In this study, we synthesized low molecular weight organogelators, pyromellitamides (PMDA-R) and investigated the effect of product composition on their viscosity-increasing ability, focusing on the differences between synthetic conditions and those used when scaling up production. We regarded PMDA-2C8/oleyl as a target material and synthesized the compound in both a 50 mL flask and a 1 L flask as laboratory-level syntheses. The effects of both temperature and stirring conditions on the composition and performance of the synthesized organogelators were evaluated by the steady flow characteristics and by the viscoelasticity of the solutions dissolved in isododecane. The experimental results showed that increasing the reaction temperature to shorten the reaction time resulted in significant differences in product composition. Although the rheological properties of the solutions showed similar trends in some cases, morphological observation by transmission electron microscopy (TEM) revealed that the self-organizing structures formed by the different compositions were completely different from each other. Synthesis was also carried out in a commercial-scale reactor. This study provided useful information for ‘process intensification’ by focusing on changes in products during scale-up.

Key Words: Organogelator / Composition / Scale-up / Spinnability / Transmission electron microscopy (TEM)

1. INTRODUCTION

Organogelators with a molecular weight of around 1000 g/mol have been studied as additives that dissolve transparently in oil and significantly increase oil viscosity. Bouteiller et al.1) reported a compound having a urea structure that those authors suspected might have both π-π interaction and hydrogen bond interaction between molecules. Hanabusa et al.2) synthesized a tricarboxamide derivative having benzene ring and three carboxamides. The compound consisted of a centrally located basic skeleton and three chemical chains coordinated around it. Other researchers introduced aromatic ring derivatives3), asymmetric carbon4-6), phenyloxazoyl groups7), alkoxyalkyl groups8), and so on at the ends of these chemical chains. These compounds consisted mainly of a centrally located basic skeleton and multiple chemical chains coordinated around it. Webb et al.9) and Tong et al.10) synthesized pyromellitic acid tetracarboxamides having four alkyl chains. Although their compounds showed suitable viscosity-increasing effects, they were not very versatile in their applicability to different types of oils. We have reported the syntheses of N,N’,N”,N’’-1,2,4,5-tetra alkyl/alkenyl pyromellitamides (PMDA-R) with four chemical side chains (homo-compounds) and two kinds of chemical chains (hetero-compounds)11). From laboratory-scale screening experiments, PMDA-R, in which two 2-ethylhexyl (2C8) and two oleyl, were introduced as side chains was proposed as an organogelator. Here, we noted the compound as PMDA-2C8(2)/oleyl(2), where the numbers in parentheses represent the number of each side chain. It has not only a sufficient viscosity-increasing effect but also excellent versatility for different oils. The next step is to scale up the synthesis of the organogelator from the laboratory level to a commercial scale. During the scale-up of a reaction field, problems in the production of by-products due to nonuniform reaction temperatures and inadequate agitation in a reactor often occur. PMDA-R molecules form laminates via noncovalent bonds, which are hydrogen bonds in the case of amide groups, and they are bundled by intertwining them12). The ability to increase the viscosity of an oil is influenced by how these bundles dissolve and spread in the oil. Therefore, the crystallinity/amorphousness of an organogelator is controlled by blending the side chains so that they are suitable for most oils. However, the formation of by-products requires deviation from the optimum conditions. In order to achieve the ‘process intensification’ that has been focused on in recent
years, it is necessary to verify changes in the compositions of products due to changes in scale-up processes and operating conditions in association with the required performance of the product.

In this study, we produced PMDA-2C₈(2)/oleyl(2) on a two-stage laboratory-scale and through commercial-scale synthesis. The compositions of the compounds were analyzed for each product, and the viscosity-increasing ability was rheologically evaluated for the solution dissolved in isododecan. Furthermore, the self-organizing structures of the organogelator products were observed by transmission electron microscopy (TEM). The objectives were to clarify the relationship between the side chain compounding ratio and the rheological properties of PMDA-2C₈/oleyl and to point out the problems with scaling up production of a target compound.

2. EXPERIMENTAL

2.1 Materials and methods

Figure 1 shows the chemical structure of N,N',N'',N'''-1,2,4,5-tetra alkyl/alkenyl pyromellitamide (PMDA-R). It has four amide groups at the end of the skeletal structure of the benzene ring. We synthesized PMDA-2C₈(2)/oleyl(2) as the target compound. The synthesis was achieved via reaction with an alkylamine (RNH₂). The amic acid obtained was condensed with an alkylamine (R'NH₂), diisopropyl carbodiimide was added as a catalyst, and the product was then washed with an organic solvent 11).

In the synthesis of PMDA-2C₈(2)/oleyl(2), by-product compounds are often produced depending on the temperature and the degree of agitation. These compounds were PMDA-2C₈(4), PMDA-2C₈(3)/oleyl(1), PMDA-2C₈(1)/oleyl(3), and PMDA-oleyl(4), where the numbers in parentheses represent the numbers of side chains before the parentheses. Therefore, high-performance liquid chromatography (HPLC, Agilent 1100, Agilent Technologies) was used to analyze the compositions of the products synthesized in this study. 1.0 wt% of a product sample was dissolved in chloroform as an eluent and then subjected to HPLC analysis with an injection volume of 10 μL. The flow rate was set to 0.7 mL/min with an oven temperature of 35 °C. Inertsil Diol 100, 5 μm (4.6 × 250) × 3 (GL Science) was used as a column.

Table I shows the synthetic operating conditions with different scales of reactors. Our first synthesis was performed at 50 °C using a 50 ml flask as the basic prescription mentioned as L1. We increased the synthesis temperature with the intention of shortening the reaction time as L2-L4. L5 and L6 were synthesized in a 1-L flask with different stirring devices. The reaction temperatures deviated up to 15 °C from the basic prescription. C1 and C2 were synthesized in a commercially used reaction tank having an inertial capacity of 20 L. A MAXBLEND® stirring device (Sumitomo Heavy Industries Process Equipment) was used to increase agitation efficiency.

The synthesized products were dissolved in a paraffin oil, isododecan (Maruzen Petrochemical). Good solubility was confirmed for each sample by both visual observation and high-value absorbance (> 90 %) at an absorption wavelength in the vicinity of 660 nm, using an ultraviolet-visible spectrophotometer (UV mini 1240, Shimadzu).

2.2 Characterization

A cone plate rheometer (NRM-2000R; Elquest) was used to measure the rheological properties of the prepared samples. The rheometer had a computerized torque motor covering six orders of magnitude from 10⁻⁴–500 rpm. The torque range was 10⁻⁹–5 × 10⁻² N·m. The diameter and angle of the cone were 17.1 mm and 3.0 degrees, respectively, while the cone tip truncation gap was 150 μm. The steady flow measurement was performed at a shear rate of 1–500 s⁻¹.

The frequency dependence of dynamic viscoelastic moduli

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Table 1 Product notations and their synthetic operating conditions.

| Notation | L1 | L2 | L3 | L4 |
|----------|----|----|----|----|
| Synthesis scale | Laboratory scale (1) | 50 mL |
| Composite scale | 50 mL |
| Synthesis temperature [°C] | 50 °C | 100 °C | 108 °C | 108 °C |
| Stirring device | Stirring bar |
| Stirring temperature °C | →50°C | →100°C | →100°C | →100°C |

* Oley addition reaction temp. → 2-ethylhexyl addition reaction temp.  ** 2-ethylhexyl addition reaction temp. → oleyl addition reaction temp.

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Fig. 1 N,N',N'',N'''-1,2,4,5-tetra alkyl/alkenyl pyromellitamide (PMDA-R).
was measured with a fixed strain of 0.1 and an angular frequency, $\omega$, ranging from 0.0628–62.8 rad/s. The measurement temperature was set to 25 ± 0.5°C with a Peltier air-bath control system. When casting a sample on the plate of the rheometer, we left it for more than 5 min until the temperature arrived at the set point. A few samples prepared showed somewhat solid-like properties for higher organogelator concentrations; however, they maintained their continuous phase and did not break up during measurement.

A JEM-140 TEM (JEOL, Tokyo, Japan) was used to observe the morphology of the sample. As a pretreatment, the sample was mounted on a support film grid and stained with osmium tetraoxide 2% aqueous solution for 4 hours, after which the surface of the self-assembled structure was coated with osmium. The measurement condition was an acceleration voltage of 100 kV.

The spinnability measuring device shown in Fig. 2 consists of an elevating device (MX2-500N, Imada), a strain gauge, and an amplifier system (maximum strain of 50 mN, LVS-56A, Kyowa Electronic Instruments). Approximately 10 mL of sample was put in a 50 mL glass container with a diameter of 30 mm and set on the stage of the device. A stainless wire was brought into contact with the liquid surface of the sample. The diameter, length, and weight of the wire were 1.2 mm, 11.8 cm, and 1.112 g, respectively. The wire was raised by the elevating device at constant speeds of 1, 3, and 5 mm/s. A strain gauge was used to measure the force with which the thread formed from the sample interface pulled on the wire. Also, the deformation of the thread was visualized with two digital cameras (DSC-RX0M2, Sony) to obtain both the spinnability stress and the length of the thread.

### 3. RESULTS AND DISCUSSION

#### 3.1 Laboratory-scale synthesized compounds (1)

Table II indicates the results of HPLC analyses for products L1–L4. L1 contained the target compound: PMDA-2C₈(2)/oleyl(2) with a high composition of 94%. L2–L4 each had a lower target compound content, around 40%. It is pointed out that the content of the 2-ethylhexyl group was higher in the order of L2, L3, and L4.

Figure 3 shows the results of the steady flow characteristics of L1–L4 with two concentrations, 0.5 wt% and 1.0 wt%, in isododecane. Isododecane showed a nearly constant viscosity value of 1.4 mPa s, which could be measured only after the shear rate $\gamma$ of 40 s⁻¹ due to the detection limit of the torque. For all the products with the addition of 0.5 wt%, similar levels of significant increases in viscosity were seen, together with typical shear-thinning properties. L1 and L4 could be measured over the entire shear rate range, whereas for the other samples, the higher shear rate range was not measured because the sample popped out from the cone-plate jig during the measurements.

**Table II** Compositions of compounds for L1–L4.

| Compound            | L1  | L2  | L3  | L4  |
|---------------------|-----|-----|-----|-----|
| PMDA-2C₈(4)          | 0.5 | 4.5 | 3.4 | 1.6 |
| PMDA-2C₈(3)oleyl(1)  | 3.9 | 22.6| 19.2| 13.0|
| PMDA-2C₈(2)oleyl(2)  | 94.0| 41.2| 40.9| 39.4|
| PMDA-2C₈(1)oleyl(3)  | 2.0 | 26.5| 30.4| 36.6|
| PMDA-oleyl(4)        | -   | 5.2 | 6.2 | 9.4 |

Figure 3  Steady flow characteristics of L1–L4 with two concentrations in isododecane.
abilities were more pronounced with 1.0 wt% addition, although slight differences were seen among the products. The tendency of L4 almost overlapped with that of L1; however, L1 was found to pop out at a lower shear rate (more than 30 s⁻¹) than L4 (more than 200 s⁻¹). L2 and L3 popped out at even lower shear rates of 2 s⁻¹ and 7.5 s⁻¹, respectively. We considered that such differences in the behavior of the samples were influenced by their viscoelastic properties.

Figure 4a displays the result of the dynamic viscoelasticity of 1.0 wt% L1 in isododecane. Since the cross point of $G'$ and $G''$ was located at the leftmost point and $G'$ gradually became independent as $\omega$ increased, we found that the sample was viscoelastic and also behaved like a gel in the high $\omega$ region.

We drew the L1 data in each figure with a dotted line ($G'$) and a dashed line ($G''$) for comparison. Fig. 4b displays the results of 1.0 wt% L2. $G'$ was always over $G''$ with no intersection and was almost independent of $\omega$, showing that the sample is a gel material.

Figure 4c and 4d show the results of 1.0 wt% L3 and L4, respectively, which were roughly in agreement with the outline of L1 except that the cross point for L4 was located in a slightly higher $\omega$ region than the other. We noted that, as the proportion of 2C₈ in the compound increased, the sample tended to behave like a solid.

Figure 5a shows a TEM image of 1.0 wt% L1 in isododecane. Self-assembled structures consisting of thick and fine fibers can be seen, which appeared to form a network structure. Fig. 5b shows a TEM image of 1.0 wt% L2, which included not only fiber materials, but also interspersed massive materials. Such a nonuniform structure may be formed by the influence of the highly crystalline alkyl group of 2C₈ in isododecane. Fig. 5c shows a TEM image of 1.0 wt% L3, which included a mesh structure with thick and thin fibers.
coexisting. Fig. 5d shows a TEM image of 1.0 wt% L4. We confirmed a precise structure but could not classify whether it was a network structure.

As described above, some mixtures of different compounds exhibited similar steady flow characteristics and viscoelasticities even when the compositions differed. On the other hand, since the morphologies of the self-assembled structures formed by the four products were quite different, we expected certain differences in their performance as organogelators owing to differences in the rheological properties evaluated in this study. As a result, we considered that it was not a good idea to increase the synthesis temperature to 100 °C to shorten the reaction time. In addition, it was necessary to increase the number of target components as much as possible.

### 3.2 Laboratory-scale synthesized compounds (2)

Table III presents the results of HPLC analyses for L5–L6. Both products contained high compositions of PMDA-2C₈(2)/oleyl(2). The reaction temperature of L5 was 20 °C higher than that of L6, and the performance of the stirring blade used for L6 was more efficient than that for L5. As a result, L5 had a slightly lower content of the target component than L1, and the amounts of PMDA-2C₈(3)/oleyl(1) and PMDA-2C₈(1)/oleyl(3) increased accordingly. L5 contained a small amount of both PMDA-2C₈(4) and PMDA-oleyl(4). Here, the crystallization temperature of PMDA-2C₈(4) was 139.2 °C, while that of PMDA-oleyl(4) was not observed. In addition, the melting points of PMDA-2C₈(4) and PMDA-oleyl(4) were 262.3 and 258 °C, respectively. Therefore, we pointed out that L5 contained a small amount of both a highly crystalline homo-compound and an amorphous homo-compound. L6 had a similar composition to L1 except that L1 contained no PMDA-2C₈(4) even in a slight amount.

Figure 6a and 6b show the steady flow characteristics of 1.0 wt% L5 and L6 for isododecane. We drew the L1 data in each figure with a dotted line for comparison. Both compounds displayed shear thinning properties; however, the viscosity-increasing abilities at the lower shear rate range

| Table III Compositions of compounds for L5 and L6. (%) |
|-------------------------------------------------------|
|            | L5  | L6  |
| PMDA-2C₈(4) | 0.7  | -   |
| PMDA-2C₈(3)/oleyl(1) | 7.4  | 2.6 |
| PMDA-2C₈(2)/oleyl(2) | 82.0 | 95.0 |
| PMDA-2C₈(1)/oleyl(3)  | 9.3  | 2.0 |
| PMDA-oleyl(4)         | 0.5  | -   |
were reduced to that of L1. Fig. 6c and 6d show the dynamic viscoelasticities of 1.0 wt% L5 and L6. We drew the L1 data in each figure with a dotted line ($G'$) and a dashed line ($G''$) for comparison. L5 displayed a viscoelastic fluid, while L6 expressed a weak gel. Also, both products showed lower $G'$ values than those of L1. This indicates that even if the proportion of the target substance is moderately increased, the slight difference in composition eventually affects the organogelator performance. Although the components of L6 were similar to those of L1, it can also be said that they gelled, probably due to the absence of trace amounts of the homocompound.

3.3 Commercial-scale synthesis

Table IV presents the results of HPLC analyses for products C1 and C2. As the scale of the reactor increased, the stirring efficiency increased and the reaction temperature was controlled accurately. Both C1 and C2 had almost the same compositions as L1. The reproducibility was good in that the same compositions were obtained even in different batches.

Table IV  Compositions of compounds for C1 and C2.

|                | C1  | C2  | (%) |
|----------------|-----|-----|-----|
| PMDA-2C₄(4)    | 0.3 | 0.3 |     |
| PMDA-2C₄(3)oleyl(1) | 3.9 | 3.7 |     |
| PMDA-2C₄(2)oleyl(2) | 94.0 | 94.0 |     |
| PMDA-2C₄(1)oleyl(3) | 2.0 | 2.1 |     |
| PMDA-oleyl(4)  | -   | -   |     |

Figure 7a shows steady flow characteristics, while
Fig. 7b shows dynamic viscoelastic moduli for 1.0 wt% C1 and C2 in isododecane. Again, we drew L1 data in each figure in the same manner as in Fig. 6. The steady flow characteristics of the three samples were in accord with each other. Also, the dynamic viscoelastic moduli of the three samples were in good agreement with each other, as each modulus had an intersection at low angular frequency and each showed gel behavior in the high angular frequency range.

Figure 8 shows a TEM image of 1.0 wt% C1 in isododecane with an enlarged view of another area of the same sample. A typical network structure consisted of thick and fine fibers that were self-assembled. We also showed a L1 image of the same scale for comparison. We can confirm that the structure of C1 is similar to L1. As described above, we successfully produced compounds having almost the same composition, rheology, and morphology as L1 by a commercial-scale synthesis.

3.4 Spinnability

Figure 9a shows the results of spinnability tests for 1.0 wt% L1 in isododecane. With a wire-pulling speed of 1 mm/s, the stress on the wire in contact with the solution (spinning stress) showed an overshoot at the beginning and gradually increased as the wire was pulled. It reached a maximum value of 1.6 mN and then gradually decreased. At this time, the thread formed by the solution was cut at a spinning length of 5.8 mm. This tendency became more pronounced at a higher wire-pulling speed, with a spinning length of 9.4 mm at a speed of 5 mm/s. However, the gradients of the stress increase were almost constant regardless of the speed. This phenomenon can be interpreted as a manifestation of the process of the spinning development from the liquid surface and
the process after the maximum stress value, in which the thin-
ning and finally the cutting of the thread occur.

Figure 9b shows the results of the spinnability tests for
1.0 wt% L2. The maximum stress was almost the same as
that of L1 at a speed of 1 mm/s; at 3 and 5 mm/s, however,
the maximum stresses were significantly lower than those of
L1. Also, the maximum stresses showed outer shapes that
plummeted after each maximum value was passed. It is un-
derstandable that the thread lengths were less than 2 mm for
all cases, because the dynamic viscoelasticity indicated that
the sample was a gel.

Figure 9c shows the results of spinnability tests for
1.0 wt% L3. Although the gradient of the stress at a speed of
1 mm/s was similar to that of L1, both the maximum stress
and the spinning length were significantly lower than those of
L1. Again, they showed an outer shape that plummeted after

Fig. 9 Spinnability tests for L1-L4, and C1 in isododecane.
the maximum value was passed. Even when the speed was increased, the tendency of the stress did not change.

Figure 9d shows the results of spinnability tests for 1.0 wt% L4. Both the maximum stresses and the spinning lengths increased slightly as the speed increased. The gradient of the stress for each speed was gentler than that of L1. Although the compositions of L3 and L4 were significantly different from that of L1, they were regarded as candidate products showing similar rheological properties to L1 as rheological control agents for isododecane. From the point of view of spinnability, however, these compositions were not similar to that of L1.

Figure 9e shows the results of spinnability tests for 1.0 wt% C1. Although the maximum stress at each speed was almost the same as that of L1, the outer shape plummeted after each maximum value was passed. We considered that the thread formed by the solution was cut after the maximum value was reached; otherwise, the stress of the thread emerging from the liquid surface was so small that we could not detect it. In this measurement, the initial gradient shows the process of spinnability development from the liquid surface, while the process after the maximum value shows the disappearance of the expressed thread. From the experimental results, we point out that even when chemical products were synthesized so that the compositions were almost the same and the solutions showed similar viscoelasticities, the outer shapes of this part did not match at all.

To synthesize the organogelator examined in this study, we consider that the reaction temperature and time are important factors in ensuring reproducibility. Furthermore, since there was a remarkable difference in composition between L5 and L6 due to the difference in the stirring blades, the stirring conditions are also among the important factors. Keeping these in mind, even if we scale up and manufacture a product like C1 or C2, it is quite difficult to make exactly the same product as L1, which we synthesized at a laboratory scale.

Since C1 and C2 had almost the same steady flow characteristics and viscoelasticities as L1, they might show almost the same performance as L1 when we use them as normal lots of rheology-controlled agents. In such cases, the inability to produce exactly the same compound is not a major problem. Rheological differences can be problematic for some applications; however, when we use them as rheology-controlling agents in a cosmetic with isododecane as a solvent, the feature of not having to pull the threads will become a convenient function for handling.

4. CONCLUSIONS

We investigated the process of scaling up the synthesis of a laboratory-developed organogelator to a commercial level. The effects of the synthetic operating conditions and the scale-up on the properties of the resultant chemical products were examined by steady flow measurement, dynamic viscoelastic measurement, and spinnability testing. The results indicated that mixtures of compounds with different side chains were likely to be formed when the reaction temperatures were raised. Also, reaction fields with different scales and stirring conditions resulted in differences in composition, which greatly affected the performance of the produced organogelators.

To obtain a target compound, it is necessary to control the reaction temperature, time, and stirring conditions so that they are the same as in laboratory-scale experiments. Although it might be quite difficult to equalize not only the rheological characteristics but also the spinnability of a product, it is important to try to do so as much as possible.

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REFERENCES

1) Bouteiller L, Adv Polym Sci, 207, 79 (2007).
2) Hanabusa K, Koto C, Kimura M, Shirai H, Kakehi A, Chem Let, 26, 429 (1997).
3) Nagarajan V, Pedireddi VR, Cryst Growth Des, 14, 1895 (2014).
4) Smulders M, Schenning A, Meijer E, J Am Chem Soc, 130, 606 (2008).
5) Wilson A, Gestel J, Sijbesma R, Meijer E, Chem Commun, 42, 4404 (2006).
6) Stals P, Smulders M, Martin-Rapun R, Palmans A, Chem Eur J, 15, 2071 (2009).
7) Tanaka M, Ikeda T, Mack J, Kobyashi N, Haino T, J Org Chem, 76, 5082 (2011).
8) Jimenez CA, Belmar JB, Ortiz L, Paulina H, Oscar F, Jorge P, Ruiz-Pérez C, Cryst Growth Des Comms, 9, 4987 (2009).
9) Webb JEA, Crossley MJ, Turner P, Thordarson P, J Am Chem Soc, 129, 7155 (2007).
10) Tong KWK, Dehn S, Webb JEA, Nakamura K, Braet F,
Thordarson P, *Langmuir*, **25**, 8586 (2009).

11) Sakanishi Y, Narusaka Y, Itoh M, Arita T, Saeki T, *Nihon Reoroji Gakkaishi (J Soc Rheol Jpn)*, **43**, 1 (2015).

12) Kaide A, Saeki T, Sakanishi Y, Nakamura R, *Rheologica Acta*, **57**, 618 (2018).