

Novel functional gels and their commercial distribution as chemical reagents

— New development of functional soft-materials —

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We have recently developed novel gel-forming materials based on organic electrolytes. The organic electrolytes can be prepared by a simple one-pot reaction applicable to large-scale production. The materials show the following remarkable characteristics. (a) They can be used for gelation of not only water but also electrolyte solutions of polar organic solvents including ionic liquids. (b) Rapid self-healing of the formed gel is possible even after collapse by mechanical stress. (c) The formed gel can be used as an efficient dispersant for single-walled carbon nanotubes. The materials have been commercially distributed as chemical reagents for gelation.

Keywords : Gels, electrolyte, electrolyte solution, ionic liquids, chemical reagents

1 Background of research

Among the diverse materials that support our daily life, the organic polymers that form the light and soft plastics belong to the generally called “soft materials.” Whereas the inorganic solids generally have hard and tough nature, soft materials are based on the flexible characteristic of organic materials. One of the soft materials called “gel” has an intermediary property between solid and liquid. It is used widely in society in various fields including the bio fields such as drugs and medicines due to its high biocompatibility, foods and cosmetics, and as viscosity regulators of several coating materials such as paints and inks (Fig. 1).

In general, a gel is a quasi-solid material in which a large amount of liquid is trapped in a chemical or a physical network structure formed by relatively small amounts of coexisting materials, and then the apparent fluidity is lost. The hydrogel where the solvent water has become quasi-solid is represented by jelly and konjac starch that are foods, hyaluronic acid used in cosmetics, and absorbent polymers used in hygienic products. The widely known example of gels made of solvents other than water is the oil-fixing agent where the food oil, a kind of organic solvent, is quasi-solidified. Considering the gel in terms of its function as a material, in addition to its water-absorbing and moisture-retaining properties, there are other applications such as for absorption and separation, various sensing functions, anti-vibration and cushioning materials, and dynamic energy converting materials such as actuators.

Active researches are being done in the academic field both

in Japan and overseas for the “functional gels” that are given various functions, and they are expected to be useful in advanced fields in the future. One example is the “functional gel” for which the importance is indicated as one of the core materials that support the environment, life science, and IT fields, as mentioned in the “Nanotechnology and Materials Research” in the “Technological Strategy Map 2010” edited by the Ministry of Economy, Trade and Industry (METI).^[1] Moreover, in the “International Comparison of Science and Technology R&D in Nanotechnology and Material Field for 2011,” a report by the Center for Research and Development Strategy, Japan Science and Technology Agency (JST-CRDS), it is written that Japan excels in the field of soft materials (supramolecules) compared to other countries,



Fig. 1 Various products in which gels are used

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and it is pointed out that “several breakthroughs have been achieved in functional gels investigations in Japan, and those have raised the level of the researches.”^[2] Therefore, the important issues are how to increase the excellence of the core research level of Japan and how to develop the functional gel to practical industrial applications.

While further advancement of functions is necessary to increase the excellence of functional gel development, the new materials must be mass-producible using a simple method, from the industrial perspective. From this perspective, the author embarked on problem solving from the synthetic chemical approach and engaged in new material manufacturing that realized the two points, achievement of novel function and simple synthesis. As a result, the “ionic gelator,” a material group that was totally unknown before, was originally developed. In this paper, the development process, efforts for the commercialization as a chemical reagent, and current issues will be explained.

2 Process in the development of a new gelator and the research goal

Gels can be roughly divided into two categories, the chemical gels and physical gels, and each has its characteristics. For example, chemical gels generally have high elasticity and excellent dynamic property but are weak against strain, because the network structure of the gel is composed of the covalent bond. On the other hand, with physical gels, because the network structure is stabilized by the non-covalent bond interaction (such as hydrogen bond or π - π interaction), it is known that they undergo reversible sol-gel transition upon heating and cooling. The material showing the physical gel forming property is normally called a “gelator,” and both the natural-occurring and artificial gelators are used industrially. Table 1 lists the characteristics of the two gelators. The natural gelators, the most well known being agar and gelatin, are highly safe, are commercialized as food additives to add starchiness, and are available at a reasonable price. However, it is known that there is restriction in the gelation, such as the acidity of the solution must be neutral, and it is not usable in acid or alkali conditions since disintegration occurs. Also, since it does not dissolve in ordinary organic solvents, there are extreme restrictions in the gelatable solvents.^[3] On the other hand, for the chemically synthesized artificial gelators, it is possible to add various functions unseen in natural gelators, by appropriate structural control and functional group introduction. However, multiple steps are usually necessary for the synthesis and refining processes of the artificial gelator. Therefore, unless a certain yield can be obtained at each step, the total yield would be low. Also, the isolation process such as column chromatography that uses large amounts of organic solvents may be inappropriate for large-scale production. As a result, although active R&Ds are done at the academic level, in most cases, the scale of

Table 1. Types of gelators and comparison of characteristics

	Natural gelators	Artificial gelators
Examples of compounds	· Agar, gelatin, etc.	· Various synthetic polymer gels, etc.
Usage	· Utilization of biocompatibility in foods, drugs, etc.	· Absorbing material, separation chromatography, actuator, etc.
Advantages	· Available at low cost · High biocompatibility	· Chemical modification is possible · Functions such as stimulus response can be added · Abundant basic research
Issues	· Unstable in acid condition · Unsuitable for gelation in solution other than water · Addition of function by chemical modification is difficult	· In general, synthesis requires multiple steps; manufacturing process design is necessary for mass-production · Only a few types of solvents can be used

synthesis remains at the laboratory level (with only a few grams of yield at most). In addition, there have been few researches on “amphiphilic gelators” that gelate in both water and organic solvents, and the gelation of multiple solvents with one gelator has been a major challenge.

The author first became involved in gel material research by coincidence, as an extension of the research of dendritic polymer called the dendrimer, during the two-year study in the United States from 2002. The material used at the time was a system that was not suitable for mass production because multiple steps were required for synthesis. Also, the gelatable solvent was limited to only the organic solvent, and gelation was impossible for water that was the most common solvent (liquid). Upon returning to Japan, the author started research to develop a new material with a gelation function that could be manufactured using a commercially available starting material and which involved as few number of steps as possible, as well as the synthesis technology that was suitable for mass production and commercialization.^{[4]-[7]}

3 Molecular design as synthesiology: Use of organic electrolyte as a gelator

From the chemical perspective, a new material is a new *molecule*, and one of the optimizing methods to achieve the new molecular design and synthesis is a way of “synthesiology.” In that sense, the author paid attention to physical gelators in which the gel formation is possible through relatively weak interaction. The spontaneous aggregation of the molecules during gel formation and the formation of three-dimensional network structure are phenomena that are drawing attention in the current nanotechnology fields, as the “self-organization” of synthetic molecules. It is thought that gels with diversity from both the structural and functional aspects can be developed if this self-organization can be finely controlled. Also, the physical gelator can dramatically alter the viscosity of the basic solvent at extremely small amounts like a catalyst during a reaction, while maintaining the basic physical property of the solvent. Therefore, if gelation that could not be accomplished

before in a certain solvent system becomes possible through the development of a new gelator, it is expected to expand the gel application further.

The author's thoughts on the guideline for the specific molecular design of a new material are shown in Fig. 2.

In this research, we focused on the "organic electrolyte compound." Hydrogen bond between the functional group and hydrophobic interactions are generally known as the intermolecular interactions that act as the driving force of molecular self-organization, and are actually used in the gelator system (Fig. 2 "Conventional gelator"). On the other hand, the self-organization of organic electrolyte compounds that easily combine the interactions is actively investigated from the perspective of biology, in extremely complex natural systems such as the double helix structure of DNA and its further hyperaccumulation. However, the self-organization in the artificially synthesized organic electrolytes had not drawn much attention compared to the neutral compounds. In the preparation of hydrogel where the solvent is water, it is important for the gelator to have both the hydrophilic and hydrophobic sections to be amphiphilic. For conventional gelators, the hydrophilic property was mainly borne by the corresponding functional groups such as the hydroxyl group or the carboxyl group. On the other hand, the characteristic of organic electrolytes as represented by various ammonium salts is to show hydrophilic property due to the salt structure (cation and anion in pair) of the molecule, even without the functional groups. We set this nature as an important element of the molecular design. While the polymeric electrolytes are expected to be applied widely to the electrolyte and separation membranes of batteries, we expected the gelation would occur by incorporating a functional group capable of interaction to such organic electrolytes, and

then oligomerizing to add multiple functions (lower part of Fig. 2). As a method to easily achieve this new concept, the one pot self-condensation reaction (reaction that takes place in one flask only, where the molecules spontaneously condense to gain relatively high molecular weight) that used commercially available starting materials was devised, as shown below. As a result, the synthesis of new organic electrolyte with oligomeric structure with a gelation property (electrolyte gelator) was established (Fig. 3).

It was found that this material actually possessed various characteristics including: 1) acid resistance, 2) solvent compatibility, 3) self-healing property, 4) complexation with carbon nanotubes, and 5) antibacterial property. These comprise the main points of synthesisology, as "functions that occur in the appropriate molecular design." The details will be explained in the following chapter.

4 Property of the electrolyte gelator (ionic gelator)

4.1 Synthesis

The polymer with a quaternary ammonium structure in the main chain is called the ionene polymer, and this is normally synthesized by the copolymerization of two monomers, diamines (nucleophilic) and dihalogen compound (electrophilic). We thought the synthesis of the new functional organic electrolyte compound would be possible by the molecular design of an amphoteric monomer with a rigid structure, where the electrophilic and nucleophilic sections coexist within a molecule, and in which intramolecular quaternization reaction will not occur. Based on this strategy, as shown in Fig. 3, we conducted synthesis by chemical reaction involving the mixing of two types of reagents (4-aminopyridine and 4-chloromethylbenzoic acid chloride) that were purchasable as chemical reagents, in

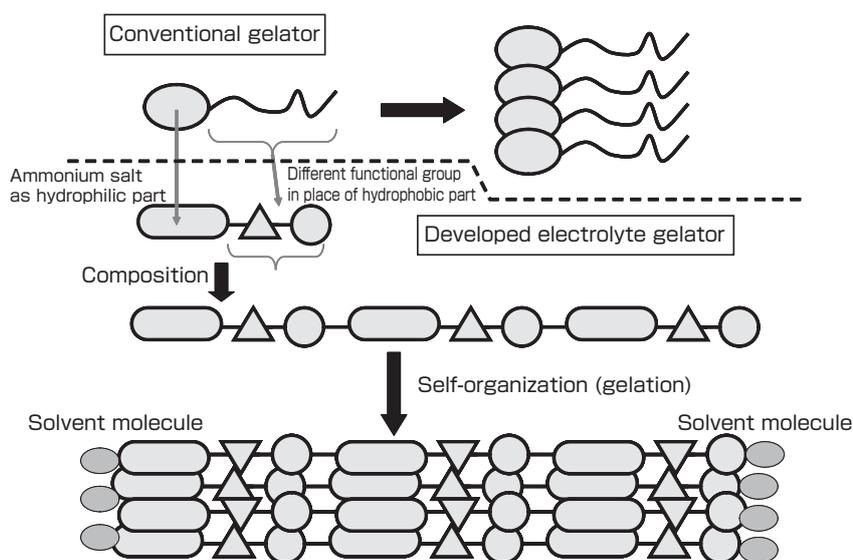


Fig. 2 Molecular design for new gel material

presence of an appropriate base under refluxed condition. To realize a new material that could be mass-produced, as mentioned before, one of the synthesiological elements was “to use the commercially (easily) available starting materials.” Precisely said, this reaction occurs in two steps of primary amidation and the following intermolecular quaternization reaction. However since the reactivity of the intermediate produced in the first reaction is high and the second step reaction ensues quickly, it looks like a single step “one pot reaction.” It is known that the material is the “oligomer” (polymer with relatively low molecular weight) with average degree of polymerization (n) of 10 to 20.^{[4][5]} There is very few case of synthesis of organic electrolytes by self-condensation, and this is a novel synthetic approach that is totally different from the conventional polymerization where two types of monomers must be prepared beforehand. This is characterized by “a small number of steps” needed to solve the problem, and can be considered an important element of synthesiology.

4.2 Gelation behavior

A hydrogel can be easily made from the organic electrolyte oligomer obtained, using a method similar to that for the conventional physical gelators. The powder is added to the water at a concentration of 1 weight % or more, the process of heating \rightarrow dissolution at high temperature \rightarrow cooling (by leaving at room temperature) is done, and the water can be gelled (Fig. 4 left).

As a general characteristic of the physical gel, this gel undergoes thermal and reversible gel-sol transition, and the once quasi-solidified gel becomes a solution without high viscosity by heating. Although the clear mechanism of gelation is not yet clarified, it is likely that the electrostatic interaction plays an important role, and other diverse interactions are involved in a complex and complementary manner. As mentioned later, this gelator possesses affinity to carbon nanotubes (CNTs). Therefore, complexation with CNTs can be done easily, and we were able to prepare a

CNT-containing gel by only the electrolyte gelator (Fig. 4 right).

4.3 Numerous functions of electrolyte gelator

The oligomeric electrolyte has interesting characteristics that were difficult or could not be achieved at all by existing gelators, as shown below.

4.3.1 Acid resistance

In naturally derived gels, the gel cannot be made using an acid solution because the main molecular structure disintegrates under acid conditions. However, it was projected that the new material would be acid resistant because it does not possess the acid labile functional groups. By using this material, the gelation of an acid water solution with about pH=1 was achieved, and application may be possible for the quasi-solidification of acid waste liquids that used to be a challenge (on the other hand, since the solubility of the gelator decreases in the base condition, gelation has not been successful).

4.3.2 Solvent compatibility control by anion exchange

The electrolyte gelator is composed of the organic part with cation and the corresponding anion, and the initial anion after the preparation is the chloride that is the same as common salt (sodium chloride). By replacing the anion with a different anion, it is possible to control the solubility (compatibility) of the gelator. This can be applied to solvents other than water, by controlling the gelator compatibility as the chloride ion of the parent compound is replaced with hydrophobic fluorinated anions such as $N(SO_2CF_3)_2$ and PF_6 that are typical counter ions in ionic liquids known as the new functional solvents.^{[4][5]} This can be used for the gelation of various organic solvents and the aforementioned ionic liquids, not just water (Fig. 5). Therefore, the characteristic distinct from the conventional artificial gelators is that the solubility can be easily adjusted even after synthesis by the counter anion exchange, and in the sense that it possesses a single molecular skeleton, it is the realization of an “amphiphilic

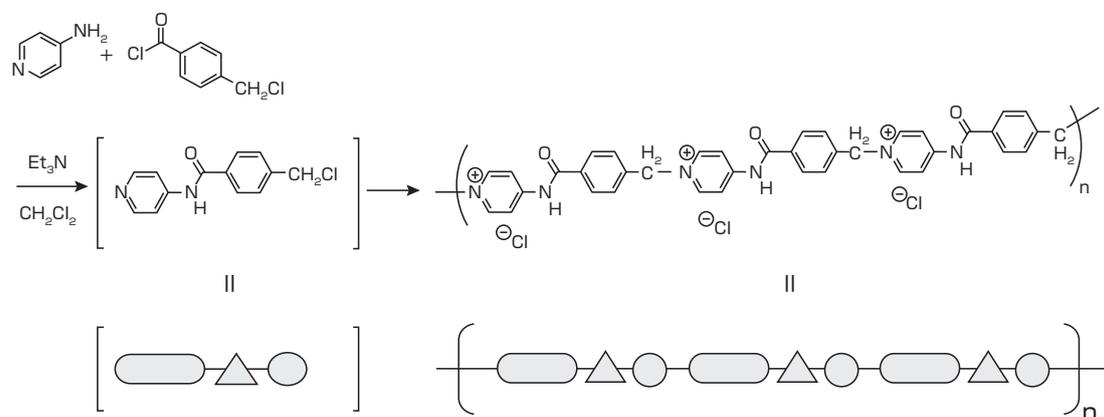


Fig. 3 Synthesis of the electrolyte gelator

gelator.” For the gelation of, for example, ionic liquids, it has been shown that the ion conductivity decreases only a few percent after gelation and is maintained.^{[4]-[6]} In conventional ionic liquids with low viscosity, there was a trade-off where the conductivity increased as the ion mobility increased in the less viscous ionic liquids but it became likely to leak in sealed conditions due to the low viscosity. On the other hand, the highly viscous ionic liquids did not leak readily but had decreased conductivity as the ion mobility decreased due to the high viscosity. For this issue, we realized a new technology using this gelator that allowed the adjustment of viscosity only while retaining ion conductivity. Therefore, it can be used in electrochemical devices (dye sensitized solar cells, capacitors, etc.) that use ionic liquids as the electrolyte solution, and application in the coating process, increased lifespan of the operation time by preventing leakage, and other improvements in performance can be expected.

4.3.3 Self-healing gel

In general, because gels have soft forms, their structures are easily destroyed by mechanical stress. Relating to the response under the mechanical stress, some gels show the “thixotropic property (thixotropy).” This is a property where the viscosity changes in response to applied stress, the substance changes into fluid sol under high stress conditions, and then returns to gel when the stress is removed. Generally, a long time is needed to return from sol to gel, and the only exception reported was the quick structural recovery of hydrogel composed of block copolymer that possesses cation charge on the side chain.^[8] The authors looked at the structural similarity between the case studies and the electrolyte gelator, and investigated whether a similar characteristic could be observed. As expected, it was found that the new material had an interesting self-healing property where the storage elasticity modulus, which indicates the solidity of gel, recovered at extremely high speed (in a few seconds) after the destruction of the gel structure.^{[4][7][9]} This structural recovery occurred at higher speed as the concentration increased.



Fig. 4 Photograph of hydrogel in inverted sample bottle (concentration at 1 wt%)

Left: Pure water gel; Right: Gel containing single walled carbon nanotubes (From Reference [5])

As a side story, the author at the time had no experience in the rheological measurement of gel elasticity, and we asked a measurement device manufacturer to measure the sample. It left a strong impression when the engineer who had experience in measuring numerous samples looked at the measurement of our sample and said, “I think this is a very rare phenomenon.” From the crystal structure analysis of the model compound (unpublished data), we believe this phenomenon occurs by the recovery of gel network by long-distance electrostatic interaction that arises from the fact that the electrolyte gelator is charged, rather than a short-distance interaction like the hydrogen bond. Since the once broken gel structure recovers instantly, this gel can be considered as a type of “indestructible gel,” and applications in various fields can be expected such as the impact absorbing material that utilizes high-speed structural recovery property. The author’s report was the precursor of the above high-speed self-healing gel, and many examples followed. In the functional gel “Aqua Material” that was jointly studied by Professor Takuzo Aida, Specially Appointed Assistant Professor Justin Lee Mynar (currently of King Abdullah University of Science and Technology, Saudi Arabia) of the University of Tokyo, and the authors, the formation of a water gel was observed by the interaction of clay derived nanoparticle and dendrimer that each possessed complementary charges. Since the high strength and self-healing properties were observed in this gel, the importance was again indicated of the electrostatic interaction that drives the gelation and allows self-healing.^[10]

4.3.4 Complexation with carbon nanotubes (CNTs)

The electrolyte gelator is found to be a specific “dispersant” to CNTs, which is gaining attention as the next-generation material in the field of nanotechnology, as well as having the gelation function described before.^[4] This result was found by inference from the previous example^[11] of a similar polymer electrolyte for which only one report was known. In this case also, the authors had no experience in CNT research at that time. However, there were researchers involved in CNT

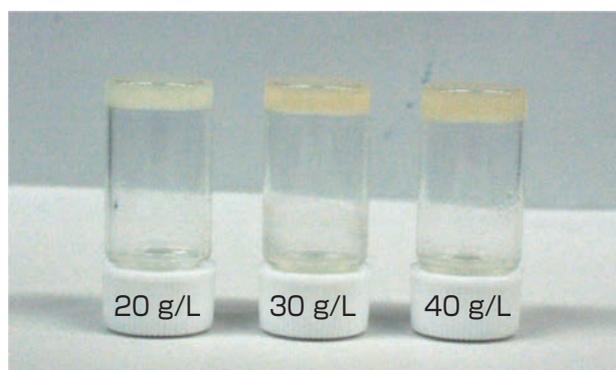


Fig. 5 Ionic liquid (EMIm-PF₆) gel in an inverted sample bottle {from Reference [4] (Supporting Information) (permitted by ACS)}

research in the same institute, and we were able to ask for a supply of CNTs and to request the evaluation of the dispersion degree, and this led to the discovery of the phenomenon. Without the presence of such researchers in a totally different field nearby, I think the discovery of this phenomenon would have been greatly delayed. In fact, it is possible to dissolve (isolated dispersion) the water insoluble single-wall carbon nanotubes (SWCNTs) by simply mixing the material with SWCNTs and then applying ultrasonic irradiation using the common ultrasonic irradiator for cleansing. In the CNT dispersion, we think organic electrolyte oligomer interacts with the π surface of the SWCNT, resulting in the dispersion in water by the surface wrapping, as in the example in Reference [11]. This solution is a highly stable solution where no precipitation occurs over a long time, and this liquid can be used to fabricate the SWCNT thin film or to prepare the SWCNT dispersed hydrogel under the condition where the concentration is maintained above a certain level. This is likely to make contributions in the preparation of CNT ink for printable electronics and the fabrication of carbon film for transparent electrode as an alternative to ITO, which is expected as a promising application of the nanocarbon material.

4.3.5 Antibacterial effect

The compound that possesses the cationic pyridinium group in the molecular structure is known to be an antibacterial agent, and is actually used. Since the new gelator also possesses a similar pyridinium group in the main chain, we subcontracted an external lab to evaluate the antibacterial property. A antibacterial effect was observed in both the Gram-positive bacteria (*E. coli*) and Gram-negative one (*S. aureus*).^[12] The minimum growth inhibitory concentration was 32 $\mu\text{g/ml}$ and 64 $\mu\text{g/ml}$, respectively, or sufficiently low, and these values were equivalent to the general surfactant-type antibacterial material.

5 Work on commercialization of the reagent considering the industrial technology application

The gelator materials with various characteristics described above were initially studied using the management grant (fund given to AIST from METI) as a core research. After obtaining a certain level of results, the research was selected for the 2005 Grant for Industrial Technology Research (Nanotechnology Material) of the New Energy and Industrial Technology Development Organization (NEDO), which greatly accelerated the research and led to further developments. At the time of application to NEDO, although we had a few patents filed, we had no published paper. So we were very lucky that we received high scores in the screening process even at an initial stage of the research. With the grant from NEDO, we participated in activities such as AIST press releases, exhibitions for nanotechnology (Nanotech 2008, 2009, and 2010; Orga Techno 2008), and AIST open

labs to publicize our research. While we had experience in the publication and discussion at academic societies, the experience of discussing specific technical issues directly with the people from companies at such exhibitions was quite invaluable. Through the buildup of such activities, we received several technical consultations about gelation from various companies, and we signed agreements to provide samples to conduct gelation performance tests with some companies. One of the major Japanese chemical reagent companies with particular experience in manufacturing and sales of ionic liquids had shown interest in the commercialization of the gelator material from the initial stages of the research, and we were able to actively exchange views and ideas. Later, a formal license agreement was signed with this company through AIST Innovations (at the time), and production was subcontracted to provide samples to companies that requested sample licensing agreements. In autumn of 2009, the product was commercialized as a chemical reagent. Initially, the authors only had experience with synthesis reaction at small-scale laboratory level of about 10~20 gram yield, and much effort was needed in optimizing the condition for large-scale reaction even if it was for a reagent. However, with the perseverance of the corporate researchers, the reproducibility and yield were improved, as the experimental conditions published in the papers were revised. As a result, commercialization of the several gelators with stable performance became possible, including the various anion exchangers (Fig. 6). In writing this paper, I sought comments from the companies on the “condition for commercializing a new reagent.” The emphasis was placed on 1) novelty, where things that could not be done before can be done, and 2) prospect, where things that did not exist before will be created. In creating the reagent of the gelator that we developed, several people commented that it could be used for electrolyte in batteries, electroconductive materials, viscosity enhancer in ink, and for research in wide-ranging areas such as cosmetics. For reference, according to the Chemical Abstracts Service that provides the database of all chemical substances managed by the American Chemical Society, at this point, there are over 65,360,000 chemical substances registered, including organic and inorganic compounds. On the other hand, in the reagent database of Sigma-Aldrich Corporation, one of the leading reagent companies in the world, there are 187,000 reagents registered and marketed. Assuming that about three times this amount is used as reagents including those of other chemical companies, the “percentage of reagents among all chemical substances” is calculated to be 0.86 %, and I think the readers can appreciate the fact that only a few compounds become available as reagents worldwide. In such a situation, our product was fortunate to become a commercially available reagent, and now it can be tested for performance by researchers of various industries, academic fields, and governments. I also think it has become widely known as a novel material.

6 Future perspectives

Although chemical reagents is a somewhat niche market, it was very encouraging for the author to see the material that we developed draw attention and then become actually commercialized, as stated in the research goal. As the reagent went on sale, it is now readily available to the external research institutions for R&D purposes, but the practical application is still in the budding stage. As a basic issue, “gelation” itself is an extremely fundamental chemical phenomenon, and this is rarely recognized to be a simple industrial technology where some specific product can be directly imaged from this phenomenon. On the other hand, through technical consultation with various companies, I am convinced that there is high expectation for the core technology of “gelation”, and I feel that sufficient contribution can be made to industry and society by advancing this “gelation” technology. Specifically, in actual industrial application, in most cases, the solvents or solutions that people wish to gelate contain various solutes, and it is necessary to fine-tune the performance of the gelators individually through feedback from the corporate users. On this point, mutual understanding cannot be obtained

merely through only the sales of the reagent, and I think it is necessary to establish a communication system between us and company researchers to promote understanding to further the practical application of the product.

In terms of the technological view, the critical issues are to increase the efficiency of gelation and the number of gelatable solvents. We are actively working on the preparation of a new electrolyte gelator, and various derivatives are prepared by a co-polymerization method using two types of monomers, and high gelation capacity has been observed.^[13] For the CNT dispersion function, we succeeded in enhancing the function such as addition of further optical responsivity by developing a material dedicated to the dispersal function,^[14] and joint research has been started with a company for industrial realization using CNTs. On the other hand, by using the gelator that was commercialized by an independent research group, an extremely fascinating phenomenon unseen before, that is the asymmetric environment (circular dichroism activity) dependent on the stirring direction of the solution, has been reported (different CD activity is observed in the solution by right- or left-rotational stirring). Interestingly, this asymmetric field can be fixed by gelation.^[15] It is becoming clear that the material that was initially developed for the objective of a new gelator discovery has diverse functions, and we wish to engage in further research for future practical applications with collaboration with other researchers inside and outside of the institute. In writing this paper, I realized that “synthetic strategy” thinking where individual elements are optimized and built up is important in developing a new material from the chemical viewpoint that involves trial-and-error of molecular design and synthesis methods. I hope this paper will be of some help for the other researches in the future.



Fig. 6 Pamphlet for the reagent (created by Kanto Chemical Co., Inc.) (top) and the commercial reagent (bottom)

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References

- [1] Technological Strategy Map 2010 METI “Nanotechnology” (in Japanese).
- [2] Center for Research and Development Strategy, Japan Science and Technology Agency (JST-CRDS):, *Nanotekunoroji Zairyo Bun'ya Kagaku Gijutsu Kenkyu-Kaihatsu No Kokusai Hikaku 2011 Nenban* (International Comparison of Science&Technology R&D in Nanotechnology and Material Field for 2011), (June 2011) (in Japanese).
- [3] Y.Osada, K. Kajiwara *et al.*: *Gels Handbook*, NTS (1997) (in Japanese).
- [4] M. Yoshida, N. Koumura, Y. Misawa, N. Tamaoki, H. Matsumoto, H. Kawanami, S. Kazaoui and N. Minami: Oligomeric electrolyte as a multi-functional gelator, *J. Am. Chem. Soc.*, 129 (36), 11039-11041 (2007).
- [5] M. Yoshida: Ionic gelators: oligomeric and polymeric electrolytes as novel gel forming materials, *The Chemical Record*, 10, 230-242 (2010) (Invited Review).
- [6] N. Koumura, H. Matsumoto, H. Kawanami, N. Tamaoki and M. Yoshida: Tuning of solubility and gelation ability of oligomeric electrolyte by anion exchange, *Polym. J.*, 42, 759-765 (2010).
- [7] S. K. Kundu, T. Matsunaga, M. Yoshida and M. Shibayama: Rheological study on rapid recovery of hydrogel based on oligomeric electrolyte, *J. Phys. Chem. B*, 112, 11537-11541 (2008).
- [8] A. P. Nowak, V. Breedveld, L. Pakstis, B. Ozbas, D. J. Pine, D. Pochan and T. J. Deming: Rapidly recovering hydrogel scaffolds from self-assembling diblock copolypeptide amphiphiles, *Nature*, 417, 424-428 (2002).
- [9] S. K. Kundu, M. Yoshida and M. Shibayama: Effect of salt content on the rheological properties of hydrogel based on oligomeric electrolyte, *J. Phys. Chem. B*, 114, 1541-1547 (2010).
- [10] Q. Wang, J. L. Mynar, M. Yoshida, E. Lee, M. Lee, K. Okuro, K. Kinbara and T. Aida: High-water-content mouldable hydrogels by mixing clay and a dendritic molecular binder, *Nature*, 463, 339-343 (2010).
- [11] V. A. Sinani, M. K. Gheith, A. A. Yaroslavov, A. A. Rakhnyanskaya, K. Sun, A. A. Mamedov, J. P. Wicksted and N. A. Kotov: Aqueous dispersions of single-wall and multiwall carbon nanotubes with designed amphiphilic polycations, *J. Am. Chem. Soc.*, 127, 3463-3472 (2005).
- [12] M. Yoshida, Patent No. 2010-143869 (in Japanese).
- [13] Y. Misawa, N. Koumura, H. Matsumoto, N. Tamaoki and M. Yoshida: Hydrogels based on surfactant-free ionene polymers with N,N'-(p-phenylene) dibenzamide linkages, *Macromolecules*, 41, 8841-8846 (2008).
- [14] Y. Matsuzawa, H. Kato, H. Ohyama, D. Nishide, H. Kataura and M. Yoshida: Photoinduced dispersibility tuning of carbon nanotubes by a water-soluble stilbene as a dispersant,

Adv. Mater., 23, 3922-3925 (2011).

- [15] K. Okano, M. Taguchi, M. Fujiki and T. Yamashita: Circularly polarized luminescence of rhodamine B in a supramolecular chiral medium formed by a vortex flow, *Angew. Chem. Int. Ed.*, 52, 12474-12477 (2011).

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Discussions with Reviewers

1 Synthesiology and molecular design

Comment (Hisao Ichijo, Tsukuba Center, Inc.)

In *Synthesiology*, you are required to describe the elemental technologies to realize the research goal, the relationships among the elements, and the process of their integration, to help the succeeding researchers. I think this paper will be valuable to the readers if you follow these points.

Comment (Toshimi Shimizu, Nanotechnology, Materials and Manufacturing, AIST)

The synthesis of chemical substance is based on diverse utilization and combination of various functional groups, and I believe the trial-and-error in molecular design and synthesis methods is the practice of synthesiology. Therefore, to rearrange the descriptions to fit the synthesis as stated in *Synthesiology*, I recommend that you discuss the scheme of molecular design that was done for the goal of achieving higher function and simplified synthesis unseen before in conventional gelators. Also, please show a diagram that breaks down the molecular structure of the gelator by elements, show how the elements of conventional gelators were converted in your research, and indicate why the new elements were added to solve which issues in executing the molecular design.

Answer (Masaru Yoshida)

The point of view of “molecular design and the synthetic approach” = “one form of synthesiology” is very informative. I created diagrams from that perspective and added descriptions to the overall text.

2 Outlet as a chemical reagent

Comment (Toshimi Shimizu)

You present the outlet for new practical use i.e. sales as a chemical reagent. If possible, please state the decisions or standards that the chemical or reagent companies use when

deciding which reagent should be commercialized. Many organic compounds have been synthesized around the world, but not all became reagents. What is the percentage of the synthesized chemical substances that became reagents (how many percentages of synthesized chemical substances become commercialized as reagents), and what is the market scale of the reagent industry? Please provide these figures as reference information.

Answer (Masaru Yoshida)

The person in charge at the reagent company mentioned that the important factors in considering reagents are: 1) things that were not possible become possible (novelty) and 2) things that did not exist before are created (prospect). A chemical substance

with novelty and prospect can be used widely in actual R&Ds as a reagent, and has the potential of generating a market.

For the percentage of chemical substances that become reagents, there are over 65,360,000 chemical substances registered in the database of Chemical Abstracts Service. On the other hand, there are currently 187,000 reagents registered in the reagent database of Sigma-Aldrich Corporation, one of the leading reagent companies in the world. Assuming that about three times this amount is used as actual reagents, the percentage can be calculated as follows: $56.1/6538 = 0.86 \%$. It can certainly be said that only a very limited number of chemical substances become reagents. This information was added to the paper.