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Synthesis and estimation of gelation ability of C_3-symmetry tris-urea compounds

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ABSTRACT

C_3-Symmetry tris-urea low molecular weight gelator (LMWG) (**1**), which shows chemical stimuli responsible for a sol–gel phase transition, was divided into five regions. Based on the division, 22 derivatives were synthesized. The gelation ability of these derivatives was tested in nine organic solvents with a wide range of values for relative static permittivity (ε_r=47.2–1.89). Some derivatives showed a better performance as LMWGs than the original tris-urea LMWG (**1**). For example, the critical gelation concentration (CGC) in acetone was improved from 1.5 wt % to 0.5 wt % by changing the core substituent (**18**). Highly versatile LMWG for a variety of solvents was obtained by changing the linker moiety (**23**). Structural information to design tris-urea LMWGs is important to create rationally a functional supramolecular gel.

1. Introduction

Research on low molecular weight gelators (LMWGs) has attracted much attention for several decades.[1] Hydrogen-bonding,[2] π–π interaction,[3] dipole–dipole interaction,[4] and van der Waals interaction[5] are major driving forces for the self-assembly of LMWGs. To design an LMWG, it is known empirically that low-symmetry structures and the introduction of long alkyl chains are generally effective. Therefore, a large number of cholesterol-based LMWGs and/or LMWGs with long alkyl chains appended have been developed. As examples of highly symmetric structures of LMWGs, Meijer,[6] van Esch and Feringa,[7] and others[4c,8] have reported C_3-symmetry LMWGs; however, many of them have long alkyl chains appended. One of the great advantages of LMWGs are stimuli-responsive reversible sol–gel phase transitions such as photo,[5a,9] redox,[10] ultrasound,[11] and chemical stimuli[12] produced by the rational design of the gelator. Previously, we reported C_3-symmetry tris-urea LMWG (**1**), which can gelate a variety of organic solvents such as acetone, methanol, etc., following brief sonication. The acetone gel of **1** was changed into a homogeneous solution by adding anions (e.g., tetrabutylammonium fluoride), and the solution was re-gelated by adding a Lewis acid (e.g., $ZnBr_2$) and irradiating with ultrasound.[13] Because of the structural features of tris-urea LMWG (**1**), a variety of derivatives can be synthesized due to the polyfunctional and highly symmetric structure of **1**. Systematic preparation of derivatives and evaluation of their gelation properties would provide valuable information about the design of a functional supramolecular gel. In this paper, we would like to report the synthesis of 22 examples of novel tris-urea derivatives, and their gelation ability for nine types of organic solvents with a wide range of values for relative static permittivity (ε_r=47.2–1.89).

2. Results and discussion

2.1. Structural division of tris-urea LMWG (1)

Tris-urea LMWG (**1**) was divided into five regions, which are (1) the hydrogen-bonding part, (2) positional isomers of the urea moiety, (3) substituent on the outer urea nitrogen, (4) substituent on the central aromatic ring, and (5) linker moiety fastened to the outer aromatic ring (Fig. 1). In the previous communication, we reported the necessity of the urea moiety for gelation. Amide derivative and *N*-methyl urea derivative showed no gelation abilities.[13] Therefore, the urea moiety was fixed as the hydrogen-bonding part. The urea moieties are combined at the *meta*-position with aromatic linkers of the original tris-urea LMWG (**1**). *ortho*- and *para*-derivatives (**2** and **3**) were planned for synthesis and to apply gelation tests. The substituent effect of the outer urea nitrogen was evaluated using a variety of substituted tris-urea derivatives (**4**–**17**), which were synthesized from the corresponding isocyanates. The ethyl groups of **1** were replaced by different substituents (**18**–**21**). Methyleneoxy linkers were replaced by inflexible ethynyl groups and nonpolar ethylene groups (**22** and **23**).

2.2. Synthesis of tris-urea compounds

Tris-urea LMWG (**1**) was synthesized in three steps from 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene (**24**).[13] Reaction of **24** and

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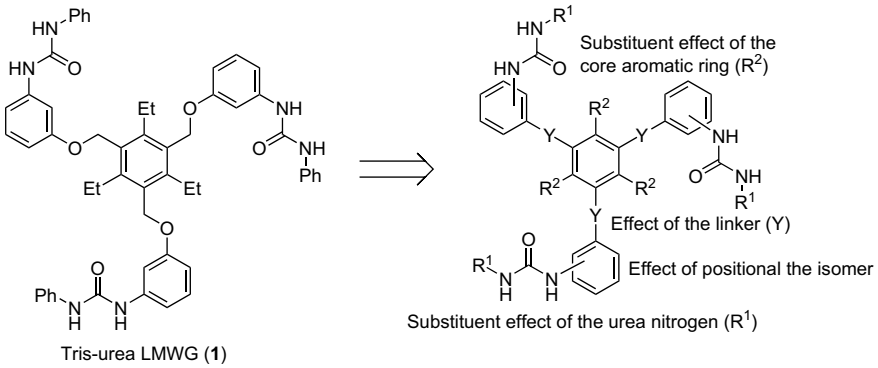
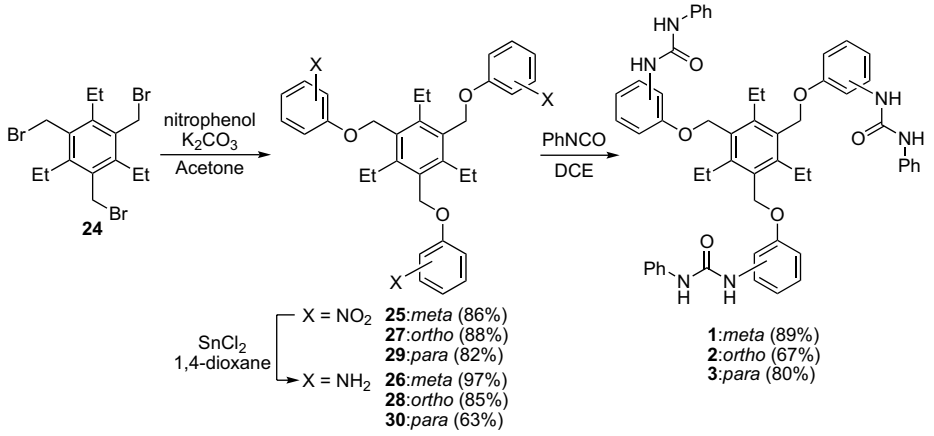


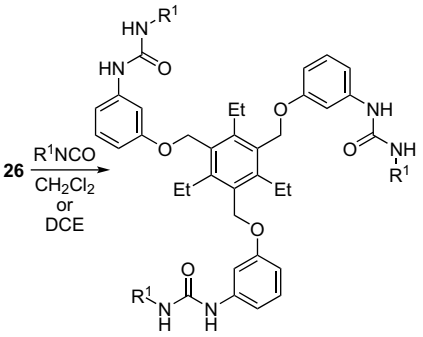
Compoud	position	R^1	R^2	Y	Compoud	position	R^1	R^2	Y
1	*meta*	Ph	Et	CH_2O	**13**	*meta*	4-$CH_3C_6H_4$	Et	CH_2O
2	*ortho*	Ph	Et	CH_2O	**14**	*meta*	4-$C_2H_5C_6H_4$	Et	CH_2O
3	*para*	Ph	Et	CH_2O	**15**	*meta*	4-$(CH_3)_2CHC_6H_4$	Et	CH_2O
4	*meta*	*n*-octyl	Et	CH_2O	**16**	*meta*	4-$C_8H_{17}C_6H_4$	Et	CH_2O
5	*meta*	*n*-dodecyl	Et	CH_2O	**17**	*meta*	1-naphthyl	Et	CH_2O
6	*meta*	benzyl	Et	CH_2O	**18**	*meta*	Ph	H	CH_2O
7	*meta*	2-FC_6H_4	Et	CH_2O	**19**	*meta*	Ph	Me	CH_2O
8	*meta*	3-FC_6H_4	Et	CH_2O	**20**	*meta*	Ph	OMe	CH_2O
9	*meta*	4-FC_6H_4	Et	CH_2O	**21**	*meta*	Ph	*i*-pentyl	CH_2O
10	*meta*	4-ClC_6H_4	Et	CH_2O	**22**	*meta*	Ph	H	C≡C
11	*meta*	4-BrC_6H_4	Et	CH_2O	**23**	*meta*	Ph	H	CH_2CH_2
12	*meta*	4-IC_6H_4	Et	CH_2O					

Figure 1. Structural division of LMWG (**1**) and structure of 22 tris-urea compounds.

3-nitrophenol gave the tris-nitrophenoxylated product (**25**). Reduction of the nitro groups of **25** proceeded in the presence of tin(II) chloride dihydrate in 1,4-dioxane solvent, and afforded tris-amine (**26**). The tris-urea LMWG (**1**) was obtained by the reaction of **26** with phenyl isocyanate. A similar procedure afforded *ortho* and *para* positional isomers (Scheme 1). Reaction of **24** and 2-nitrophenol or 4-nitrophenol gave tris-nitrophenoxylated products (**27** and **29**) in 88 and 82% yields, respectively. Reduction of the nitro groups of **27** or **29** in the presence of tin(II) chloride dihydrate in 1,4-dioxane solvent afforded tris-amines (**28** and **30**). Tris-ureas (**2** and **3**) were obtained as a result of the reaction of **28** or **30** and phenyl isocyanate in 67 and 80% yields, respectively. Synthesis of a variety of substituted tris-urea derivatives was achieved by reactions of tris-amine (**26**) and various isocyanates, and afforded tris-ureas (**4**–**17**) in 62–90% yields (Scheme 2). Reaction of 1,3,5-tris(bromomethyl)benzene (**31**) with 3-nitrophenol gave tris-nitrophenoxylated product (**32**) in 90% yield. Tris-amine (**33**) was obtained by reduction of the nitro groups of **32** in the presence of tin(II) chloride dihydrate in 1,4-dioxane solvent in 91% yield. The amino groups of **33** were converted into phenyl urea groups by a condensation reaction with phenyl isocyanate, and the proposed tris-urea (**18**) was obtained in 95% yield. Other tris-ureas (**19**–**21**) were also prepared from 1,3,5-tris(halomethyl)-2,4,6-trisubstituted benzenes (**34**, **37**, and **40**)[14] via similar three-step reactions (Scheme 3). Tris-ureas with modified methyleneoxy linkers (**22** and **23**) were synthesized from a common intermediate (**45**) (Scheme 4). The tris-amine (**45**) was prepared from the known 1,3,5-triethynylbenzene (**43**).[15] A Sonogashira cross-coupling reaction of **43** and 3 equiv of 3-bromonitrobenzene afforded the trinitrophenyl-substituted product (**44**) in 70% yield. Reduction of the nitro groups of **44** in the presence of tin(II) chloride dihydrate in 1,4-dioxane solvent gave tris-amine (**45**) in 78% yield. A tris-urea with an inflexible ethynyl linker (**22**) was obtained from the reaction of **45** and phenyl isocyanate in 83% yield. Hydrogenation of the ethynyl groups of **45** in the presence of palladium–carbon catalyst afforded the tris-amine **46**. Tris-urea with a flexible ethyl linker (**23**) was



Scheme 1. Synthetic scheme for generation of positional isomers of the urea moiety.



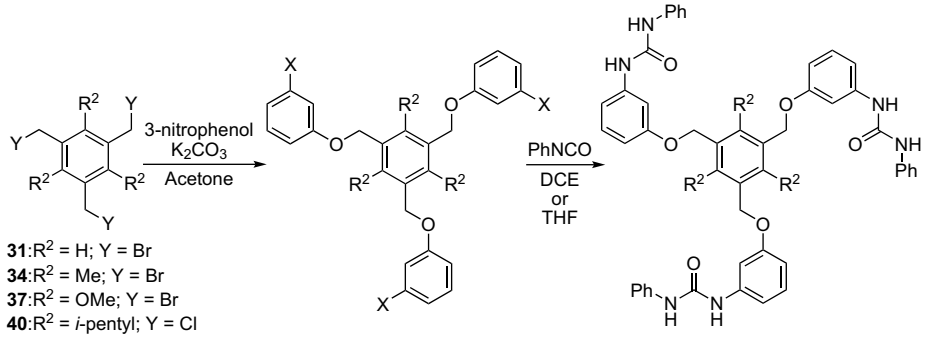
4:R^1 = *n*-octyl (77%) **11**:R^1 = 4-BrC_6H_4 (77%)
5:R^1 = *n*-dodecyl (65%) **12**:R^1 = 4-IC_6H_4 (87%)
6:R^1 = benzyl (64%) **13**:R^1 = 4-$CH_3C_6H_4$ (76%)
7:R^1 = 2-FC_6H_4 (88%) **14**:R^1 = 4-$C_2H_5C_6H_4$ (90%)
8:R^1 = 3-FC_6H_4 (78%) **15**:R^1 = 4-$(CH_3)_2CHC_6H_4$ (75%)
9:R^1 = 4-FC_6H_4 (74%) **16**:R^1 = 4-$C_8H_{17}C_6H_4$ (62%)
10:R^1 = 4-ClC_6H_4 (68%) **17**:R^1 = 1-naphthyl (82%)

Scheme 2. Synthetic scheme for generation of variety substituents on the outer urea nitrogen.

obtained from the reaction of **46** and phenyl isocyanate in 76% yield.

2.3. Gelation experiments of tris-urea compounds

Tris-urea LMWG (**1**) and 22 newly synthesized tris-urea derivatives (**2**–**23**) were used in gelation experiments (Table 1). Gel formation was tested with nine organic solvents having a wide range of values for relative static permittivity (ε_r=47.2–1.89); namely, DMSO, MeOH, acetone, diethyl phthalate (DEP), EtOAc, THF, CH_2Cl_2, toluene, and *n*-hexane. The following procedure was used as a standard condition for gelation. Tris-urea and solvent were mixed in an appropriate test tube then irradiated with ultrasound (0.39 W cm^{-2}, 42 kHz) at ambient temperature for 15 min. Gel formation was confirmed by the inverted test tube method. A stable sample upon inversion of the test tube was defined as a gel. A homogeneous solid sample that flows slowly upon inversion of the test tube was described as a soft gel. We previously reported that ultrasound irradiation is necessary for gelation of **1** and ordinary thermal dissolution and cooling did not produce a gel.[13] Some research has been reported on ultrasound-induced gel formation.[9,16] In our case, dispersion and solvation of solid tris-urea caused by ultrasound should be the principle for gelation. As support for this idea, vigorous stirring of a mixture of **1** and acetone using a vortex mixer (3200 rpm) for 10 min then standing at ambient temperature for several hours afforded an opaque gel; however, the firmness of the gel was much less than the ultrasound-induced gel of **1** and acetone. Tris-urea **1** showed gelation ability for relatively polar solvents, namely, MeOH (CGC=2.0 wt %), acetone (CGC=1.5 wt %), diethyl phthalate (CGC=2.0 wt %), and THF (CGC=5.0 wt %). Once formed, those gels were stable at ambient temperature for months. A homogeneous solution was obtained from a mixture of **1** and the very polar DMSO. Insoluble suspensions appeared from mixtures of **1** and less polar solvents, namely, EtOAc, CH_2Cl_2, toluene, and *n*-hexane. A scanning electron microscope (SEM) image of a xerogel prepared by freeze-drying an acetone gel of **1** showed intertwining nanofibers (Fig. 2a). Tris-urea **2**, which has *ortho*-substituted phenyl urea groups, formed a gel upon mixing with THF, though the gel was soft enough to flow slowly upon inversion of the test tube. Mixtures of **2** and the other solvents did not give gels, and afforded an insoluble suspension, except for soluble DMSO. Tris-urea **3** with *para*-substituted phenyl urea groups showed gelation abilities for MeOH (CGC=3.0 wt %), diethyl phthalate (CGC=4.0 wt %), EtOAc (CGC=1.5 wt %), and THF (CGC=5.0 wt %). Thus, four of the nine solvents gave gels; in general, higher concentrations of gelator (**3**) were needed for gelation than were needed for **1**. Comparison of the gelation abilities of three positional isomers (**1**–**3**) indicated the *meta*-substituted tris-urea derivative (**1**) is favorable as an LMWG, although the *para*-substituted **3** was better for gelation of EtOAc. Then we focused on the gelation abilities of derivatives with various substituents on the outer urea nitrogen (**4**–**17**). Full gelation of octyl-substituted tris-urea (**4**) was found only by mixing with THF (CGC=1.5 wt %), although soft gel formation was observed in acetone, diethyl phthalate, CH_2Cl_2, and toluene. The xerogel of toluene soft gel of **4** showed plate-shaped aggregates (Fig. 2b). Their lengths are shorter than the fibrous aggregates observed in the xerogel of the acetone gel of **1**. Longer dodecyl-substituted tris-urea (**5**) shows limited gelation ability and formed a gel only in THF (CGC=2.0 wt %). Benzyl-substituted tris-urea (**6**) gelated five of the nine solvents. Introduction of a long alkyl substituent is generally advantageous for the design of an LMWG; however, the gelation ability is not increased by introduction of a long alkyl substituent in regard to the tris-urea LMWG. Tris-urea with aryl substitution (**1** and **6**) showed



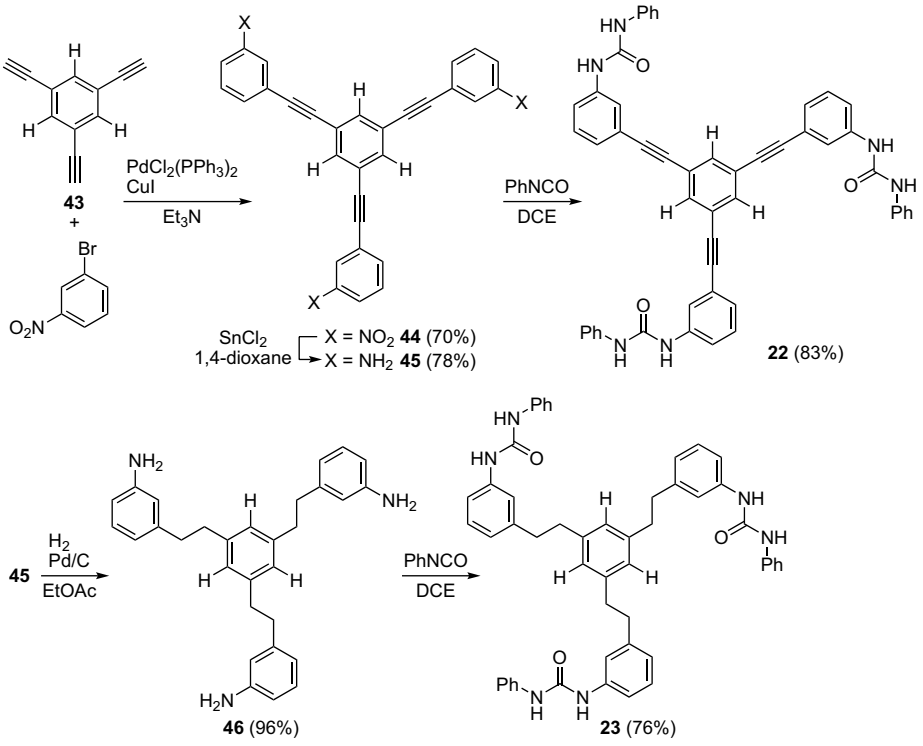
31:R^2 = H; Y = Br
34:R^2 = Me; Y = Br
37:R^2 = OMe; Y = Br
40:R^2 = *i*-pentyl; Y = Cl

32:R^2 = H (90%)
35:R^2 = Me (86%)
38:R^2 = OMe (82%)
41:R^2 = *i*-pentyl (91%)

33:R^2 = H (91%)
36:R^2 = Me (70%)
39:R^2 = OMe (92%)
42:R^2 = *i*-pentyl (84%)

18:R^2 = H (95%)
19:R^2 = Me (84%)
20:R^2 = OMe (54%)
21:R^2 = *i*-pentyl (80%)

Scheme 3. Synthetic scheme for generation of variety substituents on the central benzene ring.



Scheme 4. Synthetic scheme for generation of tris-ureas with modified linkers.

better gelation ability than those with alkyl substitution (**4** and **5**). The effect of adding substituents to the aryl groups of the urea moieties was tested. Tris-urea with *ortho*-fluorophenyl groups (**7**) formed a gel only in MeOH (CGC=1.5 wt %) in testing the nine organic solvents. Tris-urea with *meta*-fluorophenyl groups (**8**) afforded gels by mixing with MeOH (CGC=2.0 wt %), acetone (CGC=3.0 wt %), diethyl phthalate (CGC=2.0 wt %), and EtOAc (CGC=3.0 wt %). Tris-urea with *para*-fluorophenyl groups (**9**) formed a gel upon mixing with five of the nine solvents, namely, MeOH (CGC=2.5 wt %), acetone (CGC=2.0 wt %), diethyl phthalate (CGC=1.5 wt %), EtOAc (CGC=3.0 wt %), and THF (CGC=3.5 wt %). Substituents on the *para* (or *meta*) position seem conducive to maintaining gelation ability, so subsequent experiments were focused on *para*-substituted aryl ureas. Intertwining fibrous aggregates were found in the xerogels of these *meta* or *para*-fluorophenyl-substituted tris-ureas, and an SEM image of a xerogel prepared from the MeOH gel of **8** is shown in Figure 2c. Tris-urea with *para*-chlorophenyl groups (**10**) gelated only MeOH (CGC=5.0 wt %) of the nine solvents. *para*-Bromophenyl-substituted **11** showed gelation ability for MeOH (CGC=3.5 wt %),

Table 1
Gelation ability of tris-urea compounds (**1**–**23**)[a]

Compound	DMSO	MeOH	Acetone	DEP	EtOAc	THF	CH_2Cl_2	Toluene	*n*-Hexane
1	S	G (2.0)	G (1.5)	G (2.0)	I	G (5.0)	I	I	I
2	S	I	I	I	I	SG	I	I	I
3	S	G (3.0)	I	G (4.0)	G (1.5)	G (5.0)	I	I	I
4	S	I	SG	SG	I	G (1.5)	SG	SG	I
5	S	I	I	I	I	G (2.0)	I	I	I
6	S	G (4.0)	G (3.0)	G (1.5)	G (2.5)	G (3.5)	I	I	I
7	S	G (1.5)	I	I	I	S	I	I	I
8	S	G (2.0)	G (3.0)	G (2.0)	G (3.0)	S	I	I	I
9	S	G (2.5)	G (2.0)	G (1.5)	G (3.0)	G (3.5)	I	I	I
10	S	G (5.0)	I	I	I	S	I	I	I
11	S	G (3.5)	G (1.5)	I	G (4.0)	G (5.0)	I	SG	I
12	S	G (2.5)	G (1.5)	I	G (4.0)	G (3.0)	I	I	I
13	S	G (2.5)	G (2.0)	I	I	G (2.5)	I	I	I
14	S	I	G (3.0)	I	I	S	I	I	I
15	S	I	I	I	I	S	I	I	I
16	S	SG	G (2.5)	I	SG	S	I	SG	I
17	S	G (2.5)	G (2.0)	I	I	G (1.0)	I	I	I
18	S	G (1.0)	G (0.5)	G (1.5)	G (3.5)	G (1.5)	I	I	I
19	S	G (4.0)	G (1.5)	I	G (5.0)	I	I	I	I
20	S	G (3.5)	G (4.5)	G (2.5)	I	I	I	I	I
21	S	G (1.0)	G (2.5)	G (1.5)	G (2.0)	I	G (4.0)	SG	I
22	S	I	G (2.0)	I	G (4.0)	G (2.0)	I	SG	I
23	S	G (2.0)	G (2.5)	G (2.5)	G (2.5)	G (2.0)	SG	SG	I

[a] Tris-urea=up to 5 wt %; G=gel and CGCs (wt %) were shown in parentheses, SG=soft gel, S=solution, I=insoluble.

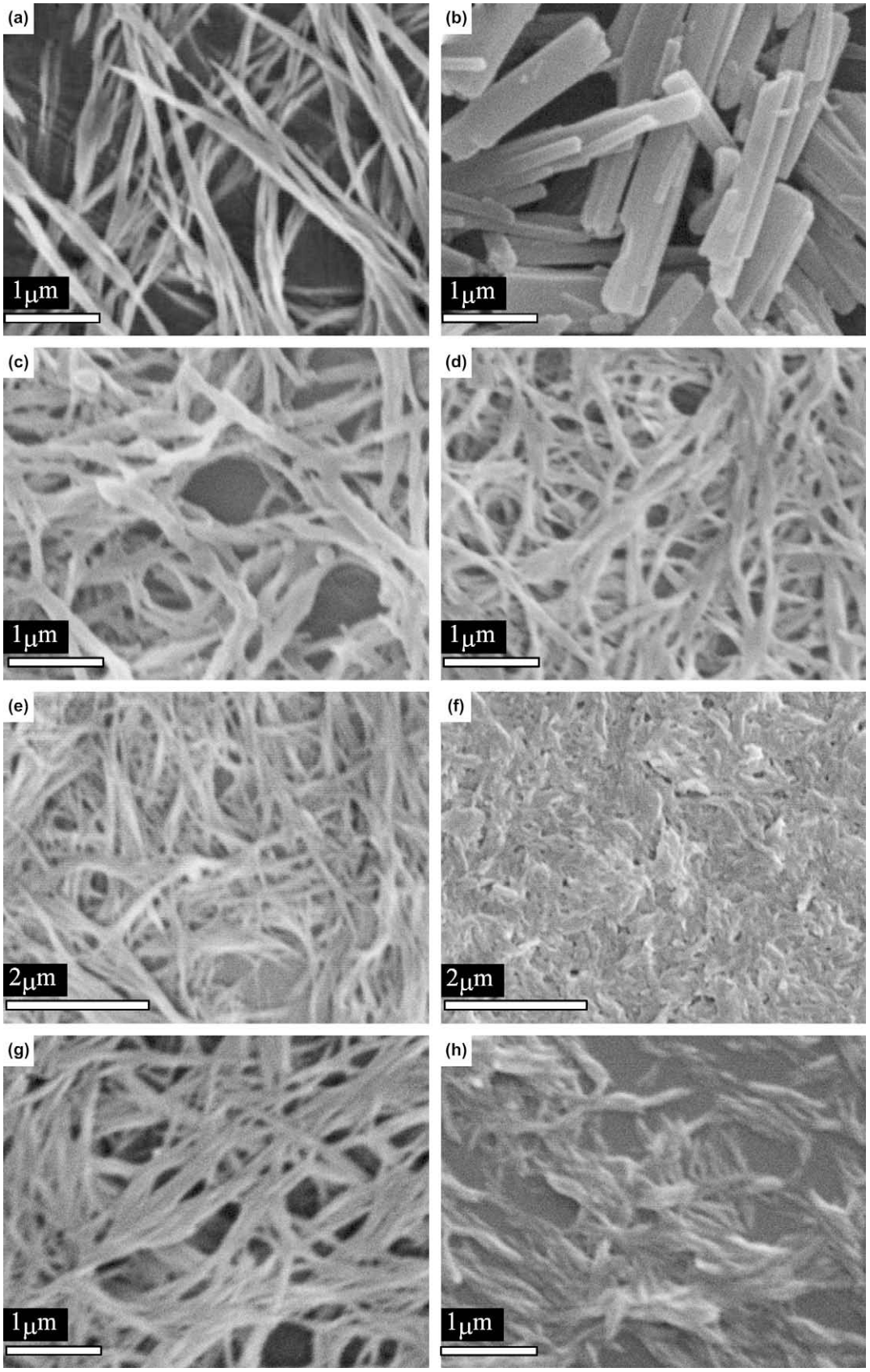


Figure 2. SEM images of xerogel prepared from (a) acetone gel of **1**, (b) toluene soft gel of **4**, (c) MeOH gel of **8**, (d) acetone gel of **18**, (e) MeOH gel of **21**, (f) toluene soft gel of **21**, (g) THF gel of **23**, and (h) CH_2Cl_2 soft gel of **23**.

acetone (CGC=1.5 wt %), EtOAc (CGC=4.0 wt %), and THF (CGC=5.0 wt %), and formed a soft gel in toluene. *para*-Iodophenyl-substituted **12** gelated MeOH (CGC=2.5 wt %), acetone (CGC=1.5 wt %), EtOAc (CGC=4.0 wt %), and THF (CGC=3.0 wt %). The gelation ability of *para*-chlorophenyl-substituted tris-urea (**10**) is markedly lower than that of the other halogen-substituted tris-ureas. A possible reason is that larger (halogen) atoms interfere with aggregation; however, bromine and iodine show halogen–π interactions or CH–halogen interactions as a secondary driving force for assembly.[17] *para*-Tolyl-substituted tris-urea (**13**) formed gels in MeOH (CGC=2.5 wt %), acetone (CGC=2.0 wt %), and THF (CGC=2.5 wt %). Tris-urea with *para*-ethylphenyl groups (**14**) gave a gel only on mixing with acetone (CGC=3.0 wt %) of the nine solvents. Tris-urea with *para*-isopropylphenyl groups (**15**) did not form a gel in the tested solvents. *para*-Octylphenyl-substituted tris-urea (**16**) formed a gel in acetone (CGC=2.5 wt %), and a soft gel in MeOH, EtOAc, and toluene. These results also support the suggestion that a bulky substituent on the aryl group of the peripheral urea prevents formation of a gel. Tris-urea with 1-naphthyl groups (**17**) gave a gel on mixing with MeOH (CGC=2.5 wt %), acetone (CGC=2.0 wt %), and THF (CGC=1.0 wt %). Considering the substituent effect on the gelation ability of the peripheral urea, aryl groups are better than alkyl groups. A bulky substituent on the aryl group reduces the gelation ability. Next, we focused on the substituent effect of the core aryl cycle of tris-urea (**1** and **18**–**21**). A remarkably enhancement of gelation ability was observed by replacing the core ethyl groups with hydrogen (**18**). Tris-urea **18** gelated MeOH (CGC=1.0 wt %), acetone (CGC=0.5 wt %), diethyl phthalate (CGC=1.5 wt %), EtOAc (CGC=3.5 wt %), and THF (CGC=1.5 wt %). The xerogel prepared from the acetone gel of **18** showed intertwining nanofibers upon SEM observation (Fig. 2d). Tris-urea with methyl substituents (**19**) gelated MeOH (CGC=4.0 wt %), acetone (CGC=1.5 wt %), and EtOAc (CGC=5.0 wt %); however, the gelation ability is lower than that of both **1** and **18**. Polar methoxy groups on the core aromatic ring are not effective for gelation, and **20** formed a gel on mixing with MeOH (CGC=3.5 wt %), acetone (CGC=4.5 wt %), and diethyl phthalate (CGC=2.5 wt %). Tris-urea with isopentyl substituents (**21**) gave a gel with MeOH (CGC=1.0 wt %), acetone (CGC=2.5 wt %), diethyl phthalate (CGC=1.5 wt %), EtOAc (CGC=2.0 wt %), and CH_2Cl_2 (CGC=4.0 wt %), and formed a soft gel in toluene. It is noteworthy that isopentyl-substituted **21** gelated not only polar solvents such as MeOH, but also nonpolar CH_2Cl_2 and toluene. Nano-size fibers were found upon SEM observation of the MeOH gel of **21**; however, a fibrous aggregate was not discovered upon SEM observation of the toluene soft gel of **21** (Fig. 2e and f). The substituent on the core aromatic ring of tris-urea plays an important role in its gelation ability. Hydrogen-substituted tris-urea (**18**) is effective as a gelator possibly because the small substituent makes **18** easy to assemble by stacking. On the other hand, a longer alkyl substituent such as isopentyl is effective in gelating nonpolar solvents. A moderate solvophilic nature of alkyl chains towards nonpolar solvents may promote its aggregation. The linker region connecting the core aromatic ring and outer aromatic ring was modified. Tris-urea with an inflexible ethynyl linker (**22**) gelated acetone (CGC=2.0 wt %), EtOAc (CGC=4.0 wt %), and THF (CGC=2.0 wt %), and formed a soft gel with toluene. Comparing the gelation ability of **18** with **22**, the flexibility of the linker region seemed important. Ethylene-linked tris-urea (**23**) formed a gel with MeOH (CGC=2.0 wt %), acetone (CGC=2.5 wt %), diethyl phthalate (CGC=2.5 wt %), EtOAc (CGC=2.5 wt %), and THF (CGC=2.0 wt %), and a soft gel with CH_2Cl_2 and toluene. Xerogel prepared from a firmly gelated mixture of **23** and THF showed intertwining nanofibers (Fig. 2g). In contrast, the xerogel prepared from a loosely gelated mixture of **23** and CH_2Cl_2 showed short fibers and their interaction seemed poor (Fig. 2h). Seven of the nine solvents were gelated, including soft gel, by **23**; however, their CGCs were moderate. A nonpolar linker has potential to construct a versatile gelator for a variety of organic solvents.

3. Conclusion

In conclusion, we divided the structure of LMWG (**1**) into five areas and synthesized 22 different derivatives. Indispensable structural characteristics were determined by testing their gelation abilities with a variety of organic solvents. The following guidelines for the design of tris-urea LMWGs were suggested by these investigations (1) The urea functional group is essential for the structure of these LMWGs.[13] (2) *meta*-Substitution of the urea moiety is effective for gelation. *ortho*-Substitution is disadvantageous for forming a gel. (3) Aryl substitution of the peripheral urea nitrogen is effective in achieving high gelation ability. A bulky substituent on the aryl group prevents gelation. (4) A small substituent group on the core aryl cycle is important to improve the gelation ability. A solvophilic alkyl substituent is effective in gelating nonpolar solvents. (5) Flexibility of the linker region is efficacious in maintaining the gelation ability. These derivatives of LMWG **1** produced improvements in the gelation ability. For example, the CGC for acetone became 0.5 wt % by changing the substituent of the core aryl ring and highly general LMWGs for a variety of solvent were obtained by modification of the linker region. Furthermore, these results enabled us to design novel functional LMWGs logically. The design and synthesis of low molecular weight hydrogelator and chiral LMWGs based on this knowledge are progressing in our laboratory.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-AL400 spectrometer or a JEOL JNM-ECA600 spectrometer. Mass spectra were measured on a JEOL JMS-T100LC AccTOF spectrometer. Ultrasound irradiation was performed using a BRANSON B2510J ultrasonic cleaner. SEM studies were carried out on a JEOL JSM-6300 spectrometer.

*4.1.1. 1,3,5-Tris(3-nitrophenoxymethyl)-2,4,6-triethylbenzene (**25**)*

To a mixture of 3-nitrophenol (9.4 g, 67 mmol) and K_2CO_3 (9.3 g, 67 mmol) in acetone (130 mL) was added 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene[18] (**24**, 9.9 g, 22 mmol) under argon atmosphere at 0 °C. The reaction mixture was stirred at room temperature for 17 h. Then the reaction mixture was diluted with chloroform, and the precipitate was removed by filtration. The solvent was removed under reduced pressure, and the crude product was purified by reprecipitation from dichloromethane and hexane to give **25** as a pale yellow solid (12 g, 86%). Mp 212–214 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J=7.6 Hz, 9H), 2.84 (q, J=7.6 Hz, 6H), 5.18 (s, 6H), 7.34 (dd, J=8.2, 2.3 Hz, 3H), 7.49 (t, J=8.5 Hz, 3H), 7.89–7.91 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 23.1, 64.8, 108.4, 116.3, 122.0, 130.2, 130.4, 146.7, 149.3, 159.2; HRMS (ESI, M+Na^+) calcd for $C_{33}H_{33}N_3NaO_9$: 638.2115, found: 638.2140.

*4.1.2. 1,3,5-Tris(3-aminophenoxymethyl)-2,4,6-triethylbenzene (**26**)*

A mixture of **25** (1.0 g, 1.6 mmol) and tin(II) chloride dihydrate (5.5 g, 24 mmol) in 1,4-dioxane (10 mL) was stirred at room temperature for 1 h. Then the mixture was kept at 50 °C for 2 h. Then the reaction mixture was poured into ice-cooled water, and neutralized with saturated sodium hydrogen carbonate solution. The precipitate was removed by filtration through Celite, and remaining solid on the Celite was washed with ethyl acetate. Organic layer and aqueous layer were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with

brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (SiO_2, hexane/ethyl acetate 1:1 to 0:1). The desired product (**26**) was obtained as a white solid (830 mg, 97%). Mp 180–182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (t, J=7.5 Hz, 9H), 2.71 (q, J=7.5 Hz, 6H), 4.95 (s, 6H), 5.06 (s, 6H), 6.19 (d, J=7.8 Hz, 3H), 6.22 (d, J=7.8 Hz, 3H), 6.25 (s, 3H), 6.93 (t, J=7.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.3, 22.4, 63.5, 99.9, 101.9, 107.1, 129.7, 131.0, 145.1, 150.1, 159.7; HRMS (ESI, M+Na$^+$) calcd for $C_{33}H_{39}N_3NaO_3$: 548.2889, found: 548.2877.

4.1.3. 1,3,5-Tris[3-(phenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**1**)

To a solution of **26** (200 mg, 0.38 mmol) in 1,2-dichloroethane (10 mL) was added phenyl isocyanate (0.14 mL, 1.3 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 4 days. Then the mixture was refluxed for 3 h. During this time, a precipitate formed in the reaction flask. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **1** as a white solid (300 mg, 89%). Mp 230–240 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.19 (t, J=7.3 Hz, 9H), 2.76 (q, J=7.3 Hz, 6H), 5.06 (s, 6H), 6.73 (d, J=8.1 Hz, 3H), 6.95 (t, J=6.8 Hz, 3H), 7.03 (d, J=8.3 Hz, 3H), 7.22–7.28 (m, 12H), 7.43 (d, J=8.3 Hz, 6H), 8.70 (s, 3H), 8.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.2, 22.4, 63.9, 104.5, 107.7, 110.9, 118.2, 121.8, 128.8, 129.7, 130.9, 139.6, 141.0, 145.4, 152.5, 159.1; HRMS (ESI, M+Na$^+$) calcd for $C_{54}H_{54}N_6NaO_6$: 905.4003, found: 905.4006.

4.1.4. 1,3,5-Tris[2-(phenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**2**)

To a solution of **28** (128 mg, 0.24 mmol) in 1,2-dichloroethane (6.4 mL) was added phenyl isocyanate (0.09 mL, 0.83 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 21 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give the desired product as a white solid (145 mg, 67%). Mp 198–199 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.20 (t, J=7.3 Hz, 9H), 2.82 (q, J=7.3 Hz, 6H), 5.15 (s, 6H), 6.91 (d, J=7.8 Hz, 3H), 6.95 (t, J=7.8 Hz, 3H), 7.04 (t, J=7.8 Hz, 3H), 7.19 (t, J=7.8 Hz, 6H), 7.34 (t, J=7.8 Hz, 6H), 7.36 (d, J=6.8 Hz, 3H), 7.74 (s, 3H), 7.95 (d, J=7.8 Hz, 3H), 9.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.4, 22.9, 65.0, 112.2, 118.1, 118.3, 120.9, 121.9, 123.0, 128.2, 128.9, 130.9, 139.8, 146.8, 148.4, 152.7; HRMS (ESI, M+Na$^+$) calcd for $C_{54}H_{54}N_6NaO_6$: 905.4003, found: 905.4027.

4.1.5. 1,3,5-Tris[4-(phenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**3**)

To a solution of **30** (160 mg, 0.30 mmol) in 1,2-dichloroethane (8.0 mL) was added phenyl isocyanate (0.11 mL, 1.0 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 28 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **3** as a white solid (215 mg, 80%). Mp 252–253 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.18 (t, J=7.6 Hz, 9H), 2.75 (q, J=7.6 Hz, 6H), 5.04 (s, 6H), 6.94 (t, J=7.6 Hz, 3H), 7.02 (d, J=8.9 Hz, 6H), 7.25 (t, J=7.6 Hz, 6H), 7.38 (d, J=8.9 Hz, 6H), 7.43 (d, J=7.6 Hz, 6H), 8.50 (s, 3H), 8.59 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.3, 22.4, 64.3, 114.6, 118.1, 120.2, 121.6, 128.7, 131.0, 133.0, 139.9, 145.3, 152.7, 153.9; HRMS (ESI, M+Na$^+$) calcd for $C_{54}H_{54}N_6NaO_6$: 905.4003, found: 905.4028.

4.1.6. 1,3,5-Tris[3-(octylureido)phenoxymethyl]-2,4,6-triethylbenzene (**4**)

To a solution of **26** (500 mg, 0.95 mmol) in dichloromethane (10 mL) was transferred a solution of *n*-octyl isocyanate (0.60 mL, 3.4 mmol) in dichloromethane (2.5 mL) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 1 day, and then refluxed for 1 h. The mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **4** as a white solid (726 mg, 77%). Mp 191–195 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 0.84 (t, J=6.5 Hz, 9H), 1.16 (t, J=6.9 Hz, 9H), 1.25 (m, 30H), 1.38–1.41 (m, 6H), 2.73 (q, J=6.9 Hz, 6H), 3.05 (q, J=6.9 Hz, 6H), 5.01 (s, 6H), 6.09 (t, J=5.5 Hz, 3H), 6.63 (d, J=8.3 Hz, 3H), 6.93 (d, J=6.9 Hz, 3H), 7.14 (t, J=8.2 Hz, 3H), 7.20 (s, 3H), 8.41 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 13.9, 16.2, 22.1, 22.4, 26.4, 28.7, 28.8, 29.7, 31.2, 63.8, 103.8, 106.9, 110.3, 129.5, 130.9, 141.9, 145.4, 155.1, 159.0; HRMS (ESI, M+Na$^+$) calcd for $C_{60}H_{90}N_6NaO_6$: 1013.6820, found: 1013.6791.

4.1.7. 1,3,5-Tris[3-(dodecylureido)phenoxymethyl]-2,4,6-triethylbenzene (**5**)

To a solution of **26** (100 mg, 0.19 mmol) in dichloromethane (3.0 mL) was added *n*-dodecyl isocyanate (133 mg, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 4 days, and then refluxed for 3 h. During this time, a precipitate formed in the reaction flask. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **5** as a white solid (143 mg, 65%). Mp 198 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 0.83 (t, J=6.9 Hz, 9H), 1.16 (t, J=7.6 Hz, 9H), 1.22 (m, 54H), 1.38–1.40 (m, 6H), 2.73 (q, J=7.6 Hz, 6H), 3.04 (q, J=6.9 Hz, 6H), 5.01 (s, 6H), 6.09 (t, J=5.5 Hz, 3H), 6.62 (d, J=8.3 Hz, 3H), 6.91 (d, J=8.2 Hz, 3H), 7.13 (t, J=8.3 Hz, 3H), 7.20 (s, 3H), 8.40 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 13.9, 16.2, 22.1, 22.4, 26.4, 28.7, 28.8, 29.0, 29.1, 29.7, 31.3, 63.8, 103.9, 106.9, 110.3, 129.5, 130.9, 141.9, 145.4, 155.1, 159.0; HRMS (ESI, M+Na$^+$) calcd for $C_{72}H_{114}N_6NaO_6$: 1181.8698, found: 1181.8705.

4.1.8. 1,3,5-Tris[3-(benzylureido)phenoxymethyl]-2,4,6-triethylbenzene (**6**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (5.0 mL) was added benzyl isocyanate (0.077 mL, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 19 h, and then refluxed for 8 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **6** as a white solid (112 mg, 64%). Mp 221–230 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.16 (t, J=7.6 Hz, 9H), 2.73 (q, J=7.6 Hz, 6H), 4.29 (d, J=6.2 Hz, 6H), 5.02 (s, 6H), 6.61 (t, J=6.2 Hz, 3H), 6.65 (d, J=7.6 Hz, 3H), 6.97 (d, J=7.6 Hz, 3H), 7.16 (t, J=8.2 Hz, 3H), 7.22 (s, 3H), 7.24 (s, 3H), 7.28–7.33 (m, 12H), 8.60 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.2, 22.4, 42.7, 63.8, 104.0, 107.1, 110.5, 126.7, 127.1, 128.3, 129.6, 130.9, 140.3, 141.8, 145.4, 155.2, 159.0; HRMS (ESI, M+Na$^+$) calcd for $C_{57}H_{60}N_6NaO_6$: 947.4472, found: 947.4473.

4.1.9. 1,3,5-Tris[3-(2-fluorophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**7**)

To a solution of **26** (200 mg, 0.38 mmol) in 1,2-dichloroethane (10 mL) was added 2-fluorophenyl isocyanate (0.14 mL, 1.3 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 4 days. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **7** as a white solid (300 mg, 88%). Mp 159–167 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.19 (t, J=7.2 Hz, 9H), 2.76 (q, J=7.2 Hz, 6H), 5.07 (s, 6H), 6.76 (d, J=7.6 Hz, 3H), 6.99–7.02 (m, 6H), 7.12 (t, J=7.9 Hz, 3H), 7.20–7.26 (m, 9H), 8.13 (t, J=8.3 Hz, 3H), 8.53 (s, 3H), 9.10 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.4, 22.6, 64.1, 104.7, 108.2, 111.1, 115.1 (d, J_{C-F}=18.9 Hz), 120.9, 122.8 (d, J_{C-F}=8.2 Hz), 124.7, 127.5 (d,

J_{C-F}=10.7 Hz), 130.1, 131.0, 140.9, 145.7, 152.2 (d, J_{C-F}=240 Hz), 152.4, 159.3; HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}F_3N_6NaO_6$: 959.3720, found: 959.3719.

4.1.10. 1,3,5-Tris[3-(3-fluorophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**8**)

To a solution of **26** (250 mg, 0.48 mmol) in 1,2-dichloroethane (13 mL) was added 3-fluorophenyl isocyanate (0.18 mL, 1.6 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 2 days. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **8** as a white solid (335 mg, 78%). Mp 202–204 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.19 (t, J=6.9 Hz, 9H), 2.76 (q, J=6.9 Hz, 6H), 5.07 (s, 6H), 6.77 (m, 6H), 7.04 (d, J=7.6 Hz, 3H), 7.10 (d, J=7.6 Hz, 3H), 7.23–7.28 (m, 9H), 7.47 (d, J=8.2 Hz, 3H), 8.76 (s, 3H), 8.90 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 22.5, 64.0, 104.7, 104.9 (d, J_{C-F}=25.9 Hz), 108.0, 108.2 (d, J_{C-F}=21.5 Hz), 111.1, 114.0, 129.8, 130.3 (d, J_{C-F}=10.1 Hz), 130.9, 140.7, 141.5 (d, J_{C-F}=11.5 Hz), 145.5, 152.3, 159.1, 162.4 (d, J_{C-F}=238 Hz); HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}F_3N_6NaO_6$: 959.3720, found: 959.3718.

4.1.11. 1,3,5-Tris[3-(4-fluorophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**9**)

To a solution of **26** (100 mg, 0.38 mmol) in 1,2-dichloroethane (5.0 mL) was added 4-fluorophenyl isocyanate (0.071 mL, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 2 days. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **9** as a white solid (126 mg, 74%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.18 (t, J=7.6 Hz, 9H), 2.76 (q, J=7.6 Hz, 6H), 5.06 (s, 6H), 6.73 (d, J=6.2 Hz, 3H), 7.02 (d, J=8.2 Hz, 3H), 7.10 (t, J=8.6 Hz, 6H), 7.22 (t, J=8.2 Hz, 3H), 7.24 (s, 3H), 7.43–7.45 (m, 6H), 8.68 (s, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 22.5, 63.9, 104.6, 107.8, 111.0, 115.3 (d, J_{C-F}=23.0 Hz), 120.0 (d, J_{C-F}=7.2 Hz), 129.7, 130.9, 135.9, 141.0, 145.4, 152.6, 157.3 (d, J_{C-F}=237 Hz), 159.1; HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}F_3N_6NaO_6$: 959.3720, found: 959.3736.

4.1.12. 1,3,5-Tris[3-(4-chlorophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**10**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (3.0 mL) was transferred a solution of 4-chlorophenyl isocyanate (96 mg, 0.63 mmol) in 1,2-dichloroethane (2.0 mL) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 18 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give the desired product as a white solid (129 mg, 68%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.18 (t, J=6.9 Hz, 9H), 2.75 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.74 (d, J=8.3 Hz, 3H), 7.01 (d, J=8.2 Hz, 3H), 7.22 (t, J=8.2 Hz, 3H), 7.24 (s, 3H), 7.31 (d, J=8.3 Hz, 6H), 7.46 (d, J=8.2 Hz, 6H), 8.73 (s, 3H), 8.81 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 22.4, 64.0, 104.7, 107.9, 111.1, 119.7, 125.4, 128.6, 129.7, 130.9, 138.6, 140.8, 145.5, 152.4, 159.1; HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}Cl_3N_6NaO_6$: 1009.2804, found: 1009.2788.

4.1.13. 1,3,5-Tris[3-(4-bromophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**11**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (5.0 mL) was added 4-bromophenyl isocyanate (125 mg, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 1 day. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **11** as a white solid (164 mg, 77%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.18 (t, J=6.9 Hz, 9H), 2.75 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.74 (d, J=8.3 Hz, 3H), 7.02 (d, J=8.2 Hz, 3H), 7.22 (t, J=8.2 Hz, 3H), 7.24 (s, 3H), 7.33–7.62 (m, 12H), 8.73 (s, 3H), 8.81 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.2, 22.4, 64.0, 104.7, 107.9, 111.1, 113.2, 120.1, 129.7, 130.9, 131.5, 139.1, 140.8, 145.5, 152.3, 159.1; HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}Br_3N_6NaO_6$: 1143.1277, found: 1143.1316.

4.1.14. 1,3,5-Tris[3-(4-iodophenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**12**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (5.0 mL) was added 4-iodophenyl isocyanate (154 mg, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 3 days, and then refluxed for 1 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **12** as a white solid (209 mg, 87%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.18 (t, J=6.9 Hz, 9H), 2.75 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.74 (d, J=8.3 Hz, 3H), 7.02 (d, J=8.2 Hz, 3H), 7.22 (t, J=8.3 Hz, 3H), 7.24 (s, 3H), 7.29 (d, J=8.2 Hz, 6H), 7.58 (d, J=8.3 Hz, 6H), 8.73 (s, 3H), 8.81 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 22.5, 64.0, 84.7, 104.7, 107.9, 111.0, 120.5, 129.8, 130.9, 137.3, 139.6, 140.8, 145.5, 152.3, 159.1; HRMS (ESI, M+Na^+) calcd for $C_{54}H_{51}I_3N_6NaO_6$: 1283.0902, found: 1283.0860.

4.1.15. 1,3,5-Tris[3-(4-methylphenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**13**)

To a solution of **26** (200 mg, 0.38 mmol) in 1,2-dichloroethane (10 mL) was added *p*-tolyl isocyanate (0.16 mL, 1.3 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 3 days. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **13** as a white solid (265 mg, 76%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.19 (t, J=6.9 Hz, 9H), 2.22 (s, 9H), 2.76 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.73 (d, J=8.3 Hz, 3H), 7.02 (d, J=8.3 Hz, 3H), 7.07 (d, J=8.2 Hz, 6H), 7.22 (t, J=8.3 Hz, 3H), 7.25 (s, 3H), 7.32 (d, J=8.2 Hz, 6H), 8.55 (s, 3H), 8.65 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 20.3, 22.5, 63.9, 104.5, 107.6, 110.9, 118.3, 129.2, 129.7, 130.7, 130.9, 137.1, 141.1, 145.5, 152.5, 159.1; HRMS (ESI, M+Na^+) calcd for $C_{57}H_{60}N_6NaO_6$: 947.4472, found: 947.4477.

4.1.16. 1,3,5-Tris[3-(4-ethylphenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**14**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (5.0 mL) was added 4-ethylphenyl isocyanate (0.090 mL, 0.63 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 1 day, and then refluxed for 3 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **14** as a white solid (165 mg, 90%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.14 (t, J=7.6 Hz, 9H), 1.19 (t, J=6.9 Hz, 9H), 2.52 (q, J=7.6 Hz, 6H), 2.76 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.72 (d, J=8.3 Hz, 3H), 7.02 (d, J=8.9 Hz, 3H), 7.10 (d, J=8.2 Hz, 6H), 7.21 (t, J=8.3 Hz, 3H), 7.23 (s, 3H), 7.33 (d, J=8.2 Hz, 6H), 8.55 (s, 3H), 8.64 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 15.8, 16.3, 22.4, 27.5, 63.9, 104.5, 107.6, 110.9, 118.4, 128.0, 129.7, 130.9, 137.2, 141.1, 145.4, 152.5, 159.1; HRMS (ESI, M+Na^+) calcd for $C_{60}H_{66}N_6NaO_6$: 989.4942, found: 989.4965.

4.1.17. 1,3,5-Tris[3-(4-isopropylphenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**15**)

To a solution of **26** (79 mg, 0.15 mmol) in 1,2-dichloroethane (4.0 mL) was added 4-isopropylphenyl isocyanate (0.079 mL, 0.50 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 2 days, and then refluxed for 3 h.

Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **15** as a white solid (114 mg, 75%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.10 (d, J=6.9 Hz, 18H), 1.13 (t, J=6.9 Hz, 9H), 2.70 (q, J=6.9 Hz, 6H), 2.75 (sep, J=6.9 Hz, 3H), 5.00 (s, 6H), 6.66 (d, J=8.3 Hz, 3H), 6.96 (d, J=8.2 Hz, 3H), 7.07 (d, J=8.2 Hz, 6H), 7.15 (t, J=8.3 Hz, 3H), 7.18 (s, 3H), 7.28 (d, J=8.2 Hz, 6H), 8.47 (s, 3H), 8.57 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.2, 22.4, 24.0, 32.7, 63.9, 104.5, 107.6, 110.9, 118.4, 126.4, 129.7, 130.9, 137.3, 141.1, 141.9, 145.4, 152.5, 159.0; HRMS (ESI, M+Na$^+$) calcd for $C_{63}H_{72}N_6NaO_6$: 1031.5411, found: 1031.5381.

4.1.18. 1,3,5-Tris[3-(4-octylphenylureido)phenoxymethyl]-2,4,6-triethylbenzene (**16**)

To a solution of **26** (100 mg, 0.19 mmol) in 1,2-dichloroethane (2.0 mL) was transferred a solution of 4-octylphenyl isocyanate (146 mg, 0.63 mmol) in 1,2-dichloroethane (3.0 mL) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 2 days, and then refluxed for 9 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **16** as a white solid (143 mg, 62%). Mp 220–222 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 0.83 (t, J=6.9 Hz, 9H), 1.18 (t, J=6.9 Hz, 9H), 1.22–1.25 (m, 30H), 1.50–1.52 (m, 6H), 2.48 (t, J=7.2 Hz, 6H), 2.75 (q, J=6.9 Hz, 6H), 5.06 (s, 6H), 6.72 (d, J=8.2 Hz, 3H), 7.01 (d, J=8.2 Hz, 3H), 7.06 (d, J=8.2 Hz, 6H), 7.21 (t, J=8.3 Hz, 3H), 7.24 (s, 3H), 7.32 (d, J=8.2 Hz, 6H), 8.54 (s, 3H), 8.64 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 13.9, 16.3, 22.1, 22.4, 28.6, 28.7, 28.8, 31.1, 31.3, 34.5, 63.9, 104.5, 107.6, 110.9, 118.4, 128.5, 129.7, 130.9, 135.8, 137.2, 141.1, 145.4, 152.5, 159.1; HRMS (ESI, M+Na$^+$) calcd for $C_{78}H_{102}N_6NaO_6$: 1241.7759, found: 1241.7732.

4.1.19. 1,3,5-Tris[3-(1-naphthylureido)phenoxymethyl]-2,4,6-triethylbenzene (**17**)

To a solution of **26** (200 mg, 0.38 mmol) in 1,2-dichloroethane (10 mL) was added 1-naphthyl isocyanate (0.18 mL, 1.3 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 3 days. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **17** as a white solid (322 mg, 82%). Mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.21 (t, J=7.7 Hz, 9H), 2.79 (q, J=7.7 Hz, 6H), 5.10 (s, 6H), 6.77 (d, J=8.3 Hz, 3H), 7.81 (d, J=7.1 Hz, 3H), 7.26 (t, J=8.1 Hz, 3H), 7.32 (s, 3H), 7.47 (t, J=7.8 Hz, 3H), 7.54 (t, J=7.3 Hz, 3H), 7.59 (t, J=6.8 Hz, 3H), 7.64 (d, J=8.3 Hz, 3H), 7.93 (d, J=7.8 Hz, 3H), 8.00 (d, J=7.8 Hz, 3H), 8.12 (d, J=7.8 Hz, 3H), 8.78 (s, 3H), 9.12 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 16.3, 22.5, 64.0, 104.5, 107.9, 110.9, 117.6, 121.3, 123.0, 125.7, 125.9, 125.9, 126.0, 128.4, 129.8, 130.9, 133.7, 134.2, 141.1, 145.5, 152.9, 159.2; HRMS (ESI, M+Na$^+$) calcd for $C_{66}H_{60}N_6NaO_6$: 1055.4472, found: 1055.4493.

4.1.20. 1,3,5-Tris[3-(phenylureido)phenoxymethylbenzene (**18**)

To a solution of **33** (360 mg, 0.82 mmol) in THF (5.0 mL) was added phenyl isocyanate (0.30 mL, 2.8 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 2 days, and then refluxed for 6 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **18** as a white solid (620 mg, 95%). Mp 247–250 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.12 (s, 6H), 6.65 (d, J=8.3 Hz, 3H), 6.93–6.97 (m, 6H), 7.17 (t, J=8.1 Hz, 3H), 7.24–7.28 (m, 9H), 7.44 (d, J=8.8 Hz, 6H), 7.53 (s, 3H), 8.65 (s, 3H), 8.66 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 68.9, 104.9, 108.0, 110.8, 118.2, 121.8, 126.3, 128.8, 129.6, 137.6, 139.6, 140.9, 152.4, 158.8; HRMS (ESI, M+Na$^+$) calcd for $C_{48}H_{42}N_6NaO_6$: 821.3064, found: 821.3081.

4.1.21. 1,3,5-Tris[3-(phenylureido)phenoxymethyl]-2,4,6-trimethylbenzene (**19**)

To a solution of **36** (300 mg, 0.62 mmol) in 1,2-dichloroethane (15 mL) was added phenyl isocyanate (0.23 mL, 2.1 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 1 day. Then phenyl isocyanate (0.15 mL, 1.4 mmol) was added and the mixture was refluxed for 1 day. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **19** as a white solid (473 mg, 84%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.39 (s, 9H), 5.10 (s, 6H), 6.72 (d, J=8.2 Hz, 3H), 6.96 (t, J=6.9 Hz, 3H), 7.00 (d, J=8.2 Hz, 3H), 7.22 (t, J=8.2 Hz, 3H), 7.26 (s, 3H), 7.28 (t, J=6.9 Hz, 6H), 7.45 (d, J=6.9 Hz, 6H), 8.66 (s, 3H), 8.68 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 15.5, 64.7, 104.7, 107.9, 110.9, 118.2, 121.8, 128.8, 129.6, 131.5, 138.7, 139.6, 141.0, 152.4, 159.3; HRMS (ESI, M+Na$^+$) calcd for $C_{51}H_{48}N_6NaO_6$: 863.3533, found: 863.3514.

4.1.22. 1,3,5-Tris[3-(phenylureido)phenoxymethyl]-2,4,6-trimetoxybenzene (**20**)

To a solution of **39** (200 mg, 0.38 mmol) in 1,2-dichloroethane (10 mL) was added phenyl isocyanate (0.14 mL, 1.3 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 4 days, and then refluxed for 3 h. The mixture was diluted with hexane, and the precipitate was filtered off. The crude product (233 mg) was reacted with phenyl isocyanate (0.10 mL, 0.92 mmol) in 1,2-dichloroethane (10 mL) again at reflux temperature for 16 h. The mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **20** as a white solid (182 mg, 54%). Mp 162–163 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 3.88 (s, 9H), 5.01 (s, 6H), 6.74 (dd, J=8.2, 2.1 Hz, 3H), 7.00 (t, J=7.6 Hz, 3H), 7.04 (dd, J=8.2, 2.1 Hz, 3H), 7.22 (t, J=8.2 Hz, 3H), 7.26–7.33 (m, 9H), 7.44 (d, J=7.6 Hz, 6H), 8.70 (s, 3H), 8.72 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 59.9, 64.0, 104.6, 107.8, 110.9, 118.2, 120.6, 121.8, 128.8, 129.7, 139.6, 141.0, 152.5, 158.9, 161.2; HRMS (ESI, M+Na$^+$) calcd for $C_{51}H_{48}N_6NaO_9$: 911.3381, found: 911.3354.

4.1.23. 1,3,5-Tris[3-(phenylureido)phenoxymethyl]-2,4,6-triisopentylbenzene (**21**)

To a solution of **42** (120 mg, 0.18 mmol) in 1,2-dichloroethane (6.0 mL) was added phenyl isocyanate (0.080 mL, 0.73 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 17 h. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **21** as a white solid (150 mg, 80%). Mp 200 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 0.77 (d, J=6.2 Hz, 18H), 1.46–1.52 (m, 9H), 2.69–2.72 (m, 6H), 5.01 (s, 6H), 6.72 (dd, J=8.2, 2.1 Hz, 3H), 6.96 (t, J=7.6 Hz, 3H), 7.01 (d, J=8.2 Hz, 3H), 7.22 (t, J=8.2 Hz, 3H), 7.26 (d, J=7.6 Hz, 6H), 7.28 (s, 3H), 7.44 (d, J=7.6 Hz, 6H), 8.66 (s, 3H), 8.68 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 22.1, 27.2, 28.2, 40.7, 64.1, 104.5, 107.5, 110.6, 118.2, 121.8, 128.8, 129.7, 131.0, 139.6, 141.0, 144.3, 152.4, 159.1; HRMS (ESI, M+Na$^+$) calcd for $C_{63}H_{72}N_6NaO_6$: 1031.5411, found: 1031.5374.

4.1.24. 1,3,5-Tris[3-(phenylureido)phenylethynyl]benzene (**22**)

To a solution of **45** (200 mg, 0.47 mmol) in 1,2-dichloroethane (10 mL) was added phenyl isocyanate (0.17 mL, 1.5 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 3 day. The reaction mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **22** as a white solid (306 mg, 83%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 6.97 (t, J=8.2 Hz, 3H), 7.21 (d, J=7.6 Hz, 3H), 7.28 (t, J=8.2 Hz, 6H), 7.36 (t, J=7.6 Hz, 3H), 7.42 (dd, J=7.6, 2.1 Hz, 3H), 7.46 (d, J=8.2 Hz,

6H), 7.80 (s, 3H), 7.81 (d, J=2.1 Hz, 3H), 8.75 (s, 3H), 8.83 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 87.1, 91.0, 118.3, 119.2, 120.7, 122.0, 122.1, 123.7, 125.1, 128.8, 129.3, 133.8, 139.5, 140.0, 152.5; HRMS (ESI, M+Na$^+$) calcd for $C_{51}H_{36}N_6NaO_3$: 803.2747, found: 803.2783.

*4.1.25. 1,3,5-Tris[3-(phenylureido)phenylethyl]benzene (**23**)*

To a solution of **46** (197 mg, 0.45 mmol) in 1,2-dichloroethane (10 mL) was added phenyl isocyanate (0.17 mL, 1.5 mmol) under argon atmosphere at 0 °C. The mixture was stirred at room temperature for 4 days and then refluxed for 3 h. During this time, a precipitate formed in the reaction flask. Then the mixture was diluted with hexane, and the precipitate was filtered off. The crude product was purified by reprecipitation from acetone and hexane to give **23** as a white solid (273 mg, 76%). Mp >250 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.80 (s-like, 12H), 6.84 (d, J=6.9 Hz, 3H), 6.94 (m, 6H), 7.16 (t, J=7.6 Hz, 3H), 7.25 (m, 9H), 7.37 (s, 3H), 7.43 (d, J=7.6 Hz, 6H), 8.58 (s, 3H), 8.63 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 37.3, 37.4, 115.9, 118.2, 121.8, 122.1, 126.1, 128.7, 128.8, 139.6, 139.7, 141.3, 142.4, 152.6; HRMS (ESI, M+Na$^+$) calcd for $C_{51}H_{48}N_6NaO_3$: 815.3686, found: 815.3663.

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Supplementary data

Experimental details and spectroscopic data can be found in the PDF format. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.10.036.

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