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Ph.D. Thesis

Synthesis of Discrete Aliphatic Polyketones and their Functionalization

(脂肪酸族ポリケトンの単分散合成と機能化)

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Chapter 1

General Introduction

1.1. Creating Molecular Structures and Functions

The creation of functional organic molecules is one of the indispensable technologies in science and engineering fields for the realization and development of sustainable societies.¹⁻³ Molecular functions, such as material conversion, luminescence, and separation, are known to be highly dependent on their molecular structures. Such a structure-function relationship is important to be understood for designing rational molecular structures to produce desired molecular functions (**Figure 1-1**). For example, capsule-like hollow molecules, such as fullerene and metal-organic cages, can encapsulate small molecules as guests within their cavities.^{4,5} As another example, planar molecules with large π -conjugation tend to stack on top of each other, providing conductive pathways for electrons/holes.⁶ In more sophisticated biological systems, proteins can selectively interact with specific ligands to control their functions, which is often referred to as a lock-and-key mechanism.⁷ Among the above examples, a key to creating desired molecular functions is the rational design and precise construction of the appropriate molecular structures. Therefore, a universal method for constructing any molecular structure will ultimately enable the production of any desired molecular function. Therefore, the development of synthetic strategies to create desired molecular structures has been a central issue in synthetic organic chemistry.

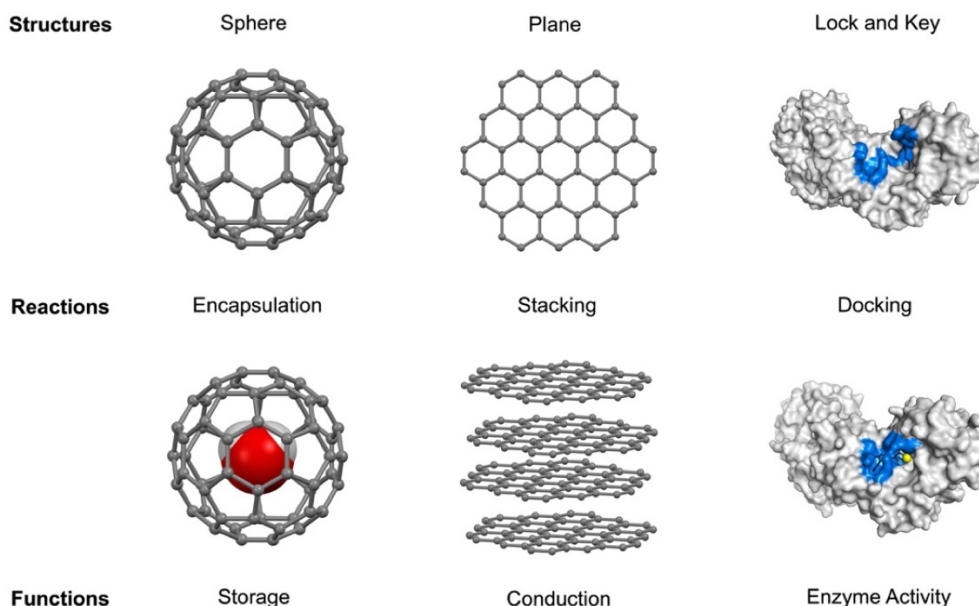


Figure 1-1. Representative examples of the structure-function relationships: (left) encapsulation of small molecules by the spherical structure of fullerene; (middle) conduction property of the stacked graphenes; (right) a lock-and-key relationship of enzymes and substrates (PDB data⁸ : 2E2N and 2E2Q).

As the mainstream of organic synthetic strategies to produce desired molecular structures, rigid molecular components, such as aromatic rings, have been mainly employed (**Figure 1-2a**).^{9,10} Transition metal catalyzed cross-coupling reactions have been developed to forge a covalent bond between rigid aromatic rings to produce various molecular structures, from simple planar structures to complicated three-dimensional architectures.¹¹⁻¹³ The development of cross-coupling reactions enabled to access various molecular structures and explore their structure-derived functions, which have been used and even manufactured as medicines, pesticides, and liquid crystals.¹⁴⁻¹⁶ To construct larger molecular structures, supramolecular interactions such as hydrogen bonds between rigid planar components have also been exploited (**Figure 1-2b**).^{17,18} By using the molecular assembly of multiple components in a programmed manner, much larger molecular architectures have been prepared that exhibit unique functions such as supramolecular catalysis, self-healing properties, and gel formation.¹⁹⁻²¹ In a similar fashion, metal ion coordination has also been used to create large molecular structures that display unique functions, exemplified by inclusion of guest molecules/ions, gas absorption, catalysis, and many related examples (**Figure 1-2c**).²²⁻²⁴ Among these synthetic strategies, a rigid component has been mainly employed to create versatile molecular structures and exert molecular functions.

As an alternative synthetic strategy, the use of flexible components to develop various types of molecular structures and functions can be considered, although this research topic is still immature compared to that of rigid components. Compared to the synthetic methodologies using rigid components, a flexible molecular chain is advantageous for shaping curved, woven, or other complicated structures. As a prominent example in nature, flexible peptide chains composed of amino acids are folded by non-covalent interactions to form highly ordered structures of proteins (**Figure 1-3a**).²⁵ However, such a sophisticated control of flexible chains to form protein-like giant yet well-ordered structures is still a difficult task in the realm of current synthetic organic chemistry due to their extraordinary complexity in selective chain folding. In an artificial system, a simple hydrocarbon chain, typified by alkanes, can induce numerous conformations such as bent, folded, or coiled conformations by rotating their C–C single bonds without increasing severe strain energies (**Figure 1-3b**). However, the induction and fixation of the desired conformation of a simple hydrocarbon chain are usually problematic because the loss of the degree of freedom of the flexible carbon chain usually causes a significant loss of entropy. In addition, the lack of effective interactions to compensate for the large entropy loss by enthalpy gains also hampers keeping the induced conformations.

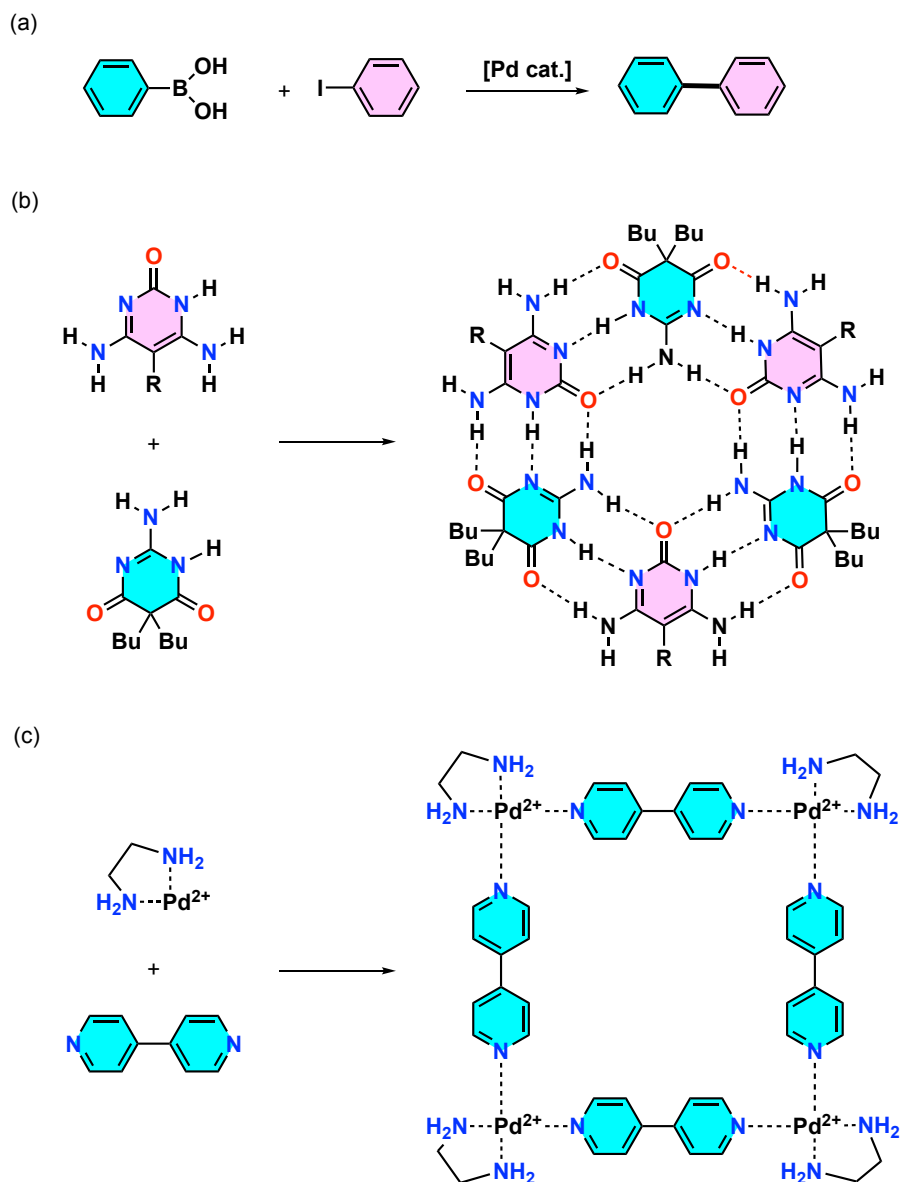


Figure 1-2. The synthetic strategies based on rigid components: (a) cross-coupling reactions, (b) molecular assemblies by supramolecular interactions, (c) metal ion complexations between ligands and metal ions.

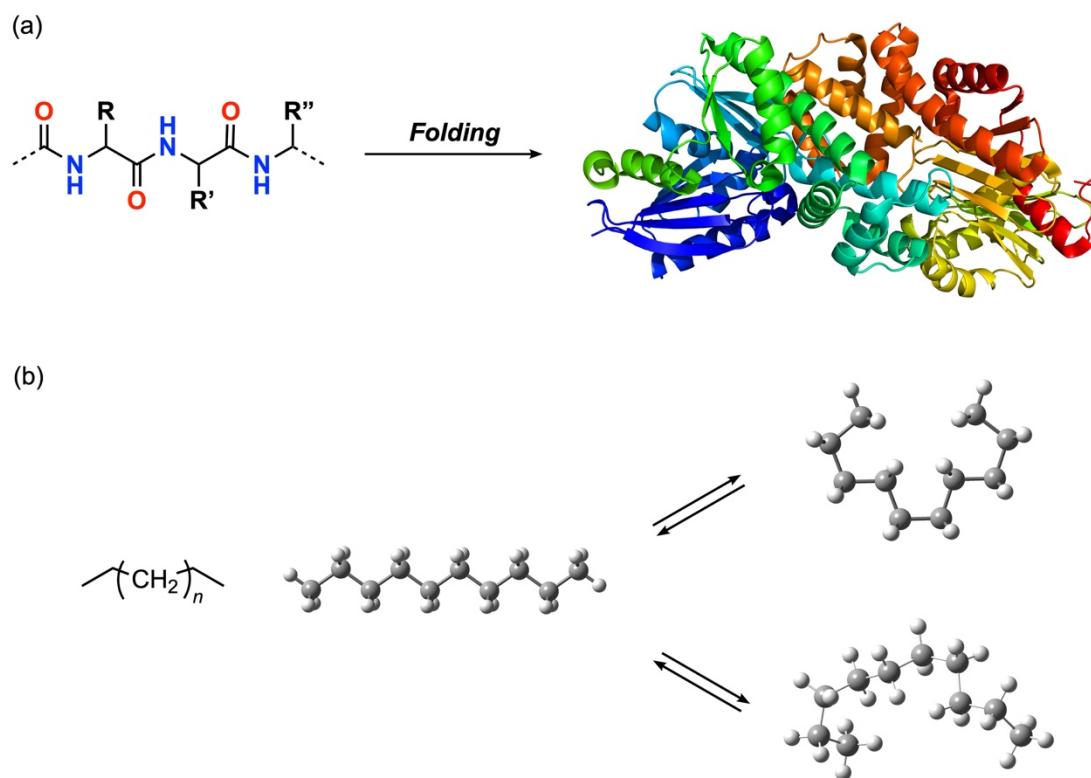


Figure 1-3. The synthetic strategies based on flexible molecular chains: (a) a folding of peptide chain into protein⁸; (b) various conformations of a simple alkane chain.

1.2. Aliphatic Polyketone as a Molecular Chain for Creating Various Structures and Functions

In an acetate-malonate biosynthetic pathway, a linear polyketide intermediate, namely an aliphatic polyketone, has been utilized as a common intermediate to create various molecular structures of secondary metabolites and structure-based biological activities, represented by Benzopyrenomycin, Enterocin, and Kendomycin as antitumor and antibiotic properties. (Figure 1-4).²⁶

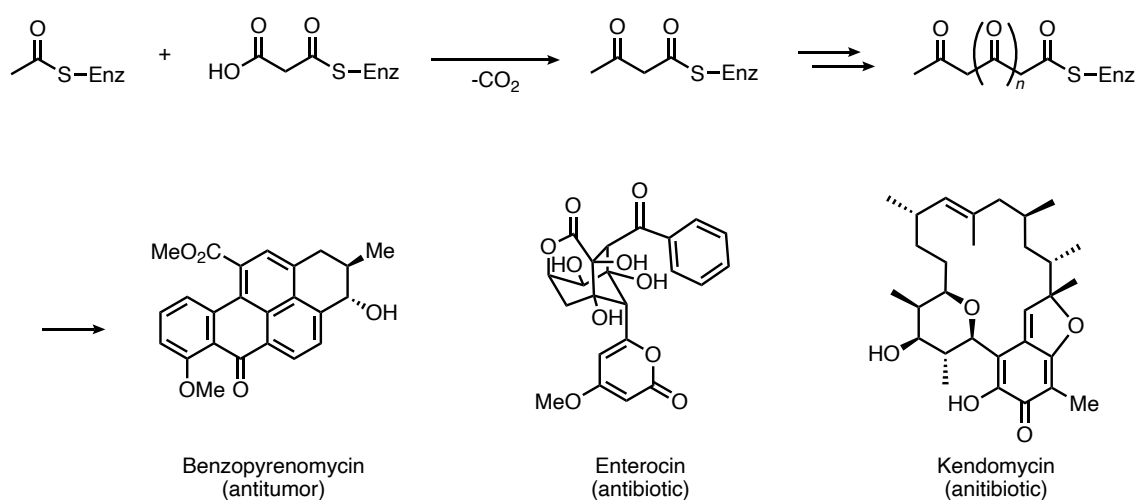


Figure 1-4. Representative acetate-malonate biosynthetic pathways for the generation of secondary metabolites of various structures from a linear polyketide intermediate.

The aliphatic polyketones can be characterized by their conformationally flexible aliphatic chains and reactivities of ketone-related reactions at multiple carbonyl groups (Figure 1-5a,b). In the biosynthetic pathways of the polyketide metabolites, the chain-length elongation and conformations of the polyketones were ingeniously controlled by enzymes, and subsequent intramolecular condensation reactions furnished diverse molecular structures (Figure 1-5c). The synergy of the conformational flexibility of the aliphatic chains and the reactions at multiple carbonyl groups enabled the induction and fixation of the desired conformations and molecular structures.

Therefore, the aliphatic polyketones also seem attractive and flexible components for organic chemists as a building block to produce versatile molecular structures and functions by ‘rope-shaping’ like synthetic strategies. However, the isolation of the linear polyketone intermediate generated in the natural biosynthetic pathways has not been reported so far, presumably due to their innate reactivities. Hence, the synthesis of natural-

type aliphatic polyketones has been attempted to investigate their intrinsic properties for chemical transformations, although many problems in their handling have been discovered during their attempts.

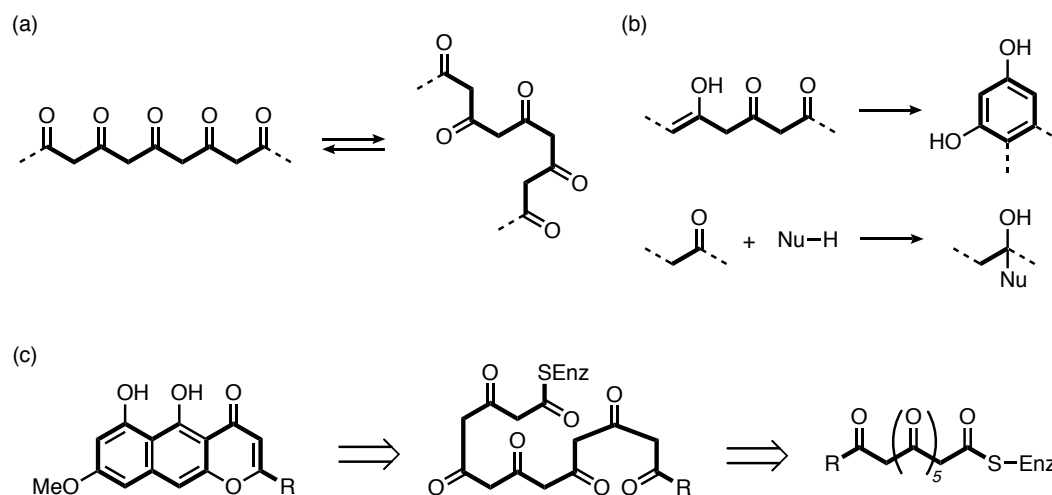


Figure 1-5. (a,b) Key features of aliphatic polyketones such as conformational flexibility and reactivity at carbonyl groups; (c) Proposed retrosynthetic analysis of the folding mode of the polyketone intermediate for the biosynthesis of Rubrofusarin.

1.3. Problems in Handling Natural-Type Aliphatic Polyketones

Since the biosynthetic pathways of the secondary metabolites from aliphatic polyketones were formulated by Birch and Donovan in 1953,²⁷ considerable efforts have been dedicated to chemical syntheses to obtain the natural-type polyketones by organic synthetic methods to produce mainly polycyclic aromatic products as well as natural polyketide syntheses.²⁸⁻³⁰ The reported synthetic routes for the natural-type polyketones can be mainly classified into two directions; (i) sequential reduction and ozonolysis of aromatic compounds and (ii) Claisen-type condensation reactions of oligoketo acids/esters as mimicking the enzymatic reactions in the biosynthesis.

In 1963, Birch and co-workers demonstrated a noble synthetic route for the preparation of linear penta- β -carbonyl derivative **2** by the ozonolysis of cyclic alkene **1** (**Figure 1-6**).³¹ In this synthetic route, aromatic compounds were recognized as synthons for 1,3-diketone units based on the reduction of aromatic compounds (i.e. Birch reduction) and subsequent ozonolysis reactions of dihydro aromatic counterparts. However, the direct synthesis of tetraketone **4** from tetraene **3** resulted in producing self-condensed products due to their innate reactivities. Although the obtained polyketones were not fully characterized due to their labile stabilities for the isolation, similar synthetic routes were later employed by White and Kirkemo,³² and Bringmann^{33,34} to produce linear poly- β -carbonyl chains upon the same concept.

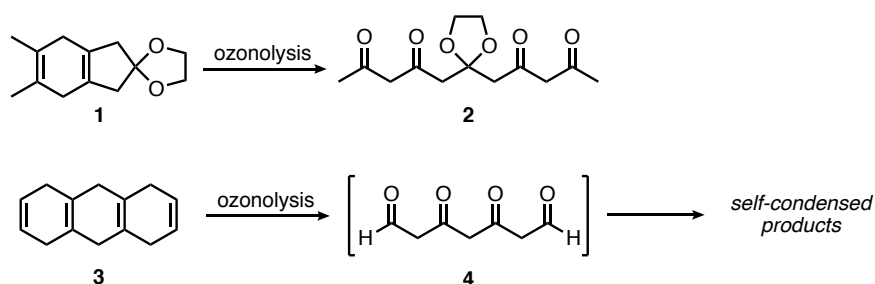


Figure 1-6. Synthetic schemes of β -polyketones by ozonolysis.

As a more direct synthetic approach to poly- β -carbonyl chains, the bioinspired Claisen-type condensation reactions of oligoketo acids/esters have also been investigated. As a pioneering work, Harris and co-workers reported the synthesis of aliphatic oligoketones up to octaketones by two-fold acylation reactions of two equivalents of ethyl benzoylacetate monoanion with polyanion species of oligoketones using *n*-butyllithium to afford hexaketone **5**, heptaketone **6**, and octaketone **7** in 40, 15, and 3% yields, respectively (**Figure 1-7**).³⁵

In their synthetic methods, the chain elongation was enabled by harnessing the differentiated reactivities of the terminal and internal positioned anions, where only the terminal anions reacted with monoanionic species while anions at internal α -carbons were virtually protected from nucleophilic attack by monoanionic species.

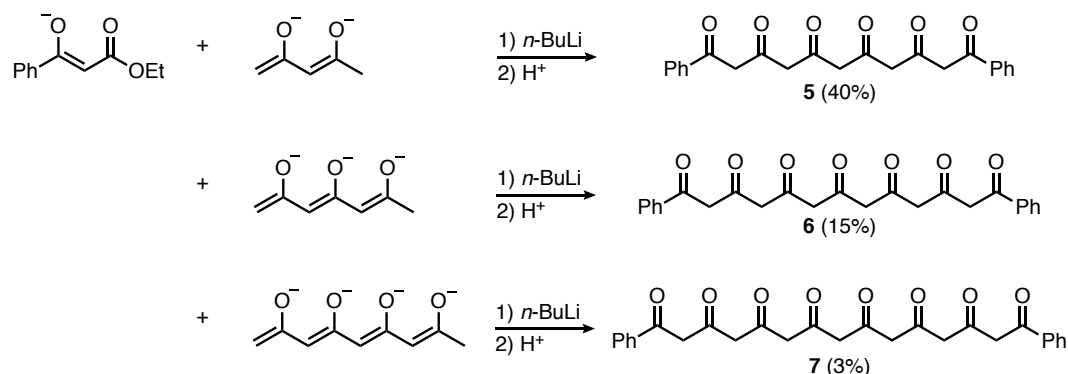
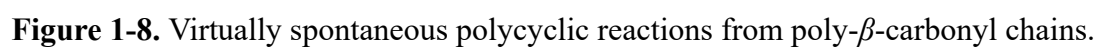


Figure 1-7. Two-fold condensation reactions to generate poly- β -carbonyl chains **5-7**.

However, in the syntheses of **5-7**, harsh reaction conditions to generate the multi-anionic species were required. On top of that, the natural-type polyketone had significant drawbacks in complicated keto-enol tautomerism and virtually spontaneous intramolecular cyclization reactions even under near-neutral conditions (**Figure 1-8**). As the number of carbonyl groups on the aliphatic chain increased, the number of possible intramolecular cyclization pathways remarkably increased, leading to a dramatic increase in uncontrolled intramolecular cyclization reactions. Therefore, further chain length elongation, isolation, and functionalization of longer poly- β -carbonyl chains became difficult as the number of repeating units of aliphatic polyketones increased.^{36,37}



1.4. Problems in Handling Artificial Aliphatic Polyketones

In section 1.3, the drawbacks of natural-type polyketones composed of 1,3-diketone repeating units were described, namely spontaneous intramolecular cyclization and complicated keto-enol tautomerism for isolation, manipulation, and further derivatization. Therefore, aliphatic polyketones with different repeating units have also been surveyed as a potential artificial molecular chain for the generation of diverse molecular structures and functions. Dicarbonyl compounds exhibit unique reactivities and properties upon the proximity of two carbonyl groups, such as a 1,2-, 1,3-, and 1,4-diketone units.³⁸ Accordingly, polyketone oligomers are expected to exhibit totally different stability and reactivity based on their differences in the repeating units.

Vicinal aliphatic polyketones, which are composed of the 1,2-diketone repeating unit, have been extensively studied since the first synthetic report of diphenyl triketone in 1890.³⁹ Reflecting their attention in organic chemistry, the enormous synthetic development, property, and derivatization of vicinal aliphatic polyketones over a century were summarized in excellent reviews.⁴⁰⁻⁴² The representative synthesis of vicinal aliphatic polyketones is illustrated in **Figure 1-9**.

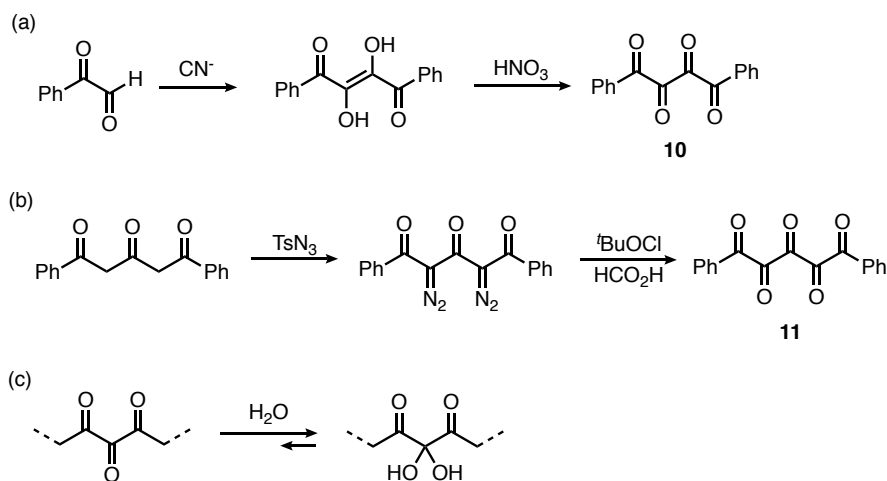


Figure 1-9. Representative synthesis of vicinal aliphatic (a) tetraketone **10** and (b) pentaketone **11**; (c) hydration reactions of 1,2,3-triketone unit.

Vicinal triketones were typically synthesized from β -dicarbonyl compounds through functional group transformations at the internal α -carbon position.⁴⁰⁻⁴² However, for vicinal tetraketones and pentaketones, the synthetic methods were severely limited compared to triketones. Vicinal tetraketones were synthesized by benzoin condensation

reactions of α -ketoaldehydes with cyanide ions and subsequent oxidation reactions (**Figure 1-9a**).⁴³⁻⁴⁶ The preparation of vicinal pentaketones was reported only from 2,4-bis(diazo)-1,3,5-triketone precursor (**Figure 1-9b**).^{47,48} Further longer vicinal polyketones have not been reported until now. The characteristics of the vicinal polyketones were dictated by their high reactivity toward nucleophiles derived from the strong electrophilicity of carbonyl carbon atoms adjacent to the other two carbonyl groups. Therefore, the strikingly activated carbonyl groups were readily hydrated even at room temperature (**Figure 1-9c**).⁴⁹ This extremely reactive nature of the vicinal polyketones hampered further chain length elongation and functionalization.

Aliphatic polyketone **12** bearing 1,4-diketone repeating units has been mainly prepared as a polymer, prepared by copolymerization of ethylene and carbon monoxide, firstly reported in 1941 (**Figure 1-10a**).⁵⁰ With the development of transition metal catalysts for the efficient copolymerization reactions,⁵¹⁻⁵⁴ polyketone polymer **12** are now widely utilized as engineering plastics.⁵⁵ Moreover, upon the Paal-Knorr type heteroaromatic ring formation at 1,4-diketone units, various post-functionalizations, such as cross-linking of copolymers, were achieved.⁵⁶ The key to their widespread utilization was their relative stability compared to other polyketones bearing 1,2- or 1,3-diketone repeating units. However, the artificial polyketone **12** was obtained as a polymer, which is not suitable for the precise synthesis of molecular structures and functions. In addition, the synthesis of discrete counterparts by polymerization reactions is nearly impossible because of the difficulties in accurate control of the degree of polymerization.

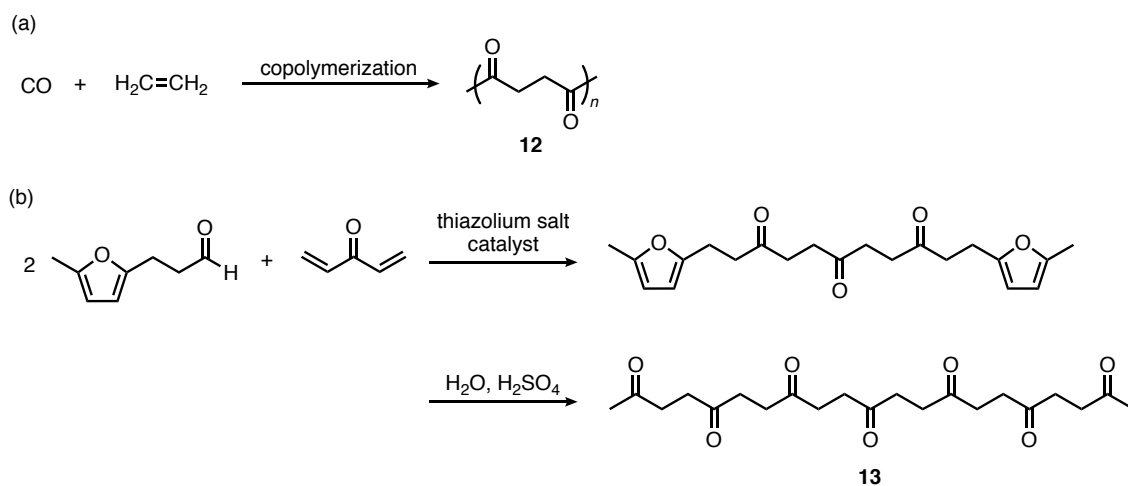


Figure 1-10. Synthesis of (a) copolymer **12** bearing 1,4-diketone repeating unit and (b) heptaketone **13**.

The discrete oligomers of aliphatic polyketones composed of 1,4-diketone repeating units have also been synthesized by stepwise reactions. Stetter and co-workers have reported the synthesis of discrete heptaketone **13** through the addition of aldehydes to vinyl ketones by Stetter reaction and the subsequent furan-ring opening reactions (**Figure 1-10b**).⁵⁷ Alder, Gordon, and their co-workers have also reported the synthesis of hexaketone and heptaketone, respectively, using a similar synthetic strategy.⁵⁸ In their synthetic routes, the furan ring was treated as a synthon for 1,4-diketone unit. However, these reported synthetic protocols were sporadic, and systematic approaches to prepare a library of polyketone chains of different lengths were still underdeveloped.

Considering the natural-type and artificial polyketones described in Sections 1.3 and 1.4, the development of more easy-to-handle, precise, yet still reactive new aliphatic polyketones are required. To overcome the discovered drawbacks of the reported polyketones, the newly designed polyketones are necessary for using aliphatic polyketones as a flexible component.

1.5. Overview of This Thesis

The objective of this thesis was to utilize an aliphatic polyketone as a molecular chain to construct versatile molecular structures and exploit their structure-derived functions. In this context, the author has firstly attempted to design and synthesize flexible, stable, and discrete aliphatic polyketones as a molecular chain. Secondly, versatile molecular structures were formed using the newly designed aliphatic polyketone chains, such as a rod, a coordination network, and a helix, for the development of structure-derived functional molecular materials, such as organic chromophores, metal ion adsorbents, and thermochromic luminescent complexes.

In Chapter 2, the design, synthesis, and structural analysis of discrete aliphatic polyketones were described. Aliphatic polyketones composed of 3,3-dimethylpentane-2,4-dione as the repeating unit were designed to overcome the critical drawbacks of natural-type polyketones with maintaining their attractive structural flexibility of the aliphatic carbon chain and reactivities at multiple carbonyl groups. The stepwise synthesis of discrete polyketones was achieved by repeating terminal-selective silylation and silver(I) oxide mediated coupling reactions. The resulting polyketones are stable colorless solids, and all carbonyl groups were present in the keto-form in contrast to the natural-type polyketones. The crystallographic analyses revealed that the polyketone oligomers longer than 5 mer adopted similar helical conformations regardless of their chain length, while shorter polyketones (2-4 mers) exhibited their own unique conformations.

In Chapter 3, the development of rigid rod-like structures from structurally flexible aliphatic polyketones was demonstrated. The rigid rod-like π -conjugated polyimines were furnished by isopyrazole ring formation at 1,3-diketone units and subsequent oxidation of bridging ethylene units. The π -conjugated polyimines displayed a bathochromic shift in the absorption spectra upon the chain length elongation, implying effective π -conjugation over the carbon chain with circumventing the quaternary carbon atoms. The similar transformation of the polydisperse polyketone polymer furnished virtually insoluble π -conjugated polyimines that exhibited a metal ion adsorption function in solution through multiple iminic nitrogen atoms at their interfaces.

In Chapter 4, large molecular assemblies were constructed by a metal ion coordination of polyimine ligands derivatized from aliphatic polyketones. Reflecting their structural flexibility and multidentate coordination modes, diverse large molecular assemblies were formed such as double-helix and mesh-like coordination structures. In particular, the complexation reaction between polyimine ligands and copper(I) iodide afforded a

luminescent two-dimensional network structure, including Cu₄I₄ tetranuclear clusters, which showed thermochromic behavior in the solid-state luminescence.

In Chapter 5, a conformational control of flexible aliphatic polyketones by a supramolecular complexation was described. Although structurally flexible aliphatic chains of aliphatic polyketones can take numerous conformations, their conformations were mechanically regulated to be linear by a rotaxane formation with pillar[5]arene, which was unambiguously determined from single crystal X-ray structures. Upon further BF₂ complexation at terminal 1,3-diketone units of polyketones, the induced conformation was locked even in the solution. Using this conformational restriction, the solvatochromic behavior of the polyketone-derived alkyl-bridged flexible chromophore dyad resulting from the folded conformation was completely suppressed.

In Chapter 6, the summary and future perspectives of this thesis were described. The polyketones developed in this thesis research have been investigated as prototypical functional materials for solid polymer electrolytes and molecular modifiers for microfluidic devices for rapid cancer diagnosis. These results have apparently displayed that aliphatic polyketones developed in the thesis research have the potential as a molecular scaffold of molecular functional materials.

1.6. References

- [1] M.-M. Titirici, R. J. White, N. Brun, V. L. Budarin, D. S. Su, F. del Monte, J. H. Clark, M. J. MacLachlan, *Chem. Soc. Rev.* **2015**, *44*, 250–290.
- [2] Z. Song, H. Zhou, *Energy Environ Sci.* **2013**, *6*, 2280–2301.
- [3] X. Gong, G. Liu, Y. Li, D. Y. W. Yu, W. Y. Teoh, *Chem. Mat.* **2016**, *28*, 8082–8118.
- [4] K. Kurotobi, Y. Murata, *Science*, **2011**, *333*, 615–616.
- [5] M. Murata, Y. Murata, K. Komatsu, *Chem. Commun.*, **2008**, 6083–6094.
- [6] K. S. Kim, Y. Zhao, H. Jang, S. Y. Lee, J. M. Kim, K. S. Kim, J.-H. Ahn, P. Kim, J.-Y. Choi, B. H. Hong, *Nature*, **2009**, *457*, 706–710.
- [7] E. Fisher, *Ber. Dtsch. Chem. Ges.*, **1894**, *27*, 2985–2993.
- [8] H. Nishimasu, S. Fushinobu, H. Shoun, T. Wakagi, *J. Biol. Chem.*, **2007**, *282*, 9923–9931.
- [9] J. P. Mathias and J. F. Stoddart, *Chem. Soc. Rev.*, **1992**, *21*, 217–225.
- [10] C. E. Schafmeister, Z. Z. Brown, S. Gupta, *Acc. Chem. Res.*, **2008**, *41*, 1387–1398.
- [11] Y. Segawa, A. Yagi, K. Matsui, K. Itami, *Angew. Chem. Int. Ed.*, **2016**, *55*, 5136–5158.
- [12] Y. Segawa, D. R. Levine, K. Itami, *Acc. Chem. Res.*, **2019**, *52*, 2760–2767.
- [13] H. Omachi, Y. Segawa, K. Itami, *Acc. Chem. Res.*, **2012**, *45*, 1378–1389.
- [14] A. Biffis, P. Centomo, A. Del Zotto, M. Zecca, *Chem. Rev.*, **2018**, *118*, 2249–2295.
- [15] S. Kotha, K. Lahli, D. Kashinath, *Tetrahedron Lett.* **2002**, *58*, 9633–9695.
- [16] P. Devender, R.-Y. Qu, W.-M. Kang, B. He, G.-F. Yang, *J. Agric. Food. Chem.* **2018**, *66*, 8914–8934.
- [17] J. M. Lehn, M. Mascal, A. DeCian, J. Fischer, *J. Chem. Soc. Perkin Trans 2.* **1992**, 461–467.
- [18] L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem. Int. Ed.* **2001**, *40*, 2382–2426.
- [19] M. Raunal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1660–1733.
- [20] L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2015**, *115*, 7196–7239.
- [21] A. J. Savyasachi, O. Kotova, S. Shanmugaraju, S. J. Bradberry, G. M. Ó' Máille, T. Gunnlaugsson, *Chem*, **2017**, *3*, 764–811.
- [22] H. Furukawa, K. E. Cordova, M. O'Keeffe, O. M. Yaghi, *Science*, **2013**, *341*, 1230444.
- [23] J.-R. Li, R. J. Kuppler, H.-C. Zhou, *Chem. Soc. Rev.* **2009**, *38*, 1477–1504.

- [24] J. Y. Lee, O. K. Farha, J. Roberts, K. A. Scheidt, S. T. Nguyen, J. T. Hupp, *Chem. Soc. Rev.* **2009**, 38, 1450–1459.
- [25] J. Venkatraman, S. C. Shankaramma, P. Balaram, *Chem. Rev.* **2001**, 101, 3131–3152.
- [26] C. Hertweck, *Angew. Chem. Int. Ed.*, **2009**, 48, 4688–4716.
- [27] A. J. Birch and F. W. Donovan, *Aust. J. Chem.*, **1953**, 6, 360–368.
- [28] T. M. Harris, C. M. Harris, *Tetrahedron*, **1977**, 33, 2159–2185.
- [29] T. M. Harris, C. M. Harris, *Pure Appl. Chem.* **1986**, 58, 283–294.
- [30] L. Kersten, K. Harms, G. Hilt, *J. Org. Chem.*, **2014**, 79, 11661–11673.
- [31] A. J. Birch, P. Fitton, D. C. C. Smith, D. E. Steere, A. R. Stelfox, *J. Chem. Soc.*, **1963**, 2209–2215.
- [32] C. L. Kirkemo and J. D. White, *J. Org. Chem.*, **1985**, 50, 1316–1319.
- [33] G. Bringmann *Angew. Chem., Int. Ed. Engl.*, **1982**, 21, 200–201.
- [34] G. Bringmann *Liebigs Ann. Chem.*, **1985**, 2105–2115.
- [35] P. J. Wittek and T. M. Harris, *J. Am. Chem. Soc.*, **1973**, 95, 6865–6867.
- [36] V. C. Fäseke, F. C. Raps, C. Sparr, *Angew. Chem. Int. Ed.*, **2020**, 59, 6975–6983.
- [37] X. Wu and C. Sparr, *Trends Chem.*, **2022**, 4, 367–370.
- [38] Y. Inokuma, T. Yonedda, Y. Ide, S. Yoshioka, *Chem. Commun*, **2020**, 56, 9079–9093.
- [39] R. de Neufville and H. Pechmann, *Ber. Dtsch. Chem. Ges.*, **1890**, 23, 3375–3387.
- [40] M. B. Rubin, *Chem. Rev.*, **1975**, 75, 177–202.
- [41] M. B. Rubin and R. Gleiter, *Chem. Rev.*, **2000**, 100, 1121–1164.
- [42] H. H. Wasserman and J. Parr, *Acc. Chem. Res.*, **2004**, 37, 687–701.
- [43] H. G. Söderbaum *Ber. Dtsch. Chem. Ges.*, **1891**, 24, 1381–1388.
- [44] H. G. Söderbaum *Ber. Dtsch. Chem. Ges.*, **1894**, 27, 658–663.
- [45] P. W. Abenius and H. G. Söderbaum, *Ber. Dtsch. Chem. Ges.*, **1892**, 25, 3468–3476.
- [46] M. Peter, R. Gleiter, F. Rominger and T. Oeser, *Eur. J. Org. Chem.*, **2004**, 3212–3220.
- [47] R. Gleiter, G. Krennrich and M. Langer, *Angew. Chem., Int. Ed. Engl.*, **1986**, 25, 999.
- [48] R. Gleiter, E. Litterst, T. Oeser and H. Irngartinger, *Angew. Chem., Int. Ed. Engl.*, **1990**, 29, 1048–1050.
- [49] C. W. Shoppee, *J. Chem. Soc.* **1936**, 269–274.
- [50] F. Ballauf, O. Bayer and L. Leichmann, *Ger. Pat.*, **1941**, 863, 711.
- [51] A. Sen, *Acc. Chem. Res.*, **1993**, 26, 303–310.
- [52] E. Drent and P. H. M. Budzelaar, *Chem. Rev.*, **1996**, 96, 663–682.
- [53] K. Nozaki and T. Hiyama, *J. Organomet. Chem.*, **1999**, 576, 248–253.
- [54] C. Bianchi and A. Meli, *Coord. Chem. Rev.*, **2002**, 225, 35–66.

- [55] Y. Yang, S.-Y. Li, R.-Y. Bao, Z.-Y. Liu, M.-B. Yang, C.-B. Tan and W. Yang, *Polym. Int.*, **2018**, *67*, 1478–1487.
- [56] Y. Zhang, A. A. Broekhuis and F. Picchioni, *Macromolecules*, **2009**, *42*, 1906–1912
- [57] H. Stetter, W. Basse, H. Kuhlmann, A. Landscheidt and W. Schlenker, *Chem. Ber.*, **1977**, *110*, 1007–1019.
- [58] R. W. Alder, N. P. Hyland, J. C. Jeffery and T. Riis-Johannessen, D. Jason Riley, *Org. Biomol. Chem.*, **2009**, *7*, 2704–2715.

Chapter 2

Design, Synthesis, and Structural Analysis of Discrete Polyketones

Abstract

The design, synthesis, and structural analysis of discrete aliphatic polyketones composed of 3,3-dimethylpentane-2,4-dione as a repeating unit were carried out. The alternating 1,3- and 1,4-diketone repeating unit suppressed intramolecular cyclization and keto-enol tautomerism, which were the major drawbacks in the natural-type polyketones. The stepwise synthesis of the discrete aliphatic polyketones was achieved by repeating terminal-selective silylation and subsequent silver oxide(I) mediated coupling reactions up to icosamer (20 mer). The resulting discrete aliphatic polyketones were stable and no keto-enol tautomerization was observed even in 20 mer. Crystallographic analyses of the discrete aliphatic polyketones revealed that polyketones longer than pentamer (5 mer) adopted similar helical conformations independent of their chain lengths while the conformations of the short polyketones (2-4 mer) were diverse, reflecting their structural flexibilities.

2.1. Introduction

The structural diversity of the natural polyketide metabolites was generated from aliphatic polyketones as a common intermediate described in section 1.2.¹ In the biosynthetic steps, the chain lengths of aliphatic polyketones were sophisticatedly controlled by enzymes because the chain length was a critical factor to generate desired carbon skeletons of aromatic products with chain folding and reactions at carbonyl groups. The produced metabolites indeed exhibited structure-derived biological activities. Similarly, the chain length control in the chemical synthesis of aliphatic polyketones is an important factor in terms of the structure constructions and their functionalization. The synthesis of discrete aliphatic polyketones will lead to the analysis of exact structure-function correlations. However, the natural-type polyketone has severe drawbacks in complicated keto-enol tautomerism and spontaneous intramolecular cyclization for synthesis, isolation, and further functionalization.

In this context, the author has focused on the aliphatic polyketones bearing alternating 1,3- and 1,4-diketone repeating unit as an alternative to the natural-type polyketones composed of 1,3-diketone repeating unit (**Figure 2-1**).² This alternating repeating unit is advantageous for the suppression of spontaneous intramolecular cyclization. Furthermore, the 3-position of 1,3-diketone unit was doubly substituted by the methyl groups to prevent complicated keto-enol tautomerism.

In this work, the synthesis of discrete aliphatic polyketones composed of 3,3-dimethylpentane-2,4-dione as a monomer unit was achieved up to icosamer (20 mer), and the structural analysis of discrete polyketones was performed. Discrete aliphatic polyketones were prepared in a stepwise fashion by repeating terminal selective silylation and silver(I) oxide mediated homo- or cross-coupling reactions. The monodisperse character of the discrete aliphatic polyketones was unambiguously confirmed by NMR, MALDI-TOF mass, and HPLC measurements. As a unique structural property of discrete aliphatic polyketones, polyketones longer than pentamer (5 mer) exhibited common helical conformations regardless of their chain length, while short polyketones (2-4 mer) showed totally different conformations upon the chain length elongation.

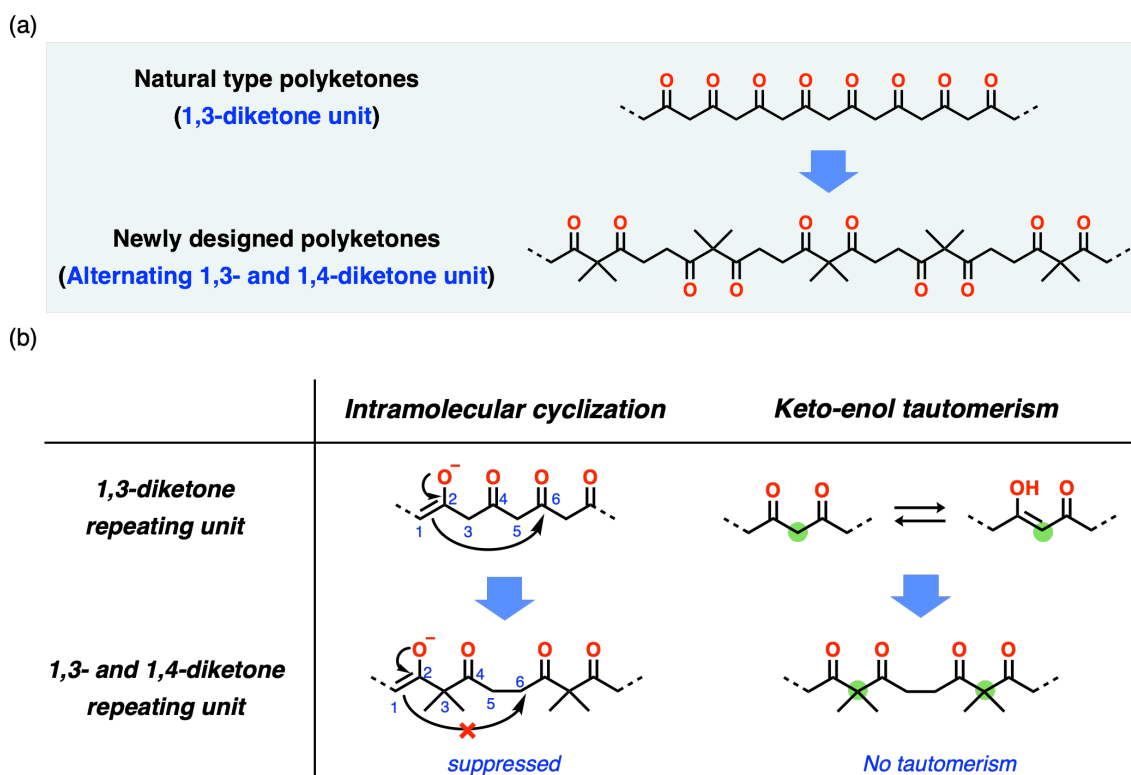
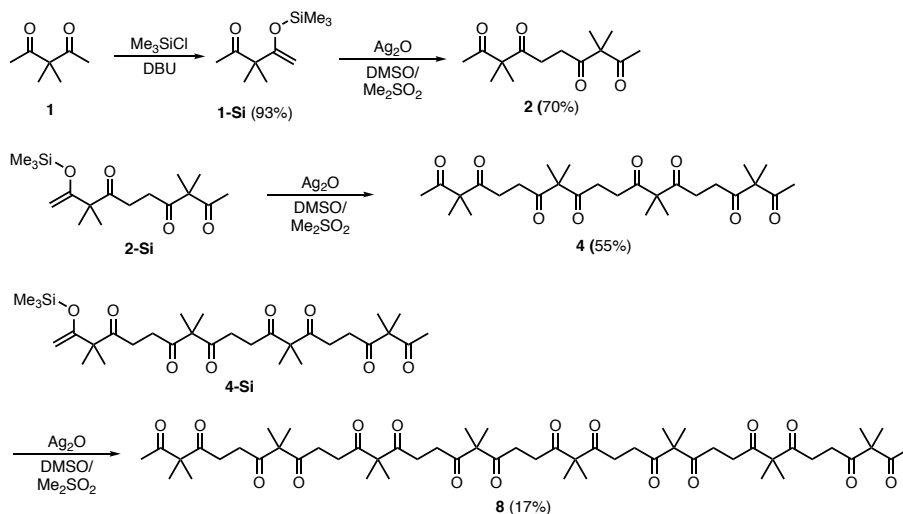


Figure 2-1. (a) Design of new polyketone chains compared with natural type polyketones; (b) comparison of two major drawbacks in natural-type polyketones.

2.2. Synthesis of Discrete Aliphatic Polyketones

As a prior synthetic route for the discrete polyketone oligomers, Uesaka *et al.* have employed a stepwise homo-coupling strategy for the oligomers in multiples of two up to octamer **8** (Scheme 2-1).² In this synthetic route, the terminal selective mono-silylation of oligomers and subsequent silver(I) oxide mediated homo-coupling reaction enabled the stepwise synthesis of discrete oligomers using 3,3-dimethylpentane-2,4-dione (**1**) as a monomer. In this work, discrete aliphatic polyketones up to decamer (10 mer) were thoroughly prepared by combining homo- and cross-coupling strategies to discriminate the synthesis of odd- or even-number oligomers. For the synthesis of even-number oligomers, a homo-coupling strategy was employed, whereas the odd-number oligomers were synthesized by a cross-coupling strategy.

The stepwise synthesis of discrete polyketone oligomers was started from the silylation of monomer **1** according to the previous work.² Monomer **1** was differently transformed into the mono- and bis-silylated products **1-Si** and **1-Si₂**.^{2,3} For the synthesis of mono-silylated monomer **1-Si**, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was used to give mono-silylated product **1-Si** selectively in 93% yield. Dimer **2** was prepared from mono-silylated monomer **1-Si** by a silver oxide(I) mediated homo-coupling reaction in 70% yield. Silylation of dimer **2** also proceeded at the only terminal positions of the carbonyl groups on dimer **2** to give silyl enol ethers **2-Si** and **2-Si₂** in 42 and 26% yields, respectively. Tetramer **4** was similarly prepared by the homo-coupling reaction of silyl enol ether **2-Si** in 55% yield. Similar to the silylation of dimer **2**, silyl enol ethers of **4-Si** and **4-Si₂** were obtained in 26 and 41% yields, respectively. Octamer **8** was afforded by the homo-coupling reaction of **4-Si** in 17% yield.



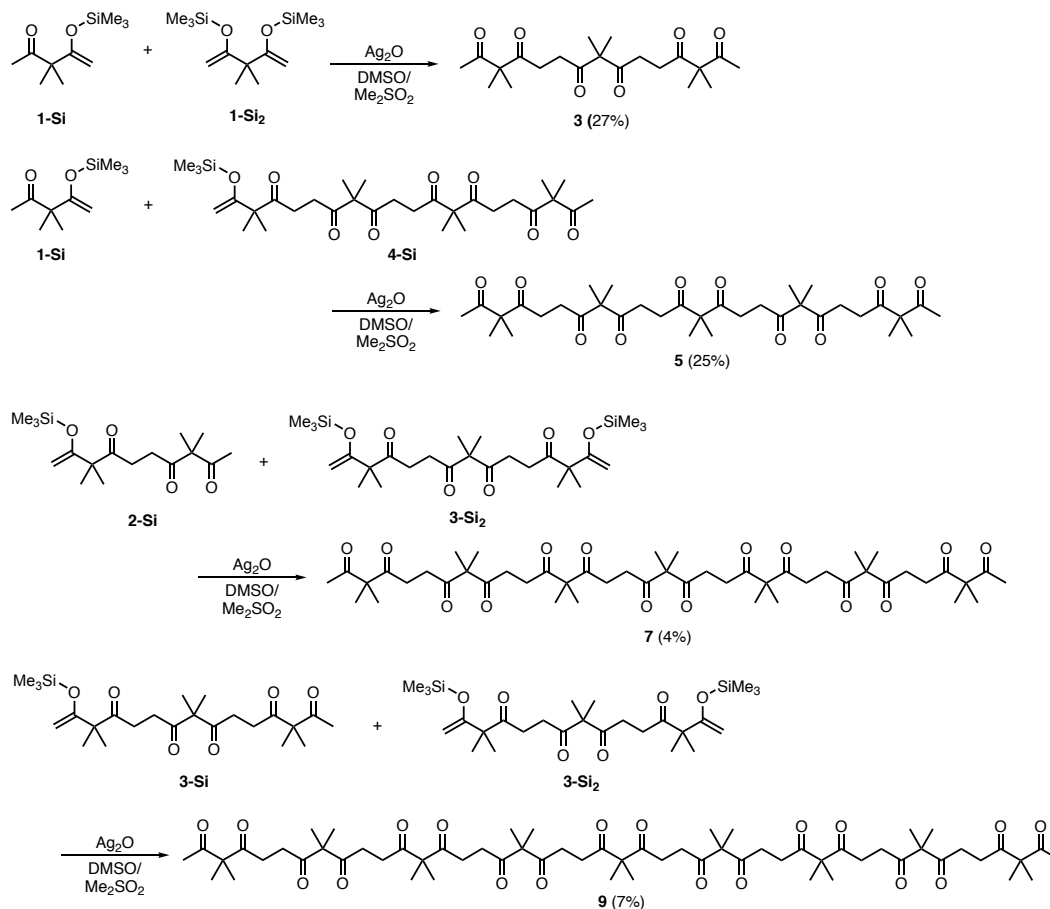
Scheme 2-1. Stepwise synthesis of discrete polyketone oligomers up to octamer **8**.²

For the synthesis of the odd-number oligomers, a cross-coupling strategy was attempted (**Scheme 2-2a**). Trimer **3** was synthesized by the cross-coupling reaction between an excess amount (5 equiv.) of mono-silylated monomer **1-Si** and bis-silylated monomer **1-Si₂** in 27% yield based on **1-Si₂** along with the formation of dimer **2**, tetramer **4**, and further longer oligomers. Trimer **3** was further silylated under the similar reaction conditions of dimer **2** and tetramer **4** to give silylated products **3-Si** and **3-Si₂** in 35 and 12% yields, respectively, for the synthesis of further longer even- and odd-number oligomers. Pentamer **5** was synthesized by the cross-coupling reaction between silyl enol ethers of **1-Si** and **4-Si** in 25% yield after a preparative size exclusion chromatography (SEC) separation. Heptamer **7** was isolated by the cross-coupling reaction between mono-silyl enol ether **2-Si** and bis-silyl enol ether **3-Si** in 4% yield based on **3-Si₂** after the SEC separation from a mixture of oligomer products **2**, **3**, **5**, desired product **7**, and higher oligomers. Nonamer **9** was prepared in a similar manner from **3-Si** and **3-Si₂** in 9% yield based on **3-Si₂**. Hexamer **6** and decamer **10** were prepared from silylated trimer **3** and pentamer **5**, which were not accessible in the previous report (**Scheme 2-2b**).² Hexamer **6** was prepared by a homo-coupling reaction of **3-Si** in 32% yield. Decamer **10** was prepared by the homo-coupling reaction of **5-Si** in 24% yield, which was synthesized from pentamer **5** in 36% yield.

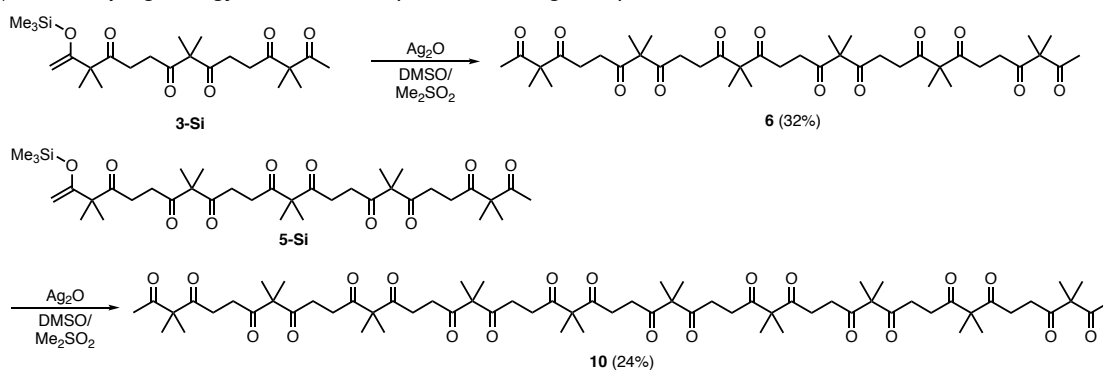
The discrete polyketone oligomers up to decamer **10** were exhaustively synthesized in a stepwise manner by repeating terminal selective silylations followed by homo- and cross-coupling reactions. However, further elongation of the polyketone chains was considered to be difficult due to two possible main issues; the terminal selectivity in the silylation reactions and the low reactivity of longer polyketone chains in the coupling reactions. Instead, the author has attempted to synthesize further longer polyketones by an oligomerization reaction of the bis-silylated oligomer **4-Si₂** followed by SEC separation (**Scheme 2-3**).

The oligomerization reaction was performed from bis-silylated tetramer **4-Si₂** under similar reaction conditions in the stepwise synthesis of discrete oligomers. The resulting crude mixture of oligomers was separated by a preparative recycling SEC to give octamer **8**, dodecamer **11**, hexadecamer **12**, and icosamer **13** in 9, 7, 5, and 3% yields, respectively. In addition to the discrete oligomers **8**, **11-13**, the polydisperse polymer containing over 20 mers was also isolated and characterized (see **Figure 2-10** and details in the Experimental Section).

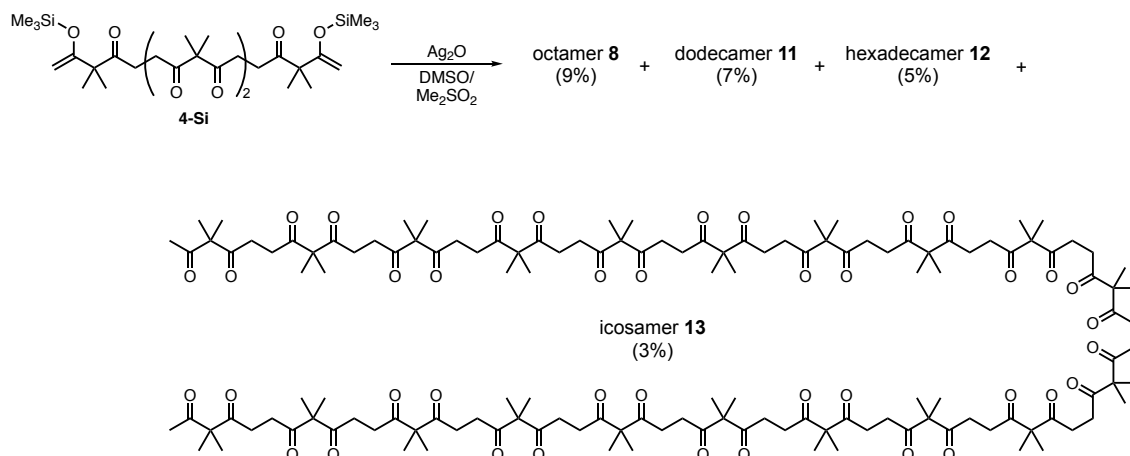
(a) Cross-coupling strategy for 3, 5, 7, and 9 mer (odd-number oligomers)



(b) Homo-coupling strategy for 6 and 10 mer (even-number oligomers)



Scheme 2-2. (a) Stepwise synthesis of odd-number discrete polyketone oligomers **3,5,7,9** by cross-coupling reactions; (b) Stepwise synthesis of even-number discrete polyketone oligomers **6** and **10** by homo-coupling reactions.



Scheme 2-3. Synthesis of further longer polyketones **8**, **11-13** by oligomerization and separation-based strategy.

The isolated discrete polyketone oligomers **2-13** were fully characterized by NMR, matrix-assisted laser time-of-flight (MALDI-TOF) mass spectroscopy, and high-performance liquid chromatography (HPLC). In the ^1H NMR spectra of discrete polyketone oligomers **2-13**, all carbonyl groups were confirmed to stand as a keto-form, even in the case of icosamer **13**, which contained 40 carbonyl groups on the C100 carbon chain. In the ^1H NMR spectrum of icosamer **13**, the terminal acetyl protons were observed as a sharp singlet signal at 2.15 ppm, while no signals were observed at 4-7 ppm region, where the olefinic protons from the enol-form of carbonyl groups could be observed (**Figure 2-2**). Moreover, all of the discrete polyketone oligomers **2-13** were stable colorless solids, and no decomposition was observed upon heating or exposure to ambient conditions, which were totally different from those of natural-type polyketones.

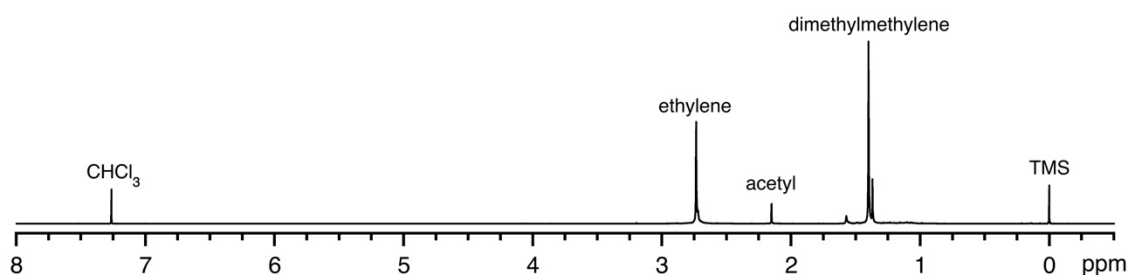


Figure 2-2. ^1H NMR spectrum of icosamer **13** in CDCl_3 (400 MHz, 298 K).

MALDI-TOF mass spectra and SEC-HPLC chromatograms clearly showed the monodisperse character of the isolated polyketone oligomers **2-13** (**Figure 2-3**). In the MALDI-TOF mass spectra of each oligomer, mono-cationic peaks were observed. These observed peaks could be assigned as sodium-adduct peaks $[M+Na]^+$ at $m/z = 277.3, 403.3, 529.3, 655.4, 781.4, 907.5, 1033.6, 1159.6, 1285.7, 1537.9, 2043.1,$ and 2547.5 for oligomers **2-13**, respectively. The SEC-HPLC chromatograms also supported their monodisperse character exhibiting monomodal peaks for each oligomer. The retention time of each peak was moderately decreased as the number of repeating units of the oligomer was increased. From NMR, MALDI-TOF mass, and SEC-HPLC measurements, the monodisperse character of the discrete polyketone oligomers **2-13** was unambiguously confirmed.

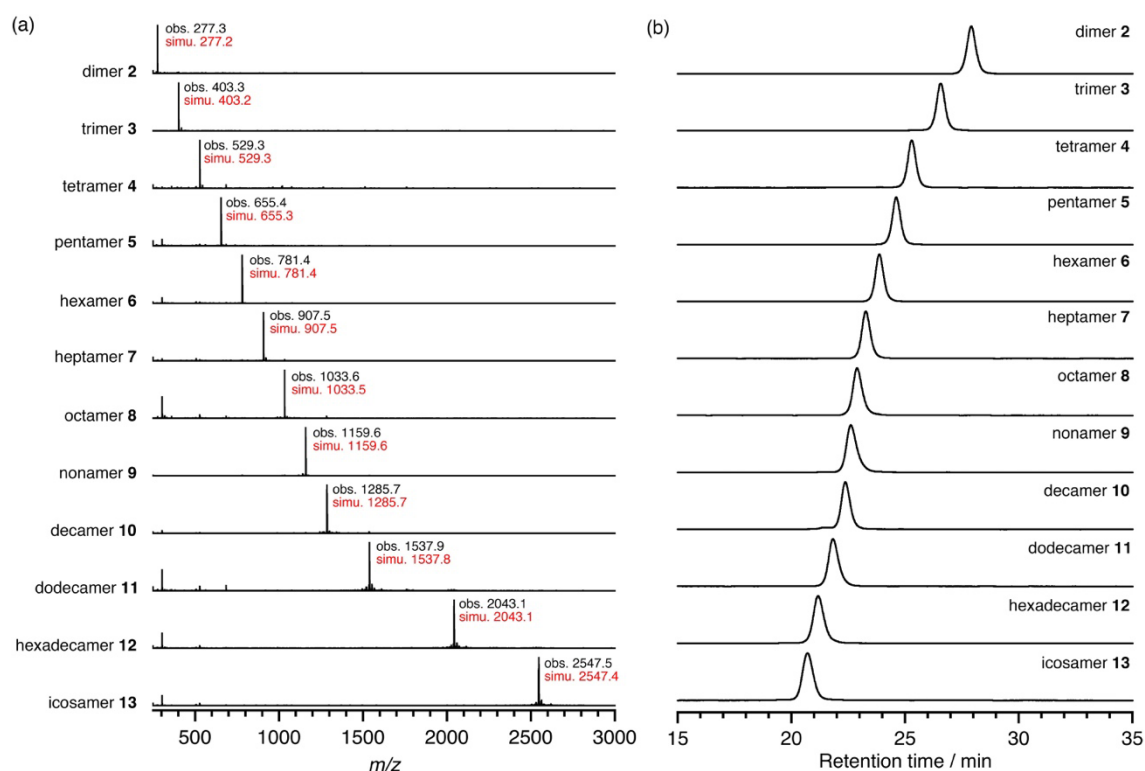


Figure 2-3. (a) MALDI-TOF mass spectra of discrete polyketone oligomers **2-13** using dithranol and $NaPF_6$ as matrixes (black values: observed m/z , red values: calculated values for corresponding sodium mono-adduct ions $[M+Na]^+$); (b) SEC-HPLC chromatograms of discrete polyketone oligomers **2-13** (Column: TOSOH TSKgel G2000HXL $\times$ 2, mobile phase: chloroform, column temperature: 55 $^{\circ}C$, detection: UV absorption at 280 nm, flow rate: 0.5 mL/min).

2.3. Structural Analysis of Discrete Aliphatic Polyketones

Polyketone oligomers **2-13** were all stable colorless solids at room temperature, whereas monomer **1** is liquid. In order to obtain the information for solid-state structures, single crystal X-ray diffraction (SCXRD) analysis of oligomers **2-6** was performed. In the single crystal structures of dimer **2**,² trimer **3**, and tetramer **4**,² they showed U-shaped, linear, and S-shaped conformations in the space groups $C2/c$, $P2_1/c$, and $P-1$, respectively (Figure 2-4).

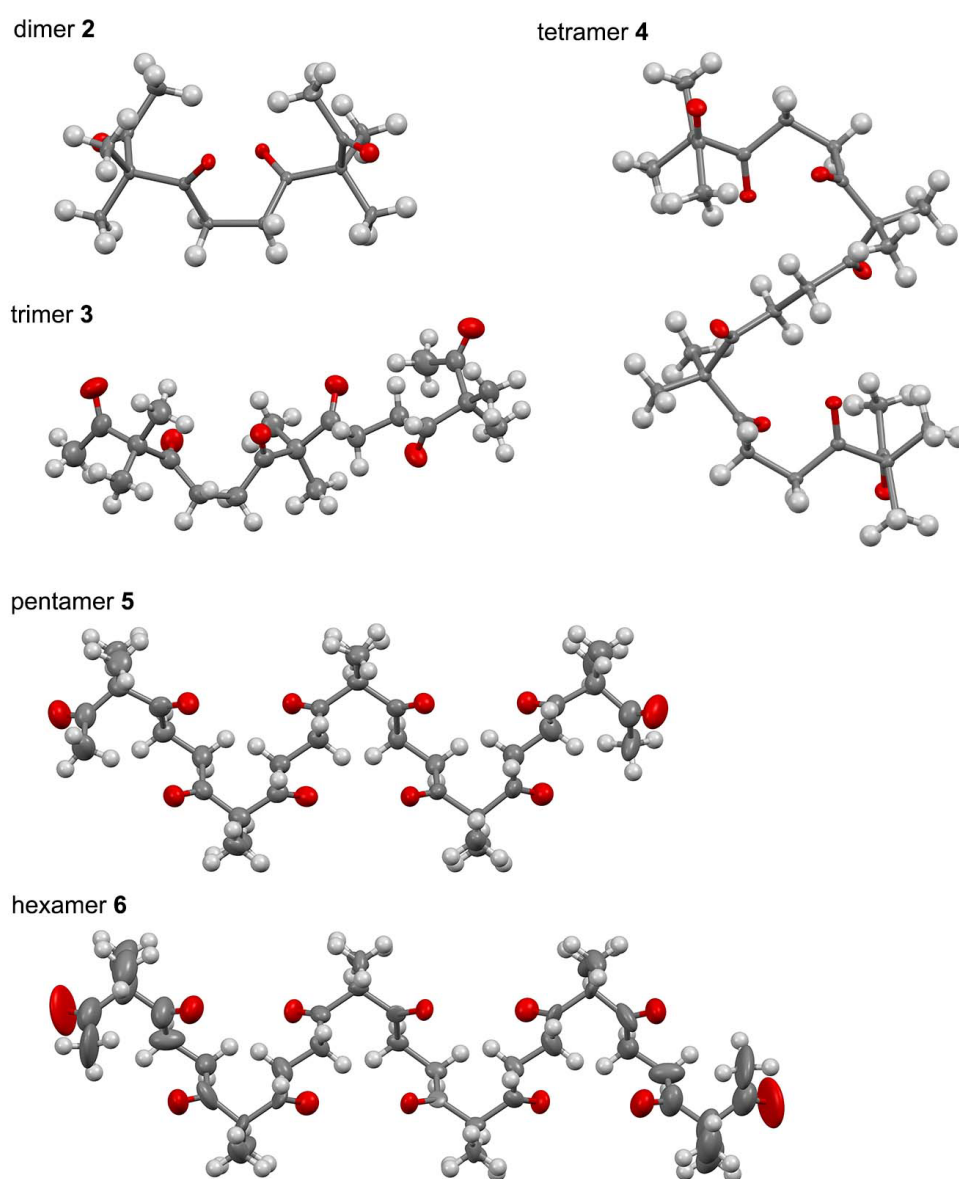


Figure 2-4. Single crystal X-ray structures of dimer **2** to hexamer **6**. Thermal ellipsoids were drawn at 50% probability.

Single crystals of pentamer **5** were grown by vapor diffusion using 1,2-dichloroethane and cyclohexene as good and poor solvents, respectively. Although the single crystals of **5** were analyzed by SCXRD analysis, the highly disordered crystal structure along the oligomer chain was observed with high R_1 values (>0.20). This disorder could be explained by pseudo infinite chain structures derived from the aperiodic arrangement of the oligomer chains. Accordingly, the author has examined a crystal thermal annealing of the crystals at various temperatures to improve the quality of the diffraction data. At last, a reasonable crystal structure of **5** was revealed using a single crystal annealed at 50 °C for 3.5 days. The solved crystal structure took the orthorhombic crystal system with space group $Pna2_1$, pentamer **5** took the two-fold helical conformation, and both left- and right-handed helices existed as a racemate in the centrosymmetric unit cell. In the unit cell, each of the two left- and right-handed helices were aligned along the c -axis (**Figure 2-5a**). In the ab plane, the left- and right-handed helices were alternatively oriented along the a -axis while the same handedness was lined up along the b -axis.

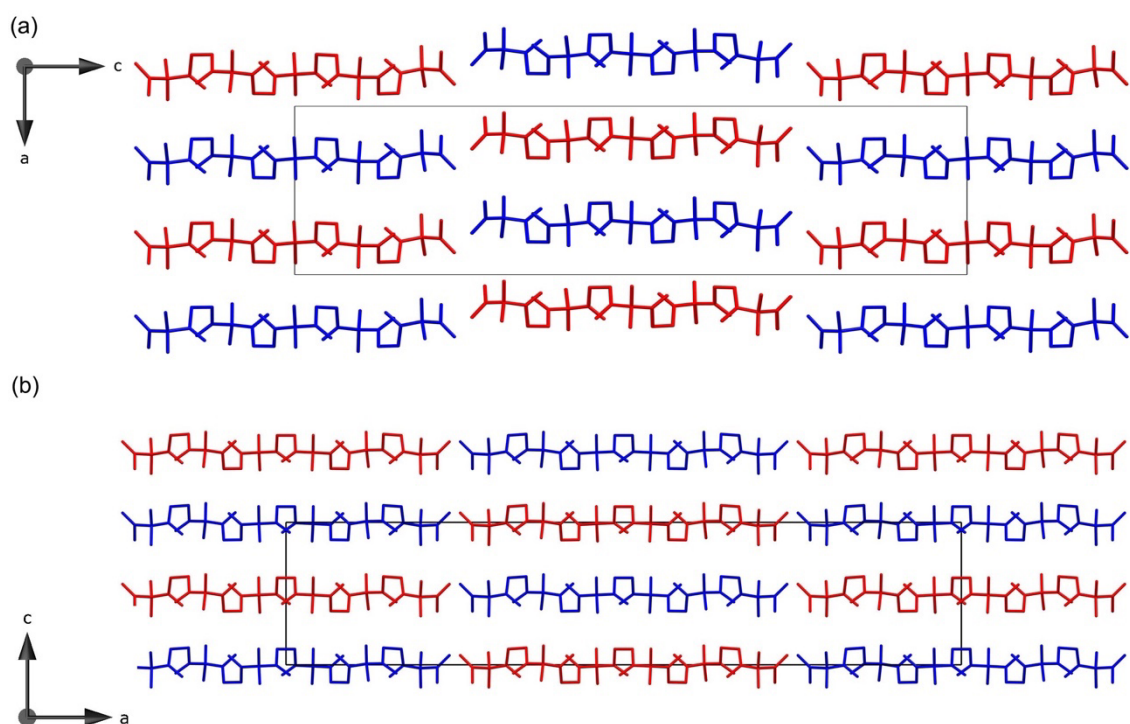


Figure 2-5. (a) Packing structure of pentamer **5** viewed along b -axis. Left- and right-handed helices are indicated in blue and red, respectively; (b) Packing structure of hexamer **6** viewed along b -axis. Left- and right-handed helices are indicated in blue and red, respectively. Hydrogen atoms are omitted for clarity.

Single crystals of **6** were also prepared by vapor diffusion using 1,2-dichloroethane and cyclohexene as good and poor solvents, respectively. Thermal annealing at 50 °C for 2 days gave the best result for the reasonable crystal structure of **6** after many attempts to improve the quality of the diffraction data. Hexamer **6** also took similar helical conformation as observed in pentamer **5** in an orthorhombic unit cell with space group *Iba*2. The packing structure of hexamer **6** was identical to that of pentamer **5** (Figure 2-5b).

To obtain further insight of the structural changes of discrete polyketone oligomers **2-13** in crystalline state upon chain length elongation, powder X-ray diffraction (PXRD) measurements were performed. The crystalline samples of oligomers **2-13** were prepared by slow evaporation of chloroform solution at room temperature over 1 day, except for trimer **3**, which was crystallized by slow cooling from the melted state. The observed PXRD patterns from the single crystal structures of dimer **2**, trimer **3**, and tetramer **4** were matched with the simulated PXRD patterns. The PXRD analysis of oligomers **2-13** showed that dimer **2**, trimer **3**, tetramer **4**, and pentamer **5** showed totally different diffraction patterns from each other. On the other hand, longer oligomers **6-13** showed similar diffraction patterns of pentamer **5**, indicating that the crystallinity of the polyketone oligomers was changed at pentamer **5** (Figure 2-6).

Although the single crystals of **5** were analyzed by SCXRD analysis and the simulated PXRD pattern was matched with the observed diffraction pattern, the highly disordered crystal structure along the oligomer chain was observed with high R_1 values (>0.20). This disorder could be explained by pseudo-infinite chain structures derived from the aperiodic arrangement of the oligomer chains. Upon the single crystal structure, the characteristic PXRD signals of **5** at $2\theta = 11.2$ and 17.0° were assigned to the (011) and (200) planes, respectively. Notably, the (200) plane corresponded to the distance between two neighboring helices of different handedness (d spacing = 5.22 Å), whose distance is virtually constant regardless of the chain length of the helices, unless the packing structure was retained. The observed PXRD diffraction pattern of **6** was also consistent with the simulation from the single crystal structure. As was it seen in pentamer **5**, the characteristic peak was again observed in hexamer **6** at $2\theta = 17.2^\circ$ (d spacing = 5.16 Å), corresponding to the distance between two helices of different handedness.

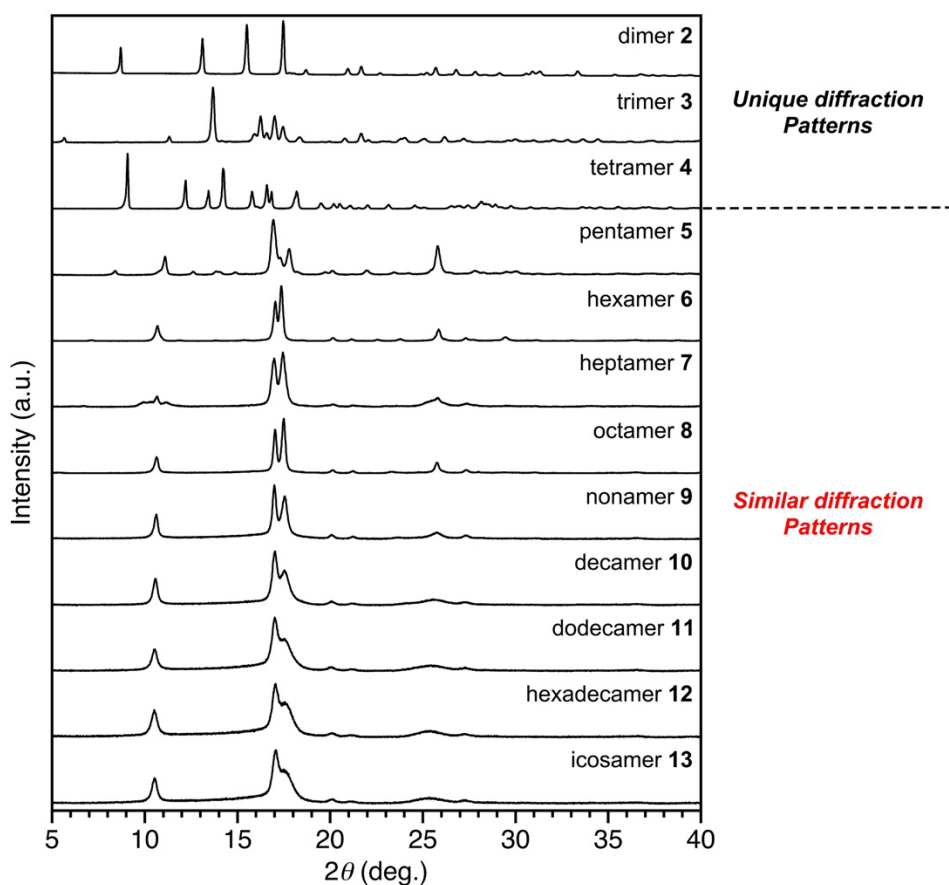


Figure 2-6. PXRD patterns of discrete aliphatic polyketones **2-13**.

While the single crystal structures of further longer polyketone oligomers **7-13** could not be obtained, theoretical calculations were performed to discuss the crystalline solid-state structures from the observed PXRD patterns. An initial packing model of infinite polyketone chains was constructed from the single crystal X-ray structure of hexamer **6**, which was constructed by considering the similar diffraction patterns of oligomers **5-13**. The initial packing model was then refined by the self-consistent-charge density functional tight binding (DFT-B) method under a periodic boundary condition with cell relaxation (See also 2.6. Experimental Section). After the structural optimization, a similar helical conformation of infinite polyketone chains like pentamer **5** and hexamer **6** was observed (**Figure 2-7a,b**). The retention of the helical conformation of the polyketone chains was implied by the stabilization effects of the multiple intramolecular hydrogen bonds between carbonyl oxygen atoms and alpha-protons from short $\text{H}\cdots\text{O}$ distances.

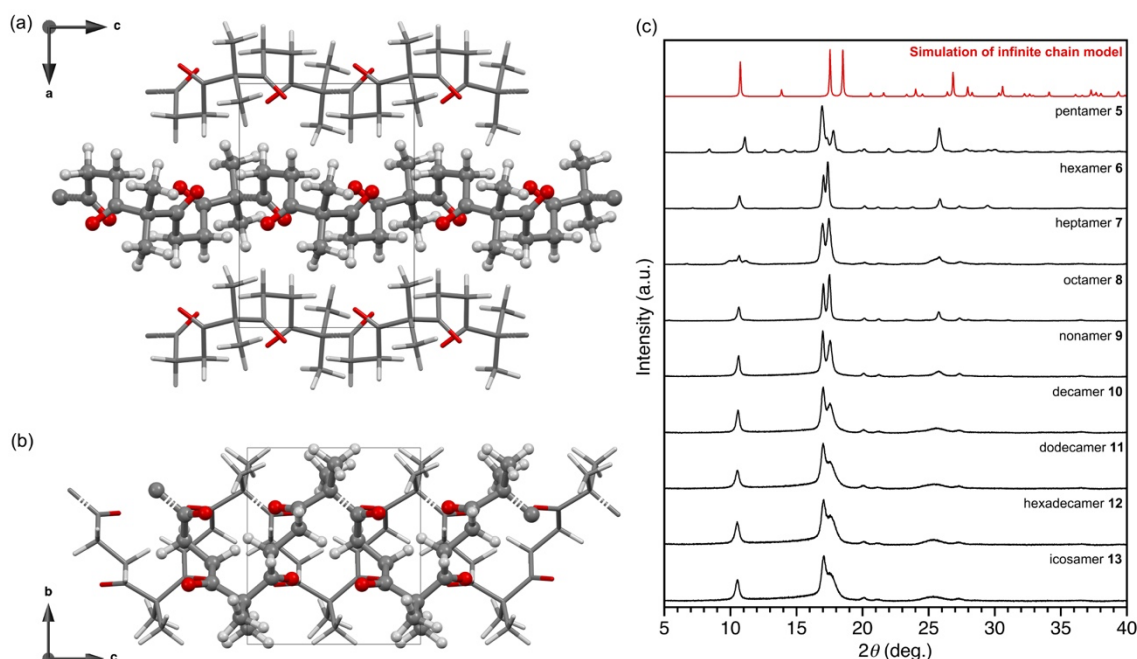


Figure 2-7. (a) Energy minimized packing structure of infinite polyketone from ac plane and (b) from bc plane; (c) Comparison of the diffraction patterns between simulation from the infinite chain model and observed patterns of oligomer **5-13**.

Upon the optimized packing structure, the PXRD pattern of the infinite chain model was calculated and compared with the measured diffraction patterns of oligomers **7-13**. The simulated PXRD pattern was in good agreement with the observed patterns of **7-13**, where the intense peaks at $2\theta = 10.8$, 17.5 , and 18.5° (d spacing = 8.19 , 5.07 , and 4.80 Å, respectively) were observed in common for **7-13** (**Figure 2-7c**). The former two peaks could be assigned to the distances between two helices of the same and different handedness, respectively. The rather sharp character of these two peaks could be explained by the independent nature of these peaks upon the chain length of polyketone chains. Based on these results, the similar helical conformation and packing structures of **5** and **6** were strongly indicated in the case of longer polyketone oligomers **7-13**.

The helical conformations of longer polyketone oligomers were also implied from small angle X-ray scattering (SAXS) measurements along with the chain length dependent long-range periodic structures. In the SAXS profiles, tetramer **4** showed no observable peaks in the range of $2\theta < 4.0^\circ$ while octamer **8**, dodecamer **11**, hexadecamer **12**, and icosamer **13** showed peaks at $2\theta = 2.6$, 1.7 , 1.4 , and 1.1° , respectively (**Figure 2-8a**). The d spacing of these peaks ($d = 3.4$, 5.2 , 6.3 , and 8.0 nm for **8**, **11-13**, respectively) was well-matched with the DFT-optimized helical conformations of each oligomer as shown in **Figure 2-8b** (3.1 , 4.5 , 6.0 , and 7.5 nm for **8**, **11-13**, respectively). Therefore,

these long-range periodic structures could be estimated to be the end-to-end distances of polyketone oligomers of helical conformations.

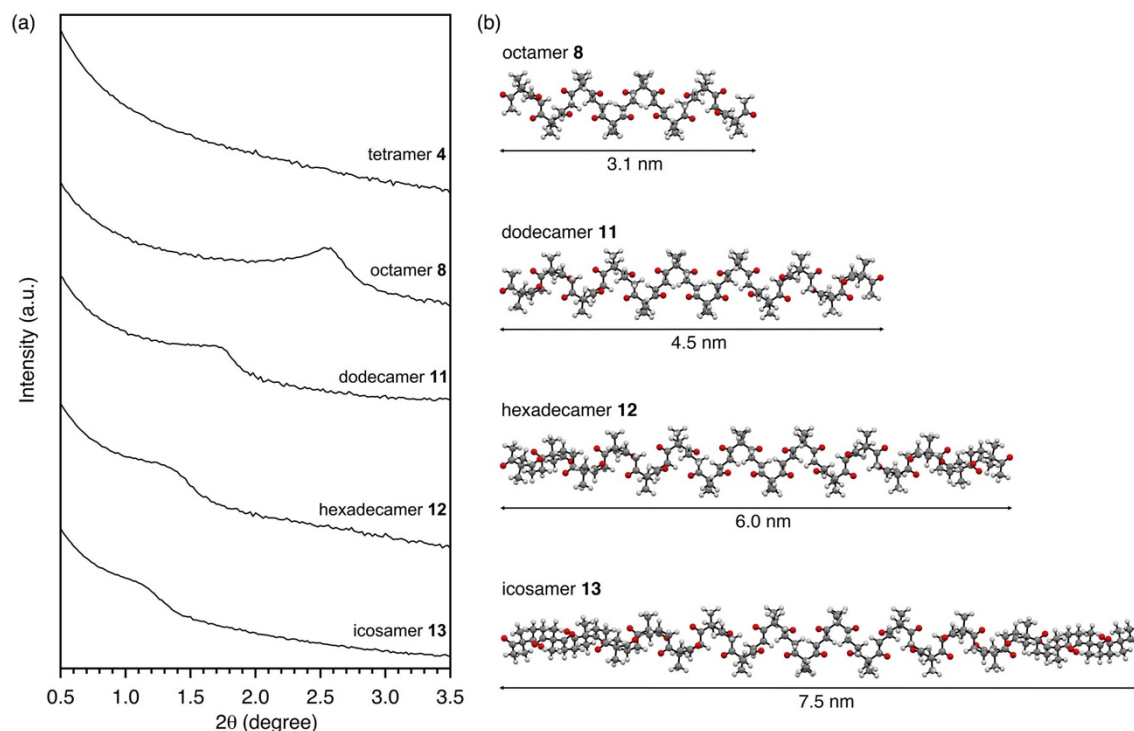


Figure 2-8. (a) SAXS profiles of the oligomers 4, 8, 11, 12, and 13. (b) Optimized structures of the oligomers 8, 11, 12, and 13.

Such a long-range periodic structure was also observed by atomic force microscopy (AFM) measurements. Onto a highly oriented pyrolytic graphite (HOPG) surface was drop-casted a 0.05 mM chloroform solution of octamer **8** (5 μ L), and the solvent was gradually evaporated over 30 seconds. In the recorded AFM images, crystalline domains with a striped texture were observed (**Figure 2-9**). The average distance and height of each domain were calculated to be 3.4, and 0.4 nm, respectively. These values were consistent with the distance between neighboring helices and the height of octamer **8** estimated from the results of SAXS, PXRD, and DFT calculation results.

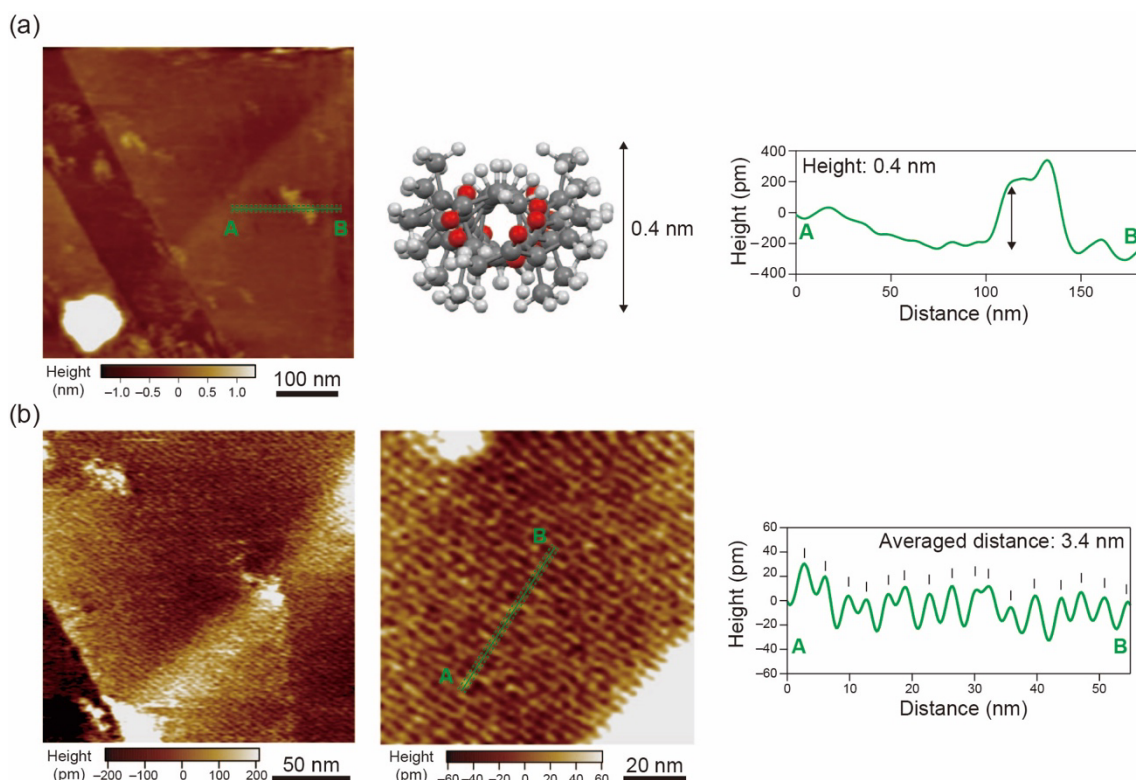


Figure 2-9. AFM images of octamer **8** in ultrapure water: (a) overview and (b) enlarged images.

Polydisperse polyketone polymer, composed of oligomers longer than 20 mer, was also indicated to form a similar helical conformation and packing structures in the analogy of the observed ones in oligomers **5-13** in the crystalline solid state. The polydisperse polymer was synthesized in a similar manner to the synthesis of oligomers **8**, **11-13** from the bis-silylated tetramer **4-Si₂** by an oligomerization reaction and SEC separation. From the MALDI-TOF mass spectrum, the isolated polydisperse polyketone polymer included at least 40 mer as the longest oligomer as a mixture (**Figure 2-10a**). In the SEC-HPLC chromatogram, the retention time of the polydisperse polyketone polymer was behind that of icosamer **20**, also indicating that the higher-molecular weight oligomers longer than 20 mer were included in the polydisperse polyketone polymer (**Figure 2-10b**). The obtained polydisperse polyketone polymer was also crystallized from a chloroform solution at room temperature over 1 day. In the PXRD patterns, two characteristic rather sharp peaks were observed at $2\theta = 10.5$ and 17.1° (**Figure 2-10c**). These peaks were estimated to correspond to the inter-helix distances of the polyketone chains, as observed in the packing model of infinite chains, where two PXRD peaks at $2\theta = 11$ and 18° . Since these two peaks were basically independent of the chain length of oligomer chains, the

longer oligomers included in the polydisperse polyketone polymer would also take a similar helical conformation and packing structure of oligomers **5-13** although they existed as a mixture of oligomers.

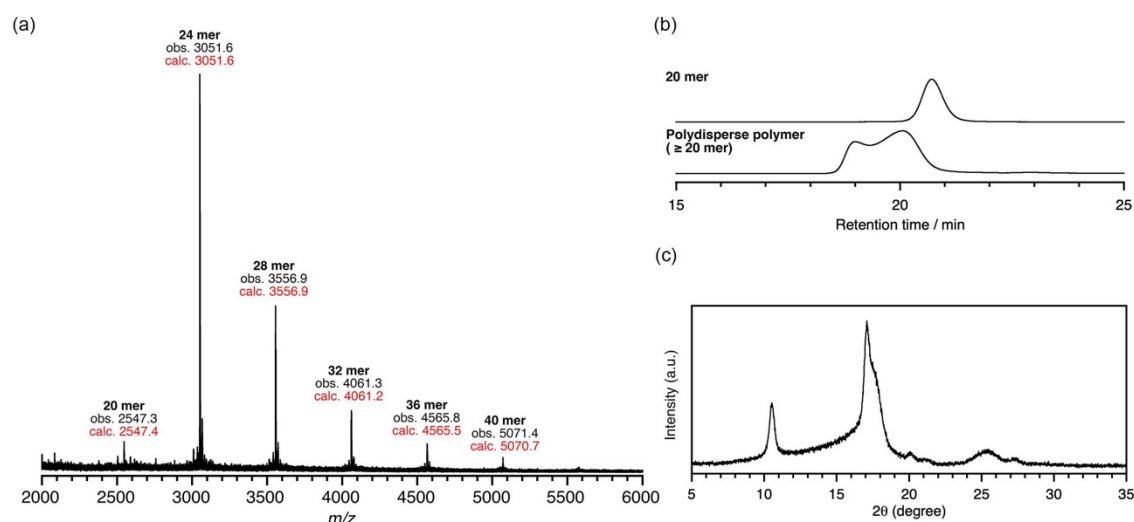


Figure 2-10. (a) MALDI-TOF mass spectrum of polydisperse polymer (≥ 20 mer) using dithranol and NaPF_6 as matrixes (black values: observed m/z , red values: calculated values for corresponding sodium mono-adduct ions $[M+Na]^+$). (b) HPLC chromatograms of icosamer **13** and polydisperse polymer (≥ 20 mer) (Column: TOSOH TSKgel G2000HXL $\times 2$, mobile phase: chloroform, column temperature: 55 °C, detection: UV absorption at 280 nm, flow rate: 0.5 mL/min). (c) PXRD pattern of polydisperse polymer (≥ 20 mer).

2.4. Correlation of Structural Changes with Thermal Properties

The chain length dependent structural changes of polyketone oligomers were found to be vital for understanding the tendency of their melting points trend upon the chain length elongation. The melting points of polyketone oligomers **2-13** were measured using differential scanning calorimetry (DSC) analysis and recorded at 87, 45, 104, 91, 119, 131, 139, 142, 148, 157, and 161 °C, respectively (**Figure 2-11a**). Along with the chain length elongation from dimer **2** to icosamer **13**, no apparent trend was observed for dimer **2** to tetramer **4**, while a clear monotonic increase in melting points was observed for pentamer **5** to icosamer **13**. Considering the changes in the packing structures of the oligomers, the irregular melting point change of oligomers **2-4** could be explained by the different crystal packings, while the monotonic melting point increase trend of oligomers **5-13** could be accounted for by the similar conformations and packing structures along with the increase of the number of monomer units. Along with the melting points, the melting enthalpy change was also investigated (**Figure 2-11b** and **2-11c**). In a similar manner to the melting point trend, an irregular change in melting enthalpies was observed in the range of oligomers **2-5**. Over pentamer **5**, the melting enthalpies were decreased monotonically as the number of repeating units was increased. These trends could also be correlated with the crystal structure changes of oligomers **2-13** as observed in melting points. While the irregular changes in the shorter oligomers **2-5** were also corresponded to the differences in crystal packings, the monotonic decrease over pentamer **5** could be derived from the decrease in the ratio of crystalline regions due to the elongation in chain length. As reflected in the trends of melting points and melting enthalpies, the structural changes of the polyketone oligomers significantly affected their thermal properties upon their chain length elongation.

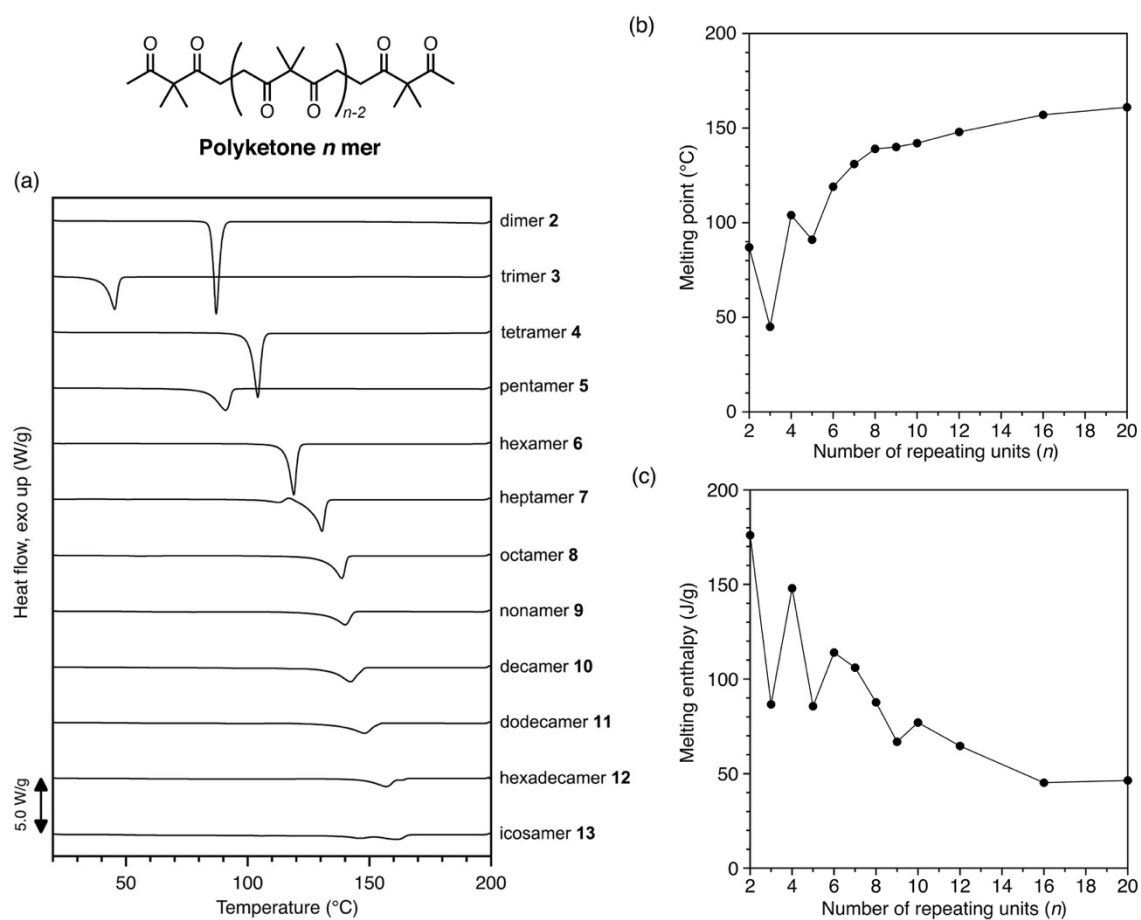


Figure 2-11. (a) DSC plots, (b) melting point plot, and (c) melting enthalpy plot of discrete aliphatic oligomers **2-13** (1st heated run, scan rate: 10 °C / min).

2.5. Conclusion

In conclusion, the synthesis of discrete aliphatic polyketone oligomers up to icosamer (20 mer) was achieved by a stepwise synthesis from 3,3-dimethylpentane-2,4-dione upon the terminal-selective silylation and following silver(I) oxide mediated homo- or cross-coupling reactions. The alternating 1,3- and 1,4-diketone repeating unit effectively suppressed the drawbacks in natural-type polyketones. The obtained discrete polyketones up to 20 mer were stable, and all carbonyl groups existed as a keto form. The monodisperse character of the discrete aliphatic polyketones was unambiguously confirmed by NMR, MALDI, and SEC-HPLC measurements. From the structural analysis of the discrete polyketones, the abrupt crystal structure change at pentamer (5 mer) was observed. Aliphatic polyketones longer than 5 mer adopted similar helical conformations, while short oligomers (2-4 mer) adopted unique conformations in the crystal structures. This unique structural change in the crystal structures also demonstrated the determination of crystallization behavior changes at 5 mer from small molecular-like and macromolecular-like crystallization.

2.6. Experimental Section

General Information

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd., TCI Co., Ltd., Kanto Chemical Co., Inc., and Sigma-Aldrich Co., and used without further purification unless otherwise noted. Compounds **2**, **4**, **1-Si**, **2-Si**, **4-Si**, and **4-Si₂** were prepared according to the reported literature.^{2,3} Single crystal structures of dimer **2** and pentamer **4** were reported in the previous literature.² All the ¹H, ¹³C NMR spectra were recorded on a JEOL JMN-ECS400 spectrometer. Chemical shifts are reported in parts per million (ppm) relative to an internal standard tetramethylsilane ($\delta=0.00$ ppm for ¹H) or a residual solvent peak ($\delta=77.16$ ppm for ¹³C in CDCl₃). Infrared spectra were measured using a JASCO Co. FT/IR-4700. ESI-TOF-MS spectra were recorded on a Thermo scientific Exactive spectrometer. Elemental analysis was performed using an Exceter Analytical, Inc. CE440 or MICRO CORDER JM10. MALDI-TOF mass spectra were recorded on a Bruker autoflex[®] maX spectrometer or Bruker Ultraflex III spectrometer. Thin layer chromatography (TLC) was performed on a silica gel sheet, MERCK silica gel 60 F₂₅₄. Preparative scale separations were performed using silica gel column chromatography (Wakosil[®] 60. 64 ~ 210 μ m), a recycling HPLC LaboACE LC-5060 equipped with two JAIGEL-2HR columns in series for pentamer **5**, or a recycling HPLC LaboACE LC-7080 equipped with JAIGEL-2.5HR and 3 HR columns in series for heptamer **7**, nonamer **9**, dodecamer **11**, hexadecamer **12**, icosamer **13**, and polydisperse polymer ($N \geq 20$). Analytical HPLC chromatograms were recorded using a JASCO MD-2018 photodiode array detector equipped with a JASCO PU-2089 pump, JASCO AS-2059 sampler, and JASCO CO-2060 column thermostat. Single crystal X-ray diffraction data were collected using a Rigaku XtaLAB P200 diffractometer equipped with a HyPix-6000HE detector using multi-layer mirror (CuK α radiation $\lambda = 1.54184$ Å). All structures were solved using a dual-space algorithm (SHELXT⁴) and refined using full-matrix least-squares method (SHELXL⁵). Powder X-ray diffraction (PXRD) and small angle X-ray scattering (SAXS) were measured using a Rigaku SmartLab X-ray diffractometer (CuK α radiation $\lambda = 1.54184$ Å) equipped with a Hypix-3000 photon counting detector. Atomic force microscopy (AFM) measurements were performed by frequency modulation mode using a laboratory-built AFM system combined with commercial AFM controllers. Differential Scanning Calorimetry (DSC) traces were recorded on a Hitachi DSC7000 instrument using an aluminum pan (sample amount: ca. 5 mg) under a nitrogen atmosphere.

Synthetic Procedures of Discrete Polyketone Oligomers

Synthesis of trimer 3

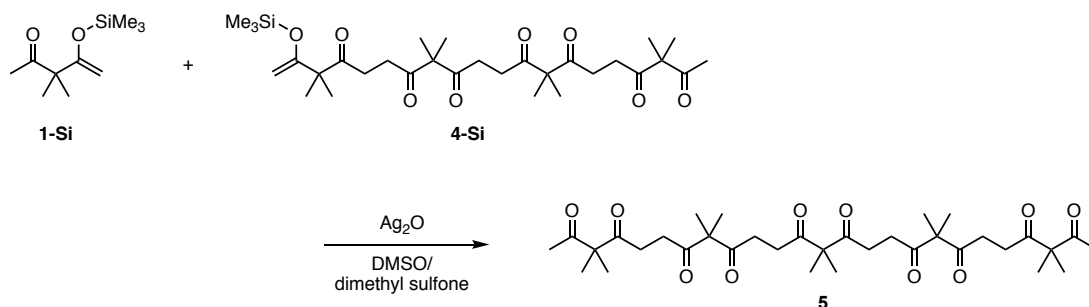


To a 300 mL round-bottom flask equipped with a reflux condenser were added enol silyl ethers **1-Si** (13.1 g, 65.5 mmol) and **1-Si₂** (3.57 g, 13.1 mmol), dimethyl sulfone (25.9 g, 275 mmol), dimethyl sulfoxide (1.43 g, 18.3 mmol), and silver(I) oxide (12.8 g, 55.0 mmol). The reaction mixture was stirred at 100 °C for 2 h. After cooling to room temperature, the reaction mixture was passed through a Celite pad using dichloromethane (100 mL). The solvent was evaporated to give the crude products as a brown solid. The solid was dissolved in diethyl ether (100 mL), and the solution was washed with water (100 mL) using an extraction funnel. The aqueous layer was further extracted with diethyl ether (50 mL $\times$ 3). The combined organic layer was washed with brine (100 mL), and dried over anhydrous sodium sulfate before evaporating the solvent. The crude product was chromatographed on a silica gel column (diameter, 4.0 cm, height, 15.0 cm) using hexane/ethyl acetate (3:1, v/v) as eluent to afford trimer **3** (1.35 g, 3.55 mmol) as a colorless solid in 27% yield based on **1-Si₂**.

3,3,8,8,13,13-Hexamethylpentadecane-2,4,7,9,12,14-hexaone (3) (trimer)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.72 (overlapping t, 8H, ethylene), 2.15 (s, 6H, acetyl), 1.41 (s, 6H, $\text{C}(\text{CH}_3)_2$), 1.37 (s, 12H, $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.3, 207.8, 62.3, 61.9, 32.3, 32.2, 26.4, 21.8, 21.7; IR (ATR, neat): 1714, 1693, 1362, 1040, 1014, 970, 504 cm^{-1} ; m.p. 42 °C; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{32}\text{O}_6\text{Na}^+$, 403.2089; found, 403.2091; Elemental analysis (%): Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_6$: C, 66.29; H, 8.48; N, 0.00. Found: C, 66.12; H, 8.55; N, 0.04; R_f = 0.24 (eluent: hexane/ethyl acetate = 3:1).

Synthesis of pentamer 5

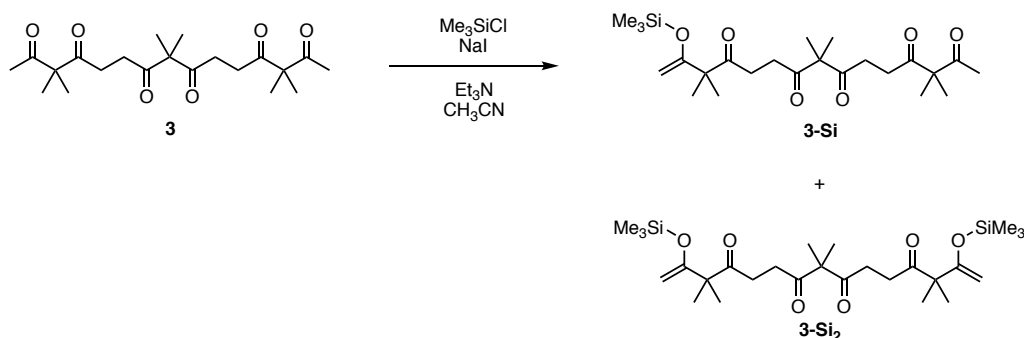


To a 50 mL round-bottom flask equipped with a reflux condenser, were added mono-silylated monomer **1-Si** (866 mg, 4.32 mmol), mono-silylated tetramer **4-Si** (500 mg, 0.864 mmol), dimethyl sulfoxide (73.9 μL , 1.04 mmol), dimethyl sulfone (1.47 g, 15.6 mmol), and silver(I) oxide (721 mg, 3.11 mmol). The reaction mixture was stirred at 100 $^{\circ}\text{C}$ for 2 h. After cooling to room temperature, the reaction mixture was filtered through a Celite pad with suction. The solid on a funnel was washed with dichloromethane (100 mL), and the filtrate was evaporated under vacuum. The resulting solid was dissolved in ethyl acetate (15 mL) and washed with water (15 mL). The aqueous layer was extracted with ethyl acetate (3×15 mL) and the combined organic layer was washed with brine (5×15 mL). The organic layer was dried over anhydrous sodium sulfate, and the solvents were evaporated *in vacuo*. The residue was purified by recycling preparative SEC using chloroform as a mobile phase. The separated product was dissolved in dichloromethane (0.5 mL) and recrystallized by adding diethyl ether (10 mL). The precipitated crystal was filtered on a funnel with suction using diethyl ether (20 mL) to give pentamer **5** (134 mg, 0.212 mmol, 25% yield) as a colorless solid.

3,3,8,8,13,13,18,18,23,23-Decamethylpentacosane-2,4,7,9,12,14,17,19,22,24-decaone (**5**) (pentamer)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.75-2.72 (m, 16H, ethylene), 2.16 (s, 6H, acetyl), 1.42-1.38 (18H, overlapping $\text{C}(\text{CH}_3)_2$), 1.37 (s, 12H, $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.4 ($2 \times \text{C}=\text{O}$), 208.2, 207.8, 62.2, 61.81, 61.76, 32.4-32.1 ($4 \times \text{CH}_2$), 26.4, 21.83, 21.81, 21.6; IR(ATR, neat) 2991, 2981, 2936, 2921, 2871, 1692, 1462, 1441, 1389, 1374, 1363, 1237, 1209, 1197, 1174, 1164, 1127, 1088, 1070, 1036, 1011 cm^{-1} ; m.p. 96-97 $^{\circ}\text{C}$; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{35}\text{H}_{52}\text{O}_{10}\text{Na}^+$: 655.3453; found, 655.3444; Elemental analysis (%): Calcd for $\text{C}_{35}\text{H}_{52}\text{O}_{10}$: C, 66.43; H, 8.28; N, 0.00; Found: C, 66.40; H, 8.34; N, 0.04; $R_f=0.30$ (hexane:ethyl acetate:dichloromethane = 3:2:2).

Silylation of trimer **3**



To a 50 mL two-necked round-bottom flask, trimer **3** (5.00 g, 13.1 mmol) and sodium iodide (3.93 g, 26.2 mmol) were added. After the flask was purged with N₂ gas, acetonitrile (20 mL) and triethylamine (4.01 mL, 28.8 mmol) were added. The resulting suspension was cooled to 0 °C and trimethylchlorosilane (3.33 mL, 26.2 mmol) was added via syringe. The reaction mixture was stirred at 0 °C for 20 min and quenched by adding water (20 mL). From the reaction mixture, products were extracted with dichloromethane (20 mL). The aqueous layer was further extracted with dichloromethane (3 × 20 mL). The combined organic layer was washed with water (20 mL), dried over anhydrous sodium sulfate, and the solvent was evaporated. The residue was purified by silica-gel column chromatography (diameter: 4.0 cm, height: 18.0 cm, eluent: hexane/ethyl acetate = 4:1) to give mono-silylated product **3-Si** (2.06 g, 4.55 mmol, 35% yield) and bis-silylated product **3-Si₂** (844 mg, 1.60 mmol, 12% yield) as pale yellow oils.

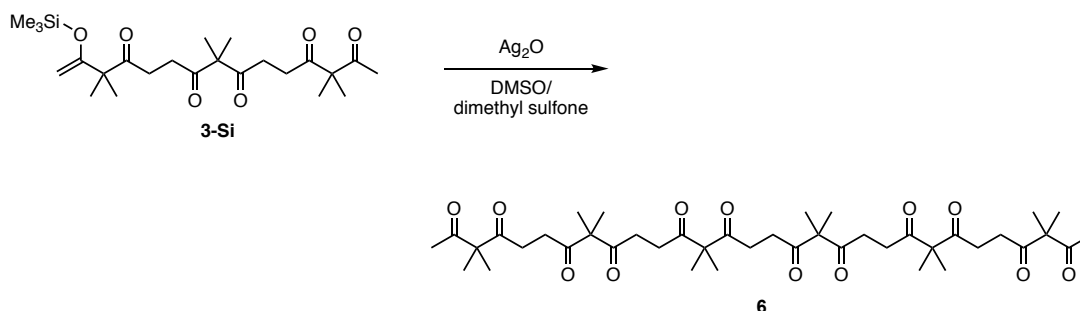
Mono-silylated product 3-Si

^1H NMR (400 MHz, CDCl_3 , 298 K) : δ 4.31 (d, $J = 2.1$ Hz, 1H, vinyl), 4.18 (d, $J = 2.1$ Hz, 1H, vinyl), 2.85-2.79 (m, 2H, ethylene), 2.77-2.67 (m, 4H, ethylene), 2.67-2.60 (m, 2H, ethylene), 2.15 (s, 3H, acetyl), 1.40 (s, 6H, $\text{C}(\text{CH}_3)_2$), 1.37 (s, 6H, $\text{C}(\text{CH}_3)_2$), 1.22 (s, 12H, $\text{C}(\text{CH}_3)_2$), 0.20 (s, 9H, $\text{Si}(\text{CH}_3)_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 211.2, 208.6, 208.5, 208.4, 207.7, 162.1, 88.9, 62.2, 61.9, 53.5, 32.32, 32.27, 32.21, 31.0, 26.3, 23.1, 21.8, 21.6, 0.03; IR(ATR, neat) 2976, 2936, 2911, 2877, 1698, 1626, 1468, 1366, 1287, 1253, 1170, 1039, 1010, 847 cm^{-1} ; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{40}\text{O}_6\text{SiNa}^+$, 475.2486; found, 475.2483; $R_f=0.30$ (hexane:ethyl acetate = 4:1).

Bis-silylated product 3-Si₂

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 4.30 (d, $J = 2.1$ Hz, 2H, vinyl), 4.17 (d, $J = 2.1$ Hz, 2H, vinyl), 2.84-2.79 (m, 4H, ethylene), 2.69-2.62 (m, 4H, ethylene), 1.40 (s, 6H, $\text{C}(\text{CH}_3)_2$), 1.22 (s, 12H, $\text{C}(\text{CH}_3)_2$), 0.20 (s, 18H, $\text{Si}(\text{CH}_3)_3$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 211.2, 208.8, 162.1, 88.9, 61.9, 53.5, 32.4, 31.0, 23.1, 21.8, 0.04; IR(ATR, neat) 2975, 2936, 2911, 2878, 1670, 1625, 1286, 1253, 1169, 1038, 1009, 842 cm^{-1} ; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{48}\text{O}_6\text{Si}_2\text{Na}^+$, 547.2882; found, 547.2878; $R_f=0.63$ (hexane:ethyl acetate = 4:1).

Synthesis of hexamer 6



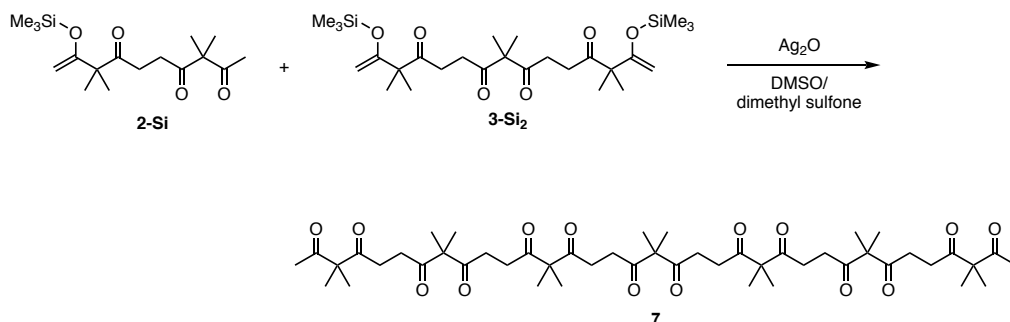
To a 30 mL round-bottom flask equipped with a reflux condenser, mono-silylated trimer **3-Si** (1.00 g, 2.21 mmol), dimethyl sulfoxide (31.4 μL , 0.442 mmol), dimethyl sulfone (624 mg, 6.63 mmol), and silver(I) oxide (308 mg, 1.33 mmol) were added. The reaction mixture was stirred at 100 $^{\circ}\text{C}$ for 2 h. After cooling to room temperature, the reaction mixture was filtered through a Celite pad with suction. The solid on a funnel was washed with dichloromethane (100 mL). The filtrate was washed with water (3×100 mL), dried over anhydrous sodium sulfate, and the solvents were removed *in vacuo*. The residue was chromatographed on a silica-gel column (diameter: 3.0 cm, height: 15.0 cm, eluent: hexane/ethyl acetate/dichloromethane = 4:3:4). The resulting crude product was washed with diethyl ether (5 mL) on a funnel with suction to give hexamer **6** (267 mg, 0.352 mmol, 32% yield) as a colorless solid.

3,3,8,8,13,13,18,18,23,23,28,28-Dodecamethyltriacontane-

2,4,7,9,12,14,17,19,22,24,27,29-dodecaone (**6**) (hexamer)

^1H NMR (400 MHz, CDCl_3): δ 2.77-2.69 (m, 20H, ethylene), 2.15 (s, 6H, acetyl), 1.42-1.38 (24H, overlapping $\text{C}(\text{CH}_3)_2$), 1.37 (s, 12H, $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 208.6, 208.4 ($3 \times \text{C}=\text{O}$), 208.2, 207.8, 62.2, 61.82, 61.76, 32.5-32.0 ($5 \times \text{CH}_2$), 26.4, 21.84, 21.81, 21.6; IR(ATR, neat) 2992, 2981, 2936, 2921, 2870, 1692, 1461, 1441, 1389, 1375, 1363, 1239, 1209, 1198, 1175, 1162, 1126, 1087, 1072, 1054, 1035, 1012, 960, 951 cm^{-1} ; m.p. 119 $^{\circ}\text{C}$; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{42}\text{H}_{62}\text{O}_{12}\text{Na}^+$, 781.4134, found, 781.4137; Elemental analysis (%): Calcd for $\text{C}_{42}\text{H}_{62}\text{O}_{12}$: C, 66.47; H, 8.23; N, 0.00; Found: C, 66.45; H, 8.30; N, 0.02; R_f =0.23 (hexane:ethyl acetate:dichloromethane = 4:3:4).

Synthesis of heptamer 7

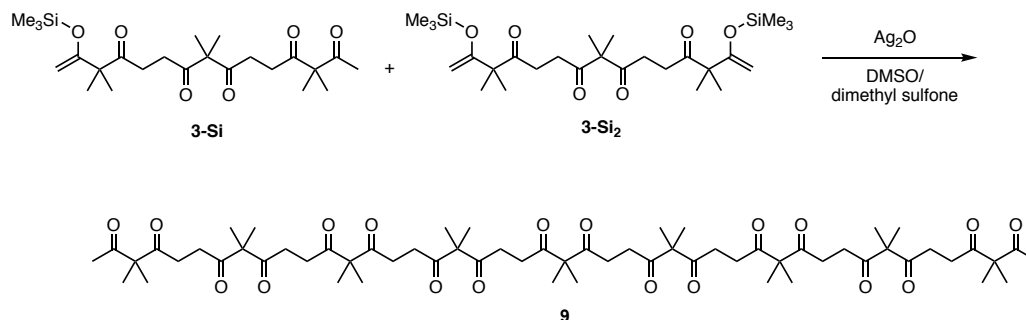


To a 50 mL round-bottom flask equipped with a reflux condenser, mono-silylated dimer **2-Si** (4.35 g, 13.3 mmol), bis-silylated trimer **3-Si₂** (1.40 g, 2.67 mmol), dimethyl sulfoxide (265 μ L, 3.74 mmol), dimethyl sulfone (5.27 g, 56.0 mmol), and silver(I) oxide (2.60 g, 11.2 mmol) were added. The reaction mixture was stirred at 100 °C for 2 h, and filtered through a Celite pad with suction. The solid on a funnel was washed with dichloromethane (200 mL). The filtrate was washed with brine (3 $\times$ 200 mL), dried over anhydrous sodium sulfate, and the solvents were removed *in vacuo*. The residue was dissolved in dichloromethane/methanol (40 mL, 1:1, v/v), and stirred with 3 M hydrochloric acid (1.1 mL) for 30 min at room temperature. The solution was neutralized with sat. aq. NaHCO₃ and the aqueous layer was extracted with dichloromethane (2 $\times$ 50 mL). The combined organic layer was washed with brine (50 mL), dried over anhydrous Na₂SO₄, and the solvents were evaporated under reduced pressure. The resulting mixture was separated by recycling preparative SEC using chloroform as a mobile phase. The separated product was passed through silica-gel column (diameter: 2.0 cm, height: 5.0 cm, eluent: hexane/ethyl acetate/dichloromethane = 1:1:1), and the resulting solid was washed with diethyl ether (5 mL) on a funnel to furnish heptamer **7** (100 mg, 0.113 mmol, 4% yield based on **3-Si₂**) as a colorless solid.

3,3,8,8,13,13,18,18,23,23,28,28,33,33-Tetradecamethylpentatriacontane-2,4,7,9,12,14,17,19,22,24,27,29,32,34-tetradecaone (7) (heptamer)

¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.78-2.68 (m, 24H, ethylene), 2.15 (s, 6H, acetyl), 1.43-1.38 (30H, overlapping C(CH₃)₂), 1.37 (s, 12H, C(CH₃)₂); ¹³C {¹H} NMR (100 MHz, CDCl₃, 298 K): δ 208.6, 208.4 (4 $\times$ C=O), 208.3, 207.8, 62.2, 61.85, 61.79 (2 $\times$ C(CH₃)₂), 32.4-32.2 (6 $\times$ CH₂), 26.4, 22.0-21.8 (3 $\times$ CH₃), 21.6; IR(ATR, neat) 2992, 2981, 2936, 2920, 2871, 1693, 1664, 1461, 1442, 1388, 1376, 1363, 1239, 1120, 1175, 1162, 1127, 1084, 1072, 1034, 1012, 959, 951 cm⁻¹; m.p. 132-133 °C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₄₉H₇₂O₁₄Na⁺, 907.4814; found, 907.4825; Elemental analysis (%): Calcd for C₄₉H₇₂O₁₄: C, 66.49; H, 8.20; N, 0.00; Found: C, 66.27; H, 8.25; N, 0.02; *R*_f=0.28 (hexane:ethyl acetate:dichloromethane = 1:1:1).

Synthesis of nonamer 9

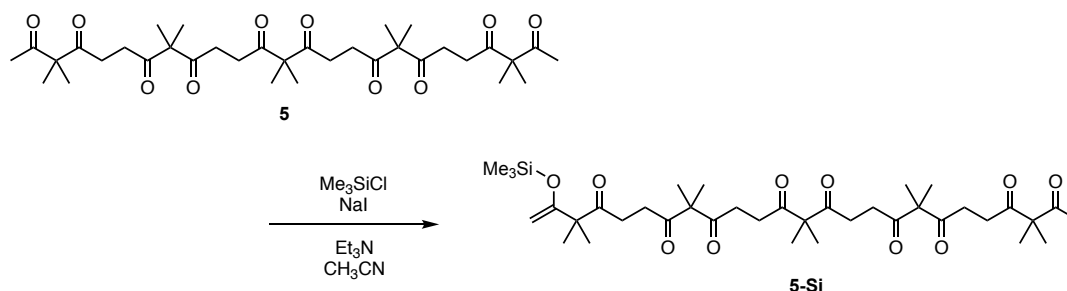


To a 50 mL round-bottom flask equipped with a reflux condenser, mono-silylated trimer **3-Si** (4.30 g, 9.50 mmol), bis-silylated trimer **3-Si₂** (997 mg, 1.90 mmol), dimethyl sulfoxide (189 μ L, 2.66 mmol), dimethyl sulfone (3.76 g, 39.9 mmol), and silver(I) oxide (1.85 g, 7.98 mmol) were added. The reaction mixture was stirred at 100 $^{\circ}$ C for 2 h and filtered through Celite pad with suction after cooling to room temperature. The solid on a funnel was washed with dichloromethane (100 mL). The filtrate was washed with brine (3 $\times$ 100 mL), dried over anhydrous sodium sulfate, and the solvents were removed *in vacuo*. The residue was dissolved in dichloromethane/methanol (28 mL, 1:1, v/v) and stirred with 3 M hydrochloric acid (0.80 mL) for 30 min at room temperature. The solution was neutralized with sat. aq. NaHCO₃ and the aqueous layer was extracted with dichloromethane (2 $\times$ 30 mL). The combined organic layer was washed with brine (60 mL), dried over anhydrous Na₂SO₄, and the solvents were evaporated under reduced pressure. The resulting mixture was separated by recycling preparative SEC using chloroform as a mobile phase. The separated product was passed through a silica gel column (diameter: 3.0 cm, height: 5.0 cm, eluent: hexane/ethyl acetate/dichloromethane = 1:1:1) and the resulting solids were washed with diethyl ether (5 mL) on a funnel to give nonamer **9** (149 mg, 0.131 mmol, 7% yield based on **3-Si₂**) as a colorless solid.

3,3,8,8,13,13,18,18,23,23,28,28,33,33,38,38,43,43-Octadecamethylpentatetracontan-2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39,42,44-octadecaone (9) (nonamer)

¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.79-2.66 (m, 32H, ethylene), 2.15 (s, 6H, acetyl), 1.42-1.38 (54H, overlapping C(CH₃)₂); ¹³C {¹H} NMR (100 MHz, CDCl₃, 298 K): δ 208.6, 208.5 (6 $\times$ C=O), 208.3, 207.8, 62.2, 61.9-61.7 (4 $\times$ C(CH₃)₂), 32.5-32.1 (8 $\times$ CH₂), 26.4, 22.0-21.8 (4 $\times$ CH₃), 21.6; IR(ATR, neat) 2992, 2980, 2937, 2920, 2871, 1693, 1462, 1441, 1388, 1375, 1362, 1240, 1200, 1175, 1160, 1127, 1073, 1032, 1014, 959, 950 cm⁻¹; m.p. 140-142 $^{\circ}$ C; HRMS(ESI-TOF): m/z [M + Na]⁺ calcd for C₆₃H₉₂O₁₈Na⁺, 1159.6176; found, 1159.6161; Elemental analysis (%): Calcd for C₆₃H₉₂O₁₈: C, 66.53; H, 8.15; N, 0.00; Found: C, 66.42; H, 8.21; N, 0.03; R_f =0.18 (hexane:ethyl acetate:dichloromethane = 1:1:1).

Silylation of pentamer **5**

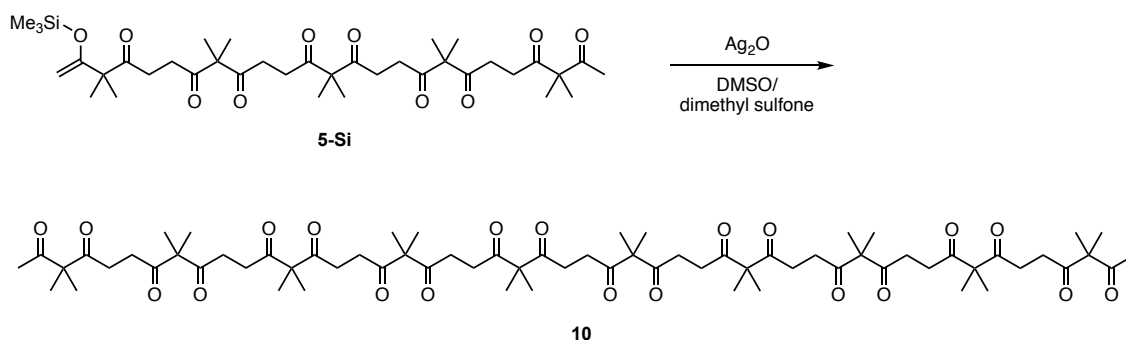


To a 20 mL two-necked round-bottom flask, pentamer **5** (1.00 g, 1.58 mmol) and sodium iodide (474 mg, 3.16 mmol) were added. After flushing the flask with N₂ gas, acetonitrile (3.0 mL) and triethylamine (485 μ L, 3.50 mmol) were added. The resulting suspension was cooled to 0 °C and trimethylchlorosilane (401 μ L, 3.17 mmol) was added via syringe. The reaction mixture was stirred at 0 °C for 2 h and quenched by the addition of water (10 mL). The products were extracted from the reaction mixture using dichloromethane (10 mL). The aqueous layer was further extracted with dichloromethane (3 $\times$ 10 mL). The combined organic layer was washed with water (10 mL), dried over anhydrous sodium sulfate, and the solvent was evaporated. The residue was purified by silica-gel column chromatography (diameter: 3.0 cm, height: 15.0 cm, eluent: hexane/ethyl acetate = 5:2) to give mono-silylated product **5-Si** (396 mg, 0.562 mmol, 36% yield).

Mono-silylated product **5-Si**

¹H NMR (400 MHz, CDCl₃, 298 K): δ 4.31 (d, J = 2.1 Hz, 1H, vinyl), 4.18 (d, J = 2.1 Hz, 1H, vinyl), 2.85-2.79 (m, 2H, ethylene), 2.77-2.67 (m, 12H, ethylene), 2.67-2.62 (m, 2H, ethylene), 2.15 (s, 3H, acetyl), 1.42-1.39 (18H, overlapping C(CH₃)₂), 1.37 (s, 6H, C(CH₃)₂), 1.22 (s, 6H, C(CH₃)₂), 0.20 (s, 9H, Si(CH₃)₃); ¹³C {¹H} NMR (100 MHz, CDCl₃, 298 K): δ 211.3, 208.7-208.4 (6 $\times$ C=O), 208.3, 207.8, 162.1, 89.0, 62.3, 61.9-61.8 (3 $\times$ C(CH₃)₂), 53.6, 32.5-32.0 (7 $\times$ CH₂), 31.0, 26.4, 23.1, 22.1-21.8 (3 $\times$ CH₃), 21.7, 0.10; IR(ATR, neat) 2976, 2935, 2913, 2874, 1697, 1627, 1468, 1389, 1366, 1254, 1039, 1011, 850 cm⁻¹; HRMS(ESI-TOF): m/z [M + Na]⁺ calcd for C₃₈H₆₀O₁₀SiNa⁺, 727.3848; found, 727.3851; Elemental analysis (%): Calcd for C₃₈H₆₀O₁₀Si: C, 64.74; H, 8.58; N, 0.00; Found: C, 64.39; H, 8.63; N, 0.00; R_f =0.30 (hexane:ethyl acetate = 5:2).

Synthesis of decamer 10

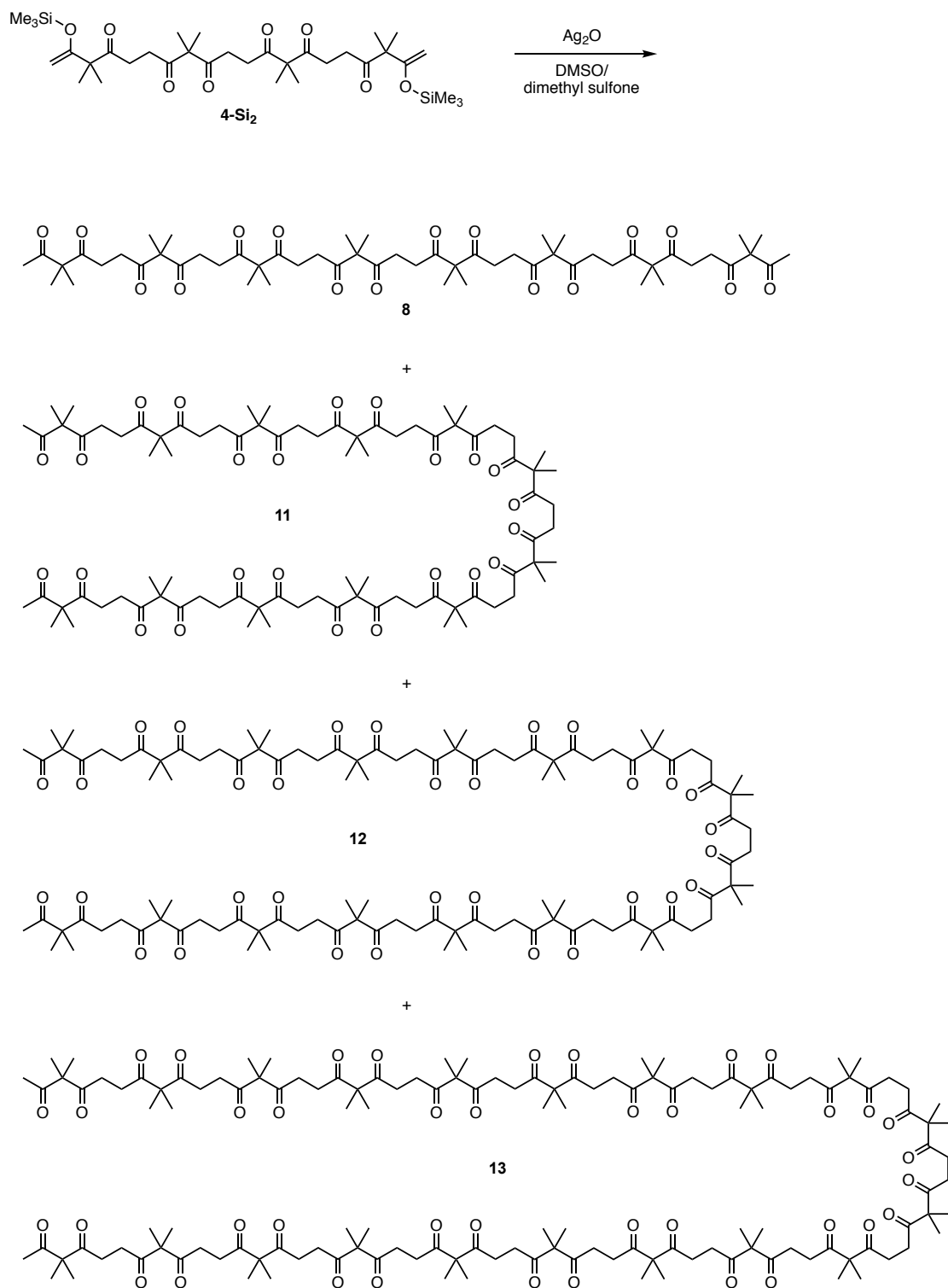


To a 10 mL round-bottom flask equipped with a reflux condenser, mono-silylated pentamer **5-Si** (300 mg, 0.426 mmol), dimethyl sulfoxide (6.04 μ L, 85.1 μ mol), dimethyl sulfone (120 mg, 1.27 mmol), and silver(I) oxide (59.1 mg, 0.255 mmol) were added. The reaction mixture was stirred at 100 $^{\circ}$ C for 2 h and, after cooling to room temperature, filtered through a Celite pad with suction. The solid on a funnel was washed with dichloromethane (80 mL) and the filtrate was evaporated under vacuum. The residue was dissolved in dichloromethane (10 mL), washed with brine (5×10 mL), and dried over anhydrous sodium sulfate. After concentrated under reduced pressure, the mixture was chromatographed on a silica gel column (diameter: 2.0 cm, height: 17.0 cm, eluent: hexane/ethyl acetate/dichloromethane = 5:6:5). The resulting solid was suspended in methanol (0.5 mL) and sonicated for 3 min. The mixture was filtered with suction and washed with methanol (3.5 mL) to give decamer **10** (64.7 mg, 51.2 μ mol, 24% yield) as a colorless solid.

3,3,8,8,13,13,18,18,23,23,28,28,33,33,38,38,43,43,48,48-Icosamethylpentacontan-2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39,42,44,47,49-icosaone (10) (decamer)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.81-2.65 (m, 36H, ethylene), 2.15 (s, 6H, acetyl), 1.40 (48H, overlapping $\text{C}(\text{CH}_3)_2$), 1.37 (12H, $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.5 ($7 \times \text{C}=\text{O}$), 208.3, 207.8, 62.2, 61.9-61.7 ($4 \times \text{C}(\text{CH}_3)_2$), 32.4-32.2 ($9 \times \text{CH}_2$), 26.4, 22.8-22.0 ($4 \times \text{CH}_3$), 21.6; IR (ATR, neat) 2992, 2980, 2937, 2920, 2871, 1693, 1462, 1441, 1388, 1375, 1363, 1240, 1201, 1175, 1160, 1128, 1074, 1015, 950 cm^{-1} ; m.p. 142-143 $^{\circ}$ C; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{70}\text{H}_{102}\text{O}_{20}\text{Na}^+$, 1285.6857; found, 1285.6804; Elemental analysis (%): Calcd for $\text{C}_{70}\text{H}_{102}\text{O}_{20}$: C, 66.54; H, 8.14; N, 0.00; Found: C, 66.30; H, 8.17; N, 0.05; R_f =0.23 (hexane:ethyl acetate:dichloromethane = 5:6:5).

Synthesis of octamer, dodecamer, hexadecamer, and icosamer (8, 11-13)



To a 50 mL round-bottom flask equipped with a reflux condenser, bis-silylated tetramer **4-Si₂** (2.00 g, 3.07 mmol), dimethyl sulfoxide (87.4 μ L, 1.23 mmol), dimethyl sulfone (1.73 g, 18.4 mmol) and silver(I) oxide (855 mg, 3.69 mmol) were added. The reaction mixture was stirred at 100 °C for 3 h, and filtered through a Celite pad using dichloromethane (150 mL) after cooling to room temperature. The filtrate was washed with brine (3 $\times$ 150 mL), dried over anhydrous sodium sulfate, and the solvent was removed under vacuum. The residue was chromatographed on a silica gel column (diameter, 4.0 cm; height, 10.0 cm) using dichloromethane/methanol (10:1, v/v) as eluent. The residue was dissolved in dichloromethane/methanol (40 mL, 1:1, v/v), and stirred with 3 M hydrochloric acid (3.0 mL) at room temperature for 20 minutes. After neutralizing with saturated aqueous sodium bicarbonate solution (10 mL), the organic layer was separated. The aqueous layer was extracted with dichloromethane (2 $\times$ 50 mL). The combined organic layer was washed with brine (100 mL), and dried over anhydrous sodium sulfate, and the solvent was evaporated *in vacuo*. The resulting mixture of oligomers was separated by recycling preparative SEC using chloroform as a mobile phase. After the separation and evaporation, the separated oligomer fractions were passed through a silica-gel column (diameter, 1.5 cm; height, 5.0 cm) using dichloromethane/methanol (25:1, v/v) as an eluent. The resulting solids were suspended in methanol (0.5 mL) and sonicated for 3 min. The mixture was filtered on a funnel with suction and washed with methanol (3.5 mL) to afford octamer **8** (137 mg, 135 μ mol, 9% yield), dodecamer **11** (106 mg, 69.9 μ mol, 7% yield), hexadecamer **12** (78.9 mg, 39.0 μ mol, 5% yield), and icosamer **13** (49.8 mg, 19.7 μ mol, 3% yield) as colorless solids.

3,3,8,8,13,13,18,18,23,23,28,28,33,33,38,38,43,43,48,48,53,53,58,58-

Tetracosamethyl-hexacontane-

2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39,42,44,47,49,52,54,57,59-tetracosane (11)
(dodecamer)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.80-2.64 (m, 44H, ethylene), 2.15 (s, 6H, acetyl), 1.43-1.35 (72H, overlapping $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.5 ($9 \times \text{C}=\text{O}$), 208.3, 207.8, 62.2, 61.8-61.7 ($5 \times \text{C}(\text{CH}_3)_2$), 32.3-32.2 ($11 \times \text{CH}_2$), 26.4, 22.0-21.7 ($5 \times \text{CH}_3$), 21.6; IR(ATR, neat) 2992, 2980, 2937, 2920, 2873, 1692, 1463, 1441, 1388, 1377, 1364, 1240, 1203, 1174, 1161, 1128, 1074, 1014, 952 cm^{-1} ; m.p. 153-155 $^\circ\text{C}$; HRMS(ESI-TOF): m/z $[\text{M} + 2\text{Na}]^{2+}$ calcd for $\text{C}_{84}\text{H}_{122}\text{O}_{24}\text{Na}_2^{2+}$, 780.4055; found, 780.4042; Elemental analysis (%): Calcd for $\text{C}_{84}\text{H}_{122}\text{O}_{24}$: C, 66.56; H, 8.11; N, 0.00; Found, C, 66.32; H, 8.15; N, 0.01; $R_f=0.33$ (dichloromethane/methanol = 25:1).

3,3,8,8,13,13,18,18,23,23,28,28,33,33,38,38,43,43,48,48,53,53,58,58,63,63,68,68,73,73
,78,78-Dotriacontamethyloctacontane-

2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39,42,44,47,49,52,54,57,59,62,64,67,69,72,74
,77,79-dotriacontane (12) (hexadecamer)

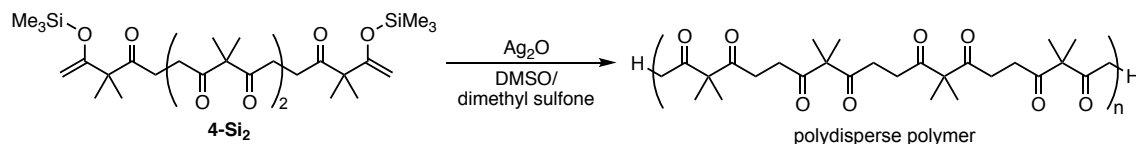
^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.82-2.64 (m, 60H, ethylene), 2.15 (s, 6H, acetyl), 1.43-1.35 (96H, overlapping $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.5-208.4 ($13 \times \text{C}=\text{O}$), 208.3, 207.8, 62.2, 62.0-61.6 ($7 \times \text{C}(\text{CH}_3)_2$), 32.4-32.2 ($15 \times \text{CH}_2$), 26.4, 22.2-21.7 ($7 \times \text{CH}_3$), 21.6; IR(ATR, neat) 2991, 2980, 2937, 2921, 2874, 1695, 1463, 1442, 1388, 1364, 1240, 1074, 1015, 951 cm^{-1} ; m.p. 158-160 $^\circ\text{C}$; HRMS(ESI-TOF): m/z $[\text{M} + 2\text{Na}]^{2+}$ calcd for $\text{C}_{112}\text{H}_{162}\text{O}_{32}\text{Na}_2^{2+}$, 1032.5417; found, 1032.5378. Elemental analysis (%): Calcd for $\text{C}_{112}\text{H}_{162}\text{O}_{32}$: C, 66.58; H, 8.08; N, 0.00; Found: C, 66.27; H, 8.13; N, 0.01; $R_f=0.33$ (dichloromethane/methanol = 25:1).

3,3,8,8,13,13,18,18,23,23,28,28,33,33,38,38,43,43,48,48,53,53,58,58,63,63,68,68,73,73,78,78,83,83,88,88,93,93,98,98-Tetracontamethylhectane-2,4,7,9,12,14,17,19,22,24,27,29,32,34,37,39,42,44,47,49,52,54,57,59,62,64,67,69,72,74,77,79,82,84,87,89,92,94,97,99-tetracontane (13) (icosamer)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.85-2.61 (m, 76H, ethylene), 2.15 (s, 6H, acetyl), 1.44-1.34 (120H, overlapping $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.6, 208.5-208.3 ($17 \times \text{C}=\text{O}$), 208.3, 207.8, 62.2, 62.0-61.6 ($9 \times \text{C}(\text{CH}_3)_2$), 32.4-32.0 ($19 \times \text{CH}_2$), 26.4, 22.0-21.7 ($9 \times \text{CH}_3$), 21.6; IR(ATR, neat) 2980, 2937, 2920, 2875, 1692, 1464, 1388, 1364, 1240, 1074, 1014, 951 cm^{-1} ; m.p. 164-167 $^\circ\text{C}$; HRMS(ESI-TOF): m/z $[\text{M} + 2\text{Na}]^{2+}$ calcd for $\text{C}_{140}\text{H}_{202}\text{O}_{40}\text{Na}_2^{2+}$, 1284.6778; found, 1284.6773; Elemental analysis (%): Calcd for $\text{C}_{140}\text{H}_{202}\text{O}_{40}$: C, 66.59; H, 8.06; N, 0.00; Found: C, 66.30; H, 8.14; N, 0.01; $R_f=0.33$ (dichloromethane/methanol = 25:1).

Preparation and Analysis of Polydisperse Polymer

Preparation of polydisperse polymer



Synthesis of octamer **8**, dodecamer **11**, hexadecamer **12**, and icosamer **13** using bis-silylated tetramer **4-Si₂** (2.00 g, 3.07 mmol), dimethyl sulfone (1.73 g, 18.4 mmol), dimethyl sulfoxide (87.4 μL , 1.23 mmol), and silver(I) oxide (855 mg, 3.69 mmol). During the SEC separation step, the high molecular weight component ($N \geq 20$) was collected. After evaporation of the solvent in vacuo, the mixture was passed through silica-gel column (diameter, 1.5 cm; height, 5.0 cm) using dichloromethane/methanol (25:1, v/v) as an eluent. The resulting solid was suspended in methanol (0.5 mL) and sonicated for 3 minutes, and then filtered with suction. The solid on a funnel was washed with methanol (3.5 mL) to give polydisperse polymer (221 mg).

Polydisperse polymer ($N \geq 20$)

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.94-2.54 (m, 88H, ethylene), 2.15 (s, 6H, acetyl), 1.46-1.28 (138H, overlapping $\text{C}(\text{CH}_3)_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 208.9-208.1, 207.8, 62.2, 62.0-61.6, 32.5-32.0, 26.4, 22.2-21.7, 21.6; IR(ATR, neat) 2979, 2937, 2915, 2876, 1692, 1465, 1442, 1388, 1364, 1241, 1074, 1014, 950 cm^{-1} . The degree of polymerization was expected as 23 from the integration ratio of ethylene and acetyl peaks.

Crystallographic Studies of Polyketone Oligomers

Single crystal preparation details of pentamer 5 and hexamer 6

The single crystal of pentamer **5** was prepared by vapor diffusion of cyclohexene into a 1,2-dichloroethane solution overnight at room temperature. The grown single crystals in a vial were then thermally annealed at 50°C for 3.5 days and slowly cooled to room temperature. The diffraction data were recorded at -150°C. Similarly, the single crystal of hexamer **6** was prepared by vapor diffusion of cyclohexene into a 1,2-dichloroethane solution overnight at room temperature. The grown single crystals in a vial were then thermally annealed at 50°C for 2 days. The diffraction data were recorded at -150 °C.

Crystallographic data of trimer 3, pentamer 5, and hexamer 6

Trimer 3

$C_{21}H_{32}O_6$, $M = 380.46$, crystal size: $0.52 \times 0.22 \times 0.05 \text{ mm}^3$, Monoclinic, space group $P2_1/c$, $a = 31.153(6) \text{ \AA}$, $b = 6.5006(14) \text{ \AA}$, $c = 10.454(2) \text{ \AA}$, $\alpha = \gamma = 90^\circ$, $\beta = 96.184(7)^\circ$, $V = 2104.7(7) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.087 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.201 \text{ g/cm}^3$, $1.973^\circ \leq \theta \leq 27.484^\circ$, 2152 unique reflections out of 4817 with $I > 2\sigma(I)$, GOF = 1.003, $R_1 = 0.0842$ and $wR_2 = 0.2428$ for all data. CCDC deposit number: 1907900.

Pentamer 5

$C_{35}H_{52}O_{10}$, $M = 632.76$, crystal size: $0.83 \times 0.10 \times 0.06 \text{ mm}^3$, Orthorhombic, space group $Pna2_1$, $a = 10.4486(3) \text{ \AA}$, $b = 8.0259(2) \text{ \AA}$, $c = 41.6406(12) \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$, $V = 3491.96(17) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.713 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.204 \text{ g/cm}^3$, $2.122^\circ \leq \theta \leq 67.494^\circ$, 5027 unique reflections out of 5956 with $I > 2\sigma(I)$, GOF = 1.083, $R_1 = 0.1315$ and $wR_2 = 0.4120$ for all data. CCDC deposit number: 2173799.

Hexamer 6

$C_{42}H_{62}O_{12}$, $M = 758.91$, crystal size: $0.38 \times 0.06 \times 0.01 \text{ mm}^3$, Orthorhombic, space group $Iba2$, $a = 48.930(9) \text{ \AA}$, $b = 8.2077(17) \text{ \AA}$, $c = 10.3345(18) \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$, $V = 4150.4(14) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.719 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.215 \text{ g/cm}^3$, $3.613^\circ \leq \theta \leq 51.377^\circ$, 1050 unique reflections out of 1893 with $I > 2\sigma(I)$, GOF = 1.619, $R_1 = 0.1571$ and $wR_2 = 0.4353$ for all data. CCDC deposit number: 2173800.

Crystalline sample preparation details for the PXRD studies

The samples of polyketone discrete oligomers **2**, **4-13** for the PXRD measurements were prepared by a slow evaporation of chloroform solution over 1 day at room temperature and further dried under vacuum overnight. The sample of trimer **3** was prepared by slow cooling from the melt and kept at $-20\text{ }^{\circ}\text{C}$ for 1 week. The resulting samples were ground and placed in the hollow of a silicon zero background sample holder for the diffraction measurements. The simulated PXRD patterns of dimer **2**, and tetramer **4** were generated using the previously reported single crystal X-ray structures.²

Details of SAXS measurement

The samples of tetramer **4**, octamer **8**, dodecamer **11**, hexadecamer **12**, and icosamer **13** for the SAXS diffraction were prepared by thermal annealing from the melt at specified temperatures over 1 day ($40\text{ }^{\circ}\text{C}$ for tetramer **4**, $100\text{ }^{\circ}\text{C}$ for octamer **8**, dodecamer **11**, hexadecamer **12**, and icosamer **13**) then slowly cooled to room temperature. The annealed samples were ground and used for the diffraction measurements.

Details of Atomic Force Microscope (AFM) Observation

AFM System

AFM measurements were performed by frequency modulation (FM) mode using a laboratory-built AFM system combined with commercial AFM controllers. The laboratory-built AFM system was equipped with an ultra-low noise deflection sensor and a photothermal excitation module. The commercial AFM controllers of Asylum ARC2 (Oxford Instruments) and Nanonis OC4.5 (SPECS GmbH) were used as a general AFM controller and a cantilever oscillation controller, respectively.

AFM cantilever and measurement condition

AFM cantilevers with a gold coating on the reflection side (160 AC-NG, MikroMasch) were used for the AFM measurements. The tip side of AFM cantilevers was coated with 30 nm thickness of Si using a magnetron sputter coater (QT150, Quorum Technologies) to improve the reproducibility of FM-AFM measurements in liquid, as reported in the previous studies.^{6,7} The cantilever vibration was oscillated by a photothermal excitation method.

Sample preparation

A 0.05 mM solution of octamer **8** was prepared with chloroform (Wako, infinity pure grade). A highly oriented pyrolytic graphite (HOPG, 7 mm × 7 mm squares, NT-MDT, GRBS/0.6) was fixed with glue on an AFM sample holder. The solution (5 μ L) was dropped onto a freshly cleaved HOPG surface and covered with a glass dish for slow evaporation. After the evaporation, the surface was rinsed three times with ultra-pure water (80 μ L) and used for the AFM measurement.

Details of Theoretical Calculation

Computational Details

To obtain a plausible packing structure of infinite polyketone chains, the crystal structure of hexamer **6** was referred. The packing structure was optimized under periodic boundary condition without cell relaxation by the self-consistent-charge density-functional tight binding (DFTB) method with the third-order expansion as implemented in the DFTB+ package version 21.1.⁸ The 3ob parameter set^{9,10} with Hubbard parameters -0.1492 for C, -0.1857 for H, and -0.1575 for O were employed. Grimme's D3 type dispersion^{11,12} was included. The optimization was followed by an optimization with cell relaxation in the same calculation conditions. After this optimization, the chains with the length of octamer **8**, dodecamer **11**, hexadecamer **12**, icosamer **13** were modeled from the optimized polymer with infinite length by termination of H atoms. All models with finite length can have C2 symmetry, and we optimized each model with C2 symmetry at the B3LYP/6-31G(d,p) level of theory with Grimme's type dispersion correction^{11,12} using Gaussian 16 Rev. C01.¹³

Optimized Structures

The chain lengths of the optimized polyketone structures were determined as the distances between the two oxygen atoms of the terminal carbonyl groups. The helical chains of the polyketones were moderately twisted after the optimizations in hexadecamer **12**, and icosamer **13**. These results are probably due to the fact that the optimization was performed under vacuum conditions without considering the packing structure. Still, the multiple intramolecular hydrogen bonds within the chains were maintained after the optimization, which were suggested in the optimized polymer model with infinite length.

2.7. References

- [1] C. Hertweck, *Angew. Chem. Int. Ed.*, **2009**, *48*, 4688–4716.
- [2] M. Uesaka, Y. Saito, S. Yoshioka, Y. Domoto, M. Fujita, Y. Inokuma, *Commun. Chem.* **2018**, *1*, 23.
- [3] Y. Manabe, M. Uesaka, T. Yoneda, Y. Inokuma, *J. Org. Chem.*, **2019**, *84*, 9957–9964.
- [4] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, **2015**, *71*, 3–8.
- [5] G. M. Sheldrick, *Acta Crystallogr. Sect. C*, **2015**, *71*, 3–8.
- [6] S. M. R. Akrami, H. Nakayachi, T. Watanabe-Nakayama, H. Asakawa, T. Fukuma, *Nanotechnology*, **2014**, *25*, 455701.
- [7] H. Asakawa, E. Holmstroom, A. S. Foster, S. Kamimura, T. Ohno, T. Fukuma, *J. Phys. Chem. C*, **2018**, *122*, 24085–24093.
- [8] B. Hourahine, B. Aradi, V. Blum, F. Bonafé, A. Buccheri, C. Camacho, C. Cevallos, M. Y. Deshayé, T. Dumitrică, A. Dominguez, S. Ehlert, M. Elstner, T. van der Heide, J. Hermann, S. Irle, J. J. Kranz, C. Köhler, T. Kowalczyk, T. Kubař, I. S. Lee, V. Lutsker, R. J. Maurer, S. K. Min, I. Mitchell, C. Negre, T. A. Niehaus, A. M. N. Niklasson, A. J. Page, A. Pecchia, G. Penazzi, M. P. Persson, J. Řezáč, C. G. Sánchez, M. Sternberg, M. Stöhr, F. Stuckenberg, A. Tkatchenko, V. W.-z. Yu, and T. Frauenheim, *J. Chem. Phys.*, **2020**, *152*, 124101.
- [9] M. Gaus, A. Goez, M. Elstner, *J. Chem. Theory Comput.*, **2013**, *9*, 338–354.
- [10] M. Kubillus, T. Kubař, M. Gaus, J. Řezáč, M. Elstner, *J. Chem. Theory Comput.*, **2015**, *11*, 332–342.
- [11] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.*, **2010**, *132*, 154104.
- [12] S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.*, **2011**, *32*, 1456–1465.
- [13] Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M.

Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

Chapter 3

From Polyketones to Polyimine: Development of π -Conjugated Chromophore and Ion Adsorbent

Abstract

Rigid, rod-like π -conjugated polyimines were developed from structurally flexible aliphatic polyketones by two-step transformations. Discrete aliphatic oligoketones were quantitatively converted into oligoimines by the reaction of hydrazine at all the 1,3-diketone sites. The ethylene bridges of the oligoimines were then fully oxidized in a *trans*-selective fashion to give linear π -conjugated oligoimines. UV-vis absorption spectroscopy confirmed that the lowest-energy absorption bands of the oligoimines continuously red-shifted as the number of repeating units increased. In addition, the generation of linear π -conjugated polyimines was also examined from polydisperse polyketone polymer longer than tetramer. The similar two-step transformation furnished virtually insoluble blown solid exhibiting a broad solid-state absorption over the whole visible region. This insoluble polymer was utilized as a functional metal-ion adsorbent at its interfaces using the coordinative imine units in the solution.

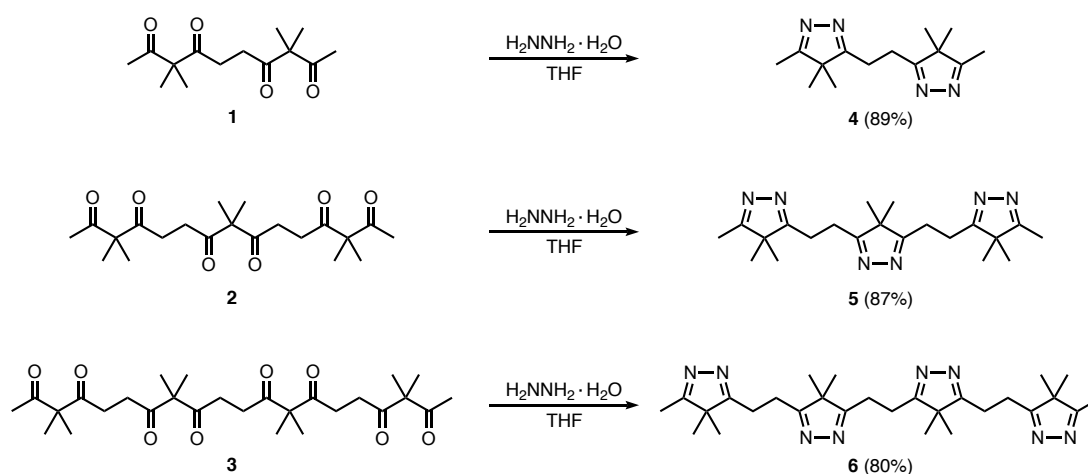
3.1. Introduction

In Chapter 2, the author has described the synthesis of stable and discrete aliphatic polyketones composed of an alternating 1,3- and 1,4-diketone repeating unit.¹ Owing to the structurally flexible nature of the polyketone, shorter oligomers exhibited various conformations in the solid state,²⁻⁶ while more extended analogs commonly adopted helical conformations in similar crystal packings.⁷⁻¹⁰ In this chapter, another important characteristic of polyketones as shapable molecular ropes, namely reactivity, was explored for the development of functional materials. Here, structurally flexible polyketones were converted to a rigid, rod-like structure by forming fully π -conjugated polyimines. Despite the presence of quaternary carbon atoms on the polyketone chain, extended π -conjugation was generated by bypassing them through the formation of isopyrazole rings¹¹ at 1,3-diketones and subsequent oxidations at bridging ethylene units.¹² The absorption spectra were bathochromic shifted, obeying the elongation of conjugation length of oligoimines. This synthetic protocol was also applicable to polydisperse polyketone polymer to transform into virtually insoluble π -conjugated polyimines, which showed the broad solid-state absorption band over the visible region. In addition, the insolubility and metal-ion coordination properties of π -conjugated polyimines led to their application as a functional metal ion adsorbent.

3.2. Development of π -Conjugated Oligoimines from Aliphatic Oligoketones

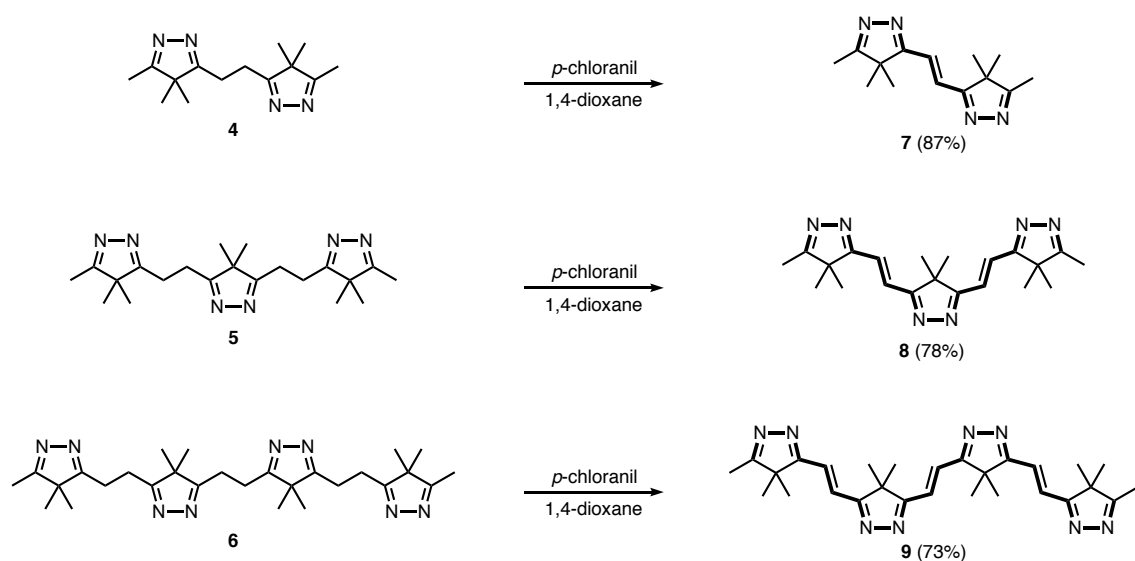
To construct a linearly extended π -conjugated system onto the carbon chain of aliphatic polyketones, the author firstly attempted to transform 1,3-diketone units into isopyrazole rings.¹¹ Upon implementing azine units on the carbon chain, subsequent oxidation of the ethylene bridges can form the desired extended π -conjugation while avoiding the quaternary carbon atoms.

By the treatment of aliphatic oligoketones **1-3** with hydrazine monohydrate, aliphatic oligoimines **4-6** were obtained in 80-89% yield (**Scheme 3-1**). Analysis of the ^1H NMR spectra of the reaction solutions showed a nearly quantitative conversion of **1-3** without the formation of detectable by-products. The complete conversion of carbonyl groups into imine groups was confirmed by the analysis of ^{13}C NMR spectra. In the ^{13}C NMR spectra, the carbonyl carbon peaks (200-210 ppm) disappeared after the transformation, and new imine carbon peaks were observed at 180-190 ppm, which was consistent with the previous report.¹



Scheme 3-1. Transformation of aliphatic oligoketones **1-3** into oligoimines **4-6**.

All the bridging ethylenes of **4-6** were stereoselectively oxidized to *trans*-vinylene bridges by treating *p*-chloranil in 1,4-dioxane (**Scheme 3-2**). When tetraimine **4** was mixed with *p*-chloranil in 1,4-dioxane at room temperature, the full conversion of **4** was observed at 1 h. In the ^1H NMR spectrum, the olefinic proton signal at 7.27 ppm was newly observed, while the ethylene proton signal at 2.98 ppm disappeared without the formation of detectable by-products.



Scheme 3-2. Synthesis of π -conjugated oligoimines **7-9**.

After the purification by silica-gel column chromatography, the oxidized product **7** was obtained in 87% yield as an off-white solid. Using the similar reaction conditions, hexamine **5** was transformed into conjugated hexamine **8** in 78% yield. In the case of octamine **6**, conjugated octamine **9** was isolated in 73% yield by heating the reaction solution to 50 °C, because the conversion of **6** was not completed at room temperature, presumably due to the low solubility of partially oxidized reaction intermediates. Analysis of the ^1H NMR spectra of **8** and **9** revealed terminal vinylene proton signals as a pair of doublet peaks (7.41 and 7.32 ppm for **8**, 7.41 and 7.33 ppm for **9** in CDCl_3). The observed coupling constant of 17.0 Hz indicated the *trans*-selective oxidation, while no *cis*-vinylene diastereomers were not observed even for octamine **9**.

The *trans* configurations of the vinylene-bridged products **7** and **8** were unambiguously determined by single crystal X-ray structure analyses (**Figure 3-1**). The bond lengths of the C=C double bond were 1.339(3) Å and 1.346(2) Å for **7** and **8**, respectively. The diazadiene subunits in the crystal structures took an all-*s-trans* conformation in both **7** and **8**. The planar structures of **7** and **8** indicated the effective extension of π -conjugation over the oligoimine carbon chains. The π -conjugated oligoimines in the X-ray structures exhibited relatively rigid and rod-like conformations in contrast to the curled or waved structures of aliphatic oligoketones **1-3**. These structural changes suggested that the structural flexibility of the carbon chain was dramatically altered by the sequential imination and oxidation transformations. By reflecting the structural rigidification, conjugated products **7-9** were less soluble in common organic solvents, such as dimethyl sulfoxide, toluene, and acetonitrile, as the repeating number of monomer unit was

increased. In contrast, structurally flexible oligoketones **1-3** and oligoimines **4-6** retained good solubility regardless of their chain length.

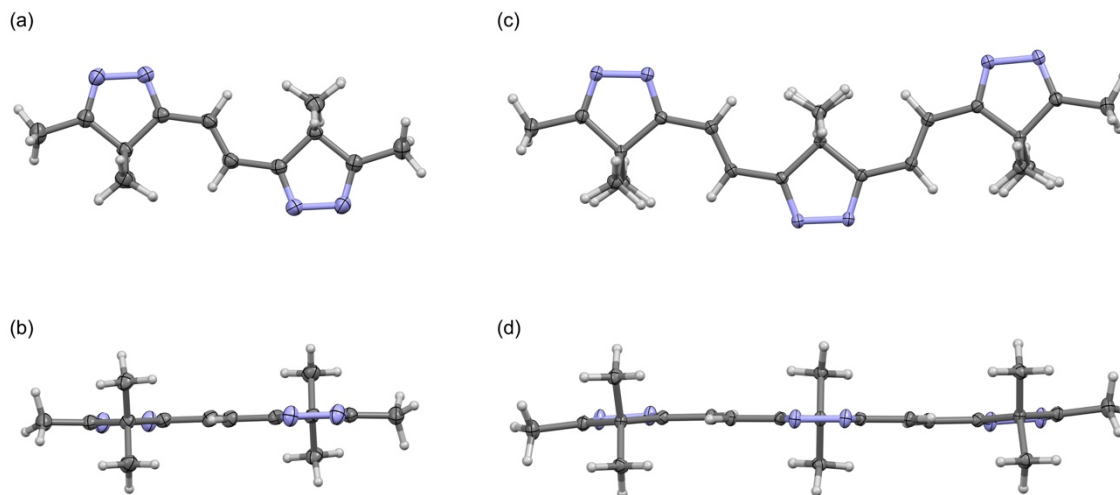


Figure 3-1. Single crystal X-ray structures of π -conjugated tetraimine **7** (a: top view, b: side view) and hexaimine **8** (c: top view; d: side view).

The π -conjugation over the carbon chains of **7-9** was also examined in UV-vis absorption spectra (**Figure 3-2**). Before the oxidation transformations, oligoketones **1-3** and oligoimines **4-6** did not exhibit any absorption band above 300 nm in CH_2Cl_2 solution. In π -conjugated tetraimine **7**, an intense absorption band was observed at $\lambda_{\text{max}} = 309$ nm with a molar extinction coefficient of $2.2 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ in CH_2Cl_2 solution. Upon the chain length elongation, the low-energy absorption band was red-shifted to 363 and 392 nm in compounds **8** and **9**, respectively, with the increase of the absorption coefficient values. According to the bathochromic shift, compounds **8** and **9** showed a yellow color in the solutions. This trend in the absorption bands was similar to that of polyenes and azines, which are nitrogen embedded analogs of polyenes. From the UV-vis absorption spectra, it was clearly shown that the π -conjugation of oligoimines **7-9** was effectively extended upon the chain length elongation by the oxidation of the ethylene bridges, although the quaternary carbons existed in the carbon chains.

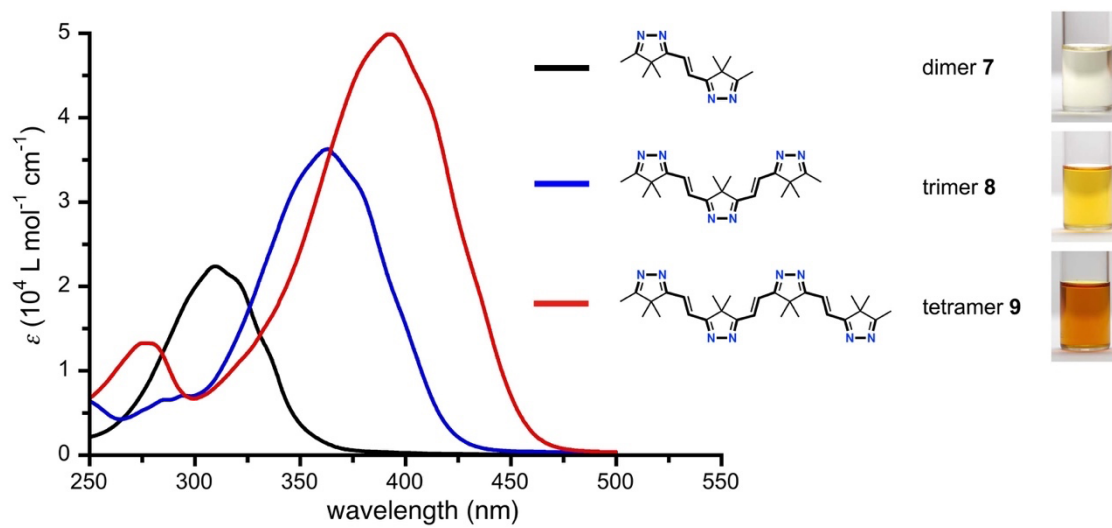
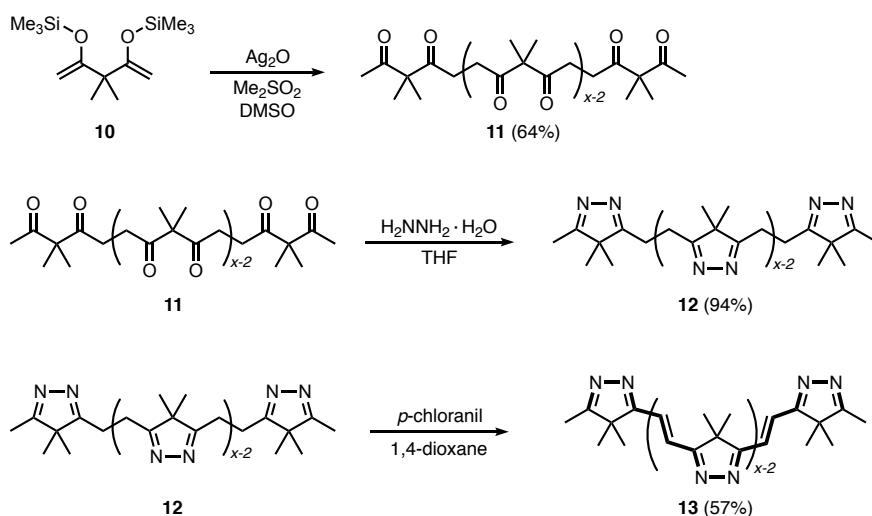


Figure 3-2. UV-vis absorption spectra of π -conjugated oligoimines **7-9** in CH_2Cl_2 and photographs of their solutions.

3.3. Transformation of Polyketone Polymers into π -Conjugated Polyimines

The author has next attempted similar chemical transformations of polydisperse polymers based on the results of the efficient transformations of aliphatic oligoketones **1-3** into π -conjugated oligoimines **7-9** (Scheme 3-3). Polyketone polymer **11** was prepared by a homo-coupling reaction from bis-silyl enol ether **10** in 64% yield. A mean degree of polymerization value was estimated to be 5.1 from the ^1H NMR spectrum (Figure 3-3).



Scheme 3-3. Synthesis of polyketone polymer **11** and its transformation into π -conjugated polyimine **13**.

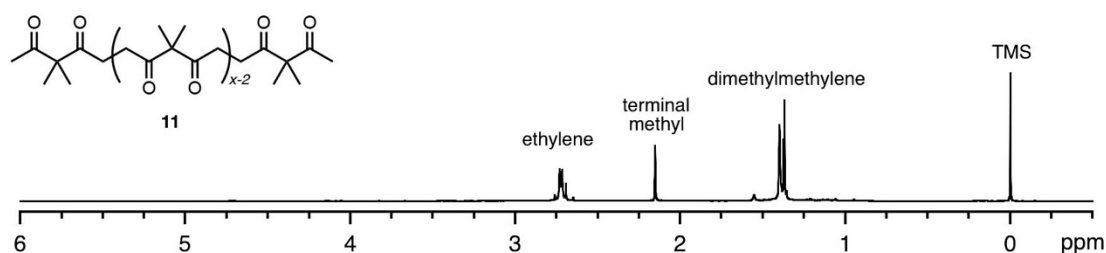


Figure 3-3. ^1H NMR spectrum of polyketone **11**.

The MALDI-TOF mass spectrum showed sodium ion adduct peaks of oligoketones up to docosamer (22 mer) (Figure 3-5a). The polydisperse index of **11** was estimated to be 1.24 from the MALDI-TOF mass spectrum. By treating polymer **11** with hydrazine monohydrate (1.2 equiv. for **11** based on monomer unit) in tetrahydrofuran, polyimine polymer **12** was obtained in 94% yield. In the ^{13}C NMR spectrum, the full conversion of

carbonyl groups into imine groups was confirmed by the disappearance of carbonyl carbon signals at 207.7-209.6 ppm and the appearance of imine carbon signals at 180.3-182.2 ppm (**Figure 3-4**). From the MALDI-TOF mass spectrum of polyimine **12**, the full conversion of 1,3-diketone unit into isopyrazole unit was indicated (**Figure 3-5b**). When polyimine **12** was treated with *p*-chloranil in 1,4-dioxane under the reflux condition, the color of the reaction solution was immediately turned into dark brown with the formation of a precipitate. The precipitate was collected by suction filtration and washed with 1,4-dioxane and methanol. Still, most of the precipitate was insoluble in common organic solvents, indicating the formation of π -conjugated polymer **13** as structurally rigid products by the extension of π -conjugation.

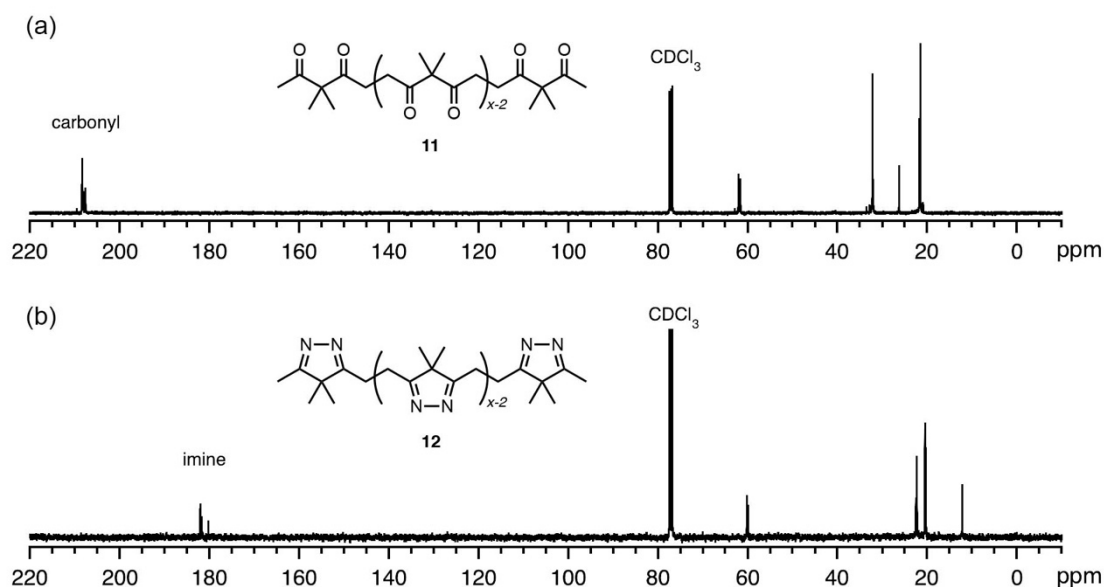


Figure 3-4. ^{13}C NMR spectra of (a) polyketone **11** and (b) polyimine **12**.

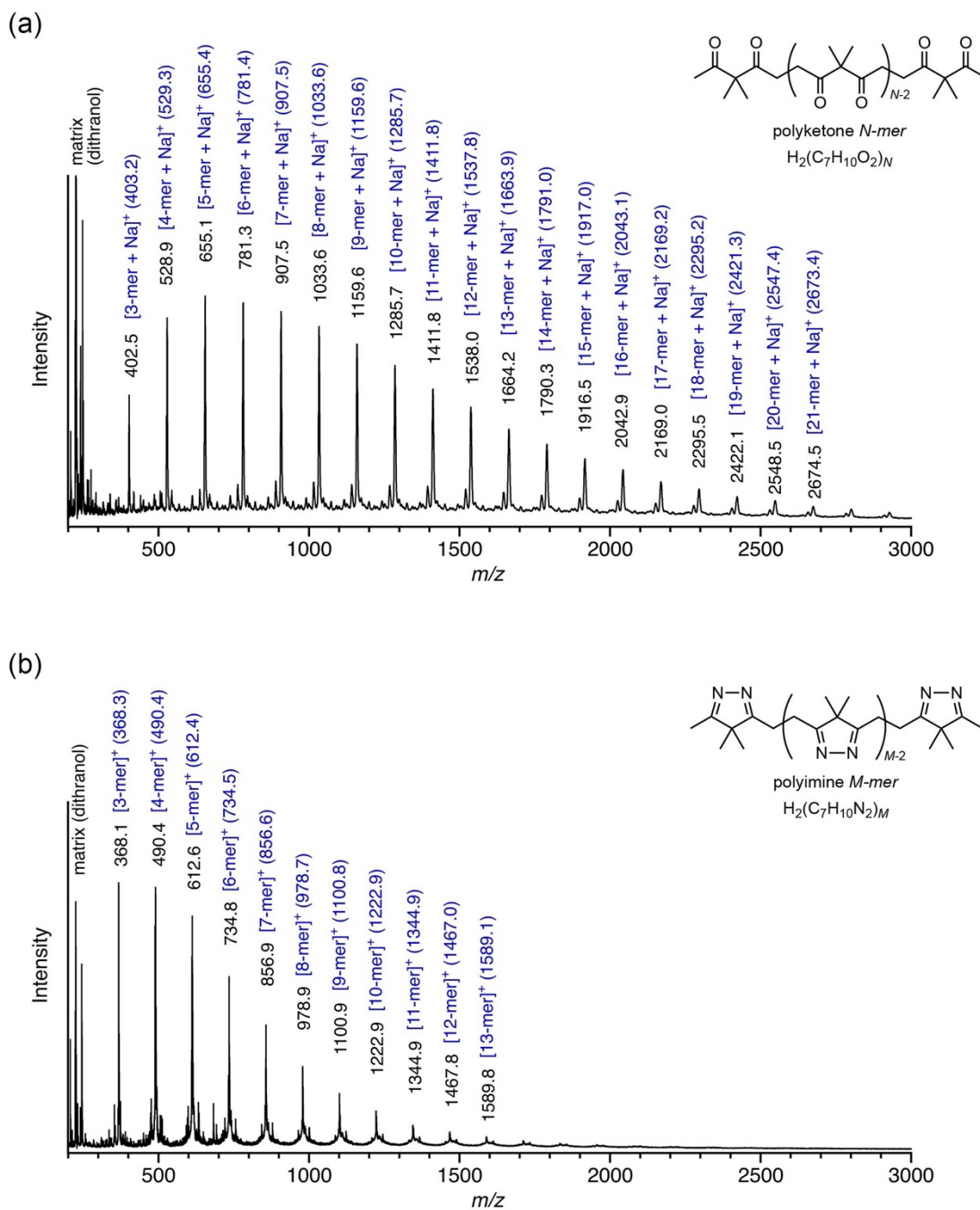


Figure 3-5. MALDI-TOF mass spectra of (a) polyketone **11** and (b) polyimine **12** using dithranol and NaPF₆ as matrixes (black: observed m/z values, blue: calculated values for the corresponding ions).

The effective π -conjugation in the oxidized polymer **13** was confirmed by solid-state diffuse reflectance spectroscopy (**Figure 3-6**). In the reflectance spectrum, the broad absorption band of **13** ($\lambda_{\text{max}} = 414 \text{ nm}$) was observed throughout the visible region, and the absorption edge reached the near-infrared region ($\sim 900 \text{ nm}$). The bathochromic shift in the absorption spectrum of **13** was remarkable compared to that of octaimine **9**, suggesting the effective long-range π -conjugation in the π -conjugated polymer **13**.

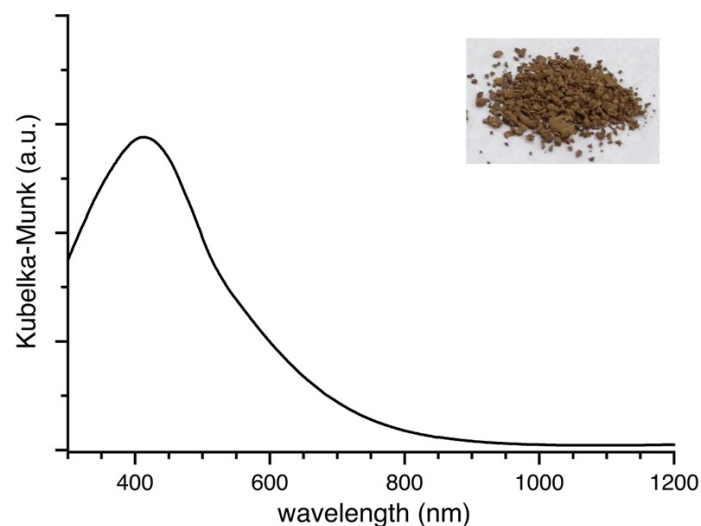


Figure 3-6. Solid-state diffuse reflectance spectrum of π -conjugated polyimine polymer **13**. The inset picture shows polymer **13** under ambient light.

Efficient oxidation of the bridging ethylene units of polyimine **12** was also suggested from IR spectroscopy (**Figure 3-7**). Before and after the oxidation, the author has focused on the signals of the imine stretching band. Tetraimine **4** showed nearly a single signal of the imine stretching band at 1572 cm^{-1} . After the oxidation, π -conjugated tetraimine **7** showed two different signals at 1566 and 1523 cm^{-1} corresponding to imine stretching signals. These two signals were assigned to terminal and *trans*-vinylene bridged internal imines, respectively. A similar trend was confirmed for the pairs of hexamines **6** and **8** and the pairs of octaimine **7** and **9**. As the number of imine subunits increased along with the chain length elongation, the relative intensities of the conjugated imines at 1513 cm^{-1} (both **8** and **9**) to the terminal imines were increased. For the π -conjugated polymer **13**, the intensity of terminal imines at 1568 cm^{-1} was very weak, but the intense signal of the conjugated imines was observed at 1510 cm^{-1} , although the unconjugated polyimine **12** showed similar signals compared to oligoimines **4-6**. This result suggested that the oxidation of the bridging ethylenes was efficiently proceeded by considering the mean degree of polymerization of the polyketone polymer **13**.

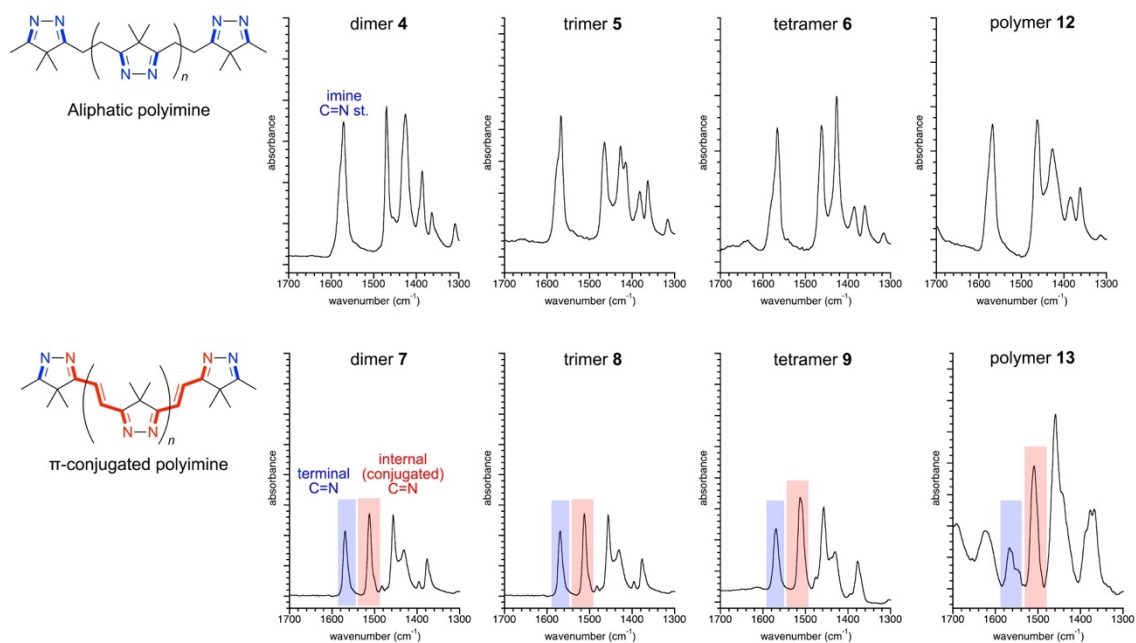


Figure 3-7. Comparison of IR spectra for aliphatic oligo- and polyimines **4-6** and **12** with π -conjugated imines **7-9** and **13**.

3.4. Theoretical Calculation Studies of π -Conjugated Polyimines

The effects of the linear π -conjugation extension were further investigated by DFT calculations. Structural optimizations of the π -conjugated oligoimines were conducted at the B3LYP/6-31G(d) level of theory. The initial structures of oligoimines were constructed from the crystal structures for **7** and **8**, and the extended structures with all *trans*-vinylene and *s-trans* conformations for **9** and longer oligomers (6, 8, 12 and 16 mer). After the structural optimizations, all oligomers exhibited planar conformations. TD-DFT calculations were then performed on the optimized structures at the same level of calculation. By plotting the energy levels of the frontier orbitals for the number of repeating units, it was clearly demonstrated that the HOMO-LUMO gaps of the π -conjugated oligomers gradually decreased with the increase of the repeating monomer units (**Figure 3-8a**). Although the stabilization of the LUMO energy level was observed up to 8 mer, the slight shift of the HOMO and LUMO energy levels was observed over 8 mer.

The Kohn-Sham orbitals for HOMOs and LUMOs of π -conjugated oligoimines **7-9** had a similar trend to that of polyenes (**Figure 3-8b**). In the 10 π -electron system of dimer **7**, the four and five nodal planes were observed in the HOMO and LUMO orbitals, respectively. The number of nodal planes in the frontier orbitals was increased in trimer **8** and tetramer **9** as the number of π -electrons was increased. These trends were also observed for polyene analogs.¹³ Although a similar trend was observed for longer oligomers, the orbital coefficients at the terminal imine units became almost negligible, whose trend was consistent with the trivial shift of the HOMO and LUMO energy level gaps for the longer oligomers (**Figure 3-9**). This result indicated that the effective conjugate length was limited although the number of imine units was increased.

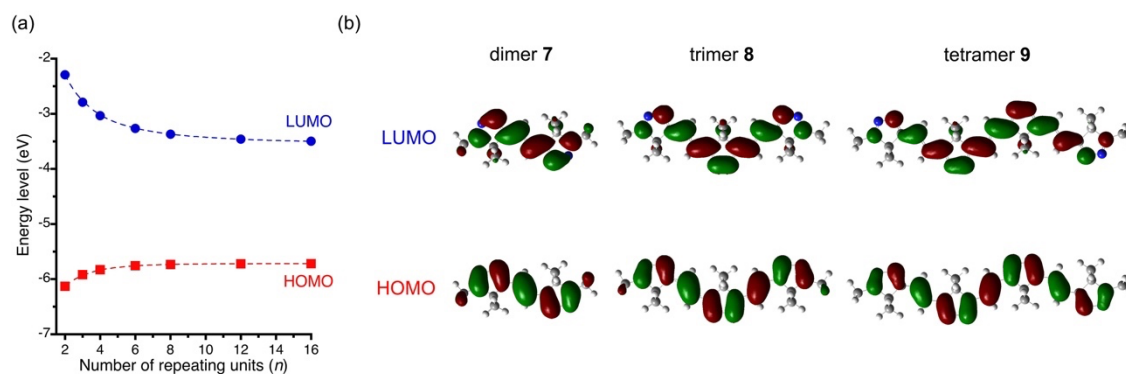


Figure 3-8. (a) Energy levels of HOMO and LUMO orbitals for π -conjugated oligoimines **7-9**; (b) Frontier orbitals of π -conjugated oligoimines **7-9**.

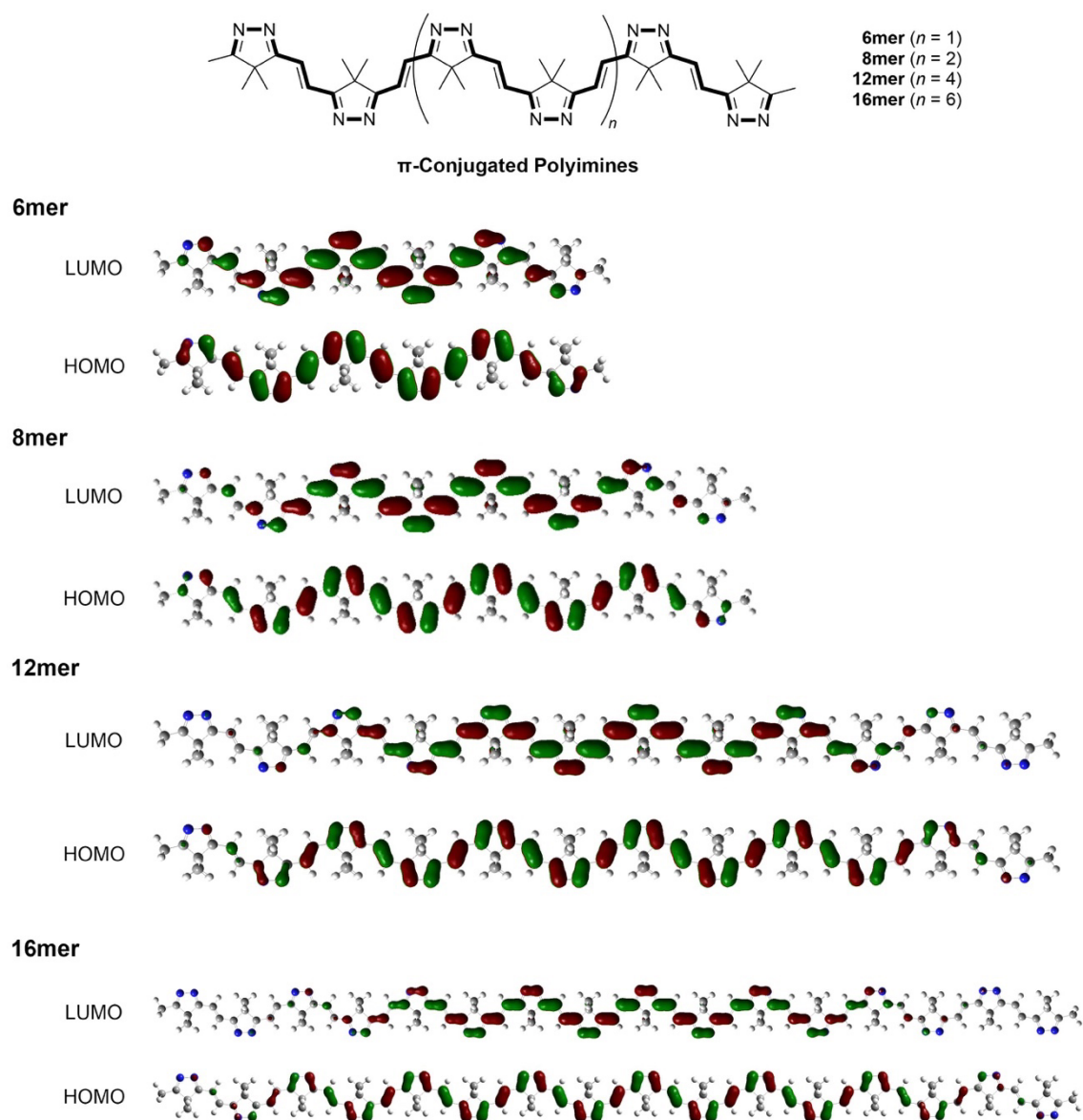


Figure 3-9. Frontier orbitals for conjugated polyimines (6-16 mers) at B3LYP/6-31G(d) level of theory.

TD-DFT calculations were performed to compare the UV-vis spectra with the calculated electronic transitions. From the TD-DFT calculations, it was implied that the lowest energy absorption bands in the UV-vis spectra were mainly attributed to the electronic transitions from HOMO to LUMO. The calculated wavelengths of the HOMO to LUMO transitions were $\lambda_{\text{max}} = 333, 420, \text{ and } 482 \text{ nm}$, with the oscillator strengths of 0.793, 1.296, and 1.815, for **7**, **8**, and **9**, respectively (**Figure 3-10**). The bathochromic shift of absorption wavelengths and increased molar coefficients, observed in the calculated results, were in a similar tendency to the observed spectra in the UV-vis

measurements. In the case of further longer polyketones, the red-shift of the lowest electronic bands from 603 to 659 nm was observed with the increase of the oscillator strengths from 6 mer to 16 mer, respectively (**Figure 3-11**). The red-shift of the lowest electronic transitions was virtually saturated at 16 mer, even the B3LYP functional tends to underestimate the molecular excitation. The results of the TD-DFT calculations can approximately explain the solid-state diffuse reflectance spectra of the π -conjugated polymer **13**, although the gas phase calculation results cannot be directly compared due to the non-negligible π -stackings of each rigid oligomer. Considering the longer oligomer components of polyketone **11**, at least docosamer, the broad absorption spectrum of **13** over the whole visible region was reasonable.

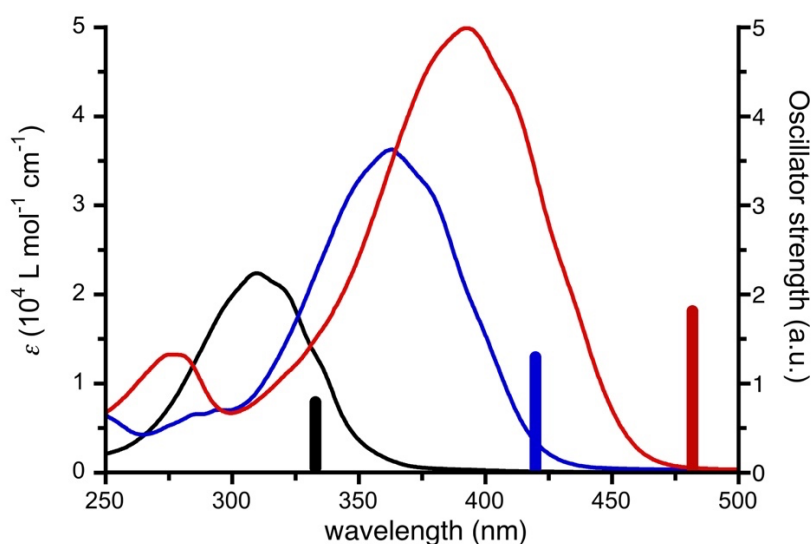


Figure 3-10. TD-DFT calculated transition (bar) and observed absorption spectra (lines; CH_2Cl_2) of π -conjugated oligoimines (**7**: black, **8**: blue, **9**: red). Calculated transition bands are listed as follows: 332.92 nm for **7**: HOMO $\rightarrow$ LUMO (99%), oscillator strength $f = 0.7927$; 419.81 nm for **8**: HOMO $\rightarrow$ LUMO (100%), oscillator strength $f = 1.2955$; 481.81 nm for **9**: HOMO $\rightarrow$ LUMO (100%), oscillator strength $f = 1.8152$.

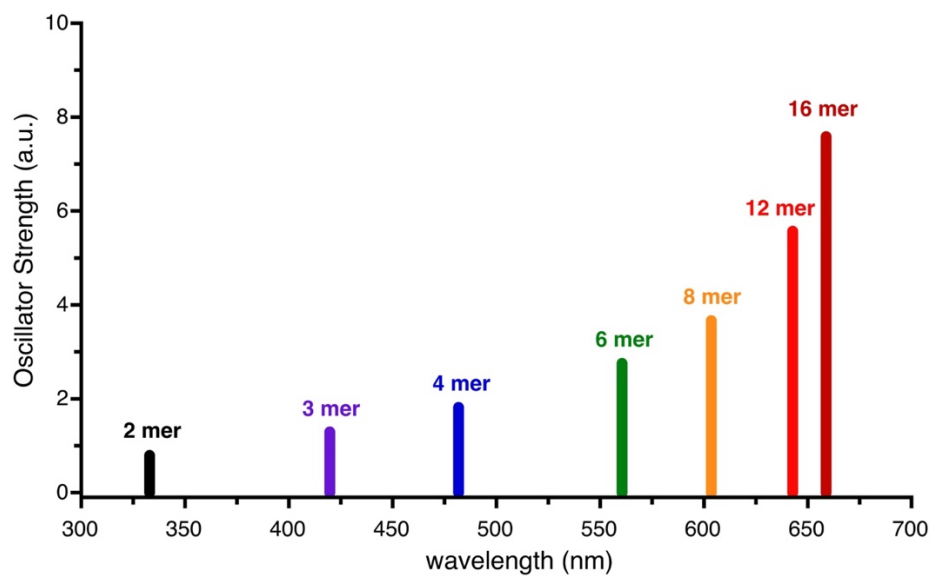


Figure 3-11. Calculated lowest energy transitions for conjugated oligoimines (6-16 mers) by TD-DFT at B3LYP/6-31G(d) level of theory.

3.5. Application of Insoluble π -Conjugated Polyimines as a Metal Ion Adsorbent

Most of the components of the polydisperse π -conjugated polyimine **13** were insoluble in common organic solvents, which would be useful for application as a metal ion adsorbent capable of extracting transition metal ions across liquid/solid interfaces.¹⁴ When as-synthesized **13** was repeatedly extracted with dichloromethane for 1 day using a Soxhlet apparatus, the soluble low molecular weight moieties were completely removed, leaving insoluble polyimine **13'**. After drying, polyimine **13'** (330 equiv. of imine unit relative to metal ion) was added to a stirred solution of $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ in acetonitrile (10.0 μM), and inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis of the supernatant indicated that 98% of the Ni^{2+} ions were adsorbed after 6 h (**Figure 3-12a**). Time-dependent analysis of the adsorption experiments revealed that the amount of adsorption reached saturation within 30 min under stirring conditions (**Figure 3-12b**). Under the optimized conditions (200 equiv. of **13'** in acetonitrile), other Group 10 metal ions, Pd^{2+} and Pt^{2+} , were also efficiently adsorbed on **13'** up to 90 and 92wt%, respectively. Adsorbed metal ions were recovered by treating the solid support with a solution of $\text{EDTA} \cdot 2\text{Na}$ in acetonitrile/water (v/v = 1:1), and the adsorbent **13'** was reused after washing with acetonitrile. Although absorption events occurred only in less polar solvents but not in water, these results demonstrated the potential applicability of polyketone-generated materials for collecting precious metal ions from waste solutions.

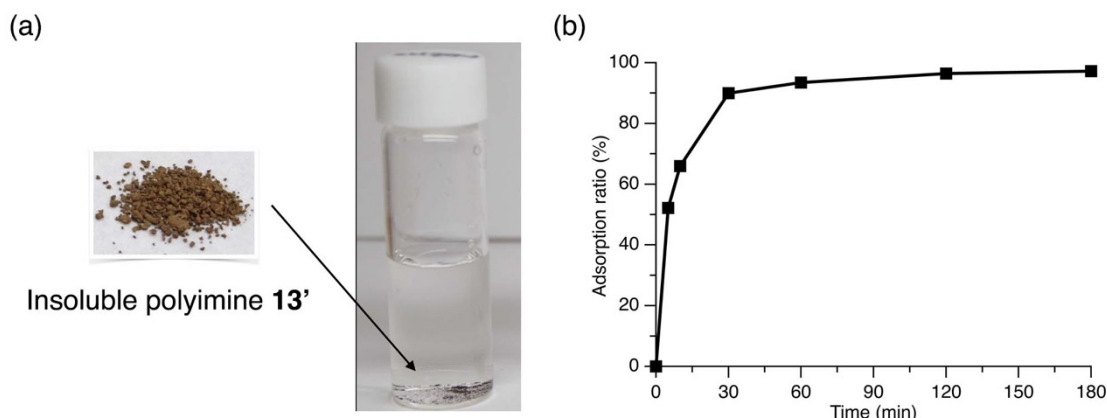


Figure 3-12. (a) Photograph of suspensions of insoluble polyimine **13'** in acetonitrile. (b) Time-dependence of Ni^{2+} ion adsorption ratios (initial concentration, 10.0 μM) using 330 equiv. of insoluble polyimine **13'** in acetonitrile.

3.6. Conclusion

In conclusion, the rigid, rod-like fully π -conjugated polyimines were generated from structurally flexible aliphatic polyketones by two-step chemical transformations. The imination reactions of all carbonyl groups and the following oxidation reactions at the ethylene bridges furnished the structurally rigid π -conjugated chromophores with circumventing the quaternary carbon atoms. The resulting π -conjugated polyimines exhibited totally different structural and optical properties by their structural changes by chemical reactions. The absorption spectra of π -conjugated oligoimines were remarkably red-shifted upon the chain length elongation, demonstrating the effective linear π -conjugation over the rigidified carbon chains. The transformation of the polydisperse polyketone polymer resulted in the formation of the virtually insoluble polymer material, which exhibited a solid-state broad absorption spectrum. Upon the full characterization by NMR, mass, and X-ray structure analyses of π -conjugated oligoimines, the obtained polymer material was also estimated to be efficiently oxidized π -conjugated polyimines. Upon the insolubility in common organic solvents and water and metal-ion coordination property of the imine groups, π -conjugated polyimines were utilized as metal-ion adsorbents of Group 10 metal ions from solution in high efficiency.

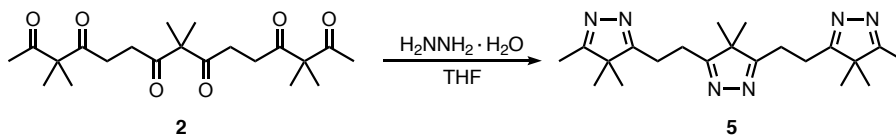
3.7. Experimental Section

General Information

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd., TCI Co., Ltd., and Sigma-Aldrich Co., and used without further purification. All the ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded using a JEOL JMNECS400 (400 MHz) spectrometer and the chemical shifts are reported in parts per million (ppm) relative to an internal standard tetramethylsilane ($\delta = 0.00$ ppm for ^1H) or residual solvent peak ($\delta = 77.16$ ppm for ^{13}C) in CDCl_3 . ESI-TOF-MS spectra were recorded on a Thermo Scientific Exactive spectrometer. Infrared spectra were measured using a JASCO Co. FT/IR-4700 spectrometer. Elemental analysis was performed using a CE440 elemental analyzer (Exeter Analytical, Inc.). Single-crystal Xray diffraction data were collected by a Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using a multilayer mirror (MoK_α radiation $\lambda = 0.71073 \text{ \AA}$) or a RAPID II diffractometer with an imaging plate detector. All structures were solved using a dual-space algorithm (SHELXT¹⁵) and refined using full-matrix least-squares method (SHELXL¹⁶). UV-vis absorption spectra were recorded on a Shimadzu UV-1800 spectrophotometer. Diffuse reflectance spectrum was measured using a JASCO V-670 spectrometer with an integrating sphere unit (JASCO ISN-723). DFT calculations were performed using Gaussian 09 software.¹⁷ MALDI-TOF mass spectra were recorded using Bruker microflex LT MALDI-TOF mass spectrometer. Oligoketones **1-3**, oligoimines **4**, **6**, and compound **10** were prepared according to the reported procedure¹ or Chapter 2 in this thesis.

Synthetic Procedures

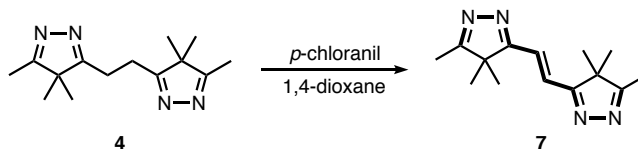
Hexaimine 5



In a 200 mL round-bottom flask equipped with a reflux condenser, compound **2** (1.70 g, 4.47 mmol) was dissolved in THF (65 mL). Hydrazine monohydrate (780 μL , 16.1 mmol) was then added and the reaction solution was stirred at 50 $^{\circ}\text{C}$ for 30 min. After cooling to room temperature, the solvent was removed using a rotary evaporator to afford the crude product as a white solid. The crude product was dissolved in chloroform (100 mL) and washed with water (100 mL). The aqueous layer was further extracted with chloroform (100 mL $\times$ 2). The combined organic layer was dried over anhydrous sodium sulfate, evaporated under reduced pressure, and the obtained solid was then washed with diethyl ether (5 mL) using an ultrasonic bath for 1 min. After filtration, rinsing with diethyl ether (20 mL) on a funnel, compound **5** $\cdot$ 0.25(H_2O) (1.45 g, 3.89 mmol) was obtained as a white solid in 87% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 3.00-2.96 (overlapping (t $\times$ 2) + s, 8H, ethylene), 2.15 (s, 6H, terminal methyl), 1.23 (s, 6H, dimethylmethylene), 1.18 (s, 12H, dimethylmethylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 182.2, 181.8, 180.3, 60.3, 59.9, 22.6, 22.4, 20.5, 20.4, 12.3; IR (ATR, neat): 2971, 2935, 2921, 2889, 2876, 1569, 1465, 1427 cm^{-1} ; m.p. 131-134 $^{\circ}\text{C}$ (decomp.); HRMS (ESI-TOF): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{33}\text{N}_6^+$, 369.2761; found, 369.2766; Elemental analysis (%): Calcd for $\text{C}_{21}\text{H}_{32}\text{N}_6 \cdot 0.25(\text{H}_2\text{O})$: C, 67.62; H, 8.78; N, 22.53. Found: C, 67.79; H, 8.70; N, 22.28; R_f = 0.19 (dichloromethane/methanol = 10:1).

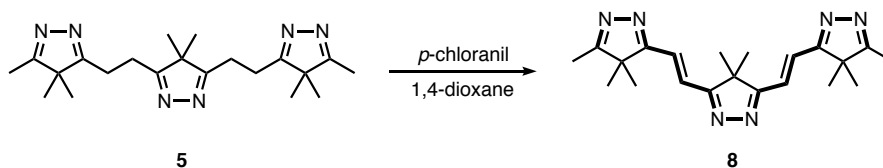
π -Conjugated tetraimine **7**



In a 500 mL round bottom flask, compound **4** (1.00 g, 4.06 mmol) and *p*-chloranil (1.10 g, 4.47 mmol) were dissolved in 1,4-dioxane (200 mL) and stirred at room temperature for 1 h. After removing the solvent using a rotary evaporator, the residual solid was dissolved in chloroform (300 mL) and washed with 5% aq NaOH (100 mL $\times$ 3). The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was chromatographed on a silica gel column (diameter, 4.0 cm, height, 5.0 cm) using dichloromethane/methanol (20:1, v/v) as eluent. The resulting solid was then washed with diethyl ether (5 mL) using an ultrasonic bath for 1 min. After filtration, rinsing with diethyl ether (10 mL), compound **7** (866 mg, 3.54 mmol) was obtained as an off-white solid in 87% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.27 (s, 2H, vinylene), 2.23 (s, 6H, terminal methyl), 1.35 (s, 12H, dimethylmethylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 182.5, 177.4, 126.1, 58.5, 21.1, 12.1; IR (ATR, neat): 3058, 2978, 2937, 2878, 1568, 1523, 1469, 1430, 980 cm^{-1} ; mp 199-201 $^\circ\text{C}$ (decomp.); HRMS (ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{20}\text{N}_4\text{Na}^+$, 267.1580; found, 267.1586; Elemental analysis (%): Calcd for $\text{C}_{14}\text{H}_{20}\text{N}_4$: C, 68.82; H, 8.25; N, 22.93. Found: C, 68.76; H, 8.24; N, 22.75; R_f = 0.09 (dichloromethane/methanol = 20:1); UV/vis (dichloromethane): λ_{max} (ϵ) 309 nm (2.2×10^4 L mol $^{-1}$ cm $^{-1}$).

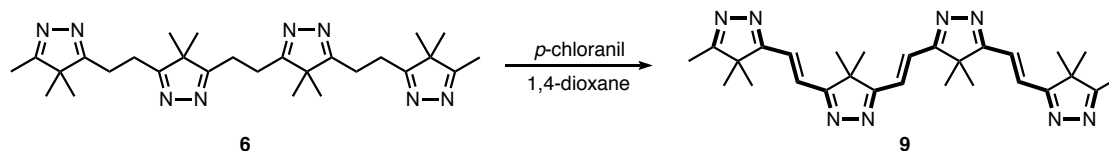
π -Conjugated hexaimine **8**



Using the synthetic procedure for compound **7**, compound **8**·0.25(H₂O) (0.77 g, 2.09 mmol) was obtained as a pale yellow solid from **8**·0.25(H₂O) (1.00 g, 2.68 mmol) in 78% yield.

¹H NMR (400 MHz, CDCl₃, 298 K): δ 7.41 (d, J = 17.0 Hz, 2H, vinylenes), 7.32 (d, J = 17.0 Hz, 2H, vinylenes), 2.25 (s, 6H, terminal methyl), 1.53 (s, 6H, dimethylmethylene), 1.36 (s, 12H, dimethylmethylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 182.6, 179.2, 177.4, 127.2, 125.0, 58.6, 57.4, 22.0, 21.1, 12.3; IR (ATR, neat): 3047, 2993, 2969, 2935, 2871, 1571, 1512, 1459, 1433, 996 cm⁻¹; m.p. 226–228 °C (decomp.); HRMS (ESI-TOF): m/z [M + H]⁺ calcd for C₂₁H₂₉N₆, 365.2448; found, 365.2446; Elemental analysis (%): Calcd for C₂₁H₂₈N₆·0.25(H₂O): C, 68.36; H, 7.79; N, 22.78. Found: C, 68.08; H, 7.63; N, 22.42; R_f = 0.24 (dichloromethane/methanol = 10:1); UV/vis (dichloromethane): $\lambda_{\max}(\epsilon)$ 363 nm (3.6×10^4 L mol⁻¹ cm⁻¹).

π -Conjugated octaimine **9**

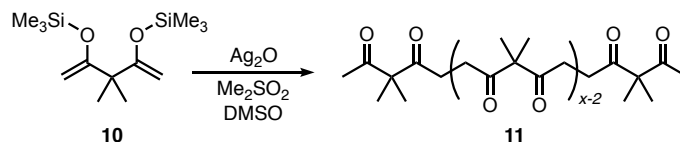


In a 300 mL round-bottom flask equipped with a reflux condenser, compound **6** (1.00 g, 2.03 mmol) was dissolved in 1,4-dioxane (100 mL) with stirring at 50 °C using an oil bath. *p*-Chloranil (1.65 g, 6.72 mmol) was then added, and the reaction mixture was stirred at 50 °C for another 30 min. After a similar workup as described in the synthesis of **8**, compound **9**·H₂O (0.74 g, 1.48 mmol) was obtained as a yellow solid in 73% yield.

¹H NMR (400 MHz, CDCl₃, 298 K): δ 7.46 (s, 2H, vinylenes), 7.41 (d, J = 17.0 Hz, 2H, vinylenes), 7.33 (d, J = 17.0 Hz, 2H, vinylenes), 2.25 (s, 6H, terminal methyl), 1.53 (s, 12H, dimethyl), 1.36 (s, 12H, dimethylmethylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 182.7, 179.2, 179.1, 177.4, 127.4, 126.0, 125.0, 58.7, 57.4, 21.9, 21.0, 12.2; IR (ATR, neat): 3048, 2988, 2933, 2873, 1570, 1512, 1459, 1430, 994 cm⁻¹; m.p. > 300 °C (decomp.); HRMS (ESI-TOF) m/z : [M + H]⁺ calcd for C₂₈H₃₇N₈, 485.3136; found, 485.3134; Elemental analysis (%): Calcd for C₂₈H₃₆N₈·(H₂O): C, 66.90; H, 7.62; N, 22.29. Found: C, 67.03; H, 7.26; N, 22.10; R_f = 0.27 (dichloromethane/methanol = 10:1); UV/vis (dichloromethane): λ_{max} (ϵ) 392 nm (5.0×10^4 L mol⁻¹ cm⁻¹).

Synthetic Procedures of Polydisperse Materials

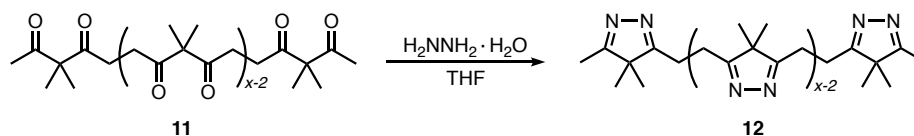
Polydisperse polyketone 11



To a 200 mL round bottom flask equipped with a reflux condenser, were added compound **10** (10.0 g, 36.7 mmol), dimethyl sulfone (20.8 g, 220 mmol), dimethyl sulfoxide (573 mg, 7.34 mmol), and silver(I) oxide (10.2 g, 44.0 mmol). The reaction mixture was stirred at 100 °C for 2 h using an oil bath. After cooling to room temperature, the reaction mixture was passed through a Celite pad using 140 mL of dichloromethane. The solvent was evaporated, the residue was washed with water (50 mL $\times$ 2) and then dimethyl sulfone was removed in vacuo ($\sim$ 1 mmHg, 150 °C). The residue was dissolved in dichloromethane/methanol (40 mL, 1:1, v/v), and stirred with hydrochloric acid (4.0 mL, 3.0 M) for 30 min at room temperature. The solution was neutralized with sat. aq. NaHCO₃ and the aqueous layer was extracted with dichloromethane (50 mL $\times$ 2). The combined organic layer was washed with brine (100 mL), and dried over anhydrous Na₂SO₄ before evaporating the solvent. The crude residue was chromatographed on a silica gel column (diameter, 4.0 cm; height, 10.0 cm) using dichloromethane/methanol (10:1, v/v) as eluent to give polymer **11** (2.99 g) in 64% yield.

¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.77-2.64 (ethylene), 2.16-2.14 (acetyl), 1.42-1.34 (dimethylmethylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 207.7-209.6, 62.1-61.7, 32.2, 26.3, 21.8-20.9; IR (ATR, neat): 2979, 2937, 2920, 2875, 1692, 1465, 1388, 1364, 1014 cm⁻¹.

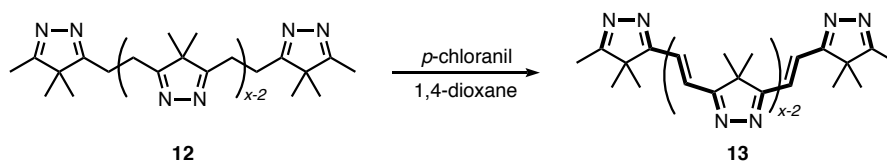
Polydisperse polyimine 12



Polymer **11** (2.00 g) was dissolved in THF (50 mL) in a 100 mL round-bottom flask equipped with a reflux condenser. Hydrazine monohydrate (0.96 mL, 19.9 mmol) was added and the mixture was stirred at 50 °C for 30 min. After cooling the solution to room temperature, the solvent was evaporated using a rotary evaporator. The residue was dissolved in CHCl_3 (100 mL) and washed with distilled water (100 mL). The aqueous layer was further extracted with CHCl_3 (100 mL $\times$ 2), and the combined organic layer was dried over anhydrous Na_2SO_4 , and the solvent was removed using a rotary evaporator to give crude product. The crude product was washed with Et_2O (30 mL) and collected by suction filtration to give polyimine **12** (1.83 g) in 94% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.99–2.94 (ethylene), 2.16–2.13 (terminal methyl), 1.24–1.16 (dimethylmethylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 182.2–180.3, 60.2–59.8, 22.6–22.2, 20.6–20.1, 12.3–12.1; IR (ATR, neat): 3281, 2966, 2929, 2911, 2871, 2364, 2356, 2342, 2333, 2325, 1699, 1569, 1463, 1427, 1385, 1362, 1099, 613 cm^{-1} .

π -Conjugated polyimine **13**



To a solution of polyimine **12** (500 mg) in 1,4-dioxane (750 mL) in a 1 L round-bottom flask, was added *p*-chloranil (2.50 g, 10.2 mmol). The mixture was refluxed for 5 h with vigorous stirring. After cooling to room temperature, the resulting precipitate was obtained by suction filtration and rinsed with 1,4-dioxane (350 mL) and methanol (250 mL) to give polymer **13** (281 mg) as a dark brown solid in 57% yield.

IR (ATR, neat): 2973, 2933, 2872, 1687, 1617, 1568, 1547, 1509, 1459, 1368, 1116, 994, 980, 614 cm^{-1} .

3.8. References

- [1] M. Uesaka, Y. Saito, S. Yoshioka, Y. Domoto, M. Fujita, Y. Inokuma, *Commun. Chem.* **2018**, *1*, 23.
- [2] R. W. Alder, N. P. Hyland, J. C. Jeffery, T. R. Johannessen, D. J. Riley, *Org. Biomol. Chem.* **2009**, *7*, 2704–2715.
- [3] T. Rahn, F. Bendrath, M. Hein, W. Baumann, H. Jiao, A. Börner, A. Villinger, P. Langer, *Org. Biomol. Chem.* **2011**, *9*, 5172–5184.
- [4] M. Peter, R. Gleiter, F. Rominger, T. Oeser, *Eur. J. Org. Chem.* **2004**, 3212–3220.
- [5] T. M. Harris, J. V. Hay, *J. Am. Chem. Soc.* **1977**, *99*, 1631–1637.
- [6] G. F. Pregaglia, M. Binaghi, *J. Org. Chem.* **1963**, *28*, 1152–1154.
- [7] M. T. Stone, J. M. Heemstra, J. S. Moore, *Acc. Chem. Res.* **2006**, *39*, 11–20.
- [8] J. M. Ren, J. Lawrence, A. S. Knight, A. Abdilla, R. B. Zerdan, A. E. Levi, B. Oschmann, W. R. Gutekunst, S.-H. Lee, Y. Li, A. J. McGrath, C. M. Bates, G. G. Qiao, C. J. Hawker, *J. Am. Chem. Soc.* **2018**, *140*, 1945–1951.
- [9] D. Zhou, M. Xu, J. Li, R. Tan, Z. Ma, X.-H. Dong, *Macromolecules* **2021**, *54*, 4827–4833.
- [10] D. Zhou, M. Xu, R. Tan, Y. Sun, Z. Ma, J. Li, X.-H. Dong, *Polymer* **2021**, *225*, 123746.
- [11] G. Cafeo, D. Garozzo, F. H. Kohnke, S. Pappalardo, M. F. Parisi, R. P. Nascone, D. J. Williams, *Tetrahedron* **2004**, *60*, 1895–1902.
- [12] T. Yoneda, T. Hoshino, S. Neya, *J. Org. Chem.* **2017**, *82*, 10737–10741.
- [13] I. Fleming, *Molecular Orbitals and Organic Chemical Reactions* Reference Edition; John Wiley & Sons, Ltd: Chichester, West Sussex, U.K., 2010; pp 1–66.
- [14] H. Shirakura, Y. Hijikata, J. Pirillo, T. Yoneda, Y. Manabe, M. Murugavel, Y. Ide, Y. Inokuma, *Eur. J. Inorg. Chem.* **2021**, *17*, 1705–1708.
- [15] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, **2015**, *71*, 3–8.
- [16] G. M. Sheldrick, *Acta Crystallogr. Sect. C*, **2015**, *71*, 3–8.
- [17] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F.

Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, J. Gaussian 09, Revision D.01; Gaussian, Inc.: Wallingford CT, 2016.

Chapter 4

Synthesis of Functional Complexes Using Polyimines

Abstract

The construction of molecular architectures was examined from oligoketone-based flexible and multidentate oligoimine ligands through a metal-ion coordination. The diverse constructed structures reflected the intrinsic characters of flexible and multidentate oligoimine ligands. The stepwise metal-ion coordination feature of oligoimines ligands furnished discrete palladium complexes in a structure-controllable manner. The structural flexibility changes by oxidation of the bridging ethylenes of the tetraimine ligand displayed the different coordination polymer formations with Cd^{2+} ions. The complexation of the flexible tetraimine ligand with copper(I) halides showed the two different coordination polymer structures upon the structural flexibility and multidentate character of the ligand. Resulting all the copper(I) complexes showed luminescence under UV irradiation, and the coordination polymer of copper(I) iodide clusters exhibited thermochromic behavior.

4.1. Introduction

The multiple carbonyl groups on aliphatic polyketone chains can interact with metal ions. Driven by metal-ion coordination, aliphatic polyketones can act as a molecular scaffold to construct various coordination structures. Cyclic aliphatic polyketones bearing alternating 1,3- and 1,4-diketone repeating unit, exhibited alkali metal ion binding as crown ethers via metal-ion coordination of carbonyl groups.¹ Linear aliphatic polyketones of the same repeating unit also exhibited lithium ion conduction as solid polymer electrolytes.² However, the interactions of linear aliphatic polyketone chains with metal ions were too weak to form stable molecular structures upon metal-ion coordination without the use of additional intra- and/or inter-molecular interactions.

Aliphatic polyimines derived from aliphatic polyketones, described in Chapter 3, also embedded the metal-ion coordinating iminic nitrogen atoms on their carbon chains with keeping their structural flexibility.³ Such iminic nitrogen atoms have much stronger interactions with transition metal ions, which prompted the author to use aliphatic oligoimines as a polyketone-based molecular scaffold to form metal-ion coordination driven versatile molecular structures. The flexible carbon chain of the oligoimine ligands allows the formation of various conformations and coordination geometries. In addition, the isopyrazole ring of the oligoimine ligands provides both convergent and divergent coordination sites, leading to the formation of discrete molecular structures or infinite coordination networks.⁴⁻⁸ Such features of the oligoimine ligands can vary on the resulting structures and structure-derived functions.

In this work, the metal-ion coordination behavior of flexible and multidentate aliphatic oligoimine ligands and the resulting molecular structures were investigated. Following the stepwise metal coordination character of isopyrazole rings, the control of coordination structures with palladium ions was investigated. The revealed correlation of the metal-ligand stoichiometry and the resulting assembled structures enabled to predict of the coordination structures when the chain length of the ligands was extended. The effects of structural flexibility on metal-ion coordination were examined using ethylene- or vinylene-bridged tetraimine ligands with cadmium ions. The resulting two coordination polymers implied that the steric hindrance of the ligands around the coordination sites differentiated the resulting structures. The structural flexibility and multidentate character of the oligoimine ligands furnished the copper(I) halide coordination polymers. Unique photophysical luminescence and thermochromic behaviors were observed.

4.2. Induction of Curved Structures of Flexible Oligoimines upon a Stepwise Metal-ion Coordination

An isopyrazole ring of the polyimine ligands has a unique stepwise metal-ion coordination feature (**Figure 4-1**).⁹ Once a metal ion was coordinated to one of the two equivalent nitrogen atoms, the electron-donating character of the other nitrogen atom was reduced. Therefore, within 1 equiv. of metal ion stoichiometry to an isopyrazole ring, one bond coordination with metal ions was preferred.

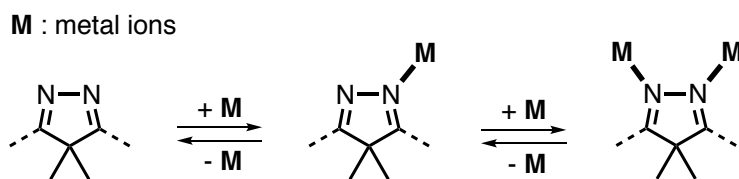
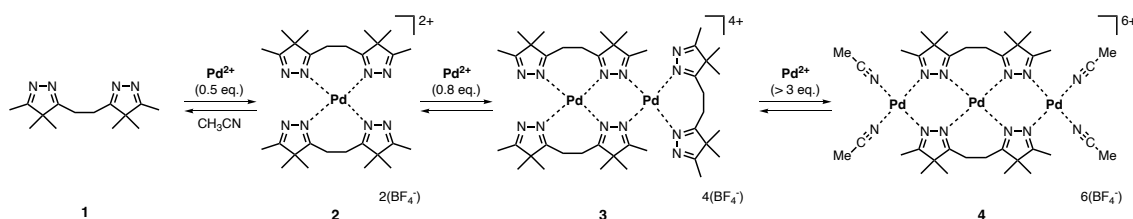


Figure 4-1. Stepwise metal-ion coordination to an isopyrazole ring of polyimine ligands

When a ligand **1** was mixed with 0.5 equiv. of $\text{Pd}(\text{CH}_3\text{CN})(\text{BF}_4)_2$ in a 60 mM CD_3CN solution for 1 h, a discrete complex **2** with a 2:1 ligand/metal ratio was complexed quantitatively in solution (**Scheme 4-1**). The single crystal structure displayed a square-planar Pd^{2+} ion was coordinated with two ligands **1** in a bidentate manner (**Figure 4-2a**). All four isopyrazole rings had one coordination to the Pd^{2+} ion, leaving one imine uncoordinated. The planar structure of complex **2** was formed upon the coordination, and the bridging ethylene unit adopted a gauche conformation. Further addition of $\text{Pd}(\text{CH}_3\text{CN})(\text{BF}_4)_2$ up to 0.8 equiv. maximized the formation of the dinuclear complex **3** with a 3:2 ligand/metal ratio. Although a uniform complex formation of **3** was not achieved, single crystals of **3** were obtained after recrystallization. In the crystal structure of **3**, two isopyrazole rings doubly coordinated to two Pd^{2+} ions, while the other four isopyrazole rings showed one coordination (**Figure 4-2b**). The whole complex structure of **3** adopted a curved rectangular structure. When an excess amount of Pd^{2+} ion was added (> 3 equiv.), a trinuclear complex **4** with a 2:3 ligand/metal ratio was formed as a converged single product. In the crystal structure, all isopyrazole rings exhibited double coordination with two Pd^{2+} ions (**Figure 4-2c**), and a curved, saddle-like structure was adopted.



Scheme 4-1. Stepwise synthetic scheme for stepwise metal-ion coordination to ligand **1**.

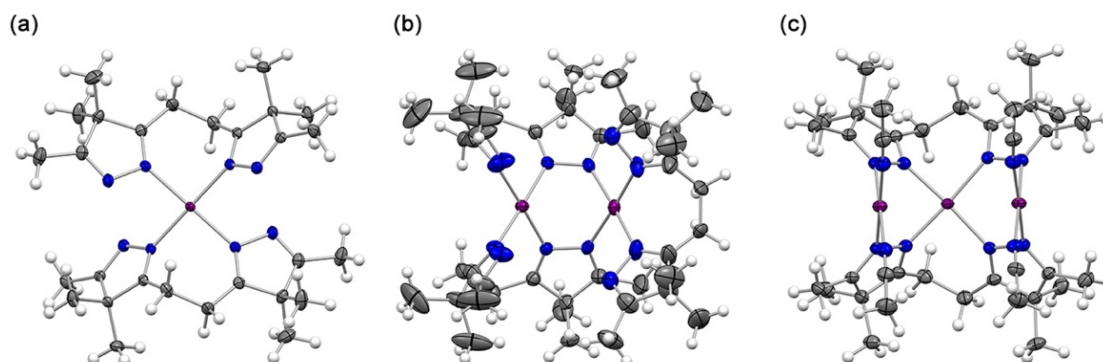
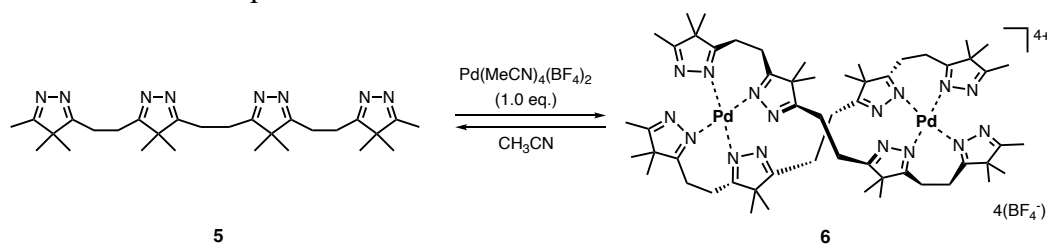


Figure 4-2. Single crystal structures of palladium complexes (a) **2**, (b) **3**, and (c) **4**. ORTEP drawings were displayed at 50% probability. Counter ions and solvents were omitted for clarity (C: grey, N: blue, H: white, Pd: purple).

From the stepwise coordination behavior of the flexible ligand **1** upon the addition of Pd^{2+} ions, the appropriate stoichiometry of metal ions and polyimine ligand can be estimated for controlling assembled structures using further longer polyimine ligands. When an octaimine ligand **5** was mixed with 1.0 equiv. of $\text{Pd}(\text{CH}_3\text{CN})(\text{BF}_4)_2$ in a 60 mM CD_3CN solution for 1 day, a discrete complex **6** with a 1:1 ligand/metal ratio was obtained (**Scheme 4-2**). Single crystal structure analysis disclosed a double helix-like structure of complex **6** composed of two ligands **5** and two Pd^{2+} ions (**Figure 4-3**). All the ethylene bridges showed gauche-like conformations, resulting in the curved conformation of ligand **5**. Each of the isopyrazole rings had one coordination to the Pd^{2+} ion, as expected in the same manner as complex **2**. As a result, complex **6** was composed of two substructures like complex **2**.



Scheme 4-2. Self-assembly of octaimine ligand **5** into Pd complex **6**.

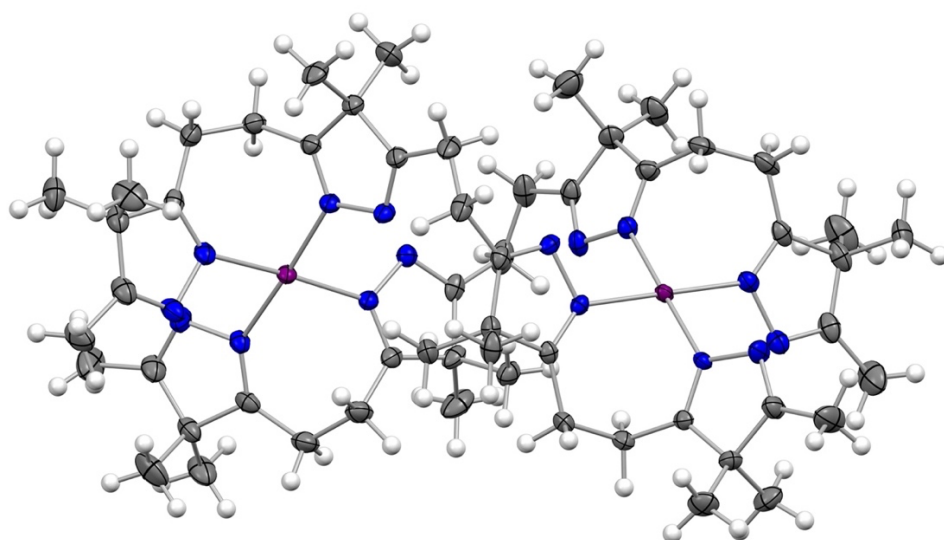


Figure 4-3. Single crystal structures of complex **6**. Counter ions and solvents were omitted for clarity. (C: grey, N: blue, H: white, Pd: purple).

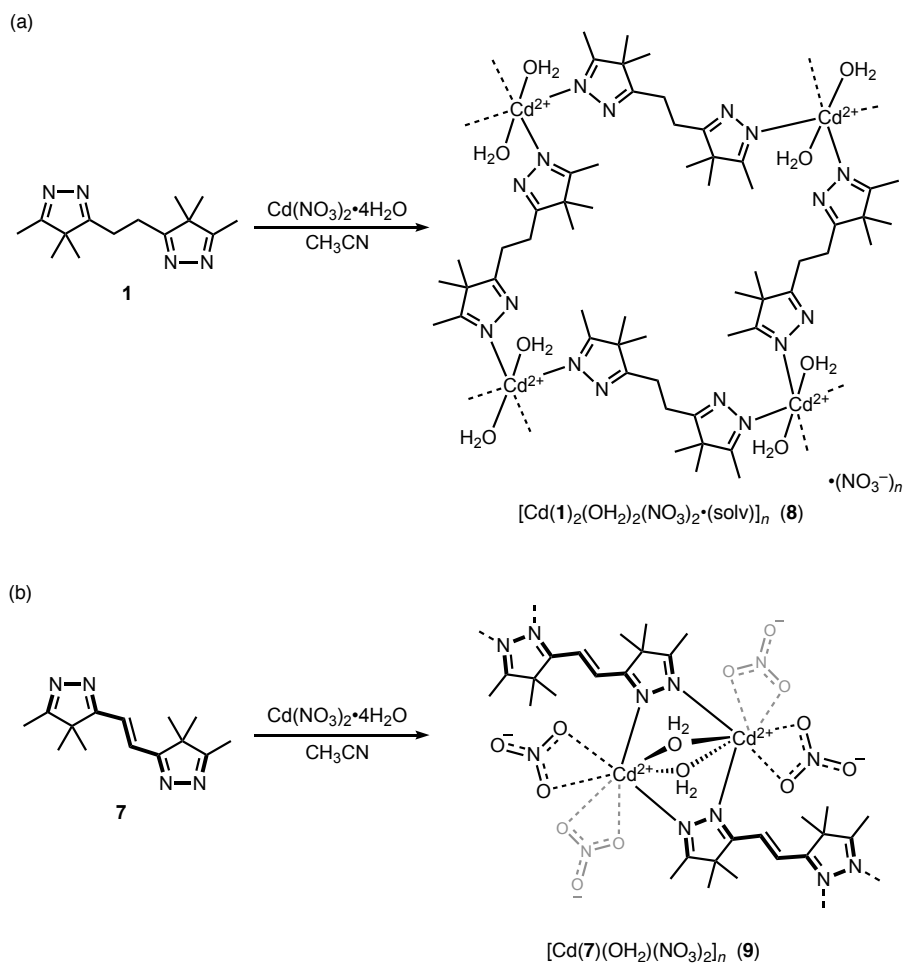
4.3. A Study of the Flexibility Effects of Polyimine Ligands for Metal-ion Coordination and Resulting Structures

The structural flexibility effects of polyimine ligands for metal-ion coordination were investigated using the flexible tetraimine **1** and the rigid tetraimine **7** for metal-ion coordination with a cadmium ion. While a ligand **1** has a flexible bridging ethylene unit, ligand **7** has rigid vinylene bridges, which would greatly affect the metal-ion coordination behavior of the ligands.

By mixing flexible tetraimine **1** and $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ in acetonitrile, cadmium complex **8** $[\text{Cd}(\text{1})_2(\text{OH}_2)_2(\text{NO}_3)_2 \cdot (\text{CH}_3\text{CN})]_n$ was obtained in 44% yield as a colorless crystal (**Scheme 4-3a**). When the rigid tetraimine **7** was mixed with $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ in acetonitrile under conditions to the synthesis of **8**, a different cadmium complex **9** $[\text{Cd}(\text{7})_2(\text{OH}_2)(\text{NO}_3)_2]_n$ was obtained as a microcrystal in 37% yield (**Scheme 4-3b**). Single crystal X-ray analysis revealed the totally different metal complex structures upon the differences in the structural flexibility of the polyimine ligands (**Figure 4-4**). From the X-ray structure analysis, complex **8** showed its two-dimensional coordination network structure. In the two-dimensional structure, each ligand **1** behaved as a bidentate ligand coordinating to two different Cd^{2+} ions using the terminal iminic nitrogen atoms, while the remaining two internal nitrogen atoms remained intact towards metal-ion coordination. The conformation of the bridging ethylene units in ligand **1** was antiperiplanar conformation. This type of coordination behavior was also observed in the previously reported Zn complex of ligand **1**.¹

In the crystal structure of complex **9**, the one-dimensional repeating substructures of di- μ -isopyrazole-di- μ -aquo-tetrakis(nitrato-*O,O'*)dicadmium¹⁰ through trans-vinylene bridges were observed as a coordination polymer. The trans-vinylene bridges exhibited all *s-trans* conformation in a similar way to its uncoordinated form. All nitrogen atoms of **9** coordinated to four Cd^{2+} ions in contrast to **8**.

The different metal coordination behaviors of **8** and **9** with Cd^{2+} ions could be derived from the lower steric hindrance of **9** in the favored *s-trans* conformation during the metal-coordination processes to internal nitrogen atoms.



Scheme 4-3. Metal Complexations of Ligand (a) **1** and (b) **7** with $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$.

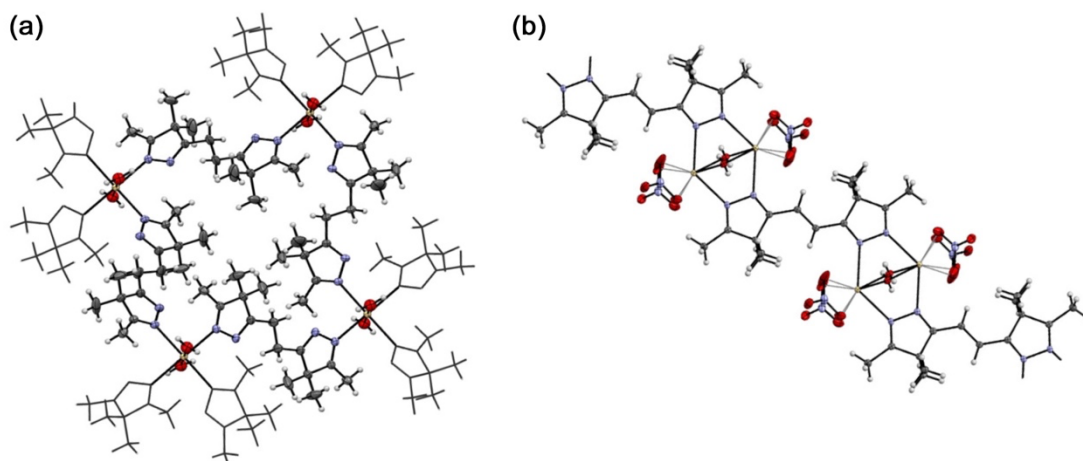
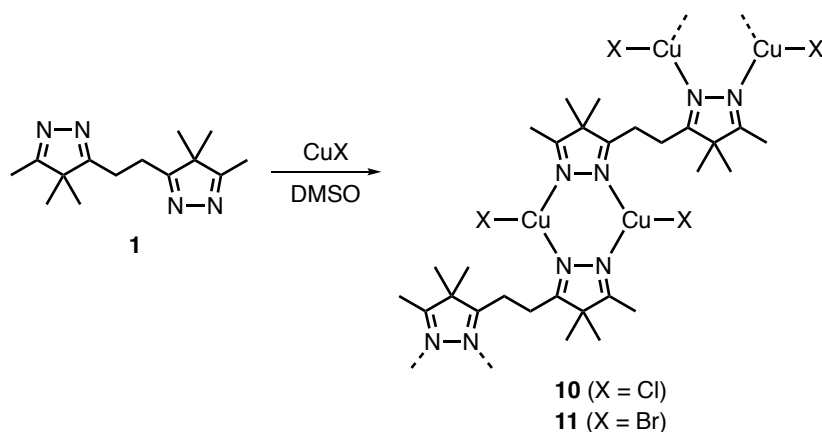


Figure 4-4. Single crystal X-ray structures of (a) two-dimensional coordination network of Cd complex **8** and (b) coordination chain of **9**. Thermal ellipsoids are shown at the 50% probability level (C: gray, N: sky blue, O: red, Cd: yellow, and H: white).

4.4. Synthesis of Luminescent Coordination Polymers from Flexible and Multidentate Polyimine Ligands and Copper(I) Halides

The coordination behavior of the tetraimine ligand **1** with copper(I) halides was investigated. The formation of various multinuclear copper(I) clusters was known upon a mixing of copper(I) halides and ligands, which exhibited unique photophysical properties due to their structural differences.¹¹⁻²⁰ When a 400 mM dimethyl sulfoxide (DMSO) solution of tetraimine **1** was mixed with a suspension of 1 equiv. of CuCl in DMSO, an immediate dissolution of all remaining solids was observed. After standing for 1 day, complex **10** was precipitated as a pale yellow solid in 63% yield (**Scheme 4-4**). The elemental analysis and IR spectrum suggested the formation of a copper complex formulated as $[(\text{CuCl})_2(\textbf{1})]_n$. Similarly, when CuBr was mixed with ligand **1** under the same conditions, complex **11** was obtained as a pale yellow solid in 62% yield.



Scheme 4-4. Synthesis of coordination chain complexes **10** and **11**.

Single crystals of complexes **10** and **11** were grown under different preparation conditions for single crystal X-ray structure analysis (see also Experimental Section). By comparing the powder X-ray diffraction data and single crystal diffractions, the identical complexes formation in both bulk syntheses and single crystal preparations was unambiguously confirmed. In the crystal structures, both complexes **10** and **11** showed the infinite coordination chain structures where ligands **1** were doubly bridged by two trigonal copper(I) ions (**Figure 4-5**). The four iminic nitrogen atoms of ligand **1** were all coordinated by four different copper(I) ions. The ethylene bridge of ligand **1** adopted an antiperiplanar conformation, and a planar conformation of ligand **1** was observed. No significant differences from the halide ion differences were observed in the crystal structures.

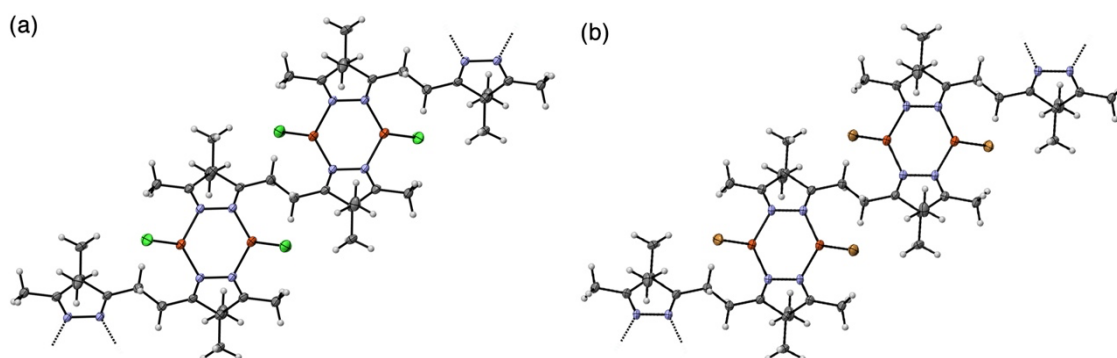
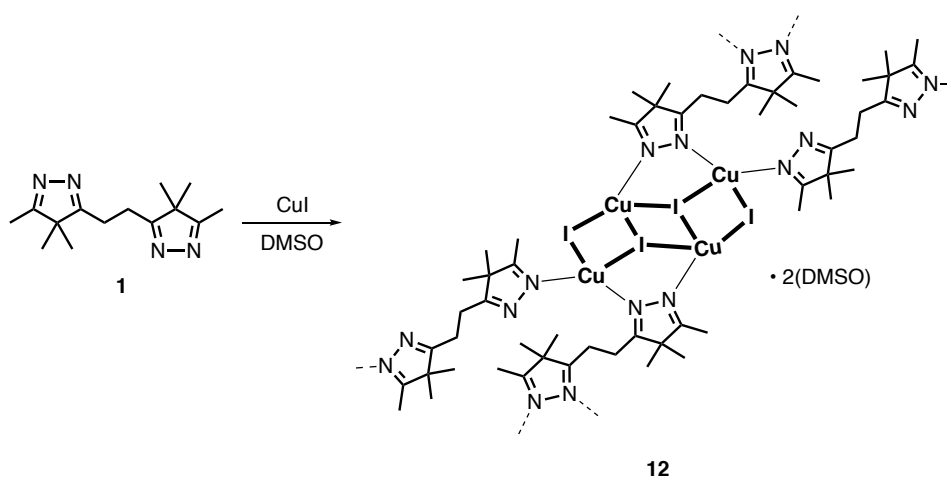


Figure 4-5. Single crystal structures of coordination polymers (a) **10** and (b) **11**. Thermal ellipsoids are drawn at the 50% probability. (C: grey, N: sky blue, Cu: orange, Cl: yellow green, Br: brown)

However, the complexation of ligand **1** with CuI in DMSO using the same complexation conditions, complex **12**, formulated as $[(\text{CuI})_2(\mathbf{1})(\text{DMSO})]_n$, was obtained as a pale yellow solid in 82% yield (**Scheme 4-5**).



Scheme 4-5. Preparation of the coordination network complex **12**.

The X-ray crystal structure of complex **12** showed a two-dimensional coordination network composed of stair-step type tetranuclear Cu_4I_4 subunits bridged by ligand **1** (**Figure 4-6a**). In the crystal structure, two different conformations of ligand **1** with different coordination modes were observed. A planar conformation, found in complexes **10** and **11**, was also observed (**Figure 4-6b**). The terminal iminic nitrogen atoms were used for bridging two different tetranuclear Cu_4I_4 subunits as a bidentate coordination mode, while the inner two nitrogen atoms were intact for metal-ion coordination. The other ligand adopted a stepped conformation, while the conformation of the bridging

ethylene was also an antiperiplanar conformation (**Figure 4-6b**). Tetradentate coordination was observed for the coordination of two adjacent Cu^+ ions in the same tetranuclear Cu_4I_4 subunits. Upon the two different conformations and coordination modes of ligand **1**, the two-dimensional coordination networks were formed.

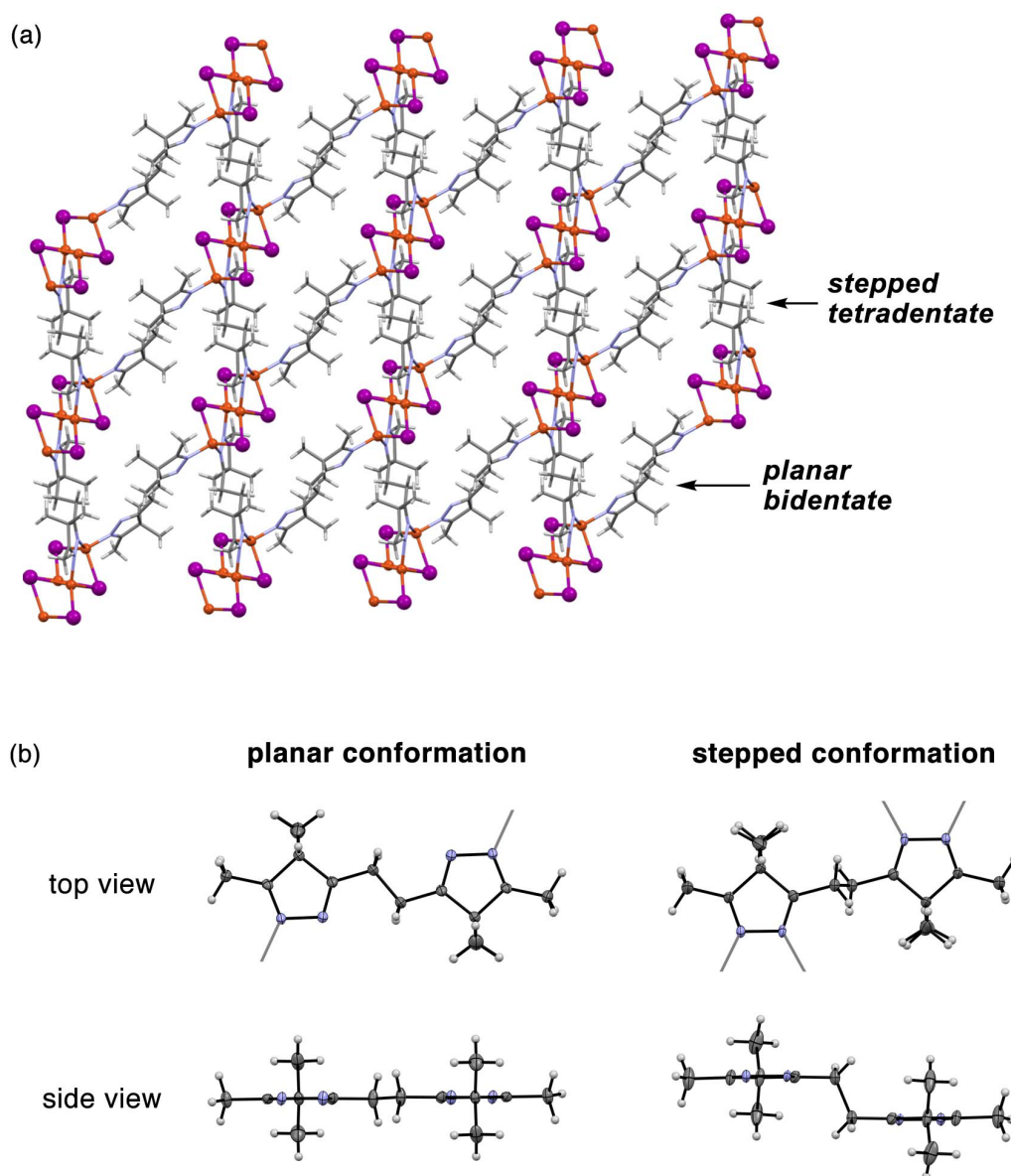


Figure 4-6. (a) Crystal structure of copper(I) coordination network **12**. (b) Planar and stepped conformations of tetramine ligand **1** in coordination network **12** (top: top views, bottom: side views). Solvent molecules were omitted for clarity. (C: gray, N: sky blue, Cu: orange, I: purple)

Upon the unique structural features found in the crystal structures, the photophysical properties of complexes **10-12** were further investigated. The copper(I) complexes have been reported to exhibit curious photophysical properties from the d^{10} electronic configuration of the copper(I) centers.²¹⁻²⁶ The obtained copper(I) complexes **10-12** were insoluble in common organic solvents or water. In the solid-state diffuse reflectance spectra, strong absorption bands in the visible region were not observed. Nevertheless, complex **10** exhibited bright green-yellow luminescence at $\lambda_{em} = 530$ nm under the excitation at 380 nm (**Figure 4-7**). In a similar manner, reflecting their structural similarity, complex **11** displayed a slightly blue-shifted luminescence at $\lambda_{em} = 513$ nm. The quantum yields of **10** and **11** in the emissions were determined to be 2.8 and 1.3% yields, respectively. The emission lifetimes were calculated to be $\tau_1 = 5.9$ and $\tau_2 = 11.8$ μ s for **10**, and $\tau_1 = 6.8$ and $\tau_2 = 14.2$ μ s for **11** (**Figure 4-8**). The emissions from complexes **10** and **11** would be attributed to the metal-to-ligand charge transfer (MLCT) and/or halogen-to-ligand charge transfer (XLCT), as observed in other various copper(I) complexes,²⁷⁻³¹ since ligand **1** itself was not emissive.

Complex **12** also showed emission at $\lambda_{em} = 572$ nm, with a quantum yield of less than 1%, and emission lifetimes of $\tau_1 = 2.6$ and $\tau_2 = 6.9$ μ s. Although the emission was low, thermochromic behavior was observed only for complex **12**. When the temperature was decreased from 298 to 93 K, the emission wavelength was slightly shifted from 572 to 580 nm along with the sharpening of the emission spectra (**Figure 4-9**). Although the spectral change was trivial, the color change was much more vivid to the naked eye.

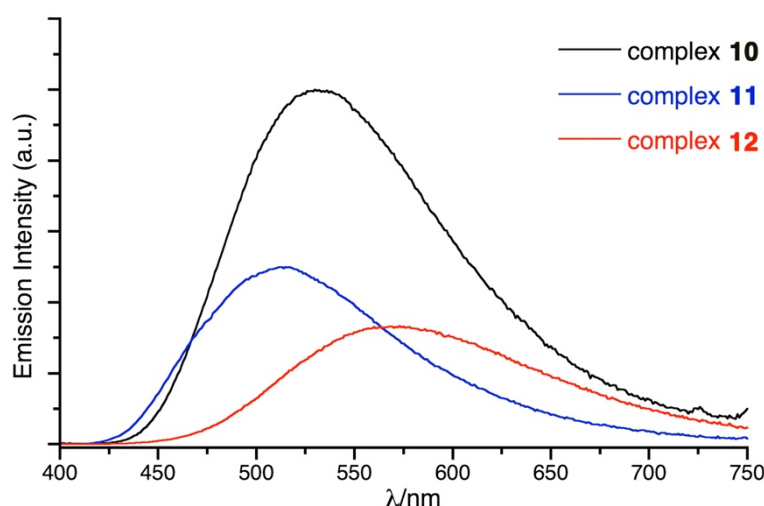


Figure 4-7. Solid-state emission spectra of copper(I) complexes **10-12** ($\lambda_{ex} = 380$ nm).

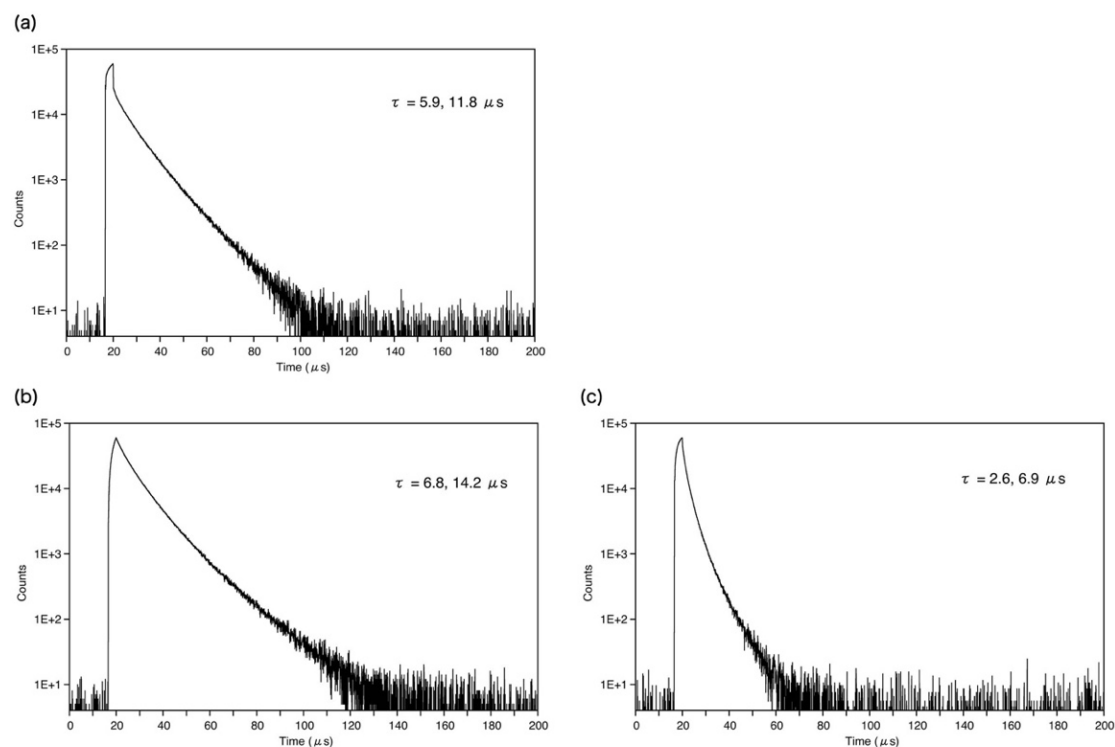


Figure 4-8. Emission decays of (a) CuCl complex **10**, (b) CuBr complex **11**, and (c) CuI complex **12**.

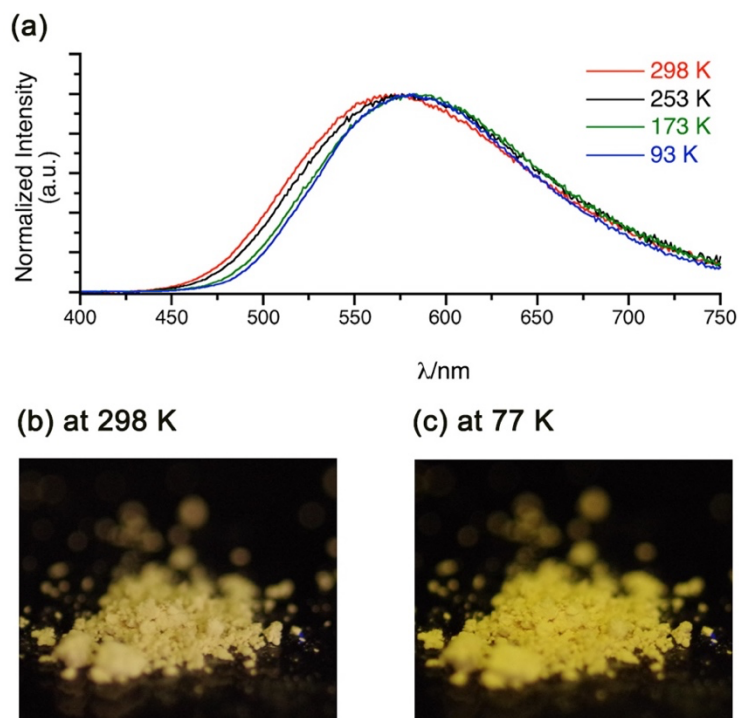


Figure 4-9. (a) Thermochromic changes of emission spectra of complex **12** ($\lambda_{\text{ex}} = 380 \text{ nm}$). Photographs of complex **12** under UV irradiation at (b) 298 K and (c) 77 K.

4.5. Conclusion

In conclusion, the diverse molecular structure formations of polyketone-based flexible and multidentate oligoimine ligands were performed by metal-ion coordination. The coordination structures of different lengths of oligoimine ligands with palladium ions were controlled by the stepwise coordination character of isopyrazole rings. Controlling the stoichiometry between metal ions and ligands was the key to controlling the assembled structures. When the structural flexibility of the tetraimine ligands was changed from ethylene to vinylene bridging units, the formed structures with cadmium ions were differentiated. The resulting structures showed different coordination modes due to the steric hindrance around the inner iminic nitrogen atoms of the isopyrazole ring. The different cluster structures of copper(I) halides and flexible and multidentate oligoimine ligands were prepared. Upon the structural differences and the character of the copper(I) halide units, unique photophysical properties were observed.

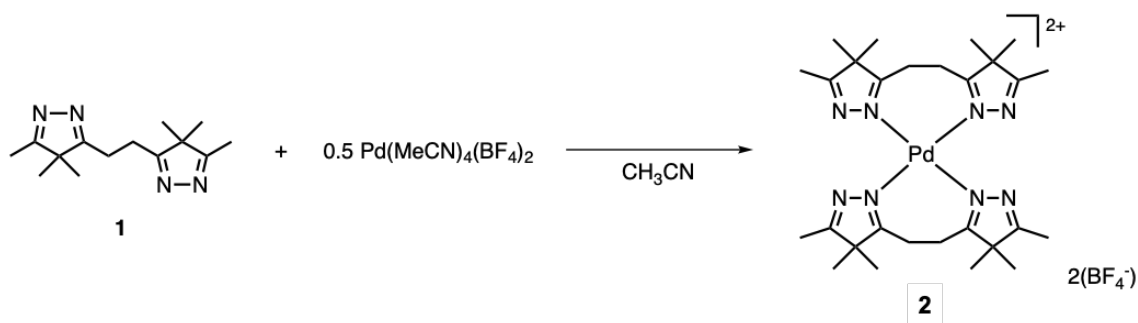
4.6. Experimental Section

General Information

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd., TCI Co., Ltd., or Sigma-Aldrich Co., and used without further purification. All the ^1H and ^{13}C and two dimensional NMR spectra were recorded using a JEOL JMN-ECS400 (400 MHz) spectrometers or ECZ600 (600 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm) relative to an internal standard tetramethylsilane ($\delta = 0.00$ ppm for ^1H in CDCl_3), or solvent residual peak ($\delta = 1.94$ ppm for ^1H in CD_3CN , $\delta = 1.32$ ppm for ^{13}C in CD_3CN , and $\delta = 77.16$ ppm for ^{13}C in CDCl_3). ESI-TOF-MS spectra were recorded on a Thermo scientific Exactive spectrometer for organic compounds in CH_3CN . Infrared spectra were measured using a JASCO Co. FT/IR-4700. Elemental analysis was performed using an Exceter Analytical, Inc. CE440. Single crystal X-ray diffraction data were collected with a Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using multi-layer mirror (MoK_α radiation $\lambda = 0.71073 \text{ \AA}$ or CuK_α radiation $\lambda = 1.54184 \text{ \AA}$) or a RAPID II diffractometer with an imaging plate detector using sealed tube MoK_α radiation. All structures were solved using a dual-space algorithm (SHELXT³²) and refined using full-matrix least-squares method (SHELXL³³). Isopyrazole ligands **1**, **5**, and **7** were synthesized according to the reported procedures. Diffuse reflectance spectra were measured using a JASCO V-670 spectrometer with an integrating sphere unit (JASCO ISN-723). Emission spectra were recorded on a HORIBA Fluorolog-3 spectrofluorometer and corrected for the response of the detector system. Quantum yields were measured using an FP-6300 spectrofluorometer with an integration sphere.

Synthetic Procedures

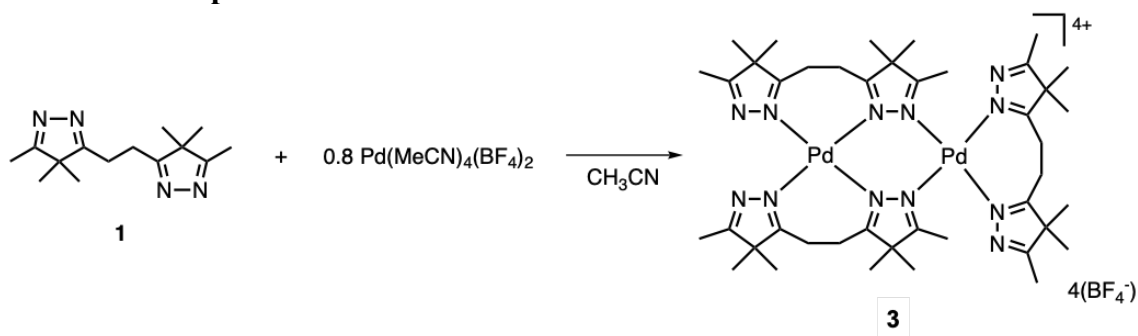
Palladium complex 2



In a 20 mL round-bottomed flask equipped with a reflux condenser, ligand **1** (50.0 mg, 203 μ mol) and [Pd(CH₃CN)₄](BF₄)₂ (45.1 mg, 102 μ mol) were dissolved in acetonitrile (3.4 mL). The solution was stirred at 60 °C with an oil bath for 1 h. After the solution was cooled to room temperature, the solution was analyzed by ¹H NMR spectroscopy and the quantitative formation of complex **2** was confirmed. The product was precipitated as a pale yellow solid by adding diethyl ether (6.0 mL) to the reaction solution. The precipitate was filtered with suction, washed with 3.0 mL of diethyl ether, and air-dried on a funnel to afford complex **2** (56.3 mg) in 71% yield.

¹H NMR (400 MHz, CD₃CN, 298 K): δ 3.46 (br s, 8H, ethylene), 2.04 (s, 12H, terminal methyl), 1.26 (s, 24H, dimethylmethylene); ¹³C{¹H} NMR (100 MHz, CD₃CN, 298 K): δ 189.8, 184.9, 63.8, 23.1, 19.6, 12.0; HRMS(ESI-TOF): m/z [M – 2(BF₄⁻)]²⁺ calcd for C₂₈H₄₄N₈Pd²⁺, 299.1367; found, 299.1357; Elemental analysis (%): Calcd for C₂₈H₄₄N₈PdB₂F₈•0.5H₂O: C, 43.02; H, 5.80; N, 14.33; Found: C, 42.95; H, 5.64; N, 14.28.

Palladium complex 3

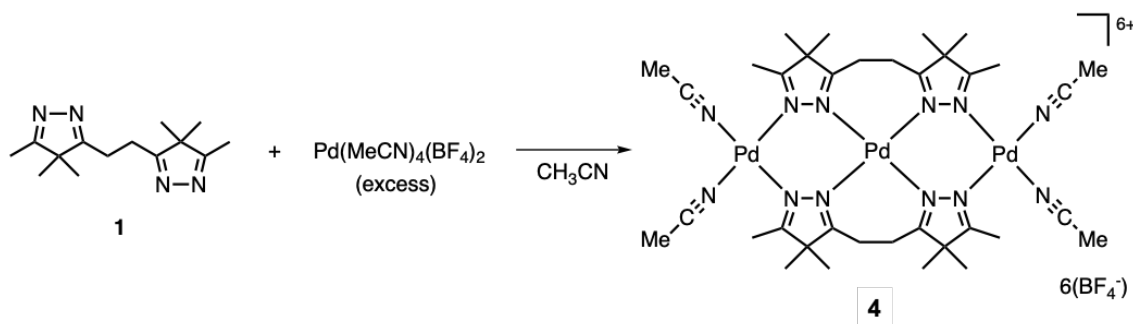


In a similar fashion to the synthesis of complex **2**, a solution of ligand **1** (50.0 mg, 203 μmol) and Pd(CH₃CN)₄(BF₄)₂ (72.0 mg, 162 μmol) in acetonitrile (3.4 mL) was stirred at 60 °C for 1 h. After the solution was cooled to room temperature, dichloromethane (12.0 mL) was slowly added via a pipette, and the resulting solution was allowed to stand at room temperature for 12 h. Pale yellow crystals formed at the bottom of the flask. The crystals were collected by suction filtration, washed with dichloromethane (3.0 mL), and dried on a funnel to give complex **3**•1.5(CH₂Cl₂) (39.9 mg) in 46% yield.

¹H NMR (600 MHz, CD₃CN, 298 K): δ 4.58 (ddd, J = 15.0, 12.1, 4.8 Hz, 2H, ethylene), 3.79 (overlapped dt, 2H, ethylene), 3.74 (m, 2H, ethylene), 3.58 (dt, J = 15.0, 4.5 Hz, 2H, ethylene), 3.25 (overlapped ddd, 2H, ethylene), 3.18 (m, 2H, ethylene), 2.50 (s, 6H, terminal methyl), 2.17 (s, 6H, terminal methyl), 1.92 (s, 6H, terminal methyl), 1.43 (s, 6H, dimethylmethylene), 1.35 (s, 6H, dimethylmethylene), 1.34 (s, 6H, dimethylmethylene), 1.30 (s, 6H, dimethylmethylene), 1.28 (s, 6H, dimethylmethylene), 1.18 (s, 6H, dimethylmethylene); ¹³C{¹H} NMR (100 MHz, CD₃CN, 298 K): δ 195.1, 194.5, 193.5, 191.9, 186.9, 186.2, 66.5, 64.9, 63.6, 25.4, 23.2, 22.6, 21.9, 21.8, 20.3, 19.4, 19.2, 19.2, 15.2, 12.4, 12.3; HRMS(ESI-TOF): m/z [M – 3(BF₄)]³⁺ calcd for C₄₂H₆₆N₁₂Pd₂B₁F₄³⁺, 346.4554; found, 346.4553; Elemental analysis (%): Calcd. for C₄₂H₆₆N₁₂Pd₂B₄F₁₆•1.5CH₂Cl₂: C, 36.63; H, 4.88; N, 11.78; Found: C, 36.59; H, 4.99; N, 12.09.

Note that complex **3** crystalized with 1.5 molecules of dichloromethane used as a crystallization solvent. Existence of dichloromethane was also confirmed by the NMR and X-ray analyses. The averaged formula was determined by elemental analysis.

Palladium complex 4

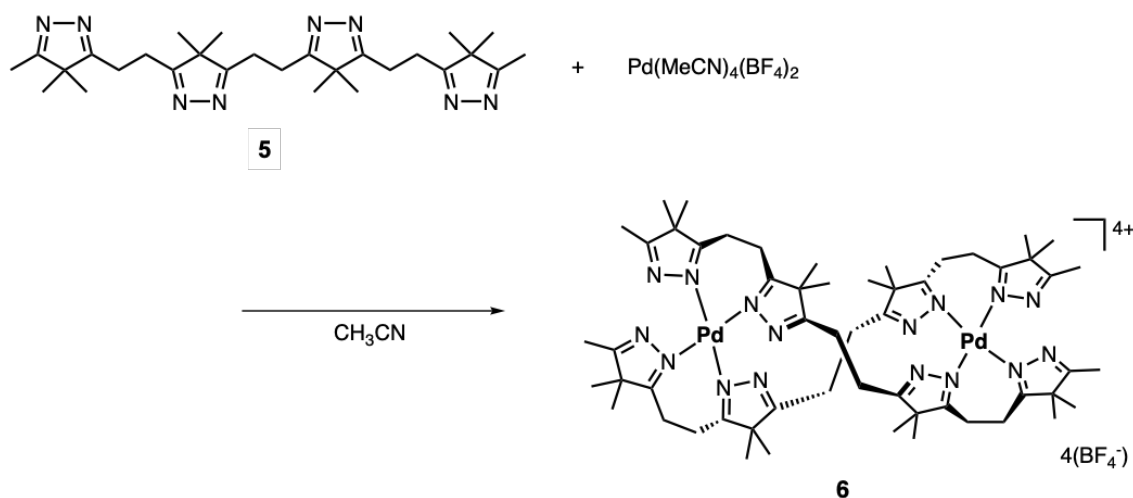


In a similar fashion to the synthesis of complex **4**, a solution of ligand **1** (100 mg, 406 μmol) and $\text{Pd}(\text{CH}_3\text{CN})_4(\text{BF}_4)_2$ (721 mg, 1.62 mmol) in acetonitrile (6.8 mL) was stirred at 60 $^\circ\text{C}$ for 1 h. After cooling the solution, pale yellow crystals formed in the flask were collected by filtration. The crystals were washed with acetonitrile (3.0 mL) and dried on a funnel to give complex **4** (181 mg) in 60% yield.

^1H NMR (400 MHz, CD_3CN , 298 K): δ 4.12 (m, 4H, ethylene), 3.25 (m, 4H, ethylene), 2.86 (s, 12H, terminal methyl), 1.96 (s, 12H, coordinated acetonitrile), 1.50 (s, 12H, dimethylmethylene), 1.46 (s, 12H, dimethylmethylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_3CN , 298 K): δ 199.6, 196.5, 126.7, 67.1, 23.8, 23.5, 19.2, 16.8; HRMS(ESI-TOF): m/z $[\text{M} - 3(\text{BF}_4^-)]^{3+}$ calcd for $\text{C}_{36}\text{H}_{56}\text{N}_{12}\text{Pd}_3\text{B}_3\text{F}_{12}^{3+}$, 412.0665; found, 412.0670; Elemental analysis (%): Calcd. for $\text{C}_{36}\text{H}_{56}\text{N}_{12}\text{Pd}_3\text{B}_6\text{F}_{24} \cdot \text{CH}_3\text{CN}$: C, 29.67; H, 3.87; N, 11.84; Found: C, 29.49; H, 3.66; N, 11.79.

The signal intensity for coordinated acetonitrile at 1.96 ppm was gradually decreased because of slow exchange with NMR solvent (CD_3CN). Due to spectral overlap and ligand exchange with CD_3CN (that causes septet signal) during overnight measurement, the methyl carbon signal for complex **4** was not observed. Attempts to measure ^{13}C NMR spectrum of **5** in other conventional solvents were not successful because of low solubility.

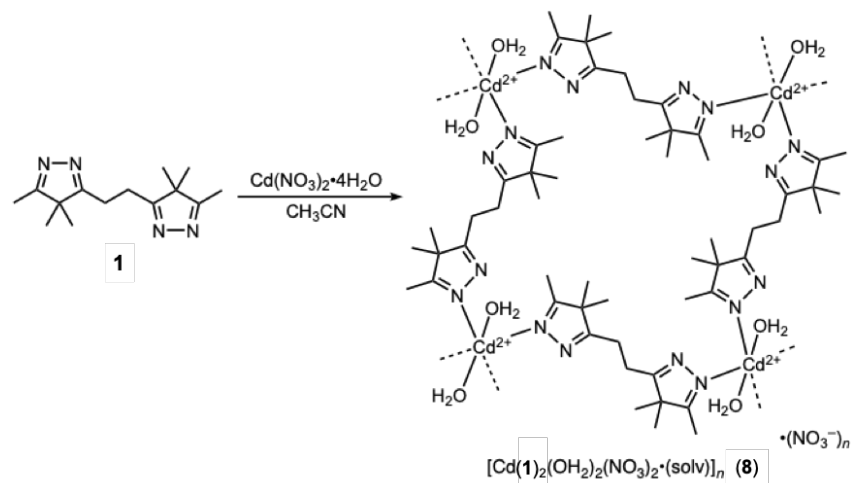
Palladium complex 6



In a 20 mL round bottomed flask equipped with a reflux condenser, ligand **5** (60.0 mg, 122 μmol) and $\text{Pd}(\text{CH}_3\text{CN})_4(\text{BF}_4)_2$ (54.3 mg, 122 μmol) were dissolved in acetonitrile (2.0 mL). The solution was stirred at reflux for 24 h. After the solution was cooled to room temperature, the product was precipitated out from the solution by slow addition of ethyl acetate (4.0 mL). The precipitate was collected by suction filtration, washed with 2.0 mL of ethyl acetate, and air-dried on a funnel to give complex **6** (61.7 mg) in 66% yield.

^1H NMR (400 MHz, CD_3CN , 298 K): δ 3.96 (ddd, $J = 15.9, 11.3, 4.2$ Hz, 4H, terminal ethylene), 3.67 (ddd, $J = 19.5, 6.2, 4.2$ Hz, 4H, terminal ethylene), 3.34 (ddd, $J = 15.9, 6.2, 4.1$ Hz, 4H, terminal ethylene), 3.07 (overlapped ddd, 4H, terminal ethylene), 2.98 (m, 2H, central ethylene), 2.74 (m, 2H, central ethylene), 2.01 (s, 12H, terminal methyl), 1.26 (s, 12H, dimethylmethylene), 1.25 (s, 12H, dimethylmethylene), 1.24 (s, 12H, dimethylmethylene), 1.19 (s, 12H, dimethylmethylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_3CN , 298 K): δ 190.5, 189.1, 187.9, 184.7, 64.0, 63.4, 24.0, 22.5, 22.5, 21.3, 20.6, 19.0, 11.9; HRMS(ESI-TOF): m/z $[\text{M} - 4(\text{BF}_4^-)]^{4+}$ calcd. for $\text{C}_{56}\text{H}_{84}\text{N}_{16}\text{Pd}_2^{4+}$, 298.6290; found, 298.6278; Elemental analysis (%): Calcd. for $\text{C}_{56}\text{H}_{84}\text{N}_{16}\text{Pd}_2\text{B}_4\text{F}_{16} \cdot 3\text{H}_2\text{O}$: C, 42.16; H, 5.69; N, 14.05; Found: C, 42.27; H, 5.39; N, 13.86.

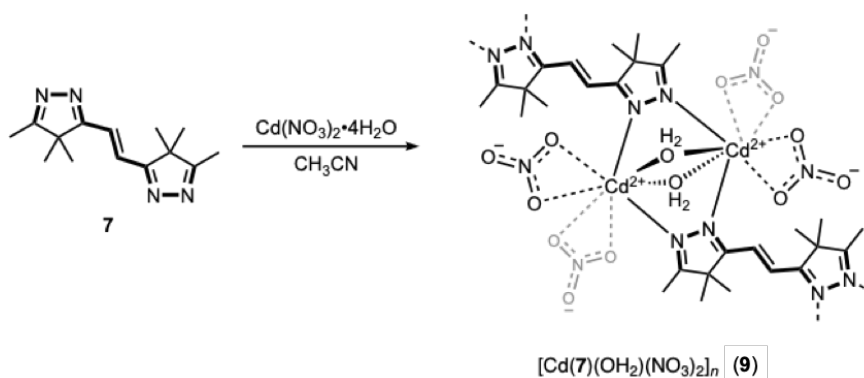
Cadmium complex **8** from unoxidized ligand **1**



To an acetonitrile solution of $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (1.0 mL, 0.30 M) in a 20 mL round-bottom flask was added a solution of ligand **1** (148 mg, 0.60 mmol) in acetonitrile (1 mL). The mixture was stirred at room temperature for 10 min, and then allowed to stand at room temperature. After 3 d, colorless crystals had formed at the bottom of the flask. The crystals were collected by filtration and rinsed with acetonitrile (10 mL) to give complex **8** $[\text{Cd}(\mathbf{1})_2(\text{OH}_2)_2(\text{NO}_3)_2 \cdot (\text{CH}_3\text{CN})]_n$ (106 mg, 0.131 mmol) in 44% yield.

IR (ATR, neat): 3365, 3218, 2974, 2935, 2876, 1595, 1577, 1467, 1422, 1386, 1302, 1187, 1114, 1037, 830, 679 cm^{-1} ; m.p. > 85°C (decomp.); Elemental analysis (%): Calcd for $\text{Cd}(\text{C}_{14}\text{H}_{22}\text{N}_4)_2(\text{OH}_2)_2(\text{NO}_3)_2 \cdot (\text{CH}_3\text{CN})$: C, 44.69; H, 6.38; N, 19.11; Found: C, 44.31; H, 6.26; N, 19.17.

Cadmium complex **9** from oxidized ligand **7**

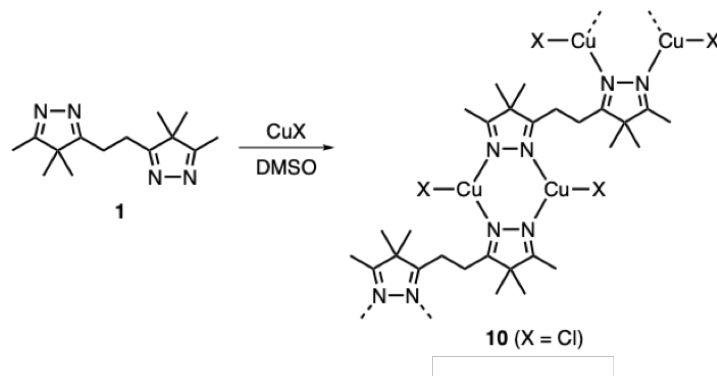


To a 4.0 mM solution of $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (136 mg, 0.44 mmol) in acetonitrile (100 mL) in a 300 mL round bottom flask, was added an acetonitrile solution of ligand **7** (100 mL, 2.0 mM). After stirring for 15 min at room temperature, brownish microcrystals were precipitated. The precipitate was collected by suction filtration, rinsed with acetonitrile (30 mL), and dried under reduced pressure (1 mmHg) at 100 °C for 1 h to give Cd complex **9** $[\text{Cd}_2(\mathbf{7})(\text{OH}_2)_2(\text{NO}_3)_4 \cdot 0.25(\text{CH}_3\text{CN})]_n$ (57 mg) in 37% yield.

IR (ATR, neat): 3174, 1584, 1538, 1411, 1389, 1328, 1304, 1043, 970, 818, 740, 714, 683, 659 cm^{-1} ; m.p. > 300 °C (decomp.); Elemental analysis (%): Calcd for $\text{Cd}_2(\text{C}_{14}\text{H}_{20}\text{N}_4)(\text{OH}_2)1.8(\text{NO}_3)_4 \cdot (\text{CH}_3\text{CN})_{0.2}$: C, 22.82; H, 3.22; N, 15.16; Found: C, 23.13; H, 3.31; N, 15.19.

For powder sample, partial substitution of neutral aqua ligand by solvent acetonitrile which cannot be removed in vacuo was observed.

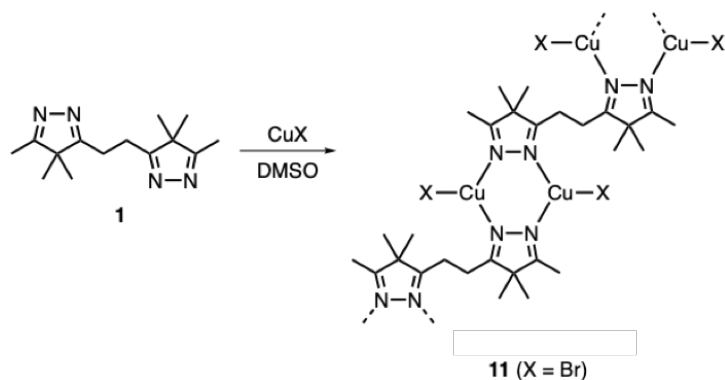
Copper complex [(1)(CuCl)₂]_n **10**



To a 400 mM DMSO solution of ligand **1** (5 mL) in a 100 mL round-bottom flask, was added a suspension of copper chloride (198 mg, 2.00 mmol) in DMSO (20 mL) with stirring at room temperature. After stirring the solution for 90 min, the reaction solution was then allowed to stand at room temperature for 24 h. A pale yellow precipitate formed from the solution was collected by suction filtration, washed successively with DMSO (10 mL) and chloroform (10 mL), and air-dried on a funnel to give complex **10** (281 mg) in 63% yield.

IR (ATR, neat): 2969, 2950, 2932, 2916, 2909, 2892, 2873, 1591, 1576, 1459, 1432, 1398, 1368, 1119, 1037, 965, 869, 768, 612 cm⁻¹; Elemental analysis (%): Calcd. for [(CuCl)₂(C₁₄H₂₂N₄)]_n: C, 37.84; H, 4.99; N, 12.61; Found: C, 37.73; H, 4.89; N, 12.41.

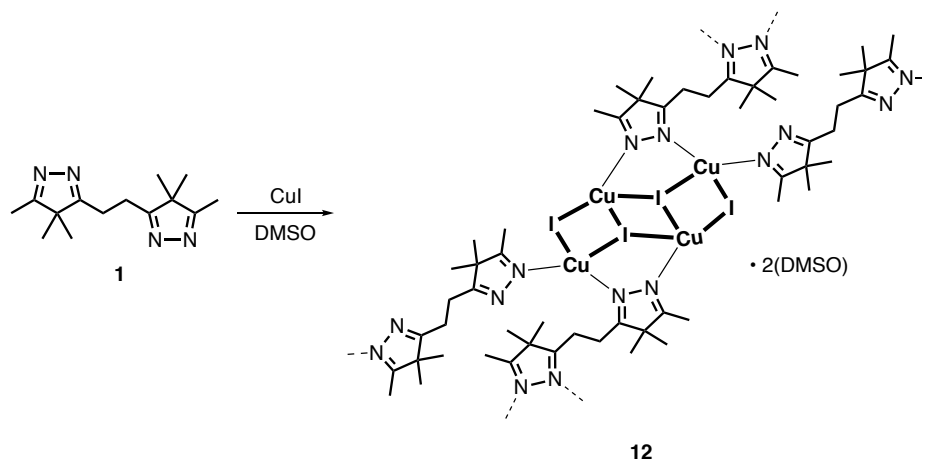
Copper complex [(1)(CuBr)₂]_n **11**



To a 200 mM DMSO solution of ligand **1** (10 mL) in a 300 mL round-bottom flask, was added a suspension of copper(I) bromide (287 mg, 2.00 mmol) in DMSO (170 mL) with stirring at room temperature. After stirring the solution for 90 min, the reaction solution was then allowed to stand at room temperature for 24 h. A pale yellow precipitate formed from the solution was collected by suction filtration, washed successively with DMSO (10 mL) and chloroform (10 mL), and air-dried on a funnel to give complex **11** (328 mg) was obtained in 62% yield as a pale yellow solid.

IR (ATR, neat): 2967, 2952, 2928, 2912, 2909, 2892, 2870, 1592, 1575, 1458, 1427, 1395, 1366, 1320, 1119, 1037, 963, 867, 763, 609 cm⁻¹; Elemental analysis (%): Calcd. for [(CuBr)₂(C₁₄H₂₂N₄)]_n: C, 31.53; H, 4.16; N, 10.51; Found: C, 31.49; H, 4.07; N, 10.26.

Copper complex [(1)₂(CuI)₄•(DMSO)₂]_n **12**



To a 200 mM DMSO solution of ligand **1** (10 mL) in a 300 mL round-bottom flask, was added a 23.5 mM DMSO solution of copper(I) iodide (170 mL). After 90 min stirring at room temperature, a pale yellow precipitate was formed. The reaction mixture was kept for 24 h at room temperature without stirring. The precipitate was collected by suction filtration, washed successively with DMSO (10 mL) and chloroform (10 mL) to afford complex **12** (1.16 g) in 82% yield.

IR (ATR, neat): 2967, 2927, 2906, 2871, 1595, 1573, 1462, 1427, 1393, 1054, 760, 609 cm^{-1} ; Elemental analysis (%): Calcd. for $[(\text{Cu}_4\text{I}_4)(\text{C}_{14}\text{H}_{22}\text{N}_4)_2 \cdot (\text{DMSO})_2]_n$: C, 27.24; H, 4.00; N, 7.94; Found: C, 26.85; H, 3.66; N, 8.09.

Single crystal X-ray diffraction analysis

Crystallographic data for complex 2

Single crystals of complex **2** for X-ray analysis were grown by slow evaporation of the solvent of an acetonitrile solution of **2** (30 mM) over 5 d at room temperature.

$[(C_{28}H_{44}N_8Pd) \cdot (BF_4)_2]$, $M = 772.73$, crystal size: $0.20 \times 0.20 \times 0.08 \text{ mm}^3$, Triclinic, space group $P-1$, $a = 6.5374(2) \text{ \AA}$, $b = 12.2580(3) \text{ \AA}$, $c = 21.5616(5) \text{ \AA}$, $\alpha = 88.574(2)^\circ$, $\beta = 85.328(2)^\circ$, $\gamma = 85.018(2)^\circ$, $V = 1715.33(8) \text{ \AA}^3$, $Z = 2$, $T = 123(2) \text{ K}$, $\mu = 0.617 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.496 \text{ g/cm}^3$, $2.548^\circ \leq \theta \leq 29.497^\circ$, 6594 unique reflections out of 7871 with $I > 2\sigma(I)$, GOF = 1.045, $R_1 = 0.0318$ and $wR_2 = 0.0827$ for all data. CCDC deposit number: 1875329.

Crystallographic data for complex 3

Single crystals of complex **3** for X-ray analysis were grown by vapor diffusion of dichloromethane into a reaction solution.

$[(C_{42}H_{66}N_{12}Pd_2) \cdot (BF_4)_4 \cdot 2.616(CH_2Cl_2) \cdot 0.692O]$, $M = 755.27$, crystal size: $0.20 \times 0.20 \times 0.13 \text{ mm}^3$, Orthorhombic, space group $Ama2$, $a = 25.6757(6) \text{ \AA}$, $b = 21.3064(6) \text{ \AA}$, $c = 11.7797(3) \text{ \AA}$, $V = 6444.2(3) \text{ \AA}^3$, $Z = 8$, $T = 123(2) \text{ K}$, $\mu = 0.839 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.557 \text{ g/cm}^3$, $1.912^\circ \leq \theta \leq 27.481^\circ$, 7069 unique reflections out of 7515 with $I > 2\sigma(I)$, GOF = 1.118, $R_1 = 0.0561$ and $wR_2 = 0.1423$ for all data. CCDC deposit number: 1875330.

Crystallographic data for complex 4

Large-sized single crystals were obtained during the synthesis of complex **4** without stirring the solution.

$[(C_{36}H_{56}N_{12}Pd_3) \cdot (BF_4)_6 \cdot 2(CH_3CN)]$, $M = 789.55$, crystal size: $0.17 \times 0.14 \times 0.06 \text{ mm}^3$, Monoclinic, space group $P2_1/m$, $a = 11.60860(10) \text{ \AA}$, $b = 21.3061(2) \text{ \AA}$, $c = 12.43950(10) \text{ \AA}$, $\beta = 102.9090(10)^\circ$, $V = 2998.95(5) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 8.260 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.749 \text{ g/cm}^3$, $3.645^\circ \leq \theta \leq 74.020^\circ$, 5930 unique reflections out of 6091 with $I > 2\sigma(I)$, GOF = 1.086, $R_1 = 0.0364$ and $wR_2 = 0.0997$ for all data. CCDC deposit number: 1875331.

Crystallographic data for complex 5

Single crystals for X-ray analysis were grown from an acetonitrile solution of **5** via vapor diffusion of ethyl acetate using a 5 mL vial.

$[(C_{56}H_{84}N_{16}Pd_2) \cdot (BF_4)_4 \cdot 2.574(H_2O)]$, $M = 1587.79$, crystal size: $0.27 \times 0.20 \times 0.07 \text{ mm}^3$, Monoclinic, space group $P2_1/c$, $a = 12.9729(3) \text{ \AA}$, $b = 14.3355(3) \text{ \AA}$, $c = 37.3886(7) \text{ \AA}$, $\beta = 91.940(2)^\circ$, $V = 6949.3(3) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.614 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.518 \text{ g/cm}^3$, $2.406^\circ \leq \theta \leq 29.541^\circ$, 14071 unique reflections out of 16533 with $I > 2\sigma(I)$, GOF = 1.130, $R_1 = 0.0472$ and $wR_2 = 0.0971$ for all data. CCDC deposit number: 1875332.

Crystallographic data for complex 10

$[C_7H_{11}CuClN_2]$, $M = 222.17$, crystal size: $0.07 \times 0.07 \times 0.05 \text{ mm}^3$, monoclinic, space group $C2/c$, $a = 23.4558(13) \text{ \AA}$, $b = 5.9720(3) \text{ \AA}$, $c = 15.3655(8) \text{ \AA}$, $\beta = 125.855(5)^\circ$, $V = 1744.50(18) \text{ \AA}^3$, $Z = 8$, $T = 123(2) \text{ K}$, $\mu = 2.744 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.692 \text{ g/cm}^3$, $F(000) = 904$, $2.143^\circ \leq \theta \leq 26.000^\circ$, 1553 unique reflections out of 1709 with $I > 2\sigma(I)$, 103 parameters, $|\Delta\rho|_{\text{max}} = 0.750 \text{ e\AA}^{-3}$, $|\Delta\rho|_{\text{min}} = -0.497 \text{ e\AA}^{-3}$, GOF = 1.139, $R_1 = 0.0349$ and $wR_2 = 0.0926$ for all data. CCDC deposit number: 1965217.

Crystallographic data for complex 11

$[C_7H_{11}CuBrN_2]$, $M = 266.63$, crystal size: $0.18 \times 0.11 \times 0.10 \text{ mm}^3$, monoclinic, space group $C2/c$, $a = 23.8021(14) \text{ \AA}$, $b = 6.0366(3) \text{ \AA}$, $c = 15.6078(8) \text{ \AA}$, $\beta = 126.140(5)^\circ$, $V = 1811.06(19) \text{ \AA}^3$, $Z = 8$, $T = 123(2) \text{ K}$, $\mu = 6.761 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.956 \text{ g/cm}^3$, $F(000) = 1048$, $2.619^\circ \leq \theta \leq 24.981^\circ$, 1401 unique reflections out of 1590 with $I > 2\sigma(I)$, 103 parameters, $|\Delta\rho|_{\text{max}} = 2.419 \text{ e\AA}^{-3}$, $|\Delta\rho|_{\text{min}} = -0.661 \text{ e\AA}^{-3}$, GOF = 1.177, $R_1 = 0.0434$ and $wR_2 = 0.1278$ for all data. CCDC deposit number: 1965218.

Crystallographic data for complex 12

$[C_{14}H_{22}Cu_2I_2N_4 \cdot (CH_3)_2SO]$, $M = 705.36$, crystal size: $0.19 \times 0.13 \times 0.04 \text{ mm}^3$, triclinic, space group $P-1$, $a = 10.7966(3) \text{ \AA}$, $b = 10.7981(3) \text{ \AA}$, $c = 12.3333(3) \text{ \AA}$, $\alpha = 69.652(3)^\circ$, $\beta = 64.233(3)^\circ$, $\gamma = 86.311(3)^\circ$, $V = 1207.65(7) \text{ \AA}^3$, $Z = 2$, $T = 123(2) \text{ K}$, $\mu = 4.416 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.940 \text{ g/cm}^3$, $F(000) = 680$, $2.605^\circ \leq \theta \leq 25.997^\circ$, 4063 unique reflections out of 4705 with $I > 2\sigma(I)$, 243 parameters, $|\Delta\rho|_{\text{max}} = 1.490 \text{ e\AA}^{-3}$, $|\Delta\rho|_{\text{min}} = -0.801 \text{ e\AA}^{-3}$, GOF = 1.031, $R_1 = 0.0251$ and $wR_2 = 0.0588$ for all data. CCDC number: 1965219.

4.7. References

- [1] N. Ozawa, K. I. Shivakumar, M. Murugavel, Y. Inaba, T. Yoneda, Y. Ide, J. Pirillo, Y. Hijikata, Y. Inokuma, *Chem. Commun.*, **2022**, 58, 2971–2974.
- [2] T. Eriksson, A. Mace, Y. Manabe, M. Y.-Fujita, Y. Inokuma, D. Brandell, J. Mindemark, *J. Electrochem. Soc.*, **2020**, 167, 070537.
- [3] Y. Manabe, M. Uesaka, T. Yoneda, Y. Inokuma, *J. Org. Chem.* **2019**, 84, 9957–9964.
- [4] B. Moulton, M. J. Zaworotko, *Chem. Rev.* **2001**, 101, 1629–1658.
- [5] A. Y. Robin, K. M. Fromm, *Coord. Chem. Rev.* **2006**, 250, 2127–2157.
- [6] Z.-J. Lin, J. Lü, M. Hong, R. Cao, *Chem. Soc. Rev.* **2014**, 43, 5867–5895.
- [7] L. Chen, Q. Chen, M. Wu, F. Jiang, H. Maochun, *Acc. Chem. Res.* **2015**, 48, 201–210.
- [8] R. Miyake, A. Ando, M. Ueno, T. Muraoka, *J. Am. Chem. Soc.* **2019**, 141, 8675–8679.
- [9] Y. Ashida, Y. Manabe, S. Yoshioka, T. Yoneda, Y. Inokuma, *Dalton Trans.* **2019**, 48, 818–822.
- [10] C. H. Wei, K. B. Jacobson, *Inorg. Chem.* **1981**, 20, 356–363.
- [11] M. Munakata, T. Kuroda-Sowa, M. Maekawa, A. Hirota, S. Kitagawa, *Inorg. Chem.* **1995**, 34, 2705–2710.
- [12] D. J. Chesnut, A. Kusnetzow, R. Birge, J. Zubieta, *Inorg. Chem.* **1999**, 38, 5484–5494.
- [13] P. M. Graham, R. D. Pike, M. Sanbat, R. D. Bailey, W. T. Pennigton, *Inorg. Chem.* **2000**, 39, 5121–5132.
- [14] J.-P. Zhang, S.-L. Zheng, X.-C. Huang, X.-M. Chen, *Angew. Chem. Int. Ed.* **2004**, 43, 206–209.
- [15] J.-P. Zhang, Y.-Y. Lin, X.-C. Huang, X.-M. Chen, *J. Am. Chem. Soc.* **2005**, 127, 5495–5506.
- [16] R. Peng, D. Li, T. Wu, X.-P. Zhou, S. W. Ng, *Inorg. Chem.* **2006**, 45, 4035–4046.
- [17] Z.-P. Deng, H.-L. Qi, L.-H. Huo, S. W. Ng, H. Zhao, S. Gao, *Dalton Trans.* **2010**, 39, 10038–10050.
- [18] R. Peng, M. Li, D. Li, *Coord. Chem. Rev.* **2010**, 254, 1–18.
- [19] S.-Q. Bai, L. Jiang, D. J. Young, T. S. A. Hor, *Dalton Trans.* **2015**, 44, 6075–6081.
- [20] R.-Y. Wang, X. Zhang, Q.-F. Yang, Q.-S. Huo, J.-H. Yu, J.-N. Xu, J.-Q. Xu, *J. Solid State Chem.* **2017**, 251, 176–185.
- [21] C. Kutal, *Coord. Chem. Rev.* **1990**, 99, 213–252.

- [22] K. R. Kyle, C. K. Ryu, J. A. Dibenedetto, P. C. Ford, *J. Am. Chem. Soc.* **1991**, *113*, 2954–2965.
- [23] P. C. Ford, A. Vogler, *Acc. Chem. Res.* **1993**, *26*, 220–226.
- [24] P. C. Ford, E. Cariati, J. Bourassa, *Chem. Rev.* **1999**, *99*, 3625–3647.
- [25] J. Conesa-Egea, F. Zamora, P. Amo-Ochoa, *Coord. Chem. Rev.* **2019**, *381*, 65–78.
- [26] T.-L. Yu, Y.-M. Guo, G.-X. Wu, X.-F. Yang, M. Xue, Y.-L. Fu, M.-S. Wang, *Coord. Chem. Rev.* **2019**, *397*, 91–111.
- [27] N. P. Rath, E. M. Holt, K. Tanimura, *J. Chem. Soc. Dalton Trans.*, **1986**, *11*, 2303–2310.
- [28] S. Yuan, S.-S. Liu, D. Sun, *CrystEngComm*, **2014**, *16*, 1927–1933.
- [29] Q. Benito, X. F. Le Goff, G. Nocton, A. Fargues, A. Garcia, A. Berhault, S. Kahlal, J.-Y. SAILARD, C. Martineau, J. Trébosc, T. Gacoin, J.-P. Boilot, S. Perruchas, *Inorg. Chem.* **2015**, *54*, 4483–4494.
- [30] B. Huitorel, H. E. Moll, M. Cordier, A. Fargues, A. Garcia, F. Massuyeau, C. Martineau-Corcos, T. Gacoin, S. Perruchas, *Inorg. Chem.* **2017**, *56*, 12379–12388.
- [31] J. Pospisil, I. Jess, C. Näther, M. Nakas, P. Taborsky, *New J. Chem.* **2011**, *35*, 861–864.
- [32] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, **2015**, *71*, 3–8.
- [33] G. M. Sheldrick, *Acta Crystallogr. Sect. C*, **2015**, *71*, 3–8.

Chapter 5

Supramolecular Conformational Control of Polyketones

Abstract

Conformational control of structurally flexible aliphatic polyketones, containing 1,3-diketone units at both terminal positions, was achieved by supramolecular complexation with pillar[5]arene. Pillar[5]arene recognized the oligomethylene chain of aliphatic oligoketones and formed pseudo-rotaxanes with association constants $K = \sim 10 \text{ M}^{-1}$. The induced linear conformations were then fixed by BF_2 complexation at 1,3-diketone sites under quasi-solid-state conditions for the rotaxane formation. Similar conformational control was performed on the polyketone-derived alkyl-bridged chromophore dyad to control its optical properties. In UV-vis absorption spectra, the solvatochromic behavior was observed for the structurally flexible chromophore dyad, presumably due to the intramolecular aggregation of the chromophore units. However, the rotaxane of the chromophore dyad did not exhibit such behavior, indicating that the conformational restriction suppressed the intramolecular aggregation.

5.1. Introduction

In Chapters 3 and 4, the author demonstrated the structural transformations of aliphatic polyketones and polyketone-derived aliphatic polyimines by chemical reactions and metal-ion coordination. As another strategy for the construction of molecular structures, the author has focused on supramolecular interactions to directly control the conformations of aliphatic chains of polyketones. In biosynthetic routes, the conformations of the aliphatic chains of structurally flexible aliphatic polyketones are sophisticatedly controlled by enzymes, and subsequent chemical transformations at carbonyl groups were performed to give diverse polyketides and structure-related bioactivities.¹⁻⁴ Inspired by the biological system, chemists have developed various types of host molecules to regulate the conformations and orientations of structurally flexible substrates.⁵⁻⁹ However, it is still a considerable challenge to induce and fix the conformation of aliphatic chains due to the lack of effective intermolecular interactions to fix their conformations.

As a host molecule for a simple aliphatic chain, the author has focused on pillar[5]arene.¹⁰⁻¹⁴ Pillar[5]arene can bind structurally flexible aliphatic guests with the multiple CH- π interactions in the tight cavity of the macrocyclic structure. Therefore, even simple hydrocarbon chains, the guest molecules can be incorporated into the cavity, and (pseudo) rotaxane structures are accordingly formed.¹⁵⁻¹⁸ This binding feature is superior to other macrocyclic hosts in terms of the recognition of neutral hydrocarbon chains. Upon the rotaxane formation, the conformation of the guest molecules can be induced to be linear from several possible conformations in their free states.

In this work, the supramolecular conformational control of structurally flexible aliphatic polyketones was performed upon the rotaxane formation with pillar[5]arene. As guest substrates, aliphatic tetraketones with different lengths of oligomethylene components between two 1,3-diketone units were selected for this study. 1,3-diketone unit is known to be functionalized by chemical modifications or metal complexations.¹⁹ The binding study of aliphatic tetraketones revealed the induction of the linear conformation of the oligomethylene chain by pseudo-rotaxane formations, although the association constant values were rather low compared to other reported guests. The induced conformations of aliphatic tetraketones were then locked by BF₂ complexations at the 1,3-diketone units. Given the conformational restriction of aliphatic tetraketones upon the rotaxane formation, the control of optical properties in an alkyl-bridged chromophore dyad was examined by suppressing its intramolecular aggregation upon rotaxane formation.

5.2. Supramolecular Conformational Induction of Polyketones by Pillar[5]arene

At first, we have investigated the binding behavior of pillar[5]arene **1** and aliphatic polyketones composed of 3,3-dimethylpentane-2,4-dione. However, the complexation was not observed, presumably due to the steric hindrance of the dimethylmethylene unit. Therefore, the binding studies of non-substituted aliphatic polyketones **2-6** of different oligomethylene chain lengths and pillar[5]arene **1** were performed (**Figure 5-1**).

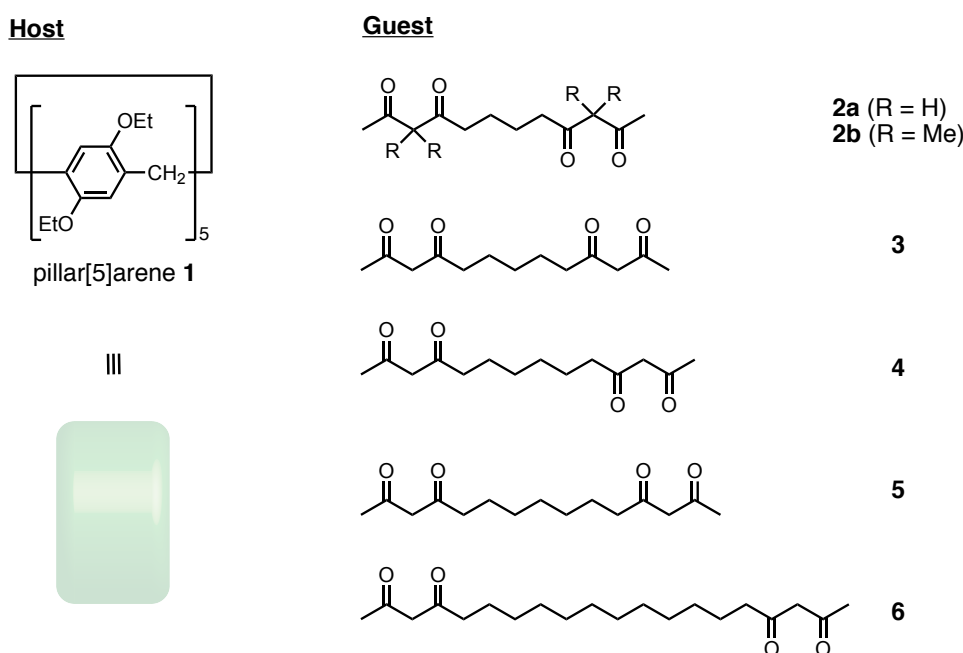


Figure 5-1. Chemical structures of pillar[5]arene **1** and aliphatic polyketones **2-6**.

Aliphatic polyketones **2-6** with different chain lengths were prepared by the reactions between acetylacetone and corresponding terminal dihaloalkanes in a similar manner to the reported procedures (see also Experimental Section).²⁰⁻²¹

The binding study was then performed using polyketone **2a** and pillar[5]arene **1** to investigate their host-guest complexation behavior. In CDCl₃ solution, polyketone **2a** existed as an 85:15 enol/keto equilibrated mixture for 1,3-diketone units at 10 mM concentration. When 1.0 equiv. of host **1** was added to the 10 mM CDCl₃ solution of **2a**, the upfield shift of the methylene proton signals from C6 and C7 positions was observed from 1.65 to 1.34 ppm in the ¹H NMR spectrum, implying the reversible formation of pseudo-rotaxane **1**⊃**2a**. The Job's plot from the ¹H NMR titration experiment suggested the 1:1 complexation of host **1** and guest **2a** (**Figure 5-2a**). Using a nonlinear curve-fitting

theorem,^{22,23} the association constant K for the complexation of **1** and **2a** was calculated to be $17.0 \pm 1.0 \text{ M}^{-1}$ (Figure 5-2b).

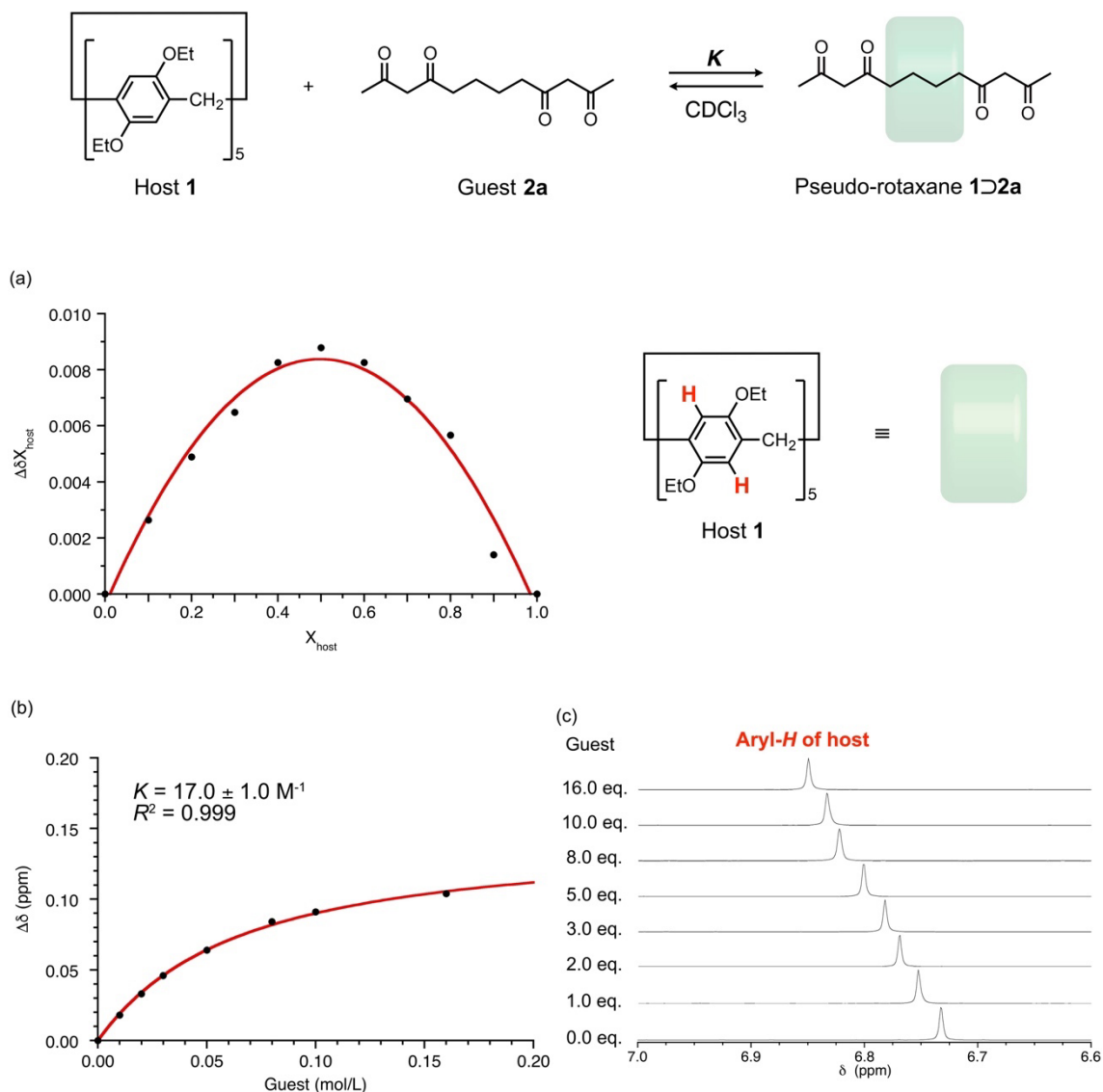


Figure 5-2. (a) Job's plot for determining host-guest ratio between **1** (host) and **2a** (guest), which indicates 1:1 binding of **1** and **2a**, $X_{\text{host}} = [\text{Host}]/([\text{Host}]+[\text{Guest}])$, $\Delta\delta$: chemical shift change of aryl proton signal of **1**; (b) Non-linear fitting curve of ^1H NMR titration; (c) Partial ^1H NMR spectra of **1** (10 mM) with increasing the ratio of **2a** from 0 to 16 equiv. in CDCl_3 at 298 K.

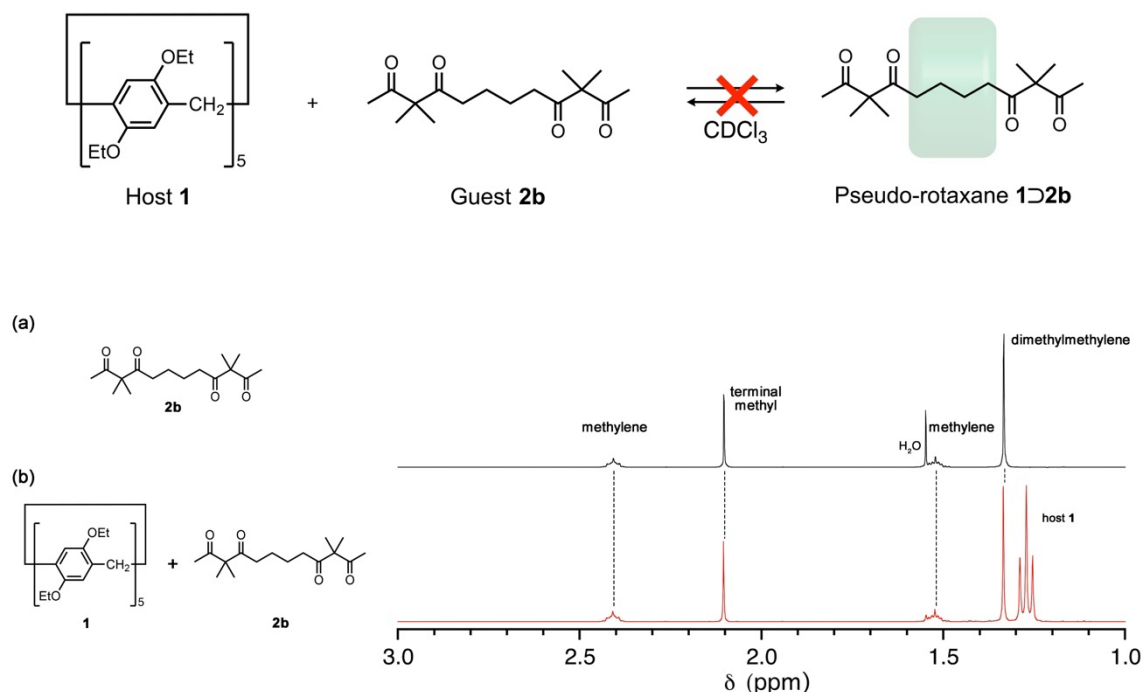


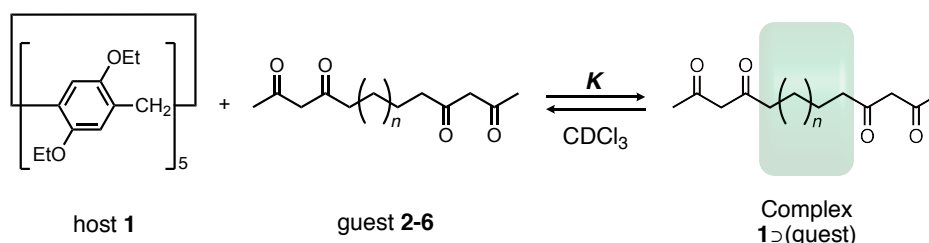
Figure 5-3. (a) Partial ^1H NMR spectrum of guest **2b** (10 mM) in CDCl_3 at 298 K; (b) Partial ^1H NMR spectrum of guest **2b** in the presence of host **1** (1:1 ratio, 10 mM) in CDCl_3 at 298 K. No chemical shift changes of methylene protons signals indicate no complexation between host **1** and guest **2b**.

When tetramethyl substituted polyketone **2b** was mixed with host **1** under the same conditions, no chemical shift change of the methylene protons was observed, as observed in the case of polyketones composed of 3,3-dimethylpentane-2,4-dione, suggesting that the substituted methyl groups at the 1,3-diketone units were too bulky to be incorporated into the cavity of host **1** (**Figure 5-3**). Similarly, the stoichiometry for the complexation and binding constants were determined for the other polyketones **3-6** with the different numbers of methylene units by ^1H NMR titrations.

In the binding constants of **2-6** with host **1**, an odd-even effect on the number of bridging methylene units was observed (**Table 5-1** and **Figure 5-11-14** in Experimental Section). While tetramethylene-bridged polyketone **2a** and hexamethylene-bridged polyketone **4** have similar binding constants, the binding constant of pentamethylene-bridged polyketone **3** was three times smaller than that of **2a**. As the chain length elongated, the odd-even effect became trivial. In the case of 12 methylene bridged polyketone **6**, the binding constant was $6.3 \pm 0.3 \text{ M}^{-1}$, which was a comparable value for odd-numbered polyketones **3** and **5**. The binding constants of polyketones **2-6** with host **1** were rather low, in the order of 10 M^{-1} , almost 90% complexation was estimated from

the binding constants at a 1.0 M concentration for both host and guest components in CDCl_3 .

Table 5-1. Association constants K between pillar[5]arene **1** and polyketone guests **2-6**.



guest	Association Constant K [M^{-1}] ^a
2a	17.0 ± 1.0
2b	—
3	5.5 ± 0.8
4	14.0 ± 0.8
5	8.1 ± 0.6
6	6.3 ± 0.3

a : Determined by ^1H NMR titration

Single crystal X-ray diffraction analysis confirmed the formation of pseudo-rotaxanes between host **1** and guest **3** and **4** (**Figure 5-4**). The colorless single crystals of pseudo-rotaxanes **1⊃3** and **1⊃4** were prepared by vapor diffusion of methanol into a chloroform solution of host **1** and guest **3** or **4** (molar ratio of host : guest = 1 : 3). In the crystal structure of **1⊃3** and **1⊃4**, the guest incorporation by host **1** was unambiguously confirmed. In both crystal structures, C_5 -symmetric conformation of host **1** with the same planar chirality of all the aromatic rings was observed. In the crystal structure of **1⊃3**, the 1,3-diketone units of guest **3** adopted planar enol forms, which was confirmed by the bond length alternation (**Figure 5-4a**). No disorder was observed in the crystal structure of the axis molecule **3**, and the tautomer was determined to be (3*Z*,11*Z*)-4,12-dihydroxytrideca-3,11-diene-2,10-dione (hereafter referred to as **3'**). Weak hydrogen bonds between the oxygen atoms of **3'** and the ethoxy groups of **1** were suggested as possible interactions considering of their short O—C distances (2.641 and 2.668 Å).

(a) Guest Conformations in the pseudo-rotaxanes

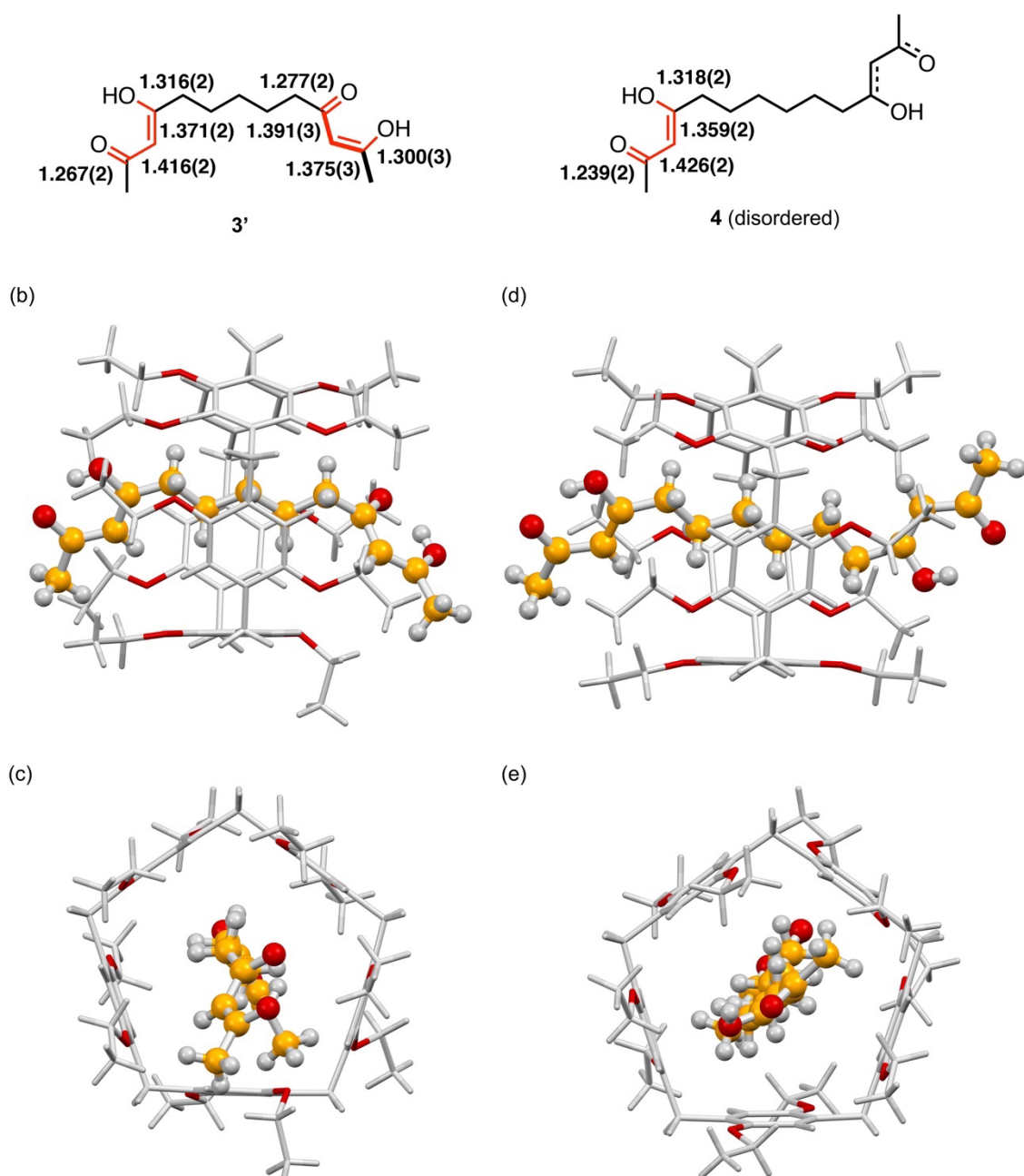


Figure 5-4. Single crystal X-ray structure of pseudo-rotaxanes **1**⊃**3** and **1**⊃**4**. (a) the guest conformations in the pseudo-rotaxanes and selected bond lengths (Å) of 1,3-diketone units. (b,d) Top views of **1**⊃**3** and **1**⊃**4**. (c,e) Side views of **1**⊃**3** and **1**⊃**4**. Host **1** and guest **3'**, **4** are drawn as line and ball-and-stick models, respectively. The major parts are shown for disordered parts of guest molecules.

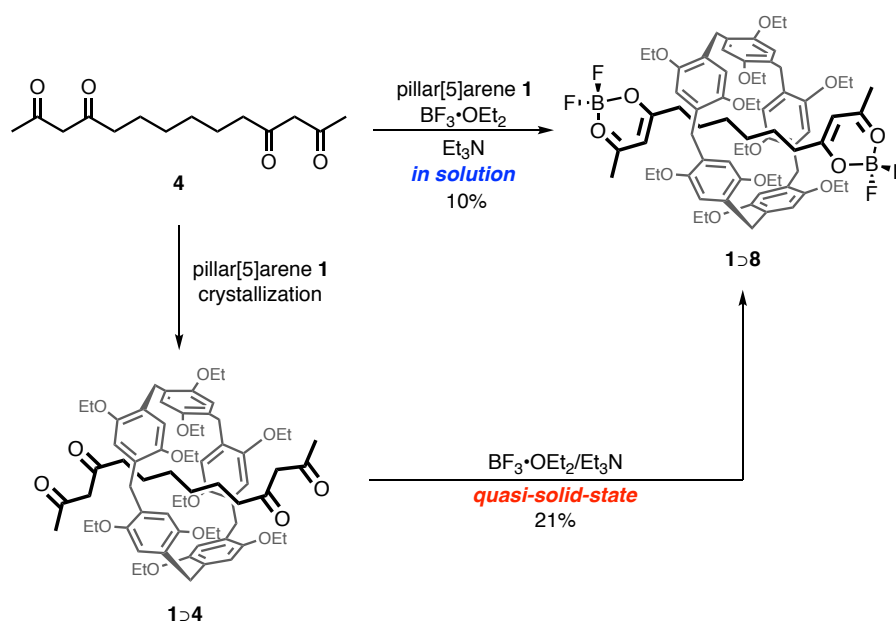
Similar to other rotaxane systems of host **1**,²⁴ CH- π interactions were indicated from the distances of the methylene carbon of **3'** and aromatic planes of **1** (2.999–3.431 Å) with all *s-trans* conformation of the pentamethylene chain. The twisted non-planar conformation of **3'** was attributed to the torsion angles of 5.4° and 84.4° for C3–C4–C5–C6 and C8–C9–C10–C11 bonds, respectively.

In the case of **1**⊃**4**, one 1,3-diketone unit of **4** was disordered, presumably due to the keto-enol tautomerism, while the other 1,3-diketone unit was clearly observed as a planar enol form with the bond length alternation (**Figure 5-4a**). In a similar manner of pseudo-rotaxane **1**⊃**3**, the hexamethylene chain showed an all-*s-trans* conformation to induce multiple CH- π interactions. The torsion angle of the non-disordered part of **4** was 0.1° for C3–C4–C5–C6 bonds, resulting in an almost planar conformation of **4**.

Considering the slight conformational differences of host **1** between **1**⊃**3** and **1**⊃**4** in the crystal structures, the observed differences in the association constants *K* were derived from the conformational stability of the incorporated guests in the cavity of host **1**.

5.3. Conformational Fixation of Polyketones by a Rotaxane Formation

After confirming the pseudo-rotaxane formations between host **1** and guest **2-6**, the author has next envisioned fixing the induced conformation of polyketones by the complexation with host **1** using BF₂ units at 1,3-diketone sites as stoppers for the rotaxane formation. Given sufficient chain length and binding constants, the rotaxane formation of hexamethylene-bridged polyketone **4** and host **1** was investigated (**Scheme 5-1**).



Scheme 5-1. Synthesis of rotaxane **1>8** under solution-state or quasi-solid-state conditions.

At first, mono-BF₂ complex **7** was prepared from **4** under the treatment of BF₃·OEt₂ and triethylamine (see Experimental Section for synthetic details) to study its binding behavior with pillar[5]arene **1** towards a rotaxane formation. The association constant between **1** and **7** was determined to be $61 \pm 2.0 \text{ M}^{-1}$, whose value was about five times larger than that of polyketone **4** (**Figure 5-5**). Therefore, the synthesis of rotaxane **1>8** was directly attempted by the reactions between guest **4** and BF₃·OEt₂ in the presence of host **1**.

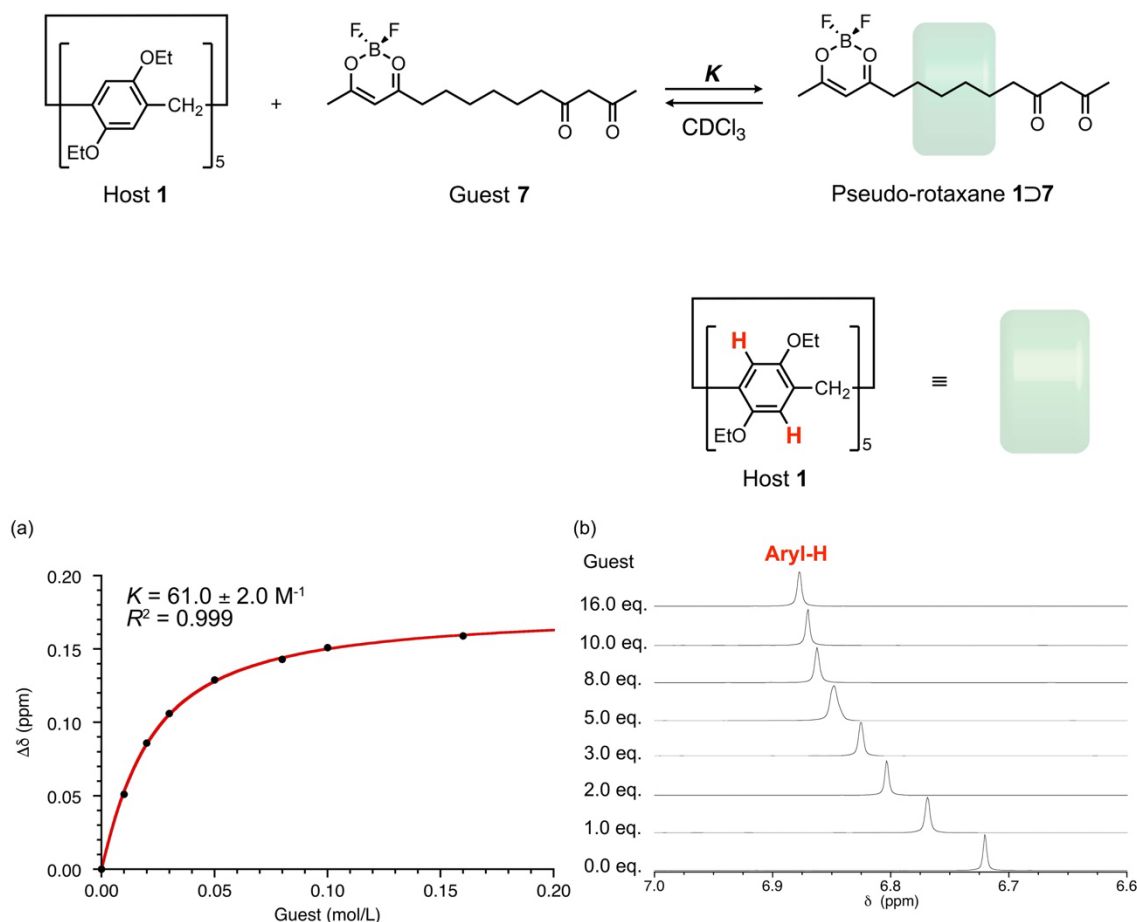


Figure 5-5. (a) Non-linear fitting curve of ^1H NMR titration with **1** (host) and **7** (guest); (b) Partial ^1H NMR spectra of **1** (10 mM) with increasing the ratio of **7** from 0 to 16 equiv. in CDCl_3 at 298 K.

When 5.0 equiv. of guest **4** and 1.0 equiv. of host **1** (200 mM) were treated with an excess amount of $\text{BF}_3 \cdot \text{OEt}_2$ in chloroform, new highly up-field shifted proton signals appeared, indicating the formation of rotaxane **1** $\supset$ **8**. In the ^1H NMR spectrum, the methylene proton signals at the C6 and C7 positions were observed at -0.102 and -2.35 ppm, respectively, due to the ring current effects of the aromatic rings of host **1**. However, the rotaxane **1** $\supset$ **8** was isolated in only 10% yield after the silica-gel chromatography separation, reflecting the still low binding constants between **1** and **4** or **7** (Scheme 5-1). Therefore, the author has performed a quasi-solid-state reaction from crystals of **1** $\supset$ **4** to increase the ratio of pseudo-rotaxane species in the reaction mixture. The crystals of **1** $\supset$ **4** were prepared in advance by mixing host **1** (1.0 equiv.) and guest **4** (5.0 equiv.) in chloroform followed by evaporation at 20 $^\circ\text{C}$. The crystals of **1** $\supset$ **4** were then ground in a mortar using a pestle with 30 equiv. of $\text{BF}_3 \cdot \text{OEt}_2$ and 10 equiv. of triethylamine. The

isolated yield of rotaxane **1**⊃**8** was slightly improved to 21% yield (Scheme 5-1). The isolated rotaxane **1**⊃**8** was stable, and no dethreading processes were not observed even in a refluxing toluene solution, indicating that the BF₂ units at the 1,3-diketone sites were sufficiently stable, and bulky to maintain the interlocked structure of **1**⊃**8**.

A single crystal of rotaxane **1**⊃**8** was prepared by vapor diffusion of cyclohexane into a toluene solution of **1**⊃**8**. The crystal structure of **1**⊃**8** showed the retention of the nearly linear conformation of the hexamethylene chain of **8** induced by host **1** even after the BF₂ complexation (Figure 5-6). Two boron atoms at the 1,3-diketone sites were separated by 12.4 Å due to the linear conformation of axis **8**, although the hexamethylene chain showed positional disorders in the crystal structure. These results ensured that the conformations of structurally flexible aliphatic chains could be constrained by the formation of the rotaxane structure by supramolecular interactions. As a result, the both ends of the axis molecule cannot contact each other even in solution due to the conformational restriction.

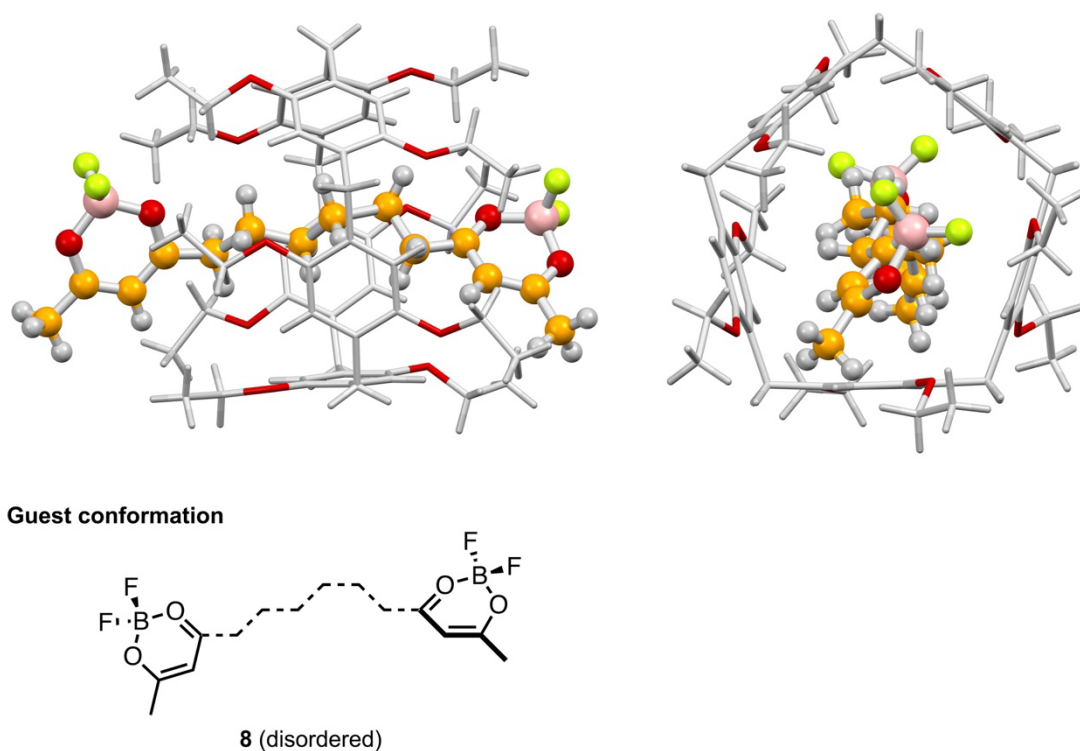
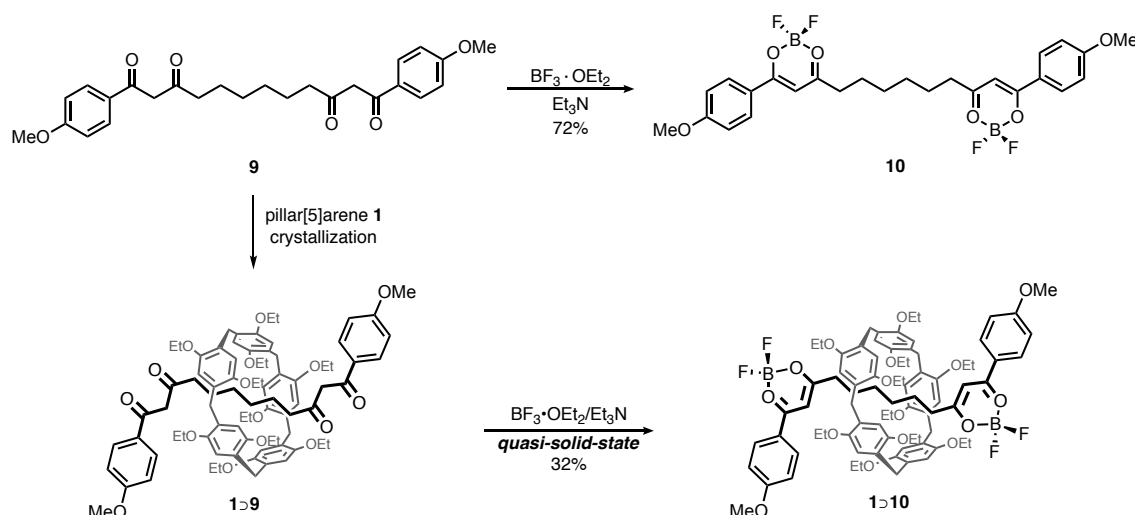


Figure 5-6. Single crystal X-ray structure of rotaxane **1**⊃**8** (left: top view, right: side view). Host **1** and guest **8** are drawn as line and ball-and-stick models, respectively. The major parts are shown for disordered parts of guest molecules.

5.4. Suppression of Solvatochromic Behavior of Polyketone-Derived Chromophore Dyads

In the X-ray crystal structure of **1**⊃**8**, the two terminal BF₂ units were well separated, so both ends cannot contact each other under the conformational restriction by the rotaxane formation. Therefore, the author attempted to utilize this conformational control by rotaxane formation to control the optical properties of the polyketone-derived alkyl-bridged chromophore dyad.

As an alkyl-bridged chromophore dyad derived from aliphatic polyketones, compound **10** was designed to evaluate its optical property control with the rotaxane counterpart **1**⊃**10** to investigate the effects of the conformational restriction on the optical property. Compound **10** was prepared from polyketone **9** in 72% yield by BF₂ complexation. (Scheme 5-2, see detailed synthetic protocols in the Experimental Section).



Scheme 5-2. Synthesis of axis **10** and rotaxane **1**⊃**10**.

In the UV–vis absorption spectrum in dichloromethane, compound **10** showed a sharp absorption band at 362 nm, which was virtually identical to that of monomer **11** (Figure 5-8). When the solvent was changed from dichloromethane to less polar THF and 1,4-dioxane, the broadening of the absorption band was observed in THF, and a new shoulder peak appeared at 349 nm in 1,4-dioxane. These changes in the absorption spectra were independent of the concentrations of compound **10**. Therefore, the solvatochromism observed in compound **10** was presumably due to intramolecular aggregation formation derived from the structural flexibility of the oligomethylene chain.²⁵⁻²⁷

Rotaxane of **1**⊃**10** was prepared through a quasi-solid-state reaction in 32% yield using

a similar synthetic protocol of **1**⊃**8** (Scheme 5-2). Rotaxane of **1**⊃**10** was crystallized in the same solvent system of **1**⊃**8** for single crystal X-ray diffraction. In the X-ray structure of rotaxane **1**⊃**10**, the hexamethylene chain adopted a rather linear conformation in a similar manner to that of **1**⊃**8** (Figure 5-7). Accordingly, the terminal boron centers were separated by a distance of 12.5 Å.

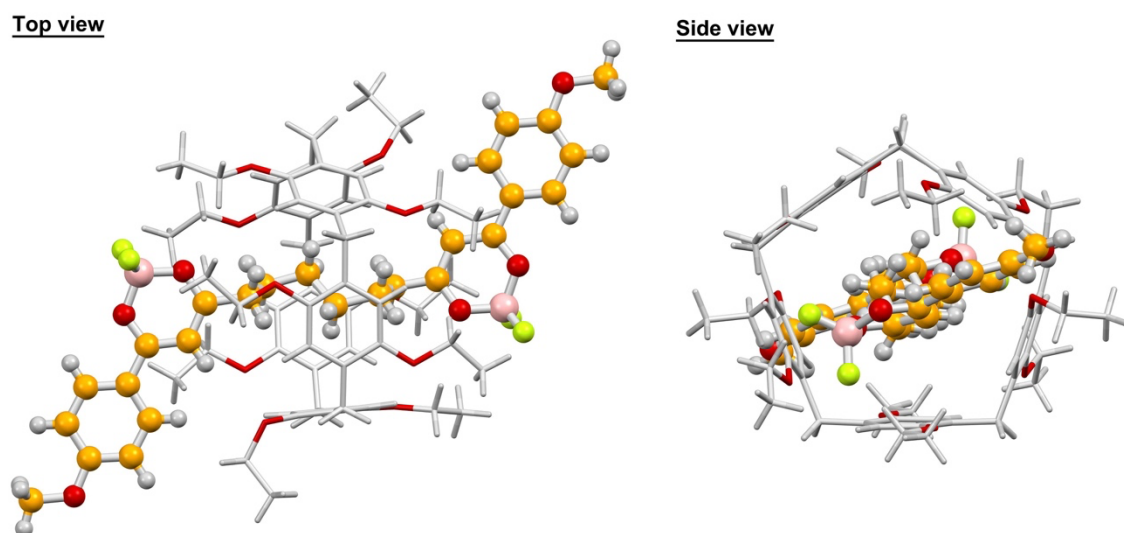


Figure 5-7. X-ray crystal structure of rotaxane **1**⊃**10** (left: top view, right: side view). Host **1** and guest **10** were drawn as line and ball-and-stick models, respectively. Solvents were omitted for clarity.

In contrast to **10**, rotaxane **1**⊃**10** showed little solvatochromic behavior in the absorption spectra. When the solvent was changed from CH₂Cl₂, THF to 1,4-dioxane, no spectral changes were observed, and each spectrum shape was virtually identical to monomer **11** (Figure 5-8). Considering these results in the absorption spectra, it was estimated that the intramolecular aggregation of axis **10** was almost suppressed by the conformational control by the rotaxane formation (Figure 5-9). Fluorescence studies were also conducted, but the evaluation of the conformational restriction could not be achieved due to the quenching of the fluorescence in the rotaxane **1**⊃**10** (Figure 5-10).

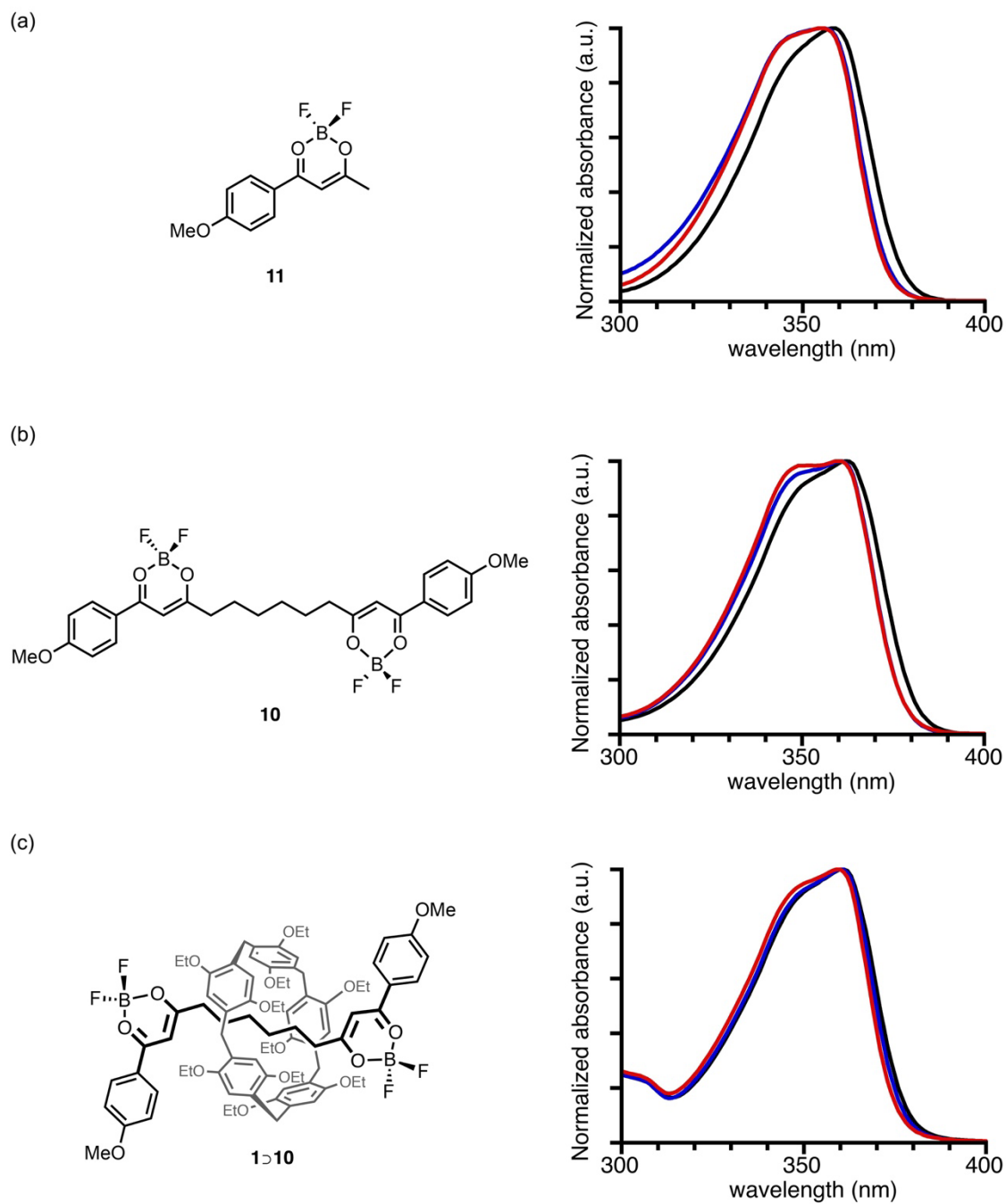


Figure 5-8. UV-vis absorption spectra of (a) monomer **11**, (b) axis **10**, and (c) rotaxane **1>10** in CH₂Cl₂, THF, and 1,4-dioxane (black, blue, and red, respectively).

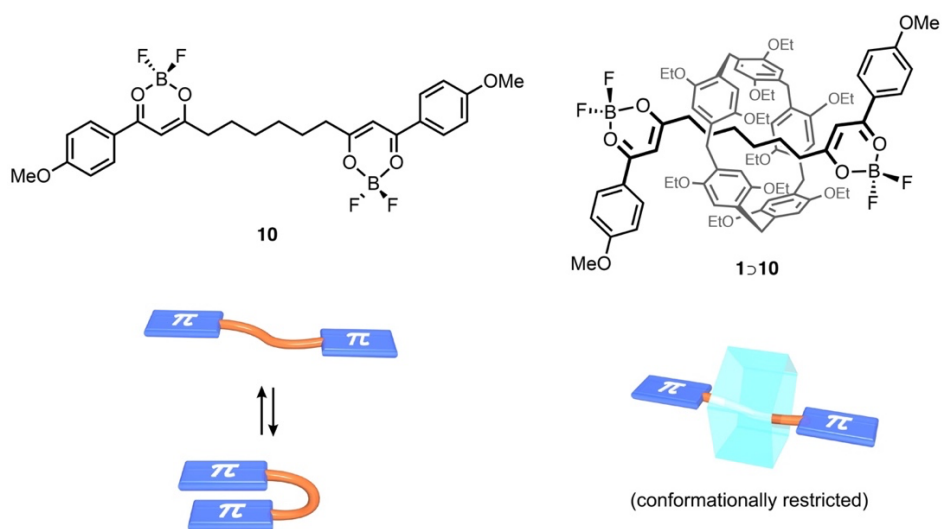


Figure 5-9. Illustration of the conformational restriction of flexible alkyl-bridged chromophore dyad by the rotaxane formation.

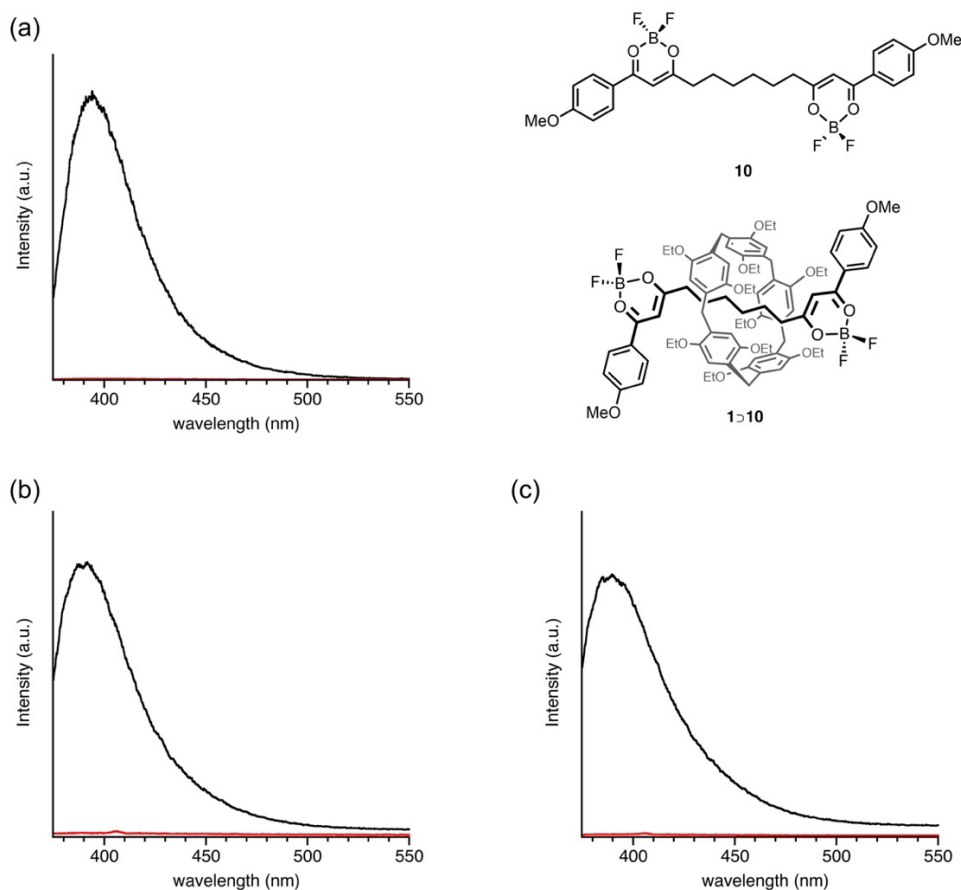


Figure 5-10. Normalized fluorescence spectra of axle molecule **10** (black) and rotaxane **1>10** (red) excited at 360 nm in (a) CH₂Cl₂, (b) THF, and (c) 1,4-dioxane. Axle molecule **10** clearly emitted visible fluorescence at 392 nm while emission was quenched in the case of rotaxane **1>10**.

5.5. Conclusion

In conclusion, the conformational control of aliphatic polyketones was achieved by supramolecular complexation with pillar[5]arene. The binding studies disclosed the conformational induction of the aliphatic polyketones to be linear by the pseudo-rotaxane formation. The quasi-solid-state BF_2 complexation reaction at the 1,3-diketone units allowed the locking of the induced conformation despite the low association constants of the pseudo-rotaxanes. Single crystal structure analysis unambiguously exhibited the locked conformation of the rotaxane structure, where the terminal BF_2 units were separated, and both terminals could not interact intramolecularly. Therefore, the optical property control of a polyketone-derived alkyl-bridged chromophore dyad was attempted by the rotaxane formation. Upon the rotaxane formation, the terminal chromophore parts of the axis molecule were separated enough to suppress their intramolecular interactions. In the UV-vis absorption spectra, the non-conformation restricted chromophore dyad exhibited solvatochromism, presumably due to the intramolecular aggregation of the chromophore units, while the restricted chromophore dyad did not show such behavior. This result indicated that the intramolecular aggregation was effectively suppressed by the conformational control of the alkyl chain of the chromophore dyad in the solution.

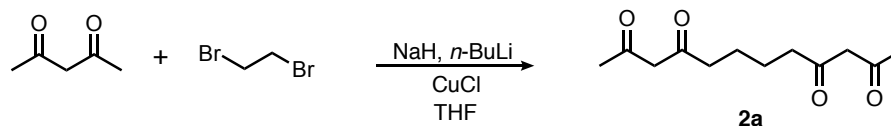
5.6. Experimental Sections

General Information

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd., TCI Co., Ltd., Kanto Chemical Co., Inc., or Sigma-Aldrich Co., and used without further purification unless otherwise noted. Pillar[5]arene **1** and monomer **11** were prepared according to the literature procedure.^{28,29} All the ¹H, ¹³C, ¹¹B and ¹⁹F NMR spectra were recorded using a JEOL JMNECS400 spectrometer. Chemical shifts are reported in parts per million (ppm) relative to an internal standard tetramethylsilane ($\delta = 0.00$ ppm for ¹H in CDCl₃), a residual solvent peak ($\delta = 2.50$ ppm for ¹H in DMSO-d₆, $\delta = 39.52$ and 77.16 ppm for ¹³C in DMSO-d₆ and CDCl₃, respectively), an external standard BF₃•OEt₂ ($\delta = 0.00$ ppm for ¹¹B), or an internal standard hexafluorobenzene ($\delta = -162.9$ ppm for ¹⁹F). Infrared spectra were measured using a JASCO Co. FT/IR-4700. ESI-TOF-MS spectra were recorded on a Thermo scientific Exactive spectrometer. Elemental analysis was performed using an Exceter Analytical, Inc. CE440 or MICRO CORDER JM10. Thin layer chromatography (TLC) was performed on a silica gel sheet, MERCK silica gel 60 F₂₅₄. Preparative scale separations were performed using silica gel gravity column chromatography (Wakosil. 60. 64 ~ 210 μ m). UV-vis absorption spectra were recorded on a Shimadzu UV-1800 spectrophotometer. Fluorescent spectra were measured on a Hitachi F-7000 spectrometer. Single crystal X-ray diffraction data were collected with a Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using multi-layer mirror (MoK α radiation $\lambda=0.71073$ Å or CuK α radiation $\lambda=1.54184$ Å). All structures were solved using a dual-space algorithm (SHELXT³⁰) and refined using full-matrix least-squares method (SHELXL³¹).

Synthetic Procedures

dodecane-2,4,9,11-tetraone (**2a**)³²

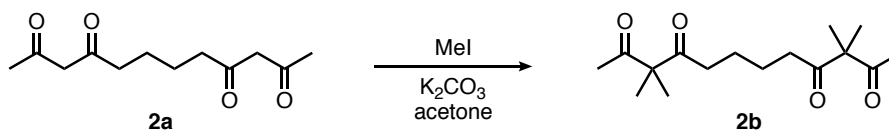


Dodecane-2,4,9,11-tetraone (**2a**) was prepared according to the literature procedure.³² Silica-gel column chromatography (eluent: hexane/ethyl acetate = 5:1) was employed for the purification instead of crystallization.

The ratio of keto-enol tautomers was calculated from ^1H NMR signals as enol : keto = 85:15 (10 mM solution of CDCl_3 after equilibrium is reached at 298 K).

^1H NMR (400 MHz, CDCl_3 , 298 K): (enol): δ 15.45 (brs, 2H, enol- OH), 5.49 (s, 2H, enol- CH), 2.30 (m, 4H, methylene), 2.05 (s, 6H, terminal methyl) 1.65 (overlapped m, 4H, methylene); (keto): δ 3.57 (s, 4H, acetoacetyl-methylene), 2.54 (m, 4H, methylene), 2.28 (s, 6H, acetyl) 1.65 (overlapped m, 4H, methylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 193.9, 191.4, 100.0, 38.1, 25.2, 25.0; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{Na}^+$, 249.1097; found, 249.1098; Elemental analysis (%): Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C, 63.70; H, 8.02; N, 0.00; Found: C, 63.73; H, 8.05; N, 0.01; R_f = 0.19 (hexane/ethyl acetate = 5:1).

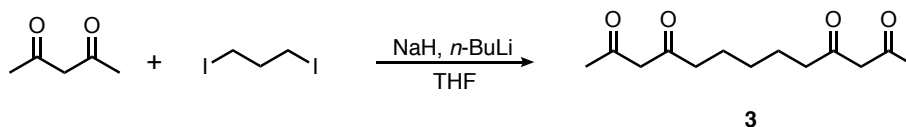
3,3,10,10-tetramethyldodecane-2,4,9,11-tetraone (**2b**)



To a 30 mL round-bottom flask equipped with a reflux condenser, compound **2a** (400 mg, 1.77 mmol), acetone (2.0 mL), and potassium carbonate (1.22 g, 8.85 mmol) were added. To the mixture, iodomethane (2.20 mL, 35.3 mmol) was added, and the reaction mixture was refluxed for 72 h. After cooling to room temperature, the reaction mixture was filtered on a funnel using acetone (10 mL), then the filtrate was evaporated. The resulting solid was dissolved in diethyl ether (30 mL), and washed with water (3 × 30 mL) and brine (30 mL). The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The crude product was purified by silica-gel column chromatography (diameter: 2.4 cm, height: 18.0 cm) using a mixture of hexane/ethyl acetate (3:1, v/v) as eluent to give 3,3,10,10-tetramethyldodecane-2,4,9,11-tetraone (**2b**) (340 mg, 1.20 mmol) as a white solid in 68% yield.

¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.41 (m, 4H, methylene), 2.10 (s, 6H, acetyl), 1.53 (m, 4H, methylene), 1.33 (s, 12H, dimethylmethylene); ¹³C {¹H} NMR (100 MHz, CDCl₃, 298 K): δ 209.5, 208.0, 62.5, 38.2, 26.3, 23.3, 21.4; IR(ATR, neat) 2979, 2939, 2873, 2359, 2341, 1692, 1468, 1457, 1448, 1385, 1365, 1356, 1245, 1125, 1062, 975, 960 cm⁻¹; m.p. 30-31°C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₆H₂₆O₄Na⁺, 305.1723; found, 305.1725; Elemental analysis (%): Calcd for C₁₆H₂₆O₄: C, 68.06; H, 9.28; N, 0.00; Found: C, 68.03; H, 9.46; N, 0.03; *R*_f = 0.21 (hexane/ethyl acetate = 3:1).

tridecane-2,4,10,12-tetraone (3)³³

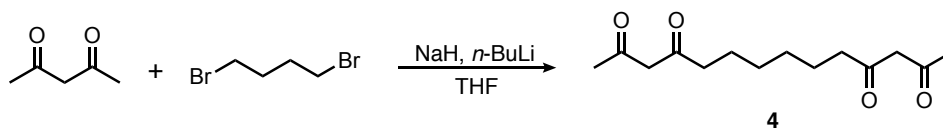


Tridecane-2,4,10,12-tetraone (**3**) was prepared according to the literature procedure.³³ Silica-gel column chromatography (eluent: hexane/ethyl acetate = 5:1) was employed for the purification instead of crystallization.

The ratio of keto-enol tautomers was calculated from ¹H NMR signals as enol : keto = 84:16 (10 mM solution of CDCl₃ after equilibrium is reached at 298 K).

¹H NMR (400 MHz, CDCl₃, 298 K): (enol): δ 15.47 (brs, 2H, enol-OH), 5.48 (s, 2H, enol-CH), 2.28 (m, 4H, methylene), 2.05 (s, 6H, terminal methyl), 1.63 (overlapped m, 4H, methylene), 1.36 (overlapped m, 2H, methylene); (keto): δ 3.57 (s, 4H, acetoacetyl-methylene), 2.51 (m, 4H, methylene), 2.24 (s, 6H, acetyl), 1.63 (overlapped m, 4H, methylene), 1.36 (overlapped m, 2H, methylene), ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 194.2, 191.5, 100.0, 38.1, 28.8, 25.5, 25.1; IR(ATR, neat) 2935, 2921, 2895, 2868, 2847, 1633, 1592, 1411, 1359, 1281, 1211, 1197, 900, 833, 779 cm⁻¹; m.p. 63-64°C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₃H₂₀O₄Na⁺, 263.1254; found, 263.1257; Elemental analysis (%): Calcd for C₁₃H₂₀O₄: C, 64.98; H, 8.39; N, 0.00; Found: C, 64.98; H, 8.48; N, 0.03; *R*_f = 0.19 (hexane/ethyl acetate = 5:1).

tetradecane-2,4,11,13-tetraone (4)³³

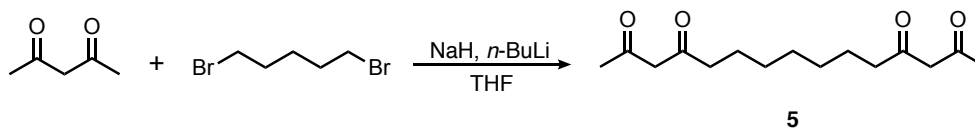


Tetradecane-2,4,11,13-tetraone (**4**) was prepared according to the literature procedure.³³ Silica-gel column chromatography (eluent: hexane/ethyl acetate = 5:1) was employed for the purification instead of crystallization.

The ratio of keto-enol tautomers was calculated from ¹H NMR signals as enol : keto = 84:16 (10 mM solution of CDCl₃ after equilibrium is reached at 298 K).

¹H NMR (400 MHz, CDCl₃, 298 K): (enol): δ 15.49 (brs, 2H, enol-OH), 5.48 (s, 2H, enol-CH), 2.26 (m, 4H, methylene), 2.05 (s, 6H, terminal methyl), 1.61 (overlapped m, 4H, methylene), 1.34 (overlapped m, 4H, methylene); (keto): δ 3.56 (s, 4H, acetoacetyl-methylene), 2.50 (m, 4H, methylene), 2.24 (s, 6H, acetyl), 1.61 (overlapped m, 4H, methylene), 1.34 (overlapped m, 4H, methylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 194.3, 191.5, 99.9, 38.3, 29.0, 25.6, 25.1; IR(ATR, neat) 2931, 2920, 2902, 2865, 2849, 1631, 1585, 1440, 1411, 1382, 1362, 1315, 1227, 1193, 1127, 1113, 1004, 902, 799, 773 cm⁻¹; m.p. 64-65 °C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₄H₂₂O₄Na⁺, 277.1410; found, 277.1414; Elemental analysis (%): Calcd for C₁₅H₂₄O₄: C, 66.12; H, 8.72; N, 0.00; Found: C, 65.92; H, 8.78; N, 0.01; *R*_f = 0.22 (hexane/ethyl acetate = 5:1).

pentadecane-2,4,12,14-tetraone (5)³⁴

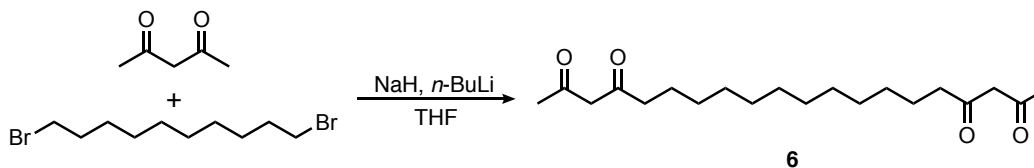


Pentadecane-2,4,12,14-tetraone (**5**) was synthesized following reported synthetic procedure.³³ To a 500 mL three-necked round-bottom flask equipped with two dropping funnels and inert gas inlet/outlet, THF (100 mL) and 60% (w/w) paraffin dispersed sodium hydride (2.08 g, 52.0 mmol) were added under nitrogen atmosphere with keeping the temperature to 0 °C using an ice/water bath. To the reaction mixture, acetylacetone (4.40 mL, 43.0 mmol) was slowly added. After stirring 20 min, 19.0 mL of *n*-BuLi solution (2.5 M in hexanes) were added dropwise to the resulting reaction mixture over 10 min. Then 1,5-dibromopentane (2.93 mL, 21.5 mmol) was added dropwise over 20 min. The reaction mixture was gradually warmed to room temperature and stirred for 4 h. After 4h, the reaction mixture was poured into an ice/water mixture (50 g) and acidified with conc. hydrochloric acid until pH ≤ 2. The organic layer was separated, and aqueous layer was extracted with diethyl ether (3 × 25 mL). The combined organic layer was washed with brine (30 mL), dried over anhydrous sodium sulfate and solvents were removed under reduced pressure. The crude mixture was chromatographed on a silica-gel column (diameter: 4.5 cm, height: 15.0 cm) using a mixture of hexane/ethyl acetate (5:1, v/v) as eluent. The resulting solid was washed on a funnel using hexane (20 mL) to give icosane-2,4,12,14-tetraone (**4**) (1.69 g, 6.30 mmol) as a white solid in 29% yield.

The ratio of keto-enol tautomers of acetylacetone unit was calculated from ¹H NMR signals as enol : keto = 84:16 (10 mM solution of CDCl₃ after equilibrium is reached at 298 K).

¹H NMR (400 MHz, CDCl₃, 298 K): (enol): δ 15.50 (brs, 2H, enol-OH), 5.48 (overlapped s, 2H, enol-CH), 2.26 (t, *J* = 7.2 Hz, 4H, methylene), 2.05 (s, 6H, terminal methyl), 1.59 (overlapped m, 4H, methylene), 1.32 (overlapped m, 6H, methylene); (keto): δ 3.56 (s, 4H, acetoacetyl-methylene), 2.50 (t, *J* = 7.2 Hz, 4H, methylene), 2.24 (s, 6H, acetyl), 1.59 (overlapped m, 4H, methylene), 1.34 (overlapped m, 6H, methylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 194.3, 191.5, 99.9, 38.3, 29.2, 29.1, 25.7, 25.1; IR(ATR, neat) 2933, 2920, 2908, 2867, 2850, 1631, 1587, 1410, 1208, 1193, 901, 787 cm⁻¹; m.p. 65-66 °C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₅H₂₄O₄Na⁺, 291.1567; found, 291.1567; Elemental analysis (%): Calcd for C₁₅H₂₄O₄: C, 67.14; H, 9.01; N, 0.00; Found: C, 66.89; H, 9.17; N, 0.05; *R*_f = 0.23 (hexane/ethyl acetate = 5:1).

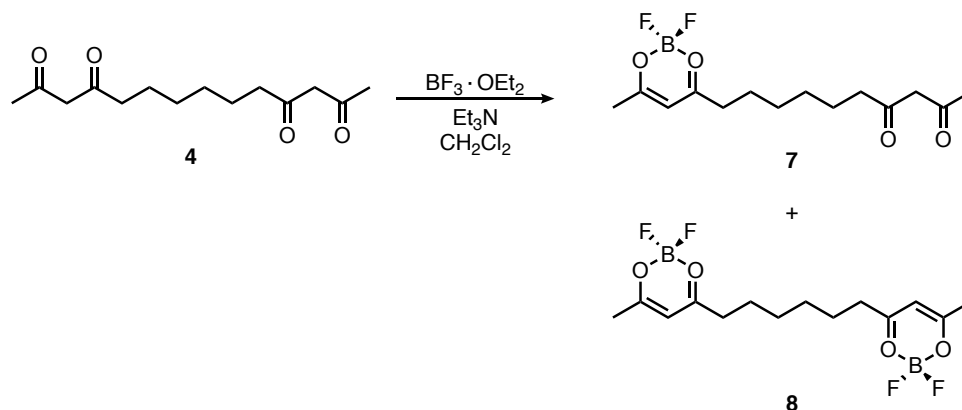
icosane-2,4,17,19-tetraone (**6**)³⁵



Icosane-2,4,17,19-tetraone (**6**) was synthesized following reported synthetic procedure.³³ To a 500 mL three-necked round-bottom flask equipped with two dropping funnels and inert gas inlet/outlet, THF (90 mL) and sodium hydride (2.08 g, 52.0 mmol) were added under nitrogen atmosphere with keeping the temperature to 0 °C using an ice/water bath. To the reaction mixture, acetylacetone (4.40 mL, 43.0 mmol) was slowly added. After stirring 20 min, 19.0 mL of *n*-BuLi solution (2.5 M in hexanes) were added dropwise to the resulting reaction mixture over 10 min. Then 10 mL THF solution of 1,10-dibromodecane (6.45 g, 21.5 mmol) was added dropwise over 20 min. The reaction mixture was gradually warmed to room temperature and stirred for 4 h. After 4 h, the reaction mixture was poured into an ice/water mixture (50 g) and acidified with conc. hydrochloric acid until pH ≤ 2. The organic layer was separated, and aqueous layer was extracted with diethyl ether (3 × 25 mL). The combined organic layer was washed with brine (30 mL), dried over anhydrous sodium sulfate and solvents were removed under reduced pressure. The crude mixture was chromatographed on a silica-gel column (diameter: 7.0 cm, height: 15.0 cm) using a mixture of chloroform/hexane (5:1, v/v) as eluent. The resulting solid was washed on a funnel using hexane (20 mL) to give icosane-2,4,17,19-tetraone (**6**) (1.61 g, 4.76 mmol) as a white solid in 22% yield. The ratio of keto-enol tautomers of acetylacetone unit was calculated from ¹H NMR signals as enol : keto = 84:16 (10 mM solution of CDCl₃ after equilibrium is reached at 298 K).

¹H NMR (400 MHz, CDCl₃, 298 K): (enol): δ 15.51 (brs, 2H, enol-OH), 5.49 (overlapped s, 2H, enol-CH), 2.26 (t, *J* = 7.2 Hz, 4H, methyl), 2.05 (s, 6H, terminal methyl), 1.59 (overlapped m, 4H, methylene), 1.39-1.21 (overlapped m, 16H, methylene); (keto): δ 3.57 (s, 4H, acetoacetyl-methylene), 2.50 (t, *J* = 7.2 Hz, 2H, methylene), 2.24 (s, 6H, acetyl), 1.59 (overlapped m, 4H, methylene), 1.39-1.21 (overlapped m, 16H, methylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 194.4, 191.6, 99.9, 38.4, 29.7, 29.6, 29.5, 29.3, 25.8, 25.1; IR(ATR, neat) 2930, 2914, 2865, 2849, 1632, 1599, 1468, 1443, 1411, 1380, 1362, 1343, 1299, 1250, 1211, 1187, 1132, 923, 903, 784 cm⁻¹; m.p. 77-78°C; HRMS(ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₃₄O₄Na⁺, 361.2349; found, 361.2348; Elemental analysis (%): Calcd for C₂₀H₃₄O₄: C, 70.97; H, 10.13; N, 0.00; Found: C, 70.98; H, 10.35; N, 0.03; *R*_f = 0.25 (hexane/ethyl acetate = 5:1).

BF₂ complexes 7 and 8



To a 50 mL two-necked round bottom flask with a reflux condenser and inert gas inlet/outlet, tetradecane-2,4,11,13-tetraone (**4**) (1.00 g, 3.93 mmol) was added and the flask was purged with nitrogen gas. To the flask, dichloromethane (8.0 mL), triethylamine (548 μL , 3.93 mmol) and boron trifluoride diethyl etherate (631 μL , 5.11 mmol) were added via syringe with keeping temperature to 0 °C using an ice/water bath. After the addition, the reaction solution was refluxed for 2 h. After cooling to room temperature, the reaction was quenched by addition of water (20 mL), and organic layer was separated. The aqueous layer was extracted with dichloromethane (2 $\times$ 20 mL). The combined organic layer was dried over anhydrous sodium sulfate, and the solvent was removed using a rotary evaporator. The crude products were chromatographed on a silica gel column (diameter: 3.0 cm, height: 15.0 cm) using a mixture of hexane/ethyl acetate (3:2, v/v) as eluent to give compound **7** (300 mg, 0.993 mmol) as a colorless oil, and compound **8** (186 mg, 0.532 mmol) as a white solid in 25% and 13% yields respectively, along with recovery of **4** (558 mg, 2.19 mmol, 56%) .

Compound 7

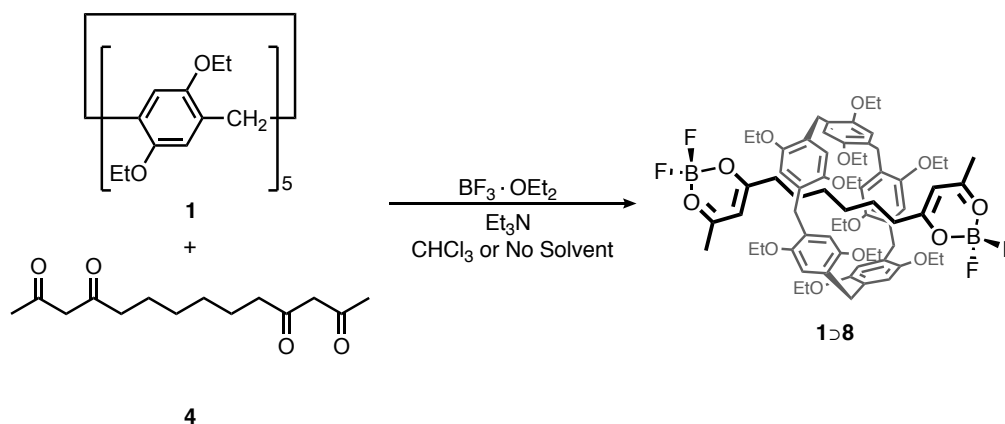
The ratio of keto-enol tautomers were calculated from ^1H NMR signals as enol : keto = 83:17 (10 mM solution of CDCl_3 after equilibrium is reached at 298 K).

^1H NMR (400 MHz, CDCl_3 , 298 K): (enol): δ 15.48 (brs, 1H, enol-OH), 5.94 (s, 1H, BF_2 -enol-CH), 5.49 (s, 1H, enol-CH), 2.50 (t, $J = 7.6$ Hz, 2H, methylene), 2.30 (s, 3H, terminal methyl), 2.27 (t, $J = 7.6$ Hz, 2H, methylene), 2.06 (s, 3H, terminal methyl), 1.71 (overlapped m, 2H, methylene), 1.61 (overlapped m, 2H, methylene), 1.44-1.30 (overlapped m, 4H, methylene); (keto): δ 5.94 (s, 1H, BF_2 -enol-CH), 3.57 (s, 2H, acetoacetyl-methylene), 2.51 (t, $J = 7.2$ Hz, 2H, methylene), 2.50 (overlapped t, 2H, methylene), 2.30 (overlapped s, 3H, terminal methyl), 2.24 (s, 3H, acetyl), 1.71 (overlapped m, 2H, methylene), 1.61 (overlapped m, 2H, methylene), 1.44-1.30 (overlapped m, 4H, methylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K) (all tautomers): δ 204.3, 202.5, 195.6, 194.1, 192.5, 191.4, 101.3, 99.9, 57.7, 43.5, 38.1, 37.3, 31.0, 28.71, 28.68, 25.6, 25.5, 24.9, 24.2, 22.9; ^{11}B NMR (128 MHz, CDCl_3 , 298 K): δ 0.51 (BF_2); ^{19}F NMR (376 MHz, CDCl_3 , 298 K): δ -139.74 (s, 2F, keto- $^{10}\text{BF}_2$), -139.77 (s, 2F, enol- $^{10}\text{BF}_2$), -139.80 (s, 2F, keto- $^{11}\text{BF}_2$), -139.83 (s, 2F, enol- $^{11}\text{BF}_2$) (Four signals were observed due to natural abundance of two boron isotopes (^{10}B and ^{11}B) and keto-enol tautomers.)^{36,37}; IR(ATR, neat) 2934, 2861, 1603, 1545, 1396, 1372, 1175, 1058, 1021 cm^{-1} ; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{O}_4\text{BF}_2\text{Na}^+$, 325.1393, found, 325.1394; Elemental analysis (%): Calcd for $\text{C}_{14}\text{H}_{21}\text{O}_4\text{BF}_2$: C, 55.66; H, 7.01; N, 0.00; Found: C, 55.35; H, 7.06; N, 0.00; $R_f = 0.31$ (hexane/ethyl acetate = 3:2).

Compound 8³⁷

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 5.96 (s, 2H, BF_2 -enol-CH), 2.50 (t, $J = 7.6$ Hz, 2H, methylene), 2.31 (s, 6H, terminal methyl), 1.71 (m, 4H, methylene), 1.37 (m, 4H, methylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 195.4, 192.8, 101.5, 37.2, 28.4, 25.4, 24.4. Spectral data were matched with the reported values.

Rotaxane 1⊃8



Synthesis in solution

To a 100 mL round-bottom flask with a gas inlet/outlet, compound **4** (1.40 g, 5.50 mmol) and host **1** (1.00 g, 1.10 mmol) were added. The flask was purged with nitrogen gas and cooled to 0 °C using an ice/water bath. To the flask, chloroform (36 mL, 200 mM for **1**), triethylamine (1.53 mL, 11.0 mmol) and boron trifluoride diethyl etherate (4.08 mL, 33.0 mmol) were added via syringe. The reaction solution was warmed to room temperature and stirred for 7 h at room temperature. After the addition of water (30 mL), resulting products were extracted from the aqueous layer using chloroform (2 × 30 mL), dried over anhydrous sodium sulfate, and evaporated using a rotary evaporator. To the mixture, chloroform (2.0 mL) was added and sonicated for 3 min and filtrated on a funnel. The residue was washed using chloroform (8.0 mL), then the filtrate was collected and evaporated. The resulting solid from filtrate was chromatographed on silica-gel (diameter 3.0 cm, height 18.0 cm, eluent: chloroform/carbon tetrachloride = 5:2) to obtain rotaxane **1⊃8** along with little amount of **1** as the first fraction while excess amount of **1** and **8** was eluted as the second fraction. The first fraction was again chromatographed on silica-gel (diameter 2.4 cm, height 18.0 cm, eluent: chloroform/carbon tetrachloride = 5:2) to give rotaxane **1⊃8** (142 mg, 0.114 mmol) as a white solid in 10% yield based on host **1**.

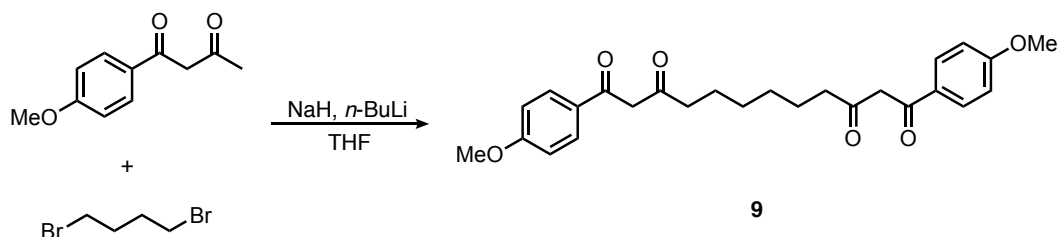
Quasi-Solid State Synthesis

In a 100 mL round-bottom flask, compound **4** (1.40 g, 5.50 mmol) and host **1** (1.00 g, 1.10 mmol) were dissolved in chloroform (10 mL). The solution was evaporated at 20 °C and further dried under vacuum for 1 h at room temperature to form pseudo-rotaxane **1**⊃**4**. After transferred the mixture to a mortar, triethylamine (1.53 mL, 11.0 mmol) and boron trifluoride diethyl etherate (4.08 mL, 33.0 mmol) were added. The resulting yellowish paste was grounded for 30 min at room temperature using a pestle. To the mixture, water (50 mL) was added and transferred to a separating funnel using chloroform (100 mL). Separated aqueous layer was extracted with chloroform (2 × 50 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. To the crude mixture, chloroform (2.0 mL) was added, sonicated for 3 min and filtered on a funnel. The residue was washed using chloroform (8.0 mL), then the filtrate was collected and evaporated. The resulting solid from filtrate was chromatographed on a silica-gel column (diameter 3.0 cm, height 17.0 cm, eluent: chloroform/carbon tetrachloride = 5:2) to obtain rotaxane **1**⊃**8** along with little amount of **1** as the first fraction while excess amount of **1** and **8** was eluted as the second fraction. The first fraction was again chromatographed (diameter: 2.4 cm, height: 19.0 cm, eluent: chloroform/carbon tetrachloride = 5:2) to give rotaxane **1**⊃**8** (284 mg, 0.231 mmol) as a white solid in 21% yield based on host **1**.

Compound data of rotaxane **1**⊃**8**

¹H NMR (400 MHz, CDCl₃, 298 K): δ 6.90 (s, 10H, host-aryl), 6.05 (s, 2H, enol-CH), 3.90 (m, 20H, ethoxy-CH₂CH₃), 3.75 (s, 10H, host-methylene), 2.37 (s, 6H, terminal methyl), 1.44 (t, *J* = 6.8 Hz, 30H, ethoxy-CH₂CH₃), 1.37 (t, *J* = 8.8 Hz, 4H, guest-methylene), -0.10 (br, 4H, guest-methylene), -2.35 (br, 4H, guest-methylene); ¹³C{¹H} NMR (100 MHz, CDCl₃, 298 K): δ 199.1, 190.4, 150.0, 129.1, 115.2, 100.2, 64.5, 36.7, 29.4, 25.1, 24.3, 24.1, 15.5; ¹¹B NMR (128 MHz, CDCl₃, 298 K): δ 0.57 (BF₂); ¹⁹F NMR (376 MHz, CDCl₃, 298 K): δ -140.26 (d, ²*J*_{FF} = 72.0 Hz, 1F, ¹⁰BF₂), -140.32 (d, ²*J*_{FF} = 72.0 Hz, 1F, ¹¹BF₂), -140.60 (d, ²*J*_{FF} = 72.0 Hz, 1F, ¹⁰BF₂), -140.66 (d, ²*J*_{FF} = 72.0 Hz, 1F, ¹¹BF₂); IR(ATR, neat) 2976, 2931, 2896, 2872, 1545, 1498, 1477, 1403, 1389, 1201, 1110, 1094, 1083, 1048, 1021, 956 cm⁻¹; m.p. 229-230°C (decomp.); HRMS(ESI-TOF): *m/z* [M - H]⁻ calcd for C₆₉H₈₉O₁₄B₂F₄⁻ 1239.6380, found, 1239.6403; Elemental analysis (%): Calcd for C₆₉H₉₀O₁₄B₂F₄: C, 66.78; H, 7.31; N, 0.00; Found: C, 66.78; H, 7.33; N, 0.02; R_f = 0.24 (chloroform/carbon tetrachloride = 5:1).

1,12-bis(4-methoxyphenyl)dodecane-1,3,10,12-tetraone (9)



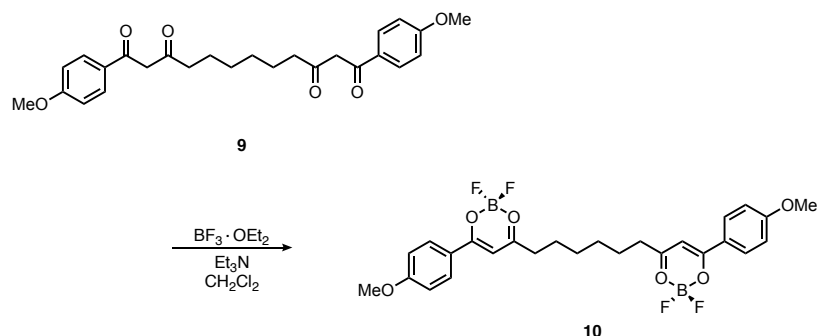
To a 200 mL three-necked round-bottom flask equipped with two dropping funnels and inert gas inlet/outlet, THF (35 mL) and 60% (w/w) paraffin dispersed sodium hydride (1.25 g, 31.2 mmol) were added under nitrogen atmosphere with keeping the temperature to 0 °C using an ice/water bath. To the reaction mixture, a 15 mL THF solution of 1-(4-methoxyphenyl)butane-1,3-dione³⁸ (5.00 g, 26.0 mmol) was slowly added. After stirring for 20 min, 11.0 mL of *n*-BuLi solution (2.6 M in hexanes, 28.6 mmol) were added dropwise to the resulting reaction mixture over 10 min. Then 1,4-dibromobutane (1.55 mL, 13.0 mmol) was added dropwise over 20 min. The reaction mixture was gradually warmed to room temperature and stirred for 4 h. After 4 h, the reaction mixture was poured into an ice/water mixture (50 g) and acidified with conc. hydrochloric acid until pH ≤ 2. The organic layer was separated, and aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layer was washed with brine (100 mL), dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. To the resulting solid, diethyl ether (2.0 mL) was added, sonicated for 3 min and filtered on a funnel. The residue was washed using diethyl ether (20 mL) to give 1,12-bis(4-methoxyphenyl)dodecane-1,3,10,12-tetraone (9) (2.09 g, 4.77 mmol) as a white solid in 37% yield.

The ratio of keto-enol tautomers was calculated from ¹H NMR signals as enol : keto = 87:13 (10 mM solution of CDCl₃ after equilibrium was reached at 298 K).

¹H NMR (400 MHz, CDCl₃, 298 K): (enol): δ 16.33 (brs, 1H, enol-OH), 7.86 (d, *J* = 8.8 Hz, 2H, aryl), 6.94 (overlapped d, *J* = 8.8 Hz, 2H, aryl), 6.10 (s, 1H, enol-CH), 3.87 (s, 6H, methoxy), 2.40 (t, *J* = 7.6 Hz, 4H, methylene), 1.70 (m, 4H, methylene), 1.42 (overlapped m, 4H, methylene); (keto): δ 16.32 (brs, 1H, enol-OH), 7.92 (d, *J* = 8.8 Hz, 2H, aryl), 6.94 (overlapped d, *J* = 8.8 Hz, 2H, aryl), 6.09 (s, 1H, enol-CH), 4.03 (s, 2H, dicarbonyl-methylene), 3.87 (overlapped s, 6H, methoxy), 2.58 (t, *J* = 7.6 Hz, 2H,

methylene), 2.36 (t, $J = 7.6$ Hz, 2H, methylene), 1.66-1.55 (overlapped m, 4H, methylene), 1.39-1.24 (overlapped m, 4H, methylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): (all tautomers): δ 194.8, 184.4, 163.2, 129.3, 127.9, 114.0, 95.3, 55.6, 38.8, 29.1, 25.9; IR(ATR, neat) 2935, 2909, 2865, 2852, 2837, 1597, 1574, 1505, 1464, 1456, 1438, 1251, 1177, 1111, 1077, 1027, 842, 802, 772 cm^{-1} ; m.p. 122-123°C; HRMS(ESI-TOF): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{30}\text{O}_6\text{Na}^+$, 461.1935, found, 461.1934; Elemental analysis (%): Calcd for $\text{C}_{26}\text{H}_{30}\text{O}_6$: C, 71.21; H, 6.90; N, 0.00; Found: C, 71.05; H, 6.90; N, 0.02; $R_f = 0.31$ (hexane/ethyl acetate = 6:1).

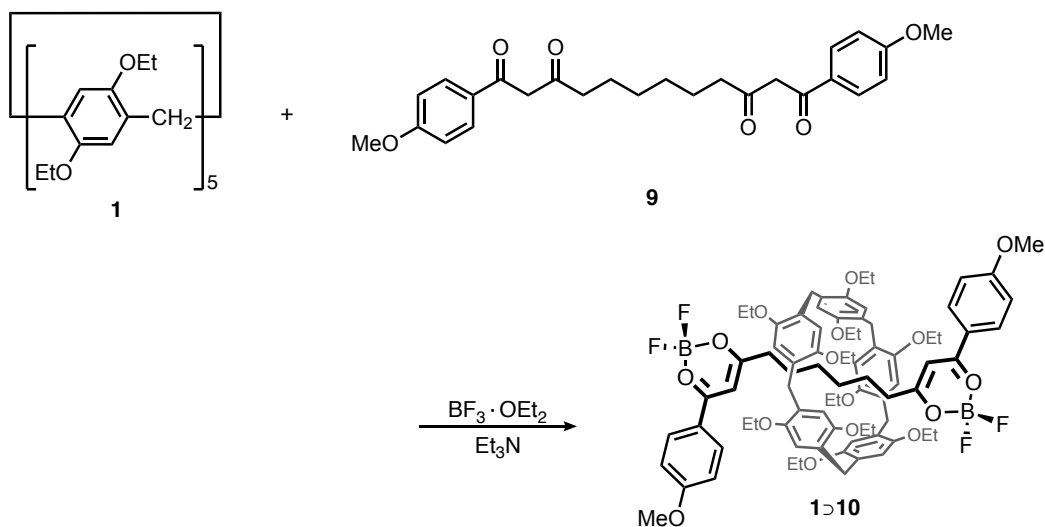
BF₂ complex **10**



To a 50 mL two-necked round-bottom flask equipped with a reflux condenser and inert gas inlet/outlet, compound **9** (100 mg, 0.228 mmol) was added and the flask was purged with nitrogen gas. To the flask, dichloromethane (15 mL), triethylamine (63.2 μL , 0.456 mmol) and trifluoroborate diethyl etherate (169 μL , 1.37 mmol) was added with keeping the temperature to 0 °C using an ice/water bath. After the addition, the reaction solution was refluxed for 2 h. The reaction mixture was cooled to room temperature and water (15 mL) was added to the flask. The organic layer was separated, and aqueous layer was extracted with dichloromethane (3 $\times$ 30 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. To the crude mixture, methanol (2.0 mL) was added, sonicated for 1 min and filtered on a funnel. The residue was washed using methanol (8.0 mL) to give compound **10** (87.2 mg, 0.199 mmol) as a yellow solid in 72% yield. Samples for UV-vis and fluorescent measurement were obtained by recrystallization from dichloromethane.

¹H NMR (400 MHz, DMSO-*d*₆, 298 K): δ 8.19 (d, J = 9.2 Hz, 4H, aryl), 7.17 (d, J = 9.2 Hz, 4H, aryl), 7.14 (s, 2H, BF₂-enol-CH), 3.91 (s, 6H, methoxy), 2.65 (t, J = 7.6 Hz, 4H, methylene), 1.69 (m, 4H, methylene), 1.39 (m, 4H, methylene); ¹³C {¹H} NMR (100 MHz, DMSO-*d*₆, 298 K): δ 194.2, 180.8, 165.7, 131.9, 122.7, 115.1, 96.5, 56.0, 36.8, 28.0, 25.3; ¹¹B NMR (128 MHz, DMSO-*d*₆, 298 K): δ 1.46 (BF₂); ¹⁹F NMR (376 MHz, DMSO-*d*₆, 298 K): δ -137.39, (s, 2F, ¹⁰BF₂), -137.46 (s, 2F, ¹¹BF₂) (Two signals were observed due to natural abundance of two boron isotopes.^{36,37}); IR(ATR, neat) 2944, 2910, 2844, 1604, 1556, 1536, 1508, 1466, 1446, 1431, 1406, 1388, 1349, 1300, 1258, 1183, 1128, 1074, 1019, 973, 959, 841, 809, 798, 750, 698 cm⁻¹; m.p. 215-216°C; HRMS(ESI-TOF): m/z [M + Na]⁺ calcd for C₂₆H₂₈O₆B₂F₄Na⁺, 557.1900, found, 557.1902; Elemental analysis (%): Calcd for C₂₆H₂₈O₆B₂F₄: C, 58.47; H, 5.28; N, 0.00; Found: C, 58.04; H, 5.21; N, 0.01; R_f = 0.15 (dichloromethane); UV/Vis (dichloromethane) λ_{max} (ϵ) 362 nm (8.2×10^4 L mol⁻¹ cm⁻¹); (THF) λ_{max} (ϵ) 361 nm (7.6×10^4 L mol⁻¹ cm⁻¹); (1,4-dioxane) λ_{max} (ϵ) 360 nm (5.8×10^4 L mol⁻¹ cm⁻¹); 349 nm (sh, 5.7×10^4 L mol⁻¹ cm⁻¹).

Rotaxane **1**→**10**



In a 100 mL round-bottom flask, compound **9** (1.23 g, 2.81 mmol) and host **1** (500 mg, 0.561 mmol) were dissolved in chloroform (50 mL). The solution was evaporated at 20 °C and further dried under vacuum for 1 h at room temperature to form pseudo-rotaxane **1**→**9**. After transferred the mixture to a mortar, triethylamine (0.779 mL, 5.62 mmol) and trifluoride diethyl etherate (4.16 mL, 33.7 mmol) were added. The resulting yellowish paste was grounded for 30 min at room temperature using a pestle. To the reaction mixture, water (50 mL) was added and transferred to a separating funnel using chloroform (50 mL). The organic layer was separated, and aqueous layer was extracted with chloroform (2 × 50 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. To the crude mixture, chloroform (3.0 mL) was added, sonicated for 3 min and filtered on a funnel. The residue was washed using chloroform (20 mL), then the filtrate was collected and evaporated. The crude mixture from filtrate was first chromatographed on a silica-gel column (diameter: 3.0 cm, height: 18.0 cm, eluent: chloroform/carbon tetrachloride = 6:1) to obtain rotaxane **1**→**10** along with little amount of **1** and **10** as the first fraction while excess amount of **1** and **10** was eluted as the second fraction. The first fraction was chromatographed again using same condition to give rotaxane **1**→**10** (253 mg, 0.178 mmol) as a yellow solid in 32% yield based on host **1**.

Note that Chemical shifts in ^1H NMR spectra was relative to deuterated solvent peak of chloroform ($\delta = 7.26$), instead of tetramethylsilane due to the overlap of the proton signal of methylene protons and tetramethylsilane.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 8.19 (d, $J = 9.2$ Hz, 4H, guest-aryl), 7.08 (d, $J = 9.2$ Hz, 4H, guest-aryl), 6.95 (s, 10H, host-aryl), 6.62 (s, 2H, enol-CH), 4.04-3.82 (overlapped s and m, 26H, guest-methoxy and ethoxy- OCH_2CH_3), 3.78 (s, 10H, host-methylene), 1.47 (t, $J = 8.8$ Hz, 4 H, guest-methylene), 1.39 (t, $J = 7.2$ Hz, 30H, ethoxy- OCH_2CH_3), 0.02 (br, 4H, guest-methylene), -2.35 (br, 4H, guest-methylene); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 298 K): δ 197.3, 180.9, 165.6, 150.1, 131.4, 129.1, 124.1, 115.3, 114.7, 95.2, 64.6, 56.0, 37.2, 29.4, 25.6, 24.3, 15.5; ^{11}B NMR (128 MHz, CDCl_3 , 298 K): δ 0.86 (BF_2); ^{19}F NMR (376 MHz, CDCl_3 , 298 K): δ -141.54 (d, $^2J_{\text{FF}} = 75.6$ Hz, 1F, $^{10}\text{BF}_2$), -141.60 (d, $^2J_{\text{FF}} = 75.6$ Hz, 1F, $^{11}\text{BF}_2$), -141.99 (d, 1F, $^2J_{\text{FF}} = 75.6$ Hz, $^{10}\text{BF}_2$), -142.06 (d, $^2J_{\text{FF}} = 75.6$ Hz, 1F, $^{11}\text{BF}_2$) ; IR(ATR, neat) 2973, 2934, 2897, 2871, 1605, 1584, 1532, 1504, 1478, 1389, 1369, 1266, 1203, 1044 cm^{-1} ; m.p. 274-275°C (decomp.); HRMS(ESI-TOF): m/z $[\text{M}]^+$ calcd for $\text{C}_{81}\text{H}_{98}\text{O}_{16}\text{B}_2\text{F}_4^+$, 1422.6977, found, 1424.7011; Elemental analysis (%): Calcd for: $\text{C}_{81}\text{H}_{98}\text{B}_2\text{F}_4\text{O}_{16}$, 68.26; H, 6.93; N, 0.00; Found: C, 67.97; H, 6.90; N, 0.03; $R_f = 0.19$ (chloroform/carbon tetrachloride = 6:1); UV/Vis (dichloromethane) λ_{max} (ϵ) 361 nm ($9.3 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$); (THF) λ_{max} (ϵ) 360 nm ($8.9 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$); (1,4-dioxane) λ_{max} (ϵ) 359 nm ($9.6 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$).

Host-Guest Complexation Experiments

General Information

In all pseudo-rotaxane formation processes in CDCl_3 at 298 K, chemical exchanges of uncomplexed and complexed were fast with respect to the NMR timescale. Therefore all ^1H NMR titration experiments were carried out by adding a CDCl_3 solution of guest compounds **2a**, **3-6** into a CDCl_3 solution of pillar[5]arene **1** (10 mM) in NMR tube using a microsyringe.

For the determination of association stoichiometry, Job's plot was employed.^{22,23} Job's plot was conducted by changing the mole fractions of the host **1** and guest **2a**, **3-6**, and the chemical shift of the proton signal of aryl proton of host **1** was used for the calculation. In job's plot, total concentration of guest **2a** and host **1** was fixed at 20 mM.

Association constants (K_a) were calculated from the chemical shift changes of aryl proton of host **1** by using non-linear curve-fitting method following the below equation.^{22,23}

$$\Delta\delta_{\text{obs}} = \frac{\Delta\delta_{11}}{2K[H]_0} [1 + K[H]_0 + K[G]_0 - \{(1 + K[H]_0 + K[G]_0)^2 - 4K^2[H]_0[G]_0\}^{0.5}]$$

where $\Delta\delta_{\text{obs}}$ is the chemical shift change of proton signal of aryl moiety of host **1** at $[G]_0$, $\Delta\delta_{11}$ is the chemical shift change of host **1** proton resonance when the **1** is completely complexed, $[G]_0$ is the fixed initial concentration of guest **2a**, **3-6**, and $[H]_0$ is the initial concentration of host **1**.

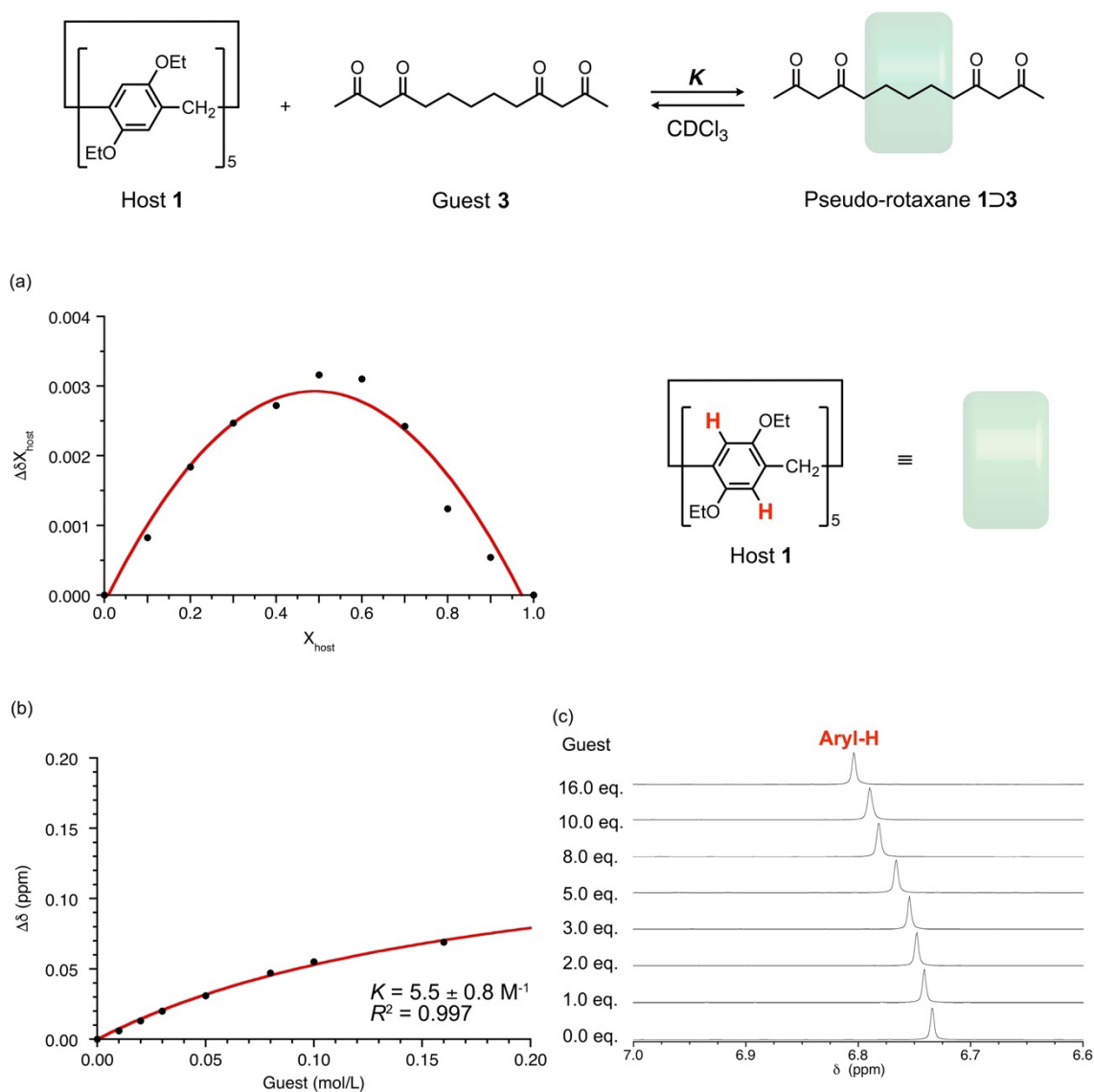


Figure 5-11. (a) Job's plot for determining host-guest ratio between **1** (host) and **3** (guest), which indicated 1:1 binding of **1** and **3**, $X_{\text{host}} = [\text{Host}]/([\text{Host}]+[\text{Guest}])$, $\Delta\delta$: chemical shift change of aryl proton signal of **1**; (b) Non-linear fitting curve of ¹H NMR titration; (c) Partial ¹H NMR spectra of **1** (10 mM) with increasing the ratio of **3** from 0 to 16 equiv. in CDCl₃ at 298 K.

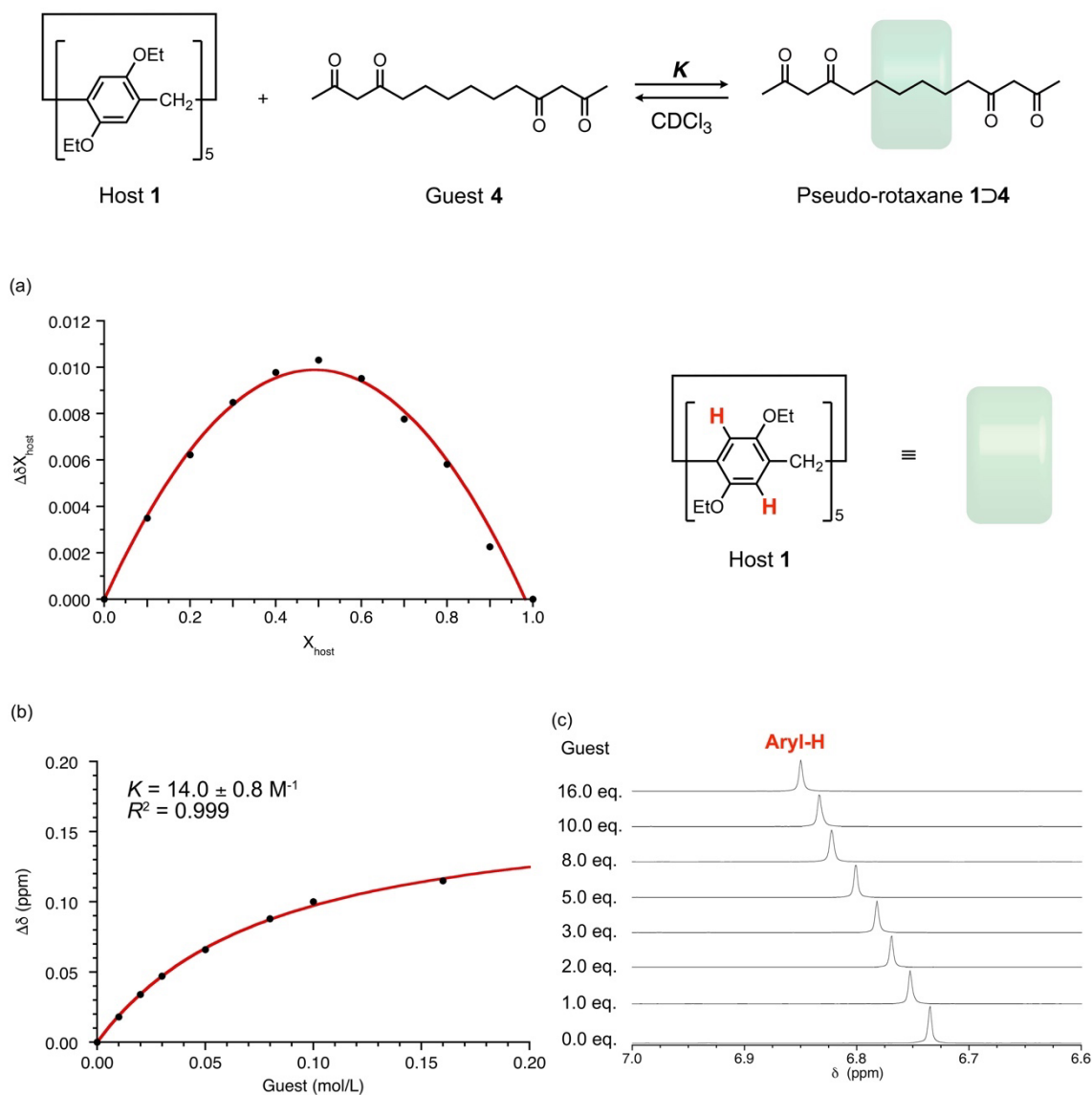


Figure 5-12. (a) Job's plot for determining host-guest ratio between **1** (host) and **4** (guest), which indicated 1:1 binding of **1** and **4**, $X_{\text{host}} = [\text{Host}]/([\text{Host}] + [\text{Guest}])$, $\Delta\delta$: chemical shift change of aryl proton signal of **1**; (b) Non-linear fitting curve of ¹H NMR titration; (c) Partial ¹H NMR spectra of **1** (10 mM) with increasing the ratio of **4** from 0 to 16 equiv. in CDCl₃ at 298 K.

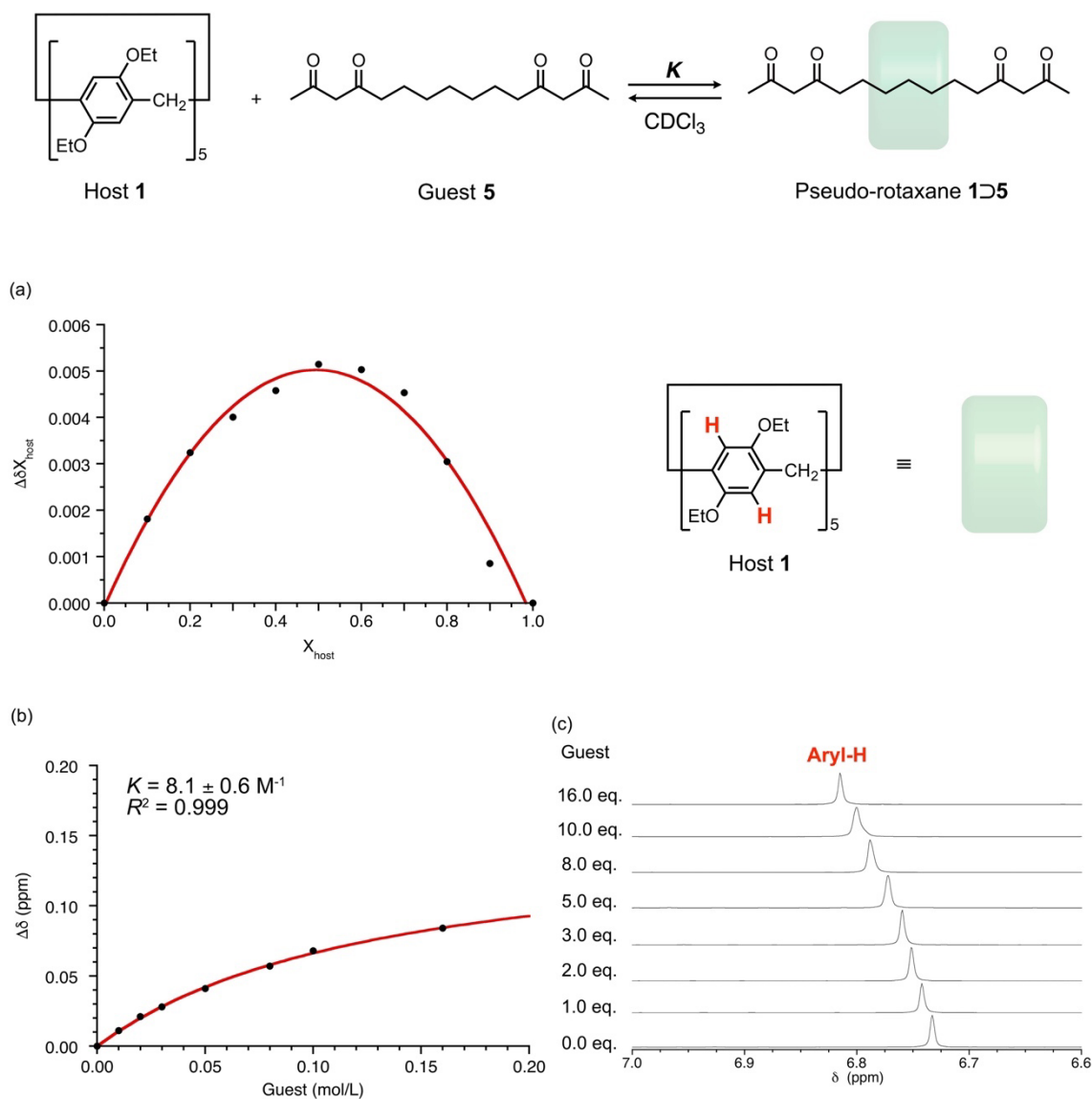


Figure 5-13. (a) Job's plot for determining host-guest ratio between **1** (host) and **5** (guest), which indicated 1:1 binding of **1** and **5**, $X_{\text{host}} = [\text{Host}]/([\text{Host}]+[\text{Guest}])$, $\Delta\delta$: chemical shift change of aryl proton signal of **1**; (b) Non-linear fitting curve of ¹H NMR titration; (c) Partial ¹H NMR spectra of **1** (10 mM) with increasing the ratio of **5** from 0 to 16 equiv. in CDCl₃ at 298 K.

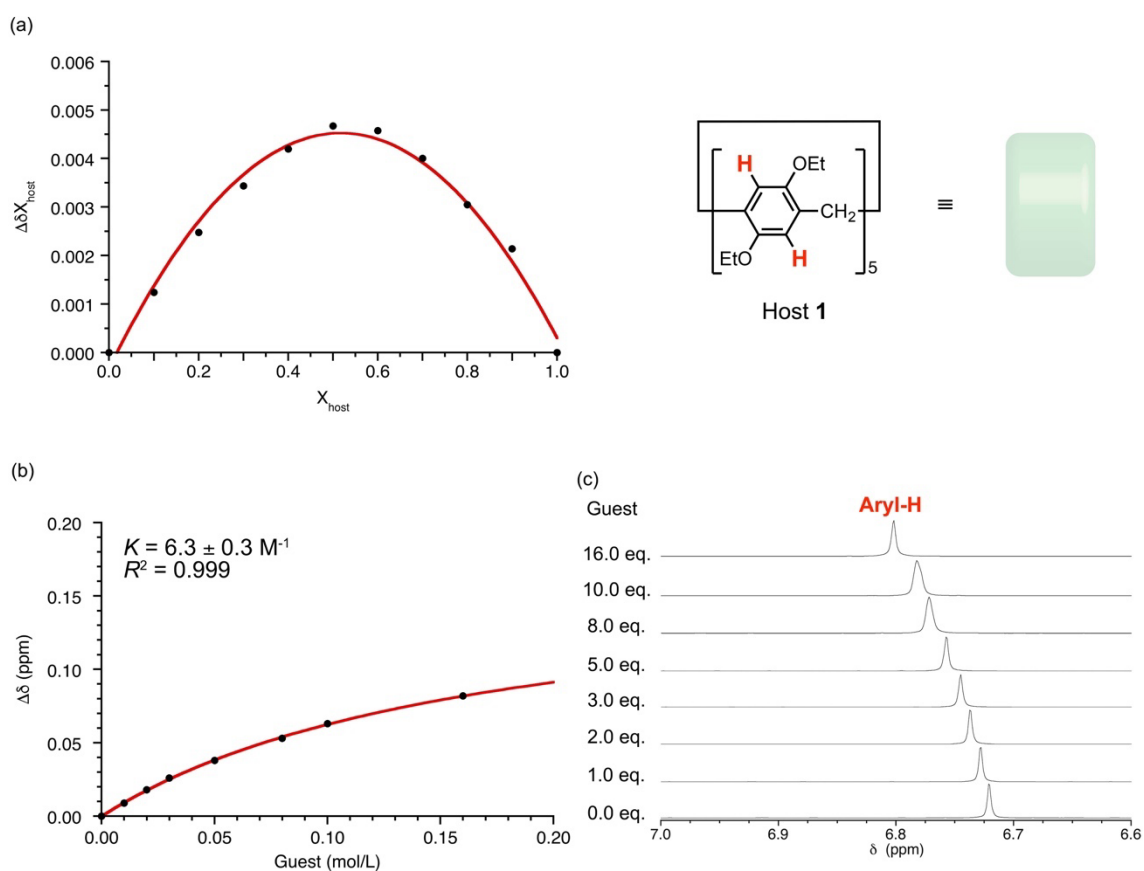
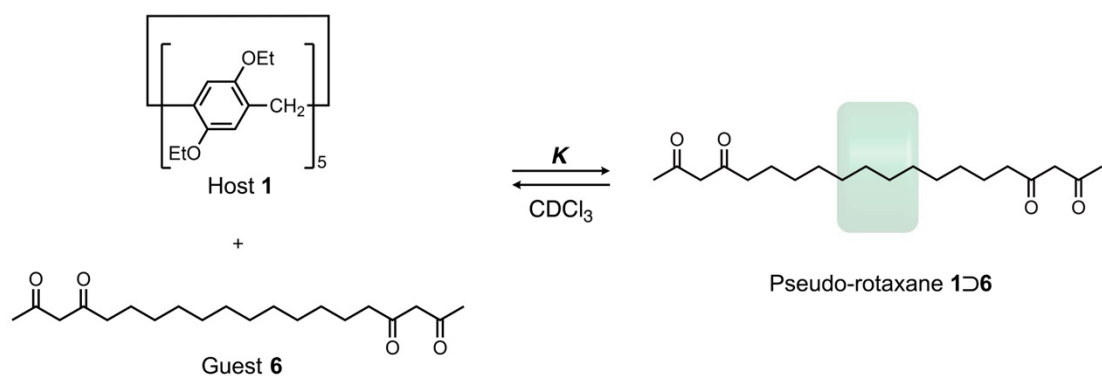


Figure 5-14. (a) Job's plot for determining host-guest ratio between **1** (host) and **6** (guest), which indicated 1:1 binding of **1** and **6**, $X_{\text{host}} = [\text{Host}]/([\text{Host}]+[\text{Guest}])$, $\Delta\delta$: chemical shift change of aryl proton signal of **1**; (b) Non-linear fitting curve of ^1H NMR titration; (c) Partial ^1H NMR spectra of **1** (10 mM) with increasing the ratio of **6** from 0 to 16 equiv. in CDCl_3 at 298 K.

X-ray Structures

Crystallographic data for pseudo-rotaxane 1⊃3

Single crystals of pseudo-rotaxane 1⊃3 were grown by vapor diffusion of methanol into a chloroform solution of host **1** and guest **3** (molar ratio 1:3).

[(C₅₅H₇₀O₁₀)•(C₁₃H₂₀O₄)], $M = 1131.39$, crystal size: $0.72 \times 0.31 \times 0.20 \text{ mm}^3$, Monoclinic, space group $P2_1/n$, $a = 13.5497(2) \text{ \AA}$, $b = 22.8417(4) \text{ \AA}$, $c = 20.6398(4) \text{ \AA}$, $\beta = 101.423(2)^\circ$, $V = 6261.45(19) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.083 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.200 \text{ g/cm}^3$, $1.774^\circ \leq \theta \leq 26.998^\circ$, 11631 unique reflections out of 13570 with $I > 2\sigma(I)$, GOF = 1.042, $R_1 = 0.0488$ and $wR_2 = 0.1346$ for all data. CCDC deposit number: 1991143.

Crystallographic data for pseudo-rotaxane 1⊃4

Single crystals of pseudo-rotaxane 1⊃4 were grown by vapor diffusion of methanol into a chloroform solution of host **1** and guest **4** (molar ratio 1:3).

[(C₅₅H₇₀O₁₀)•(C₁₄H₂₂O₄)], $M = 1145.42$, crystal size: $0.54 \times 0.45 \times 0.27 \text{ mm}^3$, Monoclinic, space group $P2_1/n$, $a = 13.6488(4) \text{ \AA}$, $b = 23.2377(6) \text{ \AA}$, $c = 20.6922(6) \text{ \AA}$, $\beta = 98.814(3)^\circ$, $V = 6485.4(3) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.081 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.173 \text{ g/cm}^3$, $2.426^\circ \leq \theta \leq 26.999^\circ$, 11373 unique reflections out of 14035 with $I > 2\sigma(I)$, GOF = 1.028, $R_1 = 0.0486$ and $wR_2 = 0.1444$ for all data. CCDC deposit number: 1991144.

Crystallographic data for rotaxane 1⊃8

Single crystals of rotaxane 1⊃8 were grown by vapor diffusion of cyclohexane into a toluene solution of rotaxane 1⊃8.

[(C₅₅H₇₀O₁₀)•(C₁₄H₂₀B₂F₄O₄)•(C₇H₈)], $M = 1333.16$, crystal size: $0.18 \times 0.11 \times 0.11 \text{ mm}^3$, Orthorhombic, space group $P2_12_12_1$, $a = 12.98580(10) \text{ \AA}$, $b = 14.01410(10) \text{ \AA}$, $c = 38.9622(3) \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$, $V = 7090.51(9) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.746 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.249 \text{ g/cm}^3$, $2.268^\circ \leq \theta \leq 65.986^\circ$, 11330 unique reflections out of 12148 with $I > 2\sigma(I)$, GOF = 1.055, $R_1 = 0.0450$ and $wR_2 = 0.1235$ for all data. CCDC deposit number: 1991145.

Crystallographic data for rotaxane 1⊃10

Single crystals of rotaxane 1⊃10 were grown by vapor diffusion of cyclohexane into a toluene solution of rotaxane 1⊃10.

$[(C_{55}H_{70}O_{10}) \cdot (C_{26}H_{28}B_2F_4O_6) \cdot 2(C_6H_{12})]$, $M = 1593.52$, crystal size: $0.23 \times 0.21 \times 0.12$ mm³, Triclinic, space group P_1 , $a = 14.4406(3)$ Å, $b = 14.9959(3)$ Å, $c = 20.1166(3)$ Å, $\alpha = 86.8830(10)^\circ$, $\beta = 85.1890(10)^\circ$, $\gamma = 80.696(2)^\circ$, $V = 4280.10(14)$ Å³, $Z = 2$, $T = 123(2)$ K, $\mu = 0.088$ mm⁻¹, $D_{\text{calc}} = 1.236$ g/cm³, $2.268^\circ \leq \theta \leq 25.499^\circ$, 13615 unique reflections out of 15916 with $I > 2\sigma(I)$, GOF = 1.087, $R_1 = 0.1043$ and $wR_2 = 0.2996$ for all data. CCDC deposit number: 1991146.

5.7. References

- [1] C. Hertweck, *Angew. Chem. Int. Ed.*, **2009**, *48*, 4688–4716.
- [2] S. G. Gilbreath, C. M. Harris, T. M. Harris, *J. Am. Chem. Soc.*, **1988**, *110*, 6172–6179.
- [3] L. Hammerer, M. Friess, J. Cerne, M. Fuchs, G. Steinkellner, K. Gruber, K. Vanhessche, T. Plocek, K. C. Winkler, W. Kroutil, *ChemCatChem*, **2019**, *11*, 5642–5649.
- [4] A. Rentmeister, F. H. Arnold, R. Fasan, *Nat. Chem. Biol.*, **2009**, *5*, 26–28.
- [5] L. Trembleau, J. Rebek, Jr. *Science*, **2003**, *301*, 1219–1220.
- [6] A. Scarso, L. Trembleau, J. Rebek, Jr. *Angew. Chem. Int. Ed.*, **2003**, *42*, 5499–5502.
- [7] Y. Yu, J. Rebek, Jr. *Acc. Chem. Res.* **2018**, *51*, 3031–3040.
- [8] R. Z. Pavlović, S. E. Border, T. J. Finnegan, L. Zhiquan, M. J. Gunther, E. Muñoz, C. E. Moore, C. M. Hadad, J. D. Badjić, *J. Am. Chem. Soc.* **2019**, *141*, 16600–16604.
- [9] M. Yamashina, S. Kusaba, M. Akita, T. Kikuchi, M. Yoshizawa, *Nat. Commun.* **2018**, *9*, 4227.
- [10] T. Ogoshi, S. Kanai, S. Fujinami, T. Yamagishi, Y. Nakamoto, *J. Am. Chem. Soc.* **2008**, *130*, 5022–5023.
- [11] P. J. Cragg, K. Sharma, *Chem. Soc. Rev.* **2012**, *41*, 597–607.
- [12] D. A. Leigh, V. Marcos, M. R. Wilson, *ACS Catal.* **2014**, *4*, 4490.
- [13] T. Ogoshi, T.-a. Yamagishi, Y. Nakamoto, *Chem. Rev.* **2016**, *116*, 7937–8002.
- [14] X. Lou, H. Chen, X. Jia, C. Li, *Chin. J. Chem.* **2015**, *33*, 335–338.
- [15] Y. Wang, G. Ping, C. Li, *Chem. Commun.* **2016**, *52*, 9858–9872.
- [16] N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros, J. F. Stoddart, *J. Am. Chem. Soc.* **2011**, *133*, 5668–5671.
- [17] S. Dong, C. Han, B. Zheng, M. Zhang, F. Huang, *Tetrahedron Lett.* **2012**, *53*, 3668–3671.
- [18] P. Wei, X. Yan, J. Li, Y. Ma, Y. Yao, F. Huang, *Tetrahedron* **2012**, *68*, 9179–9185.
- [19] Y. Manabe, M. Uesaka, T. Yoneda, Y. Inokuma, *J. Org. Chem.*, **2019**, *84*, 9957–9964.
- [20] K. G. Hampton, J. J. Christie, *J. Org. Chem.* **1976**, *41*, 2772–2773.
- [21] C. Maurer, E. Pittenauer, V. A. Du, G. Allmaier, U. Schubert, *Dalton Trans.* **2012**, *41*, 2346–2353.
- [22] P. Thordarson, *Chem. Soc. Rev.* **2011**, *40*, 1305–1323.
- [23] L. Fielding, *Tetrahedron* **2000**, *56*, 6151–6170.

- [24] M. Holler, T. Stoerkler, A. Louis, F. Fischer, J.-F. Nierengarten, *Eur. J. Org. Chem.* **2019**, 3401–3405.
- [25] K. Liang, M. S. Farahat, J. Perlstein, K.-Y. Law, D. G. Whitten, *J. Am. Chem. Soc.* **1997**, *119*, 830–831.
- [26] L. Lu, R. J. Lachicotte, T. L. Penner, J. Perlstein, D. G. Whitten, *J. Am. Chem. Soc.* **1999**, *121*, 8146–8156.
- [27] O. Uranga-Barandiaran, M. Catherin, E. Zaborova, A. D'Alé o, F. Fages, F. Castet, D. Casanova, *Phys. Chem. Chem. Phys.* **2018**, *20*, 24623–24632
- [28] T. Ogoshi, K. Kitajima, T. Aoki, S. Fujinami, T. Yamagishi, Y. Nakamoto, *J. Org. Chem.* **2010**, *75*, 3268–3273.
- [29] S. Xu, R. E. Evans, T. Liu, G. Zhang, J. N. Demas, C. O. Trindle, C. L. Fraser, *Inorg. Chem.* **2013**, *52*, 3597–3610.
- [30] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, **2015**, *71*, 3–8.
- [31] G. M. Sheldrick, *Acta Crystallogr. Sect. C*, **2015**, *71*, 3–8.
- [32] K. G. Hampton, J. J. Christie, *J. Org. Chem.* **1976**, *41*, 2772–2773.
- [33] C. Maurer, E. Pittenauer, V. A. Du, G. Allmaierb, U. Schubert, *Dalton Trans.* **2012**, *41*, 2346–2353.
- [34] R. W. Kluiber, J. W. Lewis, *J. Am. Chem. Soc.* **1960**, *82*, 5777–5779.
- [35] K. G. Hampton, R. J. Light, C. R. Hauser, *J. Am. Chem. Soc.*, **1965**, *30*, 1413–1416.
- [36] N. M. D. Brown, P. Bladon, *J. Chem. Soc. A*, **1969**, 526–532.
- [37] L. Kersten, S. Roesner, G. Hilt, *Org. Lett.* **2010**, *12*, 4920–4923.
- [38] S. Inagaki, K. Saito, S. Suto, H. Aihara, A. Sugawara, S. Tamura, T. Kawano, *J. Org. Chem.* **2018**, *83*, 13834–13846.

Chapter 6

Summary and Outlook

6.1. Summary

In this thesis, the author has demonstrated the novelty of aliphatic polyketones as a molecular chain for inducing and fixing molecular structures and discovering their structure-based functions. The structurally flexible aliphatic chain and multiple carbonyl groups allowed the induction of various structures and the fixation of the induced structures, resulting in the various functions as demonstrated in Chapters 2-6.

In Chapter 2, discrete aliphatic polyketones were synthesized and their inherent structural features were studied. Aliphatic polyketones composed of 3,3-dimethylpentane-2,4-dione as a repeating unit were synthesized up to 20 mer by repeating terminal-selective silylation and silver(I) oxide mediated coupling reactions. The resulting aliphatic polyketones were obtained as stable colorless solids, and all the carbonyl groups existed as a keto-form. Unlike natural-type polyketones, the newly developed polyketones were stable even in 20 mer. The crystallographic structural analyses showed that, although short polyketones (2-4 mer) adopted their own unique conformations, polyketones longer than 5 mer showed a similar helical conformation. This structural character of aliphatic polyketones further led to the determination of the critical chain length between small-molecular and macromolecular crystallizations in oligomer and polymer materials.

In Chapter 3, rigid rod-like structures were generated from structurally flexible aliphatic polyketones through the formation of fully π -conjugated polyimines. The resulting π -conjugated polyimines exhibited the red-shift of the absorption spectra with the chain length elongation of the parent polyketone chains. Although π -conjugated polyimines became virtually insoluble upon chain length elongation, this insoluble organic material was applied as an adsorbent to collect Group 10 metal ions from a solution. Using the metal-ion coordination character of the iminic nitrogen atoms, π -conjugated polyimines can adsorb metal ions at their interfaces.

In Chapter 4, large molecular architectures were constructed using polyimine ligands, derivatized from aliphatic polyketones, using metal-ion coordination. Upon the complexation with palladium ions, the curved structure of the ligand was fixed and formed the double-helix structure as a discrete palladium complex. Using the ligands with different structural flexibilities derived from the bridging ethylene or vinylene units for complexation with cadmium ions, the one- or two-dimensional coordination networks were formed differently. When copper(I) halides were complexed with the ligand, the coordination network of tetranuclear copper(I) iodide clusters was formed and exhibited thermochromic luminescence as a functional complex.

In Chapter 5, a conformational control of aliphatic polyketones upon supramolecular interactions was performed by a rotaxane formation with pillar[5]arene. Although the flexible aliphatic chain of aliphatic polyketones can adopt various conformations in solution, a linear conformation was selectively induced and fixed by a rotaxane formation with pillar[5]arene and BF_2 complexation at the terminal 1,3-diketone units of the polyketones. This conformational restriction was applied to the suppression of the solvatochromic behavior of polyketone-derived alkyl-bridged flexible chromophore dyads induced by the intramolecular aggregation of chromophore units by the folding of the bridging flexible alkyl chain.

6.2. Future Perspectives

The prospects of aliphatic polyketones as functional materials have been diversified through interdisciplinary collaborative research. The alkali metal ion affinity of aliphatic polyketones demonstrated their potential applicability as solid polymer electrolytes (SPE). The composite of aliphatic polyketones and lithium bis(trifluoromethanesulfonyl)imide (LiTFSI) exhibited lithium ion conductivity, which was the first example of aliphatic polyketones as a host material for SPE.¹ Upon this result, the comparison of carbonyl-containing polymers, polycarbonates, polyesters, and polyketones as SPE host materials was demonstrated to investigate the local effects of ester oxygens in main chains on the global lithium ion conductivity behavior.² Although the present aliphatic polyketones have an issue in their high crystallinity for lithium ion conduction, further chemical modifications of aliphatic polyketones will allow to improve of their ion conduction properties for the practical use of aliphatic polyketones as SPE host materials.

Aliphatic polyketones have also been applied in microfluidic devices for cancer diagnosis.³ The polyketone-coated zinc oxide nanowires have been developed as a component of microfluidic devices for efficient extraction of extracellular vesicles. In this study, the importance of the discrete chain length of aliphatic polyketones was discovered for the efficient extraction of extracellular vesicles. Furthermore, the clinical utility of this system for cancer diagnosis has been also demonstrated.

The high potential of aliphatic polyketones as a molecular scaffold for the generation of versatile, functional materials has just started to be flourished. I believe that further modifications of aliphatic polyketones will endow more unique properties not only in chemistry but also in interdisciplinary research fields.

6.3. References

- [1] T. Eriksson, A. Mace, Y. Manabe, M. Y.-Fujita, Y. Inokuma, D. Brandell, J. Mindemark, *J. Electrochem. Soc.*, **2020**, *167*, 070537.
- [2] T. Eriksson, H. Gudla, Y. Manabe, T. Yoneda, D. Friesen, C. Zhang, Y. Inokuma, D. Brandell, J. Mindemark, *Macromolecules*, **2022**, *55*, 10940–10949.
- [3] A. Yokoi[†], M. Ukai[†], T. Yasui, Y. Inokuma, K. H.-Deuk, J. Matsuzaki, K. Yoshida, M. Kitagawa, K. Chattrairat, M. Iida, T. Shimada, Y. Manabe, I.-Y. Chang, E. Asano-Inami, Y. Koya, A. Nawa, K. Nakamura, T. Kiyono, T. Kato, A. Hirakawa, Y. Yoshioka, T. Ochiya, T. Hasegawa, T. Baba, Y. Yamamoto, H. Kajiyama, *under review*. (†: Contributed equally)

List of Publications

Chapter 2

Determination of the Critical Chain Length for Macromolecular Crystallization of a Structurally Flexible Polyketone

Y. Ide, Y. Manabe, Y. Inaba, Y. Kinoshita, J. Pirillo, Y. Hijikata, T. Yoneda, K. I. Shivakumar, S. Tanaka, H. Asakawa, Y. Inokuma, *Chem. Sci.*, **2022**, *13*, 9848–9854.

Chapter 3

Two-Step Transformation of Aliphatic Polyketones into π -conjugated Polyimines

Y. Manabe, M. Uesaka, T. Yoneda and Y. Inokuma, *J. Org. Chem.*, **2019**, *84*, 9957–9964.

Chapter 4

Control over Coordination Self-Assembly of Flexible, Multidentate Ligands by Stepwise Metal Coordination of Isopyrazole Subunits

Y. Ashida, Y. Manabe, S. Yoshioka, T. Yoneda and Y. Inokuma *Dalton Trans.*, **2019**, *48*, 818–822.

Luminescent Coordination Polymers Constructed from Flexible, Tetradentate Diisopyrazole Ligand and Cooper(I) Halides

T. Yoneda, C. Kasai, Y. Manabe, M. Tsurui, Y. Kitagawa, Y. Hasegawa, S. Parantap and Y. Inokuma, *Chem. Asian J.*, **2020**, *15*, 601–605.

Chapter 5

Supramolecular Conformational Control of Aliphatic Oligoketones by Rotaxane Formation

Y. Manabe, K. Wada, Y. Baba, T. Yoneda, T. Ogoshi, Y. Inokuma, *Org. Lett.* **2020**, *22*, 3224–3228.

Other Publications

Polyketones as Host Materials for Solid Polymer Electrolytes

T. Eriksson, A. Mace, Y. Manabe, M. Y.-Fujita, Y. Inokuma, D. Brandell, J. Mindemark, *J. Electrochem. Soc.*, **2020**, *167*, 070537.

Insoluble π -Conjugated Polyimine as an Organic Adsorbent for Group 10 Metal Ions

H. Shirakura, Y. Hijikata, J. Pirillo, T. Yoneda, Y. Manabe, M. Murugavel, Y. Ide, Y. Inokuma, *Eur. J. Inorg. Chem.*, **2021**, *17*, 1705–1708.

Isopyrazole-Masked Tetraketone: Tautomerism and Fuctionalization to a Fluorophore for Metal Ion Detection

H. Shirakura[†], Y. Manabe[†], C. Kasai, Y. Inaba, M. Tsurui, Y. Kitagawa, Y. Hasegawa, T. Yoneda, Y. Ide, Y. Inokuma, *Eur. J. Org. Chem.*, **2021**, *31*, 4345–4349.

[†]: Contributed equally

Carbonyl-Containing Solid Polymer Electrolyte Host Materials: Conduction and Coordination in Polyketone, Polyester, and Polycarbonate Systems

T. Eriksson, H. Gudla, Y. Manabe, T. Yoneda, D. Friesen, C. Zhang, Y. Inokuma, D. Brandell, J. Mindemark, *Macromolecules*, **2022**, *55*, 10940–10949.

Absorption spectra of calix[3]pyrrole analogues as probes for contracted macrocycles

K. Watanabe[†], R. Saha[†], Y. Inaba, Y. Manabe, T. Yoneda, Y. Ide, Y. Hijikata, Y. Inokuma *J. Porphyrins Phthalocyanines*, **2022**, *in press*.

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[†]: Contributed equally

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