors **T1**, **T2** and **T3** was also measured in the absence and presence of various anions such as F^-, Cl^-, Br^-, I^-, HSO_4^-, AcO^- and $H_2PO_4^-$ having tetra-*n*-butyl ammonium ion as a counter cation. As shown in Figure 8, when each anion was added into the $CHCl_3$ solution containing each receptor, compound **T1** exhibits prominent response towards anions ordered as follows: fluoride > acetate > dihydrogen phosphate ions. On the other hand, compounds **T2** and **T3** showed selective and significant increase in fluorescence intensity only towards F^- ion in a polar or non-polar solvent. In polar solvents such as DMSO or DMSO:H_2O = 24:1, the ratio of the fluorescence intensity (fluoride ion vs. other

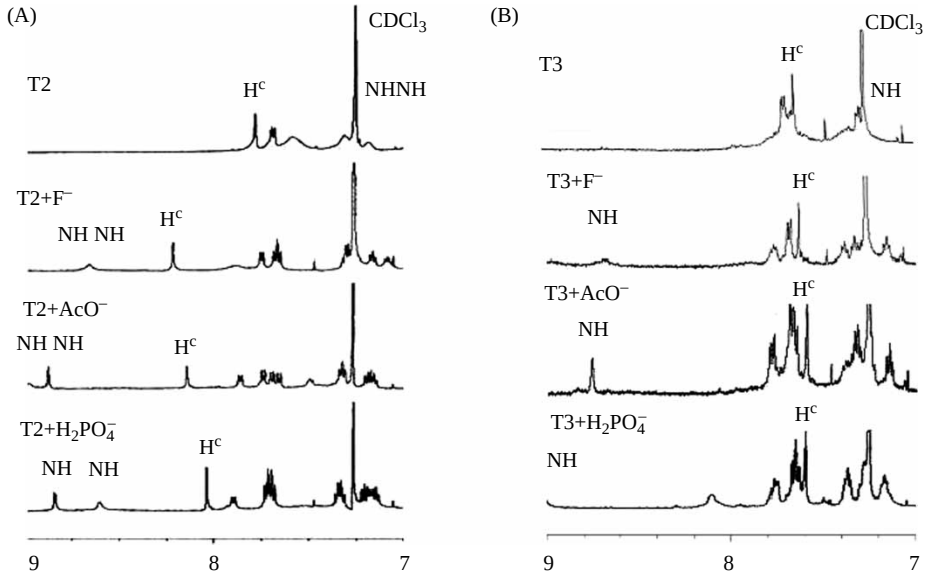


Figure 6. ^{1}H NMR spectra of (A) **T2** and **T2** added with F^-, $H_2PO_4^-$ and AcO^- and (B) **T3** and **T3** added with F^-, $H_2PO_4^-$ and AcO^-. All of the spectra are measured in $CDCl_3$.

ions) in the case of **T2** does not change so much compared with the result in $CHCl_3$, although the measured values change depending upon the conditions. On the basis of previously reported anion sensing phenomenon, the appearance of these new peaks would be just due to the formation of intermolecular excited state proton transfer (*27*) in anion complexes by weakening the intramolecular hydrogen bonding between OH and carbonyl groups. It should be noted that **T2** can be used as a fluorescent sensing agent for fluoride ion with high selectivity not only in a non-polar solvent but also in a polar solvent containing water different from **T3** which is insoluble in a polar solvent, i.e. DMSO, because it is a practically important factor that the ionic guest can be recognised selectively in a polar solvent, in particular, in an aqueous solvent.

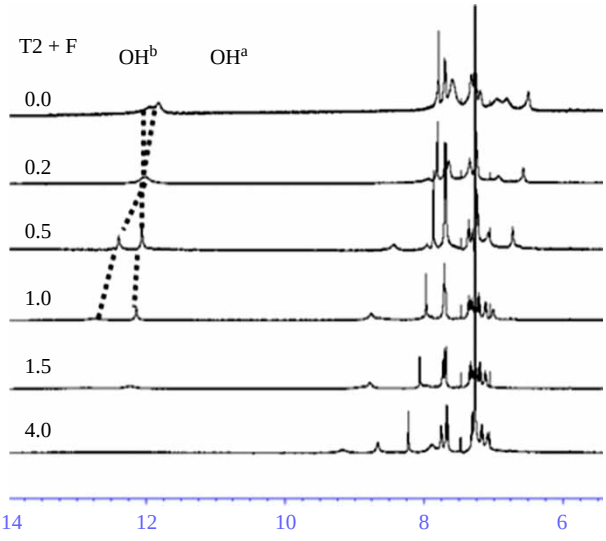


Figure 7. ^{1}H NMR spectral change with the addition of F^- to **T2** in $CDCl_3$ (conc. $= 1.25 \times 10^{-3}$ M).

3. Conclusion

Novel tripodal receptors **T2** and **T3** having multiple hydroxyl and amide groups either with *N*-dodecylamino end group or with *N*,*N*-didodecylamino end group, respectively, were successfully synthesised via TCR in order to investigate the behaviours of the interaction among three arms and the ability for complexation with anions. When the ^{1}H NMR spectrum of **T2** and **T3** was measured either in polar or non-polar solvent, the chemical shifts of outer OH^b proton changed depending upon the substituent on terminal amide group. In **T2** having *N*-monosubstituted alkyl group, the outer OH^b in each arm can form strong hydrogen bonding intramolecularly, whereas in **T3** having totally six *N*,*N*-disubstituted alkyl groups, OH^b has little hydrogen bonding interaction not only intermolecularly but also intramolecularly because of the steric hindrance. In the investigation of their anion binding behaviours, we showed that **T2** and **T3** with longer three arms compared with **T1** exhibited much higher fluorescent sensitivity towards that fluoride ion. Tripodand **T2** having two kinds of primary amide groups in one arm in a molecule can recognise anions even in a polar solvent such as DMSO and aqueous DMSO. Tripodand **T3** can exhibit fluorescent fluoride sensing in $CHCl_3$, but not in DMSO because of insolubility. In the fluorescence spectrum, **T2** exhibits highly selective emission around 500 nm towards fluoride ion among F^-, Cl^-, Br^-, I^-, HSO_4^-, AcO^- and $H_2PO_4^-$ ions.

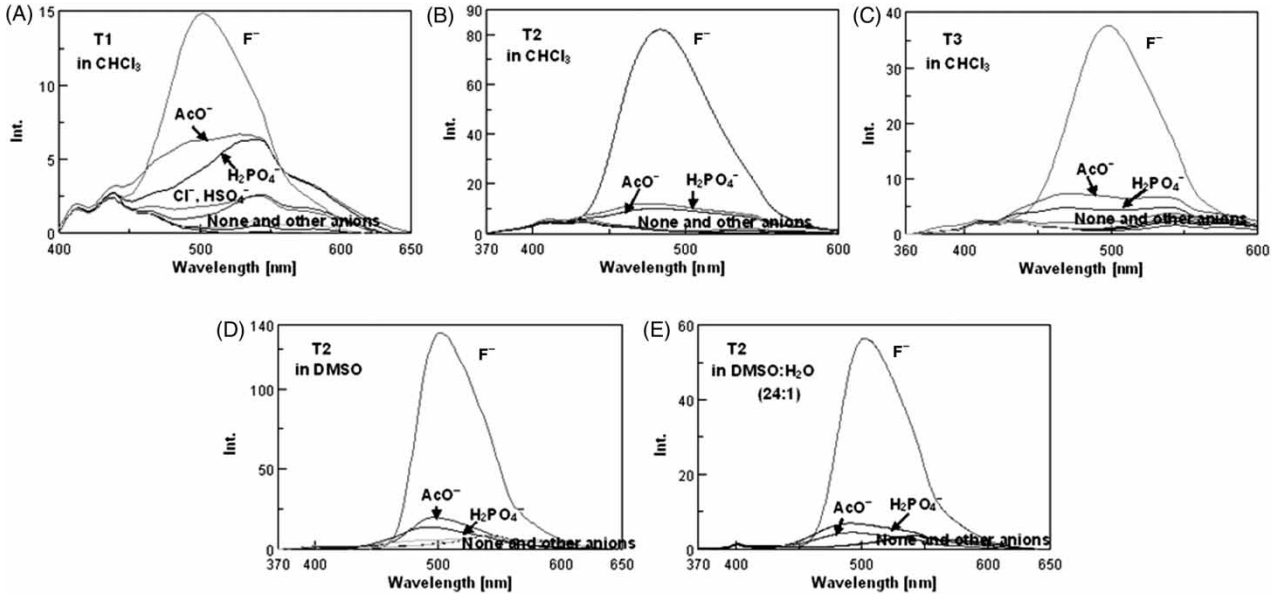


Figure 8. Emission spectral changes of (A) **T1** (1.0×10^{-5} M) upon addition of various anions in $CHCl_3$, (B) **T2** (1.0×10^{-5} M) upon addition of various anions in $CHCl_3$, (C) **T3** (1.0×10^{-5} M) upon addition of various anions in $CHCl_3$, (D) **T3** (1.0×10^{-5} M) upon addition of various anions in DMSO and (E) **T3** (1.0×10^{-5} M upon addition of various anions in DMSO:H_2O = 24:1).

4. Experimental

4.1 General information

All reagents were obtained from commercial suppliers and used without further purification unless otherwise stated. ^{1}H NMR spectrum was determined on a Varian NMR System 500. Chemical shifts from TMS in $CDCl_3$ for ^{1}H NMR are reported in parts per million (ppm), calibrated to the residual solvent peak set, with coupling constants reported in *J*-value (Hz). Column chromatography was carried out using Merck silica gel 60 Å (230–400 mesh). Recycling preparative GPC–HPLC was carried out on JAI LC-908. Mass spectrum was recorded using a Bruker Daltonics Autoflex MALDI-TOF Mass Spectrometer with Scout-MTP Ion Source. IR spectrum was recorded with a Jasco FTIR-430 spectrophotometer with samples as KBr pellets in the 4000–400 cm^{-1} range. Elemental analyses were performed on Fisons EA-1108 instrument.

4.2 3-(3-Methoxycarbonyl-2-naphthyloxy)-2-chloromethyl-1-propene (1)

To a solution of 2-hydroxy-3-naphthoic acid methyl ester (20.2 g, 0.1 mol) in dry DMF (200 ml) was added 1.2eq NaH (2.88 g, 0.12 mol), and the mixture was stirred for 1 h at room temperature. Each 10 ml of the mixture was added to the dry DMF (50 ml) solution of 3-chloro-2-chloromethyl-1-propene (37.5 g, 0.3 mol) every 30 min while stirring at 60°C under Ar. The solution was stirred at 60°C overnight after addition of the mixture. After removal of DMF under reduced pressure by a vacuum pump, the residue was dissolved in diethyl ether (100 ml) and the organic layer was washed three times with water, dried over $MgSO_4$ and evaporated under vacuum. The crude product was chromatographed on silica gel with AcOEt:hexane (1:20) as an eluent to give compound **1** (15.3 g, 0.053 mol, 55%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96 (s, 3H), 4.31 (s, 2H), 4.81 (s, 2H), 5.45 (s, 1H), 5.53 (s, 1H), 7.24 (s, 1H), 7.41 (m, 1H), 7.54 (m, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 8.36 (s, 1H).

4.3 3-(3-Hydroxycarbonyl-2-naphthoxy)-2-hydroxymethyl-1-propene (2)

Compound **1** (6.00 g, 0.02 mol) was dissolved in 50 ml of dry DMF and then potassium acetate (3.04 g, 0.04 mol) was added to the solution. The reaction mixture was stirred for 12 h at 60°C and the solvent was removed by a vacuum pump. To the residue was added water (200 ml), and the insoluble solid was separated by filtration, and washed with water (250 ml) to remove excess DMF. The solid was dried *in vacuo*. The solid obtained was used without further purification.

The solid was dissolved in EtOH and THF (200 and 20 ml, respectively) solvents and NaOH (8.00 g, 0.20 mol) was added. After stirring for 12 h at 60°C, the solvents (EtOH and THF) were removed under reduced pressure and to the aqueous solution was added conc. HCl dropwise until the pH paper indicated acidic. The white precipitate was filtered and washed with water, yielding white solid **2**

(4.80 g, 0.018 mol, 90%, for the two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.36 (s, 2H), 4.93 (s, 2H), 5.40 (s, 1H), 5.43 (s, 1H), 7.31 (s, 1H), 7.46 (m, $J = 8.3$ Hz, 1H), 7.54 (m, $J = 8.3$ Hz, 1H), 7.76 (d, $J = 8$ Hz, 1H), 7.90 (d, $J = 8$ Hz, 1H), 8.73 (s, 1H). MALDI-TOF-MS: *m/z* 259.5 $[M + H]^+$, 281.5 $[M + Na]^+$, 297.5 $[M + K]^+$.

4.4 1,3,5-Triethyl-2,4,6-tris[2-(2-chloromethyl-1-propenyl-3-oxy)naphthyl-3-carbamoylmethyl]benzene (4)

Compound **2** (4.00 g, 0.15 mol) was dissolved in $SOCl_2$ (5 ml) and heated at reflux for 4 h. The excess of $SOCl_2$ was removed by distillation and dried *in vacuo*. The remaining solid **3** was dissolved in dry THF and the solution was maintained at 0°C. To the solution were added 1,3,5-triethyl-2,4,6-trisaminomethylbenzene (1.21 g, 5.00 mmol) and Et_3N (2.93 g, 0.03 mol). The mixture was stirred overnight at room temperature and the solvent was removed under reduced pressure. To the residue was added water (200 ml), and the insoluble solid was separated by filtration, and washed with water (250 ml). The residual solid was chromatographed on silica gel with $CHCl_3$ as an eluent to give **4** (3.54 g, 0.354 mmol, 69%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26 (m, 9H), 2.87 (m, 6H), 3.61 (s, 6H), 4.67 (s, 6H), 4.79 (d, $J = 4.5$ Hz, 6H), 5.10 (s, 6H), 7.16 (s, 3H), 7.41 (m, 3H), 7.52 (m, 3H), 7.69 (d, $J = 8.5$ Hz, 3H), 7.73 (m, 3H, NH), 7.90 (d, $J = 8.0$ Hz, 3H), 8.74 (s, 3H). MALDI-TOF-MS: *m/z*: calcd for $C_{60}H_{60}Cl_3N_3O_6$: 1023.35; found: 1024.03 $[M + H]^+$.

4.5 1,3,5-Triethyl-2,4,6-tris(2-(methyloxycarbonylnaphthoxy)-2-propoxy-naphthylcarbamoyl-N-methyl)benzene (5)

To a solution of 2-hydroxy-3-naphthoeic acid methyl ester (2.02 g, 0.01 mol) in 50 ml of dry DMF was added 1.2eq NaH (0.288 g, 0.012 mol). To the stirred mixture was added compound **4** (3.00 g, 3.00 mmol). After stirring at 60°C overnight, the solvent DMF was removed under pressure to yield yellow residue. The residue was treated with water (200 ml) and filtered. The residual solid was chromatographed on silica gel with $CHCl_3$ as an eluent to give **5** (3.47 g, 2.28 mmol, 76%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.27 (m, 9H), 2.94 (m, 6H), 3.75 (s, 9H), 4.33 (s, 6H), 4.73 (s, 6H), 4.81 (d, $J = 0.4$ Hz, 6H), 4.97 (s, 3H), 5.16 (s, 3H), 6.79 (s, 3H), 7.09 (s, 3H), 7.27 (m, 3H), 7.29 (d, $J = 8.5$ Hz, 3H), 7.32 (m, 3H), 7.39 (m, 3H), 7.40 (d, $J = 8.5$ Hz, 3H), 7.47 (d, $J = 8.0$ Hz, 3H), 7.71 (d, $J = 8.0$ Hz, 3H), 7.80 (m, 3H), 7.92 (m, 3H, NH), 8.17 (s, 3H), 8.68 (s, 3H). MALDI-TOF-MS *m/z*: calcd for $C_{96}H_{87}N_3O_{15}$: 1521.61; found: 1522.28 $[M + H]^+$.

4.6 Tripodal compounds 7a–7c

To a solvent of **5** (1.00 g, 0.606 mmol) in EtOH/THF (100/20 ml) was added the solvent of NaOH (0.263 g, 6.60 mmol) in H_2O (10 ml). The reaction mixture was stirred overnight at 60°C. After removal of EtOH/THF, we added hydrochloric acid until acidification to a pH of 5. The precipitated white solid was filtered and dried *in vacuo*. The obtained compound **6** was obtained as a white solid and used without further purification. To a suspension of compound **6** (296 mg, 0.20 mmol) in dry CH_2Cl_2 (40 ml) were added 2-chloro-1-methylpyridinium iodide (204 mg, 0.80 mmol), triethylamine (121 mg, 1.20 mmol) and H-R (0.80 mmol) (R = $NHC_{12}H_{25}$, $N(C_{12}H_{25})_2$, NHC_4H_9). The mixture was stirred at 0–5°C for 4 h and at room temperature for an additional 12 h. The solvent was removed by rotary evaporation. The residue was treated with water (50 ml), filtered and washed with water (100 ml). Products **7a**–**7c** were purified by silica chromatography with $CHCl_3$ and by recycling preparative GPC.

7a (0.190 g, 48%): light yellow, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (m, 9H), 1.37–1.08 (m, 60H), 2.93 (m, 9H), 3.21 (m, 6H), 4.36 (s, 6H), 4.42 (s, 6H), 4.77 (d, $J = 4$ Hz, 6H), 5.17 (s, 3H), 5.28 (s, 3H), 6.79 (s, 3H), 6.87 (s, 3H), 7.26 (m, 3H), 7.34 (m, 3H), 7.34 (m, 3H), 7.40 (m, 3H), 7.45 (d, $J = 9$ Hz, 3H), 7.45 (d, $J = 9$ Hz, 3H), 7.74 (d, $J = 8$ Hz, 3H), 7.78 (d, $J = 8$ Hz, 3H), 7.91 (m, 3H, NH), 8.41 (s, 3H), 8.70 (s, 3H).

7b (0.463 g, 93%): white solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (m, 18H), 1.31 (m, 132H), 1.48 (m, 6H), 1.62 (m, 12H), 2.91 (m, 12H), 3.21 (m, 3H), 3.44 (m, 3H), 4.40 (m, 6H), 4.72 (m, 6H), 4.88 (m, 6H,), 4.94 (s, 3H), 5.505 (s, 3H), 6.89 (s, 3H), 7.23 (s, 3H), 7.31 (m, 3H), 7.34 (m, 3H), 7.34 (m, 3H), 7.37 (m, 3H), 7.55 (d, $J = 7.0$ Hz, 3H), 7.55 (s, 3H, naphthyl), 7.59 (d, $J = 8.0$ Hz, 3H), 7.66 (d, $J = 7.0$ Hz, 3H), 7.84 (d, $J = 8.0$ Hz, 3H), 7.98 (s, 3H, NH), 8.73 (s, 3H).

7c (0.132 g, 40%): light yellow, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.73 (m, 9H), 1.31 (m, 9H), 2.91 (m, 12H), 3.21 (m, 3H), 3.44 (m, 3H), 4.35 (m, 6H), 4.40 (m, 6H), 4.76 (m, 6H), 5.18 (s, 3H), 5.25 (s, 3H), 6.78 (s, 3H), 6.86 (s, 3H), 7.25 (m, 3H), 7.31 (m, 3H), 7.34 (m, 3H), 7.34 (m, 3H), 7.43 (m, 3H), 7.45 (m, 3H), 7.75 (d, $J = 8.5$ Hz, 3H), 7.79 (d, $J = 8.5$ Hz, 3H), 7.85 (s, 3H, NH), 8.42 (s, 3H), 8.70 (s, 3H).

4.7 Tripodal receptors T2–T5

Compounds **7a**–**7c** or **5** (100 mg) was dissolved in N-methyl-2-pyrrolidone (NMP) (5 ml) and the solution was heated at 160°C for 1 h under argon atmosphere. After removal of NMP under reduced pressure, we purified the residue by silica chromomatography with $CHCl_3$ as an eluent to give **T2**, **T3**, **T4** or **T5**, respectively.

T2 (94 mg, 94%): yellow sticky liquid. Mp 110–112°C, ^{1}H NMR (500 Hz, DMSO-d_6): δ 0.81 (m, 9H),

1.28–1.15 (m, 60H), 1.56 (m, 9H), 2.96 (s, 6H), 3.85 (s, 6H), 4.20 (s, 6H), 4.86 (s, 6H), 7.29 (m, 3H), 7.32 (m, 3H), 7.42 (m, 3H), 7.42 (m, 3H), 7.67 (d, $J = 8.0$ Hz, 3H), 7.67 (d, $J = 8.0$ Hz, 3H), 7.74 (d, $J = 9.0$ Hz, 3H), 7.81 (d, $J = 8.5$ Hz, 3H), 8.44 (s, 3H), 8.54 (s, 3H), 9.16 (m, 3H, NH), 9.21 (m, 3H, NH), 12.77 (s, 3H, OH), 12.95 (s, 3H, OH). IR (KBr): 3401, 2924, 2853, 1633 and 1466 cm^{-1}. Elemental analysis: Anal. Calcd for $C_{129}H_{156}N_6O_{12}\cdot H_2O$: C, 77.44; H, 7.96; N, 4.20. Found: C, 77.41; H, 7.74; N, 4.15. MALDI-TOF-MS *m/z*: calcd for $C_{165}H_{228}N_6O_{12}$: 1982.65; found: 1983.91 $[M + H]^+$.

T3 (93 mg, 93%): yellow sticky liquid. Mp 78–80°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.87 (br s, 18H), 1.02–1.67 (br s, 270H), 2.96 (br s, 6H), 3.49 (br s, 6H), 3.96 (br s, 12H), 4.40 (br s, 6H), 4.84 (br s, 6H), 7.27–7.34 (br s, 9H), 7.54–7.74 (br s, 24H), 9.16 (br s, 3H, OH), 11.95 (br s, 3H, OH). IR (KBr): 3393, 2925, 2853, 1650 and 1533 cm^{-1}. Elemental analysis: Anal. Calcd for $C_{165}H_{228}N_6O_{12}$: C, 79.67; H, 9.24; N, 3.38. Found: C, 79.43; H, 9.66; N, 3.40. MALDI-TOF-MS *m/z*: calcd for $C_{165}H_{228}N_6O_{12}$: 2485.74; found: 2487.05 $[M + H]^+$.

T4 (91 mg, 91%): yellow solid. Mp 134–136°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (br s, 9H), 1.32 (br s, 6H), 3.00 (br s, 6H), 3.26 (br s, 6H), 3.79 (br s, 6H), 3.88 (br s, 6H), 4.27 (m, 6H), 4.84 (s, 6H), 6.46 (br s, 3H), 6.76 (br s, 3H), 7.01 (br s, 3H), 7.16 (br s, 3H), 7.31 (br s, 9H), 7.56 (br s, 9H), 7.71 (d, $J = 8.0$ Hz, 3H), 7.79 (s, 3H), 11.87 (br s, 6H, OH). IR (KBr): 3409, 2908, 1690 and 1447 cm^{-1}. Elemental analysis: Anal. Calcd for $C_{105}H_{108}N_6O_{12}$: C, 76.62; H, 6.61; N, 5.11. Found: C, 76.89; H, 6.43; N, 4.84. MALDI-TOF-MS *m/z*: calcd for $C_{105}H_{108}N_6O_{12}$: 1646.01; found: 1647.62 $[M + H]^+$.

T5 (96 mg, 96%) white solid. Mp 152–154°C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.36 (m, 9H), 2.91 (m, 6H), 3.98 (s, 12H), 4.00 (s, 9H), 4.40 (s, 6H), 4.80 (s, 6H), 6.42 (m, NH, 3H), 7.17 (br s, 3H), 7.29 (m, 3H), 7.41 (m, 6H), 7.56 (br s, 3H), 7.78 (m, 12H), 8.41 (s, 3H), 10.76 (s, OH, 3H), 11.83 (s, OH, 3H). IR (KBr) 3053 and 1728 cm^{-1}. Elemental analysis: Anal. Calcd for $C_{96}H_{87}N_3O_{15}$: C, 75.72; H, 5.76; N, 2.76; found: C, 75.01; H, 5.54; N, 2.32. MALDI-TOF-MS: *m/z* calcd for $C_{96}H_{87}N_3O_{15}$: 1521.61; found: 1544.60 $[M + Na]^+$.

4.8 Compound L1

1,3-Bis[2-(3-chlorocarbonyl) naphthoxy]-2-methylenepropane[3a] (0.465 g, 1.00 mmol) was added to the 50 ml THF solution of *p*-methylbenzylamine (0.185 g, 1.00 mmol) and stirred at room temperature for 4 h. Then, *N*-dodecylamine (0.740 g, 4.00 mmol) was added to the mixture and stirred overnight at room temperature. THF was evaporated and water was added into the residue to give a solid. The solid was subjected to column chromomatography on silica gel with $CHCl_3$ as an eluent and then separated by recycling preparative GPC to give 0.217 g of asymmetric isobutenyl ether derivative as a white solid (0.310 mmol, 31%). The white solid was heated at 160°C under vacuum for 1 h and then purified by silica chromatography with $CHCl_3$ as an eluent to give **L1** (0.98 g, 98%). Compound **L1**: light yellow solid, mp 60–62°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (m, 3H), 1.30 (m, 10H), 1.50 (m, 2H), 1.16 (s, 2H), 2.22 (s, 2H), 3.41 (m, 2H), 4.61 (m, 2H), 4.64 (s, 2H), 4.86 (s, 2H), 6.51 (d, $J = 6.5$ Hz, 2H), 7.04 (s, H), 7.04 (s, H), 7.08 (s, H), 7.2 (s, H), 7.21 (s, H), 7.26 (s, H), 7.45 (m, H), 7.45 (m, H), 7.54 (m, H), 7.54 (m, H), 7.68 (d, $J = 9.0$ Hz, H), 7.70 (s, H), 7.70 (d, $J = 9.0$ Hz, H), 7.92 (d, $J = 8.5$ Hz, H), 7.93 (d, $J = 8.0$ Hz, H), 8.07 (s, H, NH), 8.70 (s, H), 8.79 (s, H). IR (KBr): 3413, 2922, 2811, 1690 and 1454 cm^{-1}. Elemental analysis: Anal. Calcd for $C_{58}H_{78}N_2O_4\cdot 0.5H_2O$: C, 79.50; H, 9.09; N, 3.20. Found: C, 79.43; H, 9.04; N, 3.32. MALDI-TOF-MS: *m/z* calcd for $C_{58}H_{78}N_2O_4$: 866.60; found: 889.63 $[M + Na]^+$, 905.64 $[M + K]^+$.

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