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Recognition of hydrophilic amino and *N*,*N*-dimethylamino compounds by the self-assembled aggregates of fluoroalkylated end-capped *N*-(1,1-dimethyl-3-oxobutyl)acrylamide oligomer

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Abstract

Self-assembled aggregates of new fluoroalkylated end-capped *N*-(1,1-dimethyl-3-oxobutyl)acrylamide oligomer can recognize selectively hydrophilic amino and *N*,*N*-dimethylamino compounds such as methylene blue, methyl orange, acriflavine hydrochloride and 3-aminophenylboronic acid, and transfer these compounds from aqueous solutions to organic media; in contrast, these aggregates were not able to recognize hydrophilic compounds such as 4-hydroxyazobenzene-4′-sulfonic acid sodium salt, acridine hydrochloride, 4-methoxyphenylboronic acid, 4-methyl-3-nitrophenylboronic acid, and phenylboronic acid.

Keywords: Self-assembled fluorinated aggregates; Hydrophilic amino compounds; Fluoroalkyl end-capped oligomer

Macromolecules are identified by other molecules through the recognition of their main chains and side chain segments, and recognition of side chains plays an important role in constructing supramolecular structures, achieving various functions, and maintaining their lives in biological systems [1]. Therefore, it is in particular interest to explore novel macromolecules recognition, especially fluorinated macromolecules recognition by artificial systems, because it is well known that fluorinated macromolecules have various unique properties which cannot be achieved in the corresponding non-fluorinated ones [2–4]. Hitherto, our studies actively focussed on the synthesis and applications of fluorinated polymeric compounds by the use of fluoroalkanoyl peroxides as key intermediates [5]. For example, we reported that fluoroalkylated end-capped acrylic acid–trimethylvinylsilane co-oligomers, which are prepared by using fluoroalkanoyl peroxides, exhibit not only unique properties imparted by fluorine but also a biological activity, although they have only two fluoroalkylated end-caps [6,7]. Furthermore, we have found that fluoroalkylated end-capped oligomers containing betaine segments or hydroxy segments could lead to gelation where strong aggregation of the end-capped fluoroalkyl segments is involved in establishing the physical gel network [8–13]. Recently, we have also found that fluoroalkylated end-capped acryloylmorpholine oligomers show an excellent solubility in not only water but also common organic solvents, including non-polar solvents, and are applicable to non-ionic fluorinated amphiphilic surfactants owing to reducing the surface tension of both water and in particular *m*-xylene effectively [14], although usual fluorinated polymers are well known to exhibit extremely low solubility in various solvents [2–4]. Therefore, it is very important to apply these fluoroalkylated end-capped oligomers to the artificial receptors.

Now, we were interested in the synthesis of new fluoroalkylated end-capped *N*-(1,1-dimethyl-3-oxobutyl)-acrylamide oligomers [R_F–(DOBAA)$_n$–R_F; R_F = fluoroalkyl groups] from the viewpoint of the development of a novel fluorinated artificial receptor system. In the course of this study, unexpectantly, we obtained the surprising finding that the aggregates formed by these fluoroalkylated end-capped oligomers are applicable to novel

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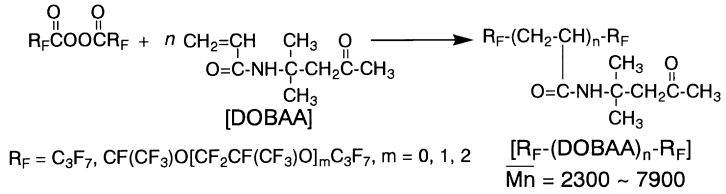


Scheme 1.

fluorinated macromolecules recognition by artificial systems, and can recognize hydrophilic amino and *N*,*N*-dimethylamino compounds as guest molecules.

A series of fluoroalkylated end-capped *N*-(1,1-dimethyl-3-oxobutyl)acrylamide oligomers were prepared in 22–60% isolated yields by the reaction of the corresponding acrylamide monomer (DOBAA) with fluoroalkanoyl peroxides as shown in Scheme 1.[1]

These fluoroalkylated end-capped DOBAA oligomers thus obtained were insoluble in water; however, these oligomers were easily soluble in common organic solvents such as chloroform, tetrachloromethane, MeOH, EtOH, 1,2-dichloroethane, dichloromethane, acetone, THF, AcOEt, PhH, PhMe, xylene, DMF and DMSO except for hexane. Furthermore, these DOBAA oligomers were able to reduce the surface tension of *m*-xylene quite effectively from 28 around to 15 mN/m levels with a clear break point resembling a CMC at 30°C. Therefore, these fluorinated DOBAA oligomers are expected to form molecular aggregates in organic media.

In fact, static light scattering measurements at a scattering angle of 90° were conducted to confirm the formation of molecular assemblies in *m*-xylene solutions of R_F–$(DOBAA)_n$–R_F; [$R_F = CF(CF_3)OC_3F_7$; $\bar{M}_n = 6900$]. The ratio of the strength of the scattered light from the oligomer solution to that from benzene (standard substance) was small and almost constant at low oligomer concentrations (0.01–0.5 g/dm^3) and it increased abruptly above a certain oligomer concentration (ca. 1.0 g/dm^3). On the other hand, in the corresponding non-fluorinated DOBAA oligomer ($\bar{M}_n = 6900$), the ratio of the strength of the scattered light did not increase significantly above a concentration of 1.0 g/dm^3. This finding suggests formation of molecular assemblies of fluoroalkylated end-capped DOBAA oligomer above this concentration because the strength of scattered light depends on the number and size of particles in the medium, and the value of this concentration was almost the same as that of a break point resembling a CMC in the surface tension measurements of *m*-xylene solutions of R_F–$(DOBAA)_n$–R_F. Very recently, we have reported that molecular assemblies formed in aqueous solution of the fluoroalkylated end-capped acrylic acid–trimethylvinylsilane co-oligomers have an ellipsoidal shape with the aggregations of terminal fluoroalkyl segments [15,16]. Thus, it is suggested that our present oligmers should form the similar molecular aggregates imparted by the aggregation of end-capped fluoroalkyl segments.

Furthermore, we tried to investigate the potential of fluoroalkylated end-capped oligomers as a host system for polar guests in organic media. We have concentrated on the molecular aggregate-assisted transfer of guest molecules between two immiscible phase. Quite surprisingly, we have found that fluoroalkylated end-capped oligomers can

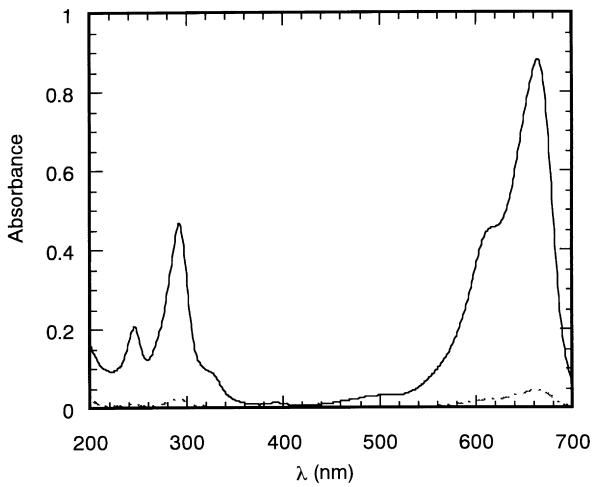
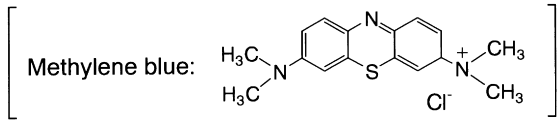


Fig. 1. UV–Vis spectra illustrating the transfer of methylene blue from an aqueous phase into an organic phase with R_F–$(DOBAA)_n$–R_F; $R_F = CF(CF_3)OC_3F_7$



—: aqueous solution of methylene blue, - - -: aqueous solution of methylene blue after the liquid–liquid extraction with R_F–$(DOBAA)_n$–R_F.

[1] A typical experiment for the synthesis of R_F–$(DOBAA)_n$–R_F is as follows: perfluoro-2-methyl-3-oxahexanoyl peroxide (5 mmol) in 1:1 mixed solvents (AK-225) of 1,1-dichloro-2,2,3,3,3-pentafluoropropane–1,3-dichloro-1,2,2,3,3-pentafluoropropane (30 g) was added to a mixture of *N*-(1,1-dimethyl-3-oxobutyl)acrylamide (15 mmol) and AK-225 (100 g). The solution was stirred at 45°C for 5 h under nitrogen. After evaporating the solvent, the crude products were reprecipiated from AK-225–hexane to give bis(perfluoro-1-methyl-2-oxapentyl)-*N*-(1,1-dimethyl-3-oxobutyl)acrylamide oligomers (3.01 g). This oligomer showed the following spectral data: IR ν (cm^{-1}): 1711, 1658 (C=O), 1365 (CF_3), 1236 (CF_2); ^{1}H NMR($CDCl_3$) δ(1.02–2.00 (CH_2), 1.31(CH_3), 2.09 (CH_3), 2.38–2.83 (CH, CH_2); ^{19}F NMR($CDCl_3$, ext. CF_3CO_2H) δ −5.71 to −7.35 (16F), −54.26 (6F); average molar mass ($\bar{M}_n$) = 6900 [determined by gel permeation chromatography (GPC) calibrated with standard polystyrenes by using tetrahydrofuran as the eluent].

Table 1
Solvent extraction of hydrophilic compounds by perfluoro-1-methyl-2-oxapentylated DOBAA oligomer (org. layer: [oligomer] = 2.0 g/dm^3; aq. layer (hydrophilic compound): [HPC] = 0.1 mmol/dm^3; Extractability = ([HPC]$_0$ − [HPC]$_{aq}$)/[HPC]$_0$ × 100; [HPC]$_0$ = initial concentration of hydrophilic compound in the aqueous layer; [HPC]$_{aq}$ = concentration of hydrophilic compound in the aqueous layer as equilibrium)

Run	Hydrophilic compound	λ_{max} (nm)	Extractability (%)[a]
1	Methylene blue	644	97
2	Methyl orange	463	74
3	4-Hydroxyazobenzene-4′-sulfonic acid sodium salt	352	0
4	2,4-Dihydroxyazobenzene-4′-sulfonic acid sodium salt	387	0
5	Acriflavine hydrochloride	449	54
6	Acridine hydrochloride	193	0
7	Lucigenin	430	0
8	3-Aminophenylboronic acid	294	80
9	3,5-bis(trifluoromethyl)phenylboronic acid	193	0
10	4-Methoxyphenylboronic acid	234	0
11	4-Methyl-3-nitrophenylboronic acid	194	0
12	2,4-Dichlorophenylboronic acid	193	0
13	Ferroceneboronic acid	193	0
14	Phenylboronic acid	195	0

[a] Each extractability was 0% not only in the absence of fluoroalkylated end-capped DOBAA oligomer but also in the presence of non-fluorinated DOBAA oligomer.

transfer hydrophilic compounds, especially recognize selectively hydrophilic amino and *N*,*N*-dimethylamino compounds from aqueous solution into 1,2-dichloroethane.

A typical experiment for the liquid–liquid extraction behavior of R_F–(DOBAA)$_n$–R_F [R_F = $CF(CF_3)OC_3F_7$; $\bar{M}_n$ = 6900] is as follows: in a 10 ml vial, 5 ml of an aqueous solution of methylene blue (0.1 mmol/dm^3) and 5 ml of an 1, 2-dichloroethane solution of R_F–(DOBAA)$_n$–R_F (2.0 g/dm^3) were mixed vigorously for 20 min at 25°C. After standing for 24 h at 25°C, the aqueous phase was separated, and then the concentration of hydrophilic compound in the aqueous phase was determined by UV–Vis spectroscopy to give the extractability.

As shown in Fig. 1, it was found that perfluoro-1-methyl-2-oxapentylated DOBAA oligomer has an extremely higher extraction ability (97% extractability) toward methylene blue. On the other hand, non-fluorinated DOBAA oligomer [–(DOBAA)$_n$–] does not have an extraction ability at all, and in the absence of oligomers, methylene blue was not extracted at all from water to organic layer under similar conditions. To calculate the maximum number of methylene blue that could occupy the fluorinated aggregates core, experiments were conducted with varying molar ratios of methylene blue and the fluorinated oligomer in the aqueous/1,2-dichloroethane phases. These experimental results showed that one mole of methylene blue interacts with ca. 1 mol of oligomer. Thus, it is suggested that the molecular aggregate could occupy around 10 dye molecules per aggregate core; because this molecular aggregate is considered to consist of around 10 fluorinated oligomeric molecules since the molecular weight of the aggregate formed by the fluorinated DOBAA oligomer determined by the static light scattering measurements and the molecular weight of the oligomer determined by GPC measurements are 66 900 and 6900 ($\bar{M}_n$), respectively.

On the other hand, fluoroalkylated end-capped alkyl ester oligomers, for example, fluoroalkylated end-capped methyl methacrylate oligomer [R_F–(MMA)$_n$–R_F; R_F = $CF(CF_3)OC_3F_7$; $\bar{M}_n$ = 2300] was found to have an extraction ability toward methylene blue under similar conditions; however, its extractability is extremely lower (24%) compared to that of R_F–(DOBAA)$_n$–R_F. This finding suggests that R_F–(DOBAA)$_n$–R_F oligomers are likely to form more stable molecular assemblies with the aggregations of the end-capped fluoroalkyl segments in organic media, including the inter-molecular hydrogen-bondings through not only the interactions between the amido segments but also the interactions between the amido [–(C=O)N*H*–] and the carbonyl [–CH_2C(=*O*)Me] segments.

In addition, we examined the liquid–liquid extraction behavior of fluoroalkylated end-capped DOBAA oligomer for various hydrophilic compounds, and these results were shown in Table 1.

As shown in Table 1, fluoroalkylated DOBAA oligomer was found to extract not only methylene blue but also methyl orange, acriflavine hydrochloride, and 3-aminophenylboronic acid, effectively. However, interestingly, this oligomer was not able to extract hydrophilic polar guests such as 4-hydroxyazobenzene-4′-sulfonic acid sodium salt, 2,4-dihydroxyazobenzene-4′-sulfonic acid sodium salt, acridine hydrochloride, lucigenin, 3,5-bis(trifluoromethyl)-phenylboronic acid, 4-methoxyphenylboronic acid, 2,4-dichlorophenylboronic acid, ferroceneboronic acid, and phenylboronic acid. This finding suggests that our present fluorinated molecular assemblies formed by the DOBAA oligomer can recognize the hydrophilic amino and *N*,*N*-dimethylamino compounds. In contrast, R_F–(MMA)$_n$–R_F was not able to extract methyl orange, acriflavine hydrochloride and 3-aminophenylboronic acid under similar conditions. This finding would depend upon it that this oligomer possesses no amido or carbonyl segments. A acidic amido proton [–C(=O)–N*H*–] and carbonyl segments in the aggregates of R_F–(DOBAA)$_n$–R_F, which are constructed by the aggregations of end-capped fluoroalkyl segments and the intermolecular hydrogen bondings of the amido and carbonyl segments, could interact with a basic amino or *N*,*N*-dimethylamino nitrogen [:*N*H_2–Ar or :*N*Me_2–Ar] and a proton (or a methyl proton) of guest molecules, respectively, via intermolecular hydrogen bondings. This interaction would devoted to the selective recognition of the hydrophilic amino and *N*,*N*-dimethylamino compounds by the aggregates of R_F–(DOBAA)$_n$–R_F. Furthermore, it is suggested that water could act as a

guest molecule for the molecular aggregates formed by fluoroalkylated end-capped DOBAA oligomers. In fact, it has been already reported that acrylamide polymers such as poly(*N*-vinyl-2-pyrrolidone) provide a very good site for hydrogen bonding, which is one of the major type of forces causing association in polymer, and water is attached to poly(*N*-vinyl-2-pyrrolidone) chains through hydrogen-bonding interactions [17,18]. The presence of water in these aggregates could provide suitable host moieties to interact strongly with amino and *N*,*N*-dimethylamino compounds as guest molecules.

Very recently, it has been reported that fluorinated dendritic surfactant can extract methyl orange into liquid CO_2 [19]; however, to our knowledge, this is the first example of fluorinated oligomers that possess the extraction ability for hydrophilic polar compounds, especially a recognition ability. Moreover, this finding is in particular interest from the viewpoint of biological applications, because it is well known that in biological systems, antigens are identified by antibodies through recognition of their side chains, and DNAs recognize each other through the sequence of the side chains [1].

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