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Structure and reactivity of bis(iodozincio)methane solution ☆

Seijiro Matsubara [a],*, Hideaki Yoshino [a], Yuhei Yamamoto [a], Koichiro Oshima [a],
Hideki Matsuoka [b], Kozo Matsumoto [b], Kazuhiko Ishikawa [c], Eiichiro Matsubara [c,d]

[a] *Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoudai-Katsura, Nishikyo, Kyoto 615-8501, Japan*
[b] *Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University, Kyoudai-Katsura, Nishikyo, Kyoto 615-8501, Japan*
[c] *Institute for Materials Research, Tohoku University, Sendai 980-8577, Japan*
[d] *Department of Material Science and Technology, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606-8501, Japan*

Abstract

Bis(iodozincio)methane, which has been shown to be an efficient reagent for organic synthesis, is obtained as THF solution. The structural information about the reagent as THF solution was corrected by small angle neutron scattering and by anomalous X-ray scattering. Those scattering experiments implied that the prepared bis(iodozincio)methane exists without forming any oligomer or aggregate. A coordination of tetrahydrothiophene to bis(iodozincio)methane enhances the nucleophilicity of the reagent and stabilizes its monomeric structure in the solution.
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1. Introduction

Methylene dimetal reagents have been developed as carbonyl methylenation reagents to compensate for some drawbacks of Wittig reagents [1,2]. The ylide naturally exhibits a strong basicity, which often leads to an enolization of the starting carbonyl compound. At the same time, the ylid often suffers from a lack of nucleophilicity. These points can be overcome by use of a *gem*-dimetal compound or a metal carbene complex [3,4]. Cainelli and co-workers [5] had reported methylenation of ketones and aldehydes with *gem*-dimagnesium reagent which was prepared from diiodomethane and Mg/Hg in ether. More conveniently, Fried and co-workers [6] and Miyano and co-workers [7] demonstrated

that treatment of diiodomethane with excess zinc gives *gem*-dizinc species in their Wittig-type methylenation reaction. Since then, the reduction of dihalomethane with zinc has been investigated by Nysted, [8] Takai, Oshima, Nozaki, [9,10] Eische and Piotrowski [11] and Lombardo, [12] from a view point of methylenation of carbonyl compounds. These researchers concluded that methylene dizinc species is a reactive species. While these procedures had used in situ formation of methylene dizinc species during methylenation reaction, we showed the preparation of methylene dizinc as THF solution from diiodomethane and zinc dust in the presence of lead catalyst [13]; we analyzed its structure by ^{1}H NMR (Fig. 1) [14,15]. We then performed several types of molecular transformations using this THF solution of methylene dizinc [16].

The broad signal at higher field (−1.1 ppm) in Fig. 1 was understood as a signal of a methylene which is substituted with two electropositive zinc atoms. However, it is impossible to tell from this ^{1}H NMR spectrum,
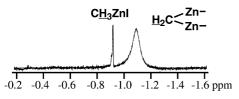
Fig. 1. ^1H NMR of the dizinc reagent in THF-d_8 (0.45 M), which was prepared from diiodomethane, zinc powder, and a catalytic amount of PbCl$_2$in THF-d_8.

what is the other substituent on the zinc atoms. The structure of the zinc reagent in THF should be determined considering equilibrate transmetallation between the molecules of **1**, that is, Schlenk equilibrium. [17] The equilibrium in this case would be discussed not only by Eq. (1) but also by Eq. (2) in Scheme 1. Schlenk equilibrium of **1** may induce a polymeric structure such as a linear compound **3** or cyclic compound **4**. We tried to determine the structure of **1** in solution by direct X-ray and neutron scattering technique [18].

In general, structural studies of organometallics in solution have not progressed so well [18,19]. For this purpose, both macroscopic and microscopic structural information should be obtained. In other words, the size of a solute and the distance between atoms in the solute should be determined. The former reflects their aggregation including Schlenk equilibrium and the latter is a single molecular structure of the corresponding reagent (Fig. 2). We tried to determine the sizes of **1** in THF solution by small angle neutron scattering (SANS) [20], and the distances between atoms by anomalous X-ray scatterings by synchrotron radiation [21]. The method will be available not only for this specific case but also for many structural studies concerning organometallic reagents in solution [22].

2. Results and discussion

We tried to determine the size of the solute in the prepared solution of *gem*-dizinc prepared from diiodomethane and zinc in the presence of lead catalyst. Such information will also tell us about the homogeneity of the solution. Small-angle neutron scattering (SANS) will give information concerning the sizes of the aggregate of the solute [19,20]. The result is shown in Fig. 3. Most of the SANS profile, where $q > 0.07$ Å^{-1} was well identified with the simulated scattering curve of the sphere particles which have the radius of gyration (R_g) of 9.2 Å. At the smaller angle regions, those where q is less than 0.07, two components with $R_g = 15$ and 60 Å can be recognized, although the data are scattered due to weak scattering intensity. However, the contributions from both of these components with larger R_g can be said to be very small. The results show that only small particles (R_g: about 9.2 Å) exist with high homogeneity in a THF solution of dizinc species. This means that the Schlenk equilibrium in Scheme 1 stays with bis(iodozincio)methane molecules **1** which do not aggregate with each other so much. To investigate the inside of the small particles, we used X-ray scattering technique.

To obtain a good scattering of the solute, one needs a strong X-ray beam. Although X-ray scattering by white X-rays of synchrotron radiation give the radial distribution function of the solute in large region, a difficulty
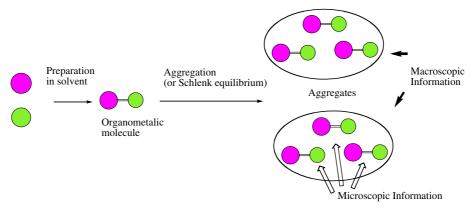

Scheme 1.

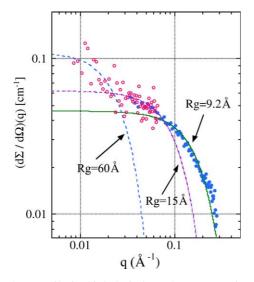Fig. 2. Structural study of an organometallic reagent in a solution.

Fig. 3. SANS profile for bis(iodozincio)methane (0.4 M) in THF-d_8. The two data sets plotted by dots were obtained at two different camera lengths (the sample-detector distance, ●: 1 m, large angle region, ○: 4 m, small angle region). These camera lengths cover different scattering vector, q, range ($q = 4\pi\sin\theta/\lambda$, where 2θ is the scattering angle and λ is the wavelength of neutron). Three lines are simulated scattering curves. The data was collected by SANS-U of the Institute for Solid State Physics, University of Tokyo, Tokai, Ibaraki.
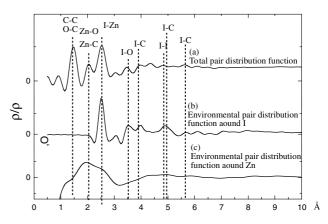

Fig. 4. (a) Pair distribution function of bis(iodozincio)methane (**1**). (b) Pair distribution function based on AXS at Zn-atm K-edge. (c) Pair distribution function based on AXS at I-atm K-edge. The data collected by Photon Factory of the Institute of Material Structure Science, High Energy Accelerator Research Organization, Tsukuba, Ibaraki.

arises to assign each peaks of the radial distribution function to the corresponding atoms in the solution. To solve this problem, we applied anomalous X-ray scattering (AXS) [21]. After we obtained the normal X-ray scattering in the area from small to large angle at 32.867 keV, anomalous X-ray scatterings around heavy atoms were measured to identify the peaks of the radial distribution function. The AXS was measured under irradiation of X-rays near the K-edge of zinc atom (9.961 keV) at 9.661 and 9.931 keV and near the K-edge of iodine atom (33.167 keV) at 33.117 and 32.867 keV. In Fig. 4, the total pair distribution function (a) is shown in comparison with the Zn (zinc) environmental pair distribution function (b) and the I (iodine) environmental pair distribution function (c). Comparing these functions, one can easily assign the peaks in (a) to distances between each pair of atoms.

Thus, two scattering measurements of the dizinc species in THF will tell us the detailed structure in solution. Before these scattering analyses, we cannot tell the structure of gem-dizinc species which was prepared as shown in Eq. (1) (Scheme 1), as the Schlenk equilibrium may change the structure of **1** into **2**, **3**, or **4**. The SANS experiment (Fig. 3) concluded that the solution of the dizinc consisted of small homogeneous particles. That is, it is not necessary to consider the possibility of polymeric structure via Schlenk equilibrium. The radius of gyration of these small homogeneous particles was 9.2 Å, as shown in Fig. 3, and it is hard to decide if the structure of the particle is monomeric **1** or dimeric **2**. The AXS data in Fig. 4 showed that the molecule in the

solution has atoms within 6–7 Å. This means the reduction of diiodomethane with zinc in THF (Scheme 1) gave monomeric bis(iodozincio)methane (**1**). In other words, under the conditions of bis(iodozincio)methane preparation, it is not necessary to consider the contributions of the Schlenk equilibrium which form polymethylene zinc.

Removal of the solvent from the THF solution of dizinc **1** in vacuo gave a white solid **5**. The solid **5** would not dissolve into THF. This fact means that the structure had changed during the concentration process. Various other solvents: DMI (1,3-dimethyl-2-imidazolidinone), CS_2, 1,2-dichloroethane, pyridine, DMF, and DMSO, were examined in attempts to dissolve the solid **5**. Among them, DMSO showed reasonable solubility. The solid was considered to be a polymeric dizinc species (**3** or **4**). An addition of tetrahydrothiophene (THT) changed the situation dramatically. After an addition of the same volume of THT to the THF solution of the dizinc which was prepared from diiodomethane and zinc, the solvent was removed in vacuo. This procedure also gave a white solid **6**. The solid **6** was soluble in THF or THT. Extended X-ray absorption fine structure (EXAFS) gives us new information about a solution at the atomic level around the selected center atom [17,18c]. EXAFS spectroscopy of these solutions (Fig. 5, (a) the THF solution of **1**, (b) **5** in DMSO, and (c) **6** in THT) was used to get some information regarding the structure. The comparison of (a) and (b) results showed that signals beyond 3.5 Å were stronger in (b) than in (a). This result implies that the solution in (b) has the larger molecules that may be the polymeric species such as **3** or **4**. It is notable that the spectrum in (c) has very weak signals beyond 3.5 Å. This fact means that the dimetal species in (c) remained as small molecules in solution, that is, **1** in a
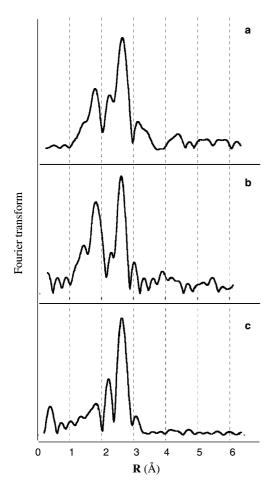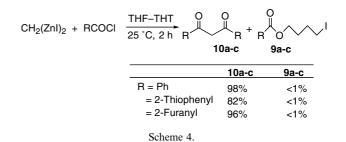
Fig. 5. Fourier transform of the EXAFS spectra at Zn K-edge: (a) the THF solution of dizinc from diiodomethane (0.1 M), (b) **5** in DMSO (0.1 M), and (c) **6** in THT (0.1 M). The data were collected at Spring 8, Sayo, Hyogo.

Scheme 4.

the formation of **2**, **3**, or **4** via Schlenk equilibrium, [25] the function of tetrahydrothiophene is very unique.
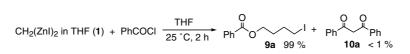
A coordinated solvent such as tetrahydrothiophene (THT) may strengthen the nucleophilicity of bis(iodozincio)methane. The effect was obvious in the reaction with acyl chloride [17,26]. Treatment of acyl chloride with bis(iodozincio)methane (**1**) in THF led to the direct reaction of acyl chloride with THF (Scheme 3). A Lewis acid existing in a THF solution of **1**, such as zinc(II) iodide or **1** itself mediated the formation of **9a**. To the reagent **1** in THF (0.5 M, 4 mL, 2.0 mmol), which was prepared from diiodomethane and zinc in THF, 5 ml of tetrahydrothiophene (THT) was added at 25 °C. The mixture was stirred for 10 min. At the same temperature, benzoyl chloride (2.0 mmol) in THF (1.0 ml) was added dropwise. The resulting solution was stirred for 2 h at the same temperature. An aqueous work-up afforded 1,3-diketone **10a** in 98% yield, and no formation of **9a** was observed (Scheme 4). Other examples are also shown in Scheme 4.

3. Conclusion

The information obtained about the structure of **1** in solution will be useful for the design of the reaction. At the same time, the profiling of the reaction pathway using **1** by ab initio calculation requires such information [27]. The activation of **1** with tetrahydrothiophene arises not only from an electrodonating effect to zinc atom via coordination but also from the stabilization of monomeric form of **1**. Thus, the structural studies of bis(iodozincio)methane help the deeper understanding of the

monomeric form with having some THT as a ligand, even after concentration procedure. An addition of THT inhibits the formation of any polymeric species such as **3** or **4**. The effect of THT can be understood as follows. As shown in Scheme 2, Schlenk equilibrium [23] may proceed via aggregation [24]. A strongly coordinated solvent like THT, however, may inhibit the formation of aggregation. As some solvent may form stable ZnI_2–solvent complexes, which would benefit

Scheme 2. Possible pathway for Schlenk equilibrium.

Scheme 3. Reaction of benzoyl chloride with tetrahydrofuran in the presence of **1**.

reaction. The method is useful not only for the analysis of **1** but also for the general organometallics studies, although the measurements require neutron and synchrotron beam lines [28].

4. Experimental

The SANS measurements were performed by SANS-U of Institute for Solid State Physics, The University of Tokyo, at the research reactor JRR-3, Tokai, Japan. The wavelength of neutron beam was 7 Å. Solutions were measured in quartz cells with a pass length of 4 mm at 25 °C [29]. The AXS experiments under irradiation of X-rays were carried out on the BL-9C at Photon Factory of the Institute of Material Structure Science, High Energy Accelerator Research Organization, Tsukuba, Ibaragi. Solutions were measured in quartz cells (0.05 mm) with a pass length of 1 mm at 25 °C [30]. The EXAFS at Zn K-edge experiments was carried out on the BL-01B1 at Spring 8 (Hyogo, Japan) operated at 8 GeV, stored current 70–100 mA. Solutions were measured in polypropylene bag at 25 °C [31].

5. Preparation of bis(Iodozincio)methane (1)

A mixture of Zn (25 mmol), diiodomethane (1.0 mmol), and $PbCl_2$ (0.005 mmol) in THF (2.0 ml) was sonicated for 1 h in an ultrasonic cleaner bath under Ar. To the mixture, diiodomethane (10 mmol) in THF (20 ml) was added dropwise over 15 min at 10 °C with vigorous stirring. The mixture was stirred for 2 h at 25 °C. After the stirring was stopped, the reaction vessel was stood undisturbed for several hours. Excess zinc was separated by sedimentation. ^1H NMR spectra of the obtained supernatant showed a broad singlet at −1.1 ppm at 0 °C, which corresponded to the methylene proton of **1**. The concentration was determined by ^1H NMR using 2,2,3,3-tetramethylbutane as an internal standard. The supernatant was used for the further reaction as a solution of **1** in THF (0.4–0.5 M). In a sealed vessel, a solution of **1** can be stored at room temperature at least for two months.

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