

3_Mother, Tadako

Grandfather of mother's side, Kametaro Yoshida worked about 50 years as a Christian missionary around East-Northern area started at Sendai from 1879. It was only about 6 years after lifting of the embargo on Japanese Christianity in 1873, Grandmother, Machi Yoshida followed him for all her life and they left one son and five daughters and our Mother Tadako was born as the last daughter in Soma Fukushima in 1897. Kametaro as a Christian missionary whose activities has been extended to Odawara(Kanagawa), Mejiro(Tokyo) so on and final at 6 grade she went to Kaminoyama (Yamagata) , so far Tadako changed school six times at primary school stage. However, she told us that the district at that time, had many objectives for the activities of Christians that she was given hard time not only by children but also by many adults. Everyday all day long, she usually stayed at home to play music with a small organ and draw paintings.



When Tadako was young, there were many bullies surrounding her circumstances, that's why she used to play by herself with music and drawing in house. She was strongly affected by Yumeji Takehisa who was a famous leading Japanese poet and painter during the Taisho era. The model of this picture may be her elder sister Misao who was a good friend of Tadako all her life. Misao was loved not only by her children but also all her nephews and nieces.

In 1913, Kametaro had a position at Urawa Saitama Church and his family lived nearby the Church except Tadako who started a life in a dormitory of Kyoritsu Yokohama Woman's School⁴). As it was her mother Machi also had studied in the same school that they immersed in the culture of the same western school life without Japanese language and got the sense of value. When we were young, Mother Tadako used to tell us "Find your individuality try to discover your own idea". This idea was completely different from days before the world war II⁵) in Japan. In her youth, she made her life full in school and later she became a teacher for Sunday school for the children at the Church.

One day she heard about the big news in the Church that she will have an opportunity to study music by a certain sponsor. However, Kyoritsu Woman's School had no license of qualification for further upgrade school. She needed to change school and went to Aoyama Gakuin. She studied basic music very hard and passed Ueno music College entrance exam (now, Tokyo University of Arts). An unfortunate matter had happened one year later that

her sponsor failed in business and no back up was available for Tadako. She had to leave the College immediately with tears. She just drew pictures all daylong to forget about her mind thinking music. After several months, her Father received a missionary assignment for Yamagata area.

Thus, her Mother, Machi asked Tadako "Come with us to Yamagata to ease your mind from thinking about music". Tadako just obeyed her mother, they went to Tateoka, Nakamachi etc. in Yamagata. There was a young person who owned a property who was Mr. M which was love at first sight to Tadako. He desired to marry her, although his family especially his Father resisted to his action, since his old established family were resistant to the Christian religion. Instead, Mr. M tried to visit Sadako's house bringing something she would like, so she was gradually liking him. This was very tiring for him since he was at the threshold between his Father's strong will and love to Tadako. He suffered from inflammation of the lung and it became very serious. A certain great man was unable to let it pass unnoticed so he arranged to get his Father's permission of marriage for them to get engaged. However, only a few months later, he passed away as I told in the story in the Father's section. Tadako had a big experience that before she got married, she had to wear Kimono all in white to help to send her husband-to-be to Heaven. She was exhausted and suffered from an acute nephritis which made her to be bedridden for two whole weeks because she was in a dangerous state.

Tadako had experienced many hardships in her life, such as quitting to study music, unable to learn painting, lose the job at the nursery school, suffered from illness and the biggest one was her fiancé passed away. However, she refused to be discouraged in her later life. She explained to us later, " These battles which I faced, I believed they were trials sent by God".

After several months passed, her Mother asked Tadako "Recently we have known, the behavior of Mr. Kotaro Tamura who have changed much and being more noble man, I think he is the best person for you why don't you marry him? " She accepted her mother's proposal since her impression about Kotaro was similar to her Mother. They were married on 7th April 1920.

4) The woman's Union Missionary Society of America for Heathen Lands established the Mission Home at Yokohama, Japan in 1871, later the name changed to the Kyoritsu woman's school in 1875. because of that three American women fully gave services establishing the school.

5) When we were young, people said "Give no one cause to gossip about you behind

your back.

4 Brothers

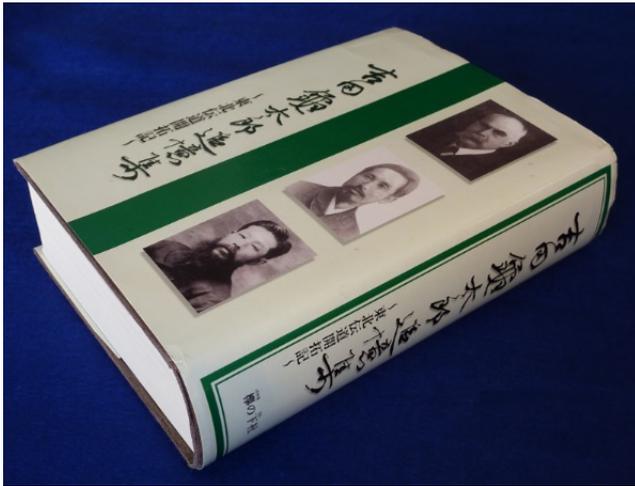
We were four brothers whose names were Tadayuki, Yoshiya, Akira and Chihiro in order of their birth. Hence the name of our eldest brother came from our Mother's and Father's names from each one of their Chinese character. I saw that my Father loved my Mother so much that when the first baby came he had been named after both of them. The source of the name, Yoshiya came from the Bible in English would be Josiah, at the time of our parents were very faithful to God, since that the Taisho era could hear about the beginning of the war. The origin of the name of Akira was described already in the first chapter. Chihiro the last son of our parents, they actually hoped the next baby would be a girl, since they had already three sons, that's why Father had decided to name the coming baby would be accepted, either a boy or a girl in our society. Adding to his idea he saw Heaven in Akira's case, next he saw ocean. The name at ending of the name "hiro" means the unit (about 1.8m) of measuring of the depth of the sea, and "Chi" means a thousand. We thanked our father that he had selected names for all his children through his best ideas, experiences, and faith.

4-1 Tadayuki



Tadayuki became a smart business man which he got in Daiei Movie Co. as a delivery salesman. He built a house when he was over 30 years old in Tokyo. He liked to read many books especially about Chinese poetry which was his favorite. When Yoshiya launched "Home News" for our family, he tried to sent newsletters to his close cousin Kenzo Hyodo by post letters. The name was "Under the Zelkovaserrata"

Tadayuki was born on 7th August 1921 at Keio hospital as the first child of the family of Tamura. The same as usual in a new family, he was expected a lot from his parents. He grew up to be a very honest child to his parents and he had a mild manner. When he was two years old, at that time, there was the great Kanto earthquake and at the same time a vicious rumor has spread out around our residential area. My mother carried Yoshiya her second baby on her back and Tadayuki who was just learning to walk going towards the community hall. Tadayuki was affected by this incident that he always was very sensitive to earthquakes and when a small earthquake occurred, immediately he turned pale. During his younger age, our Father's income was very unstable that our Mother always complained about it. Because of that Tadayuki might have strong image for importance of making



Abstract of Kametaro Yoshida his Posthumous Work

For 250 years in the whole of Japan, Tokugawa Shogunate had made a time of peace. It was put in force by a skillful management to all feudal lords, also the national isolation policy and exclusionism for Christianity was put in affect. There was so called "Genroku" which was brilliant time in Edo era even though they spent money and time on amusements. Later on, certain feudal lords made a draft in financial matters and victims of natural disasters suffered by it. Yoshinobu, the last Tokugawa-Shogun returned political power to the Emperor Meiji after several wars and battles.

In such a historical background, I, Kametaro Yoshida, was born in Hanamaki, Iwate on 1857. When I was 7 or 8, all Japanese feudal lords were in utter chaos because of their lifestyle would be completely destroyed. In the religious world, it was put on the notice board that the Imperial Covenant Consisting of Five Articles. However, exclusionism for Christianity, was continued and some believers were arrested and killed.

(omission)

When I became 16-year-old, I came up to the capital Tokyo. I learned Chinese Character and had a certain job but I wanted to study chemistry more precisely. I got a job at chemical laboratory in Tsukiji in a good luck.

money later. When we were younger, he used to play games with Akira and Chihiro but not with Yoshiya. Usually we played a game at home which Tadayuki made his original one. For instance a Sumo game using millet stalks and at bottom with a thumbtack to make it stand, and flipping it down or pushing out the opponent of the Sumo ring. One time he made a baseball game with rolling the dice

Mr. Kalsol lived there, as a neighbor who was a missionary, so occasionally hymn songs could be heard. By chance, I had read the Bible then I could get to know Jesus Christ was crucified for all mankind. I felt much sorrow for this and shed tears.

(Many things had happened after this and he became a Christian as well as a missionary for Northern-East Japan. He and Mr. Oshikawa who was a powerful evangelist went to Sendai to establish a Christian Church in 1881)

The missionary activities for the Northern-East part of Japan was supposed to be the most difficult where people were more conservative about the future. Actually, people stared at me with extremely hostile look on their faces. Not only booing could be heard but also many stones were thrown. However, there were a number of people who were looking for peaceful mind in their lives as neighbors and even in their family which had problems.

(omission)

I had finished the missionary activities for Northern-East of Japan where I have born and bred, then I transferred to Urawa in 1913. I continued further twelve years of ministry, I retired from these duties in 1925.

translated by Chihiro

with his own rules, later, Akira improved the rule to have a probability factor which was much close to real baseball. This game continued to be played for about 3 years until the start of the World War II

Tadayuki entered Aoyama-shihan attached primary school, Azabu middle school, and finally he went Aoyamagakuin college (for the merchant of faculty) When he was 20 years old he was enlisted in the army. He went to Sumatra where the surroundings were rather peaceful, almost no war around that area. When he came home he commented, he knew that he was the smallest one. He had a job at Daiei Movie Company Ltd. to distribute films to all movie theaters. He saved diligently so he made much money. However, the movie industry was on the decline for a decade, he changed the job to Ebara Industry Co. Ltd. and contributed to the establishment of a new company called Ebara Infilco Co., Ltd.

He married Toshiko Nakayama who was his father's best friend's daughter, from the Murakami Middle school days. They had two daughters, Mamiko and Machiko. When they were young, both daughters had very different upbringings. The eldest daughter Mamiko lived with grandmother Tadako's residence all the time and the youngest, Machiko lived with her parents. Later, this caused a very complicated situation not only in their family but also affected the whole of Tamura's family. After he retired from Ebara Infilco Co. Ltd, he had his own theme to work for that he wished to publish for long time, which was his Grandfather "Kametaro Yoshida's reminiscences" who worked as a missionary for North-East Japan.

4-2 Yoshiya



Our Parents were prohibited to drink wine and smoke at home throughout their lives. Yoshiya had broken this rule during his life in the army. Our mother abhorred his behavior and never permitted him to smoke in any room except his own room. When he started to work at Iwanami Publishing Co., his first job as an editor, was editing a book and the title was "Japanese Sake" by Prof. Sakaguchi. He started to drink Sake in large amounts because of this job. After a little while Akira also broke the rule in our family that a small amount of alcoholic drinking was accustomed on the dinner table in our family. Chihiro in every circumstance always followed these two elder brothers. Since Yoshiya worked for Prof. Sakaguchi, he experienced the culture of drinking Japanese Sake quite a lot. After all he began to bring all likeminded people together and enjoyed Sake and having a chat.

It seems our father might have had some emotional stability after he married and had his first son, Tadayuki since that he had suffered various kind of difficulties. Then he had a second son, whose name was Yoshiya, since our father felt overflowing thanks to God, as he remembered the past times bearing solitude and being led by the Bible. Yoshiya was born at Keio hospital on 3rd April 1923. As we could see in Japanese society, during Taisho roman certain modern people were able to expressed about the beginning of their own life style.

Yoshiya, similar to Tadayuki, entered Aoyama-shihan attached primary school. When Yoshiya was in second grade in primary school, there was a request box where all pupils could write to the teacher any half-secret proposal. He wrote "Teacher! Would



When Yoshiya was 4 grader of middle school, he launched a newspaper and announced that "I am going to publish this paper called 「Home News」 , please read it” . The contents were each person's states and affairs as likely that "Tadayuki has spoken about our family in school, the teacher, Mr. Tabata gave him praise". This story might be told by his mother, that she heard from Tadayuki of his matter in school. When the World War II started, the news, only came by a Journal that controlled military government, the accent was in accord with that line.

you please become a Christian?" Mr. Numata, his teacher, made a mock of him to his class mates announcing, "I will never be a Christian, A-ha-ha". This incident was the theme in his parents and teachers meeting. My mother worried about Yoshiya’s mental health, but there was no other way for it to be solved because of that time of social circumstances. Later on we got to know that Mr. Numata was deeply involved with emperor-centered activities. Yoshiya had been deeply exposed by these activities during his 6 years of primary school days.

He entered Azabu Middle school like his brother. He liked to take photos, he borrowed a Kodak camera from his father and he made a very small boxed shaped room for developing and printing photos. He also started in the spring a small green house to plant cactus which grew up in summer season but withered away in the winter season. At that time, he could not set up a heating apparatus for the green house. His most remarkable activity was a family newspaper which he published called "Katei Shimbun (Home News)" which started when he was 15 years old on the 7th of Oct 1938. It

continued until June 1948 because of suspension of publication by his span of military services. In these articles, his thoughts were included every time, however we see not only Yoshiya himself but also most Japanese young men were affected by the thoughts of militaristic promotion. He wanted to go to Yamagata High School as an old system but failed and finally he entered Keio University. However, after a short time in the University, he was enlisted in the army. He was going to be a candidate for an executive officer in 1942. This meant that he was willing to die for his nation. Here are some notes of Yoshiya's Diary which explain how complicated his life was when he started the army.

Yoshiya's Diary in army

>on 10th May 1944

Today, I feel a little feverish, before I join the army, all the days I felt like that. I had been in strong indignation at any affairs like usual young men. But, now, I knew I had lost such strong feeling of anger. I was against soldiers, I used to do that. Now, am I making a picture of self-criticism upon me? Yes, was it that I've used to be disgusted, about such things?

>date? unknown

What is it the meaning of death for Japanese people? When I used to read the writings of Katsuichiro Kamei, I felt moved in my soul which were not ordinary words but these are full of life. To the pure minded they would be motivated to be passionate through reading his writings.

>on 5th June 1945

Air raid was made on the Koroen area, then inventory of the number 8 was burned out, we as the inventory number 4 was still in a safe zone, but only destiny knows. Deep in my brain I felt heat that made me keep wide awake, however I felt a big thick gray wall facing me. I felt heaviness in my head and neck just like effect of a bad wine.

The style which he wrote in the diary was very abstract, because he was worried about the censorship of the army which usually checked about ideological and religious back grounds. His mother let him carry a New Testament which was hidden like an amulet. But earlier during his life time in the army, it was confiscated by an inspector. On the 12th of June 1945, he visited a house of relative for taking rest and say good-bye to one of his aunts, Misao, who he liked the most. Two months after this, Japan was defeated as a country.

World war II ended, he was still alive because suicide boats could not be produced in the final stages of the War. He could come back home without external wounds but his mind was completely hay-wired. He confessed what was on his mind at that time with deep groanings which he wrote on his paper "Katei Shimbun" in which a certain part will be as follows.

Katei Shimbun No..500

editor Yoshiya

I made it, Yes, I'm here, I cannot express it with the words. I was in a small shell which was protected by those consolidated systems of Japan, but I jumped into that system after deep consideration, then, I found I was changed a lot compared from before. My feelings and intellect is completely different from the past also. It seems like I was put into a smelting furnace. It was not only me, but all Japanese people might have felt the same as me.

(omission)

Where are we now? I know, we are still in a lost battle and became a defeated nation. Where are we going to go to? I've understood that I've lost the principal for living. Now, I almost gave in to love nihilism, indeed, I couldn't control the deep feelings of my soul. There is no hope, only chaos, this is reality for me. However, I could see a small light in the distance. This made me move my hands to write and produce certain sentences. This gave me comfort. Because of this it gave me a certain direction in my writing. Yes! I must start. This newspaper again and

Around his circumstances, many comrades died by the War. His painful reminiscences might be "Am I still alive? Why did you let me live? Why?". Once he was going to give his life for his Nation. His questions were like "What was a soldier meant to be? What was the reason of his passing time as a soldier?" A small light could be seen by writing of his pen which started since he was 15years old.

He succeeded with an entrance examination of Iwanami Publishing Co. Ltd. Our father was deeply gratified with the result because to work at Publishing company was his dream when he was a young man. Yoshiya worked to publish of "Iwanami Shinsho" (pocket size books) as an editor from 1956 to 1971 and the number of books attempted was 43.

A first big work of Yoshiya was to publish a book titled "Sake of Japan" by Kinichiro Sakaguchi, who was famous person who received the Cultural Medal of Japan. In the beginning, Yoshiya was given curt treatments from Sakaguchi because he interrupted his researcher's activity. However, after he published his book, Sakaguchi

changed his behavior and became very friendly to Yoshiya. It could be said that Yoshiya forced Dr. Sakaguchi this famous biological researcher into the cultural world of Japan.

After quarter century in his company, he became an editor of "Bungaku (magazine in Literature)", and "Sekai (magazine in the World)". His life work as an editor with a journalistic manner and the position to stand and fight for the down trodden. A big incident happened was that Mr. Mishima who was a Nobel-prize winner, committed suicide at the building of Japan Self-Defense Forces in 1970. Yoshiya was determined as the top editor of Iwanami Publishing Co. to stay out of this topic. He did not want it to be a big topic at that time. Since it could form into commercial base a social movement. Before he announced it, he asked his boss' approval of in case of disagreement he carried a letter of resignation. The president wholeheartedly followed Yoshiya's decision.

He published a book titled "No no Ji Monogatari (the story of "No" which English refers to "of"). An essay was written about his soul and the life as an editor and his idea of designing forms to advocate our society.



A part of his messages will be described which would come out by his professional style. The activity of editing starts from planning, getting a manuscript, proofreading and book binding with a conspicuously fitted design. At the beginning stages, when you see the books then you can find the intention and/or intelligence of the authors and they should not be diminished at all. Letters and words are used as mediators for people to understand. As a designer of book binding, I know that to fit the "title" on the top cover is the most important part of the work. Through these jobs,

these things used to weigh on my mind which are about the letter/word "の=no", in English, "of". This is because there are many book titles using the letter/word "no" such as, "watashi no naka no---" in English, "inside of my---", "kono jidai No naka no", in English, "inside of this span of life" and "Nihon no ---" in English, "Japanese ---". When we use the letter "no" we have various styles of handwriting with historical backgrounds even just a single stroke of the pen. Therefore, I am pleased with constructing such unique letters which fit from the mind of the author but usually it is needed to be modified by the mode of style of the letter.

Yoshiya retired from Iwanami publishing Co. A several months later he started to work for book binding of a designing cover.



1) Shotaro Yasuoka was a famous essayist, the title is “Kansei No Kokkaku”, means

“A skeletal Frame work of Sensitiveness” : His writing is full of humor and easy to read. Yoshiya commented that “Here, I use deformed drawing letters which I knew Mr. Yasuoka will accept my sensitivity in this special case but drawing letters cannot be used much before knowing the author’s character or background of their lives”. Yasuoka was 3 years older than Yoshiya and experienced a very close soldier’s life that they may link with each other in their certain deep feelings. They had a good relationship till the end. Yoshiya made 36 book covers which were half of Yasuoka’s productions.

2) Hyakken Uchida was also a famous novelist and essayist, the title is “Yoake No Inazuma” means “Flash of Lightning in the Dawn” : He published it in 1969 which was his final stage of his life. On the book cover, was an abstract drawing pattern of the flash of lightning. Uchida was born in 1889, he was just the same age as our father Kotaro, that why Yoshiya might had some respect towards him. Yoshiya designed 66 book covers for him

3) Minpei Matsuura wrote the title “Bora No Koushou”, which means “A Loud laugh from the Strip mullet” : Yoshiya surmised that reading public thoughts would be difficult to understand the intention of the author by seeing the letters of this title. He asked the editor to bring a drawing of the strip mullet to present the supposition of the author. Slightly upward stroke of the letters was deliberately made which gave the sense of making you laugh.

4) Sekihan Kim was Korean essayist born in Osaka in 1925, the title is “U No Shi”, which means “The Death of a Cormorant”: “U” and the “Shi” these both characters exposed a very strong message to the audience, how to arrange and insert between them soft Japanese character of “No”.

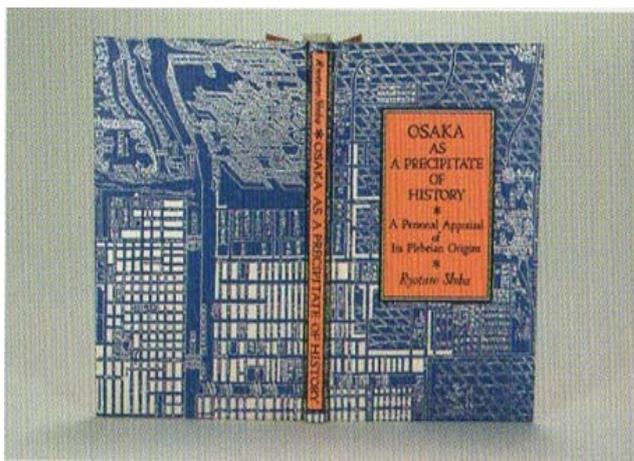
Yoshiya tried to express “*の*” like a bird-bill because of the tragic and dreadful story which was expressed in this book.

5) Minako Oba was a female novelist and essayist, who wrote the title “Kiri No Tabi” which means “a Journey in the Fog” : Yoshiya was satisfied with the letter “*の*” here for Oba in an intrinsic motivation of this book. The figure of this letter might cause Japanese to see the female character.

6) A Japanese report writer and Journalist who wrote the book the title was “Nihon No Heiki-Kojo” which means “the Weapon-Factories of Japan”: Yoshiya tried to show some heinous mind-sets on the book cover that the author wanted to introduce the problem between the government and enterprises or corporations under the Japanese peace constitution. The letter “*の*” was changed when he tried to make it in the above sense, thus all letters were deformed to give the Evil message.

7) Shunsuke Tsurumi was a critical, political activist and philosopher that he was a deep man, the title is “Watashi No Chiheisen No Ueni” which means “Above My Horizon” the editor made a comment to Yoshiya that Mr. Tsurumi said to the editor “Don’t be in hurry to finish for Mr. Tamura, so then he will be sure to give a good quality cover”. From the image of Tsurumi, Yoshiya put an idea of art Déco or like lyricism. After he met the elder sister of Mr. Tsurumi, she said “Thanks a lot for your job for my younger brother, you made him a very cute book---”.

8) Ryotaro Shiba was famous author in Japan who as a person wrote about historical events and cultural essays. The



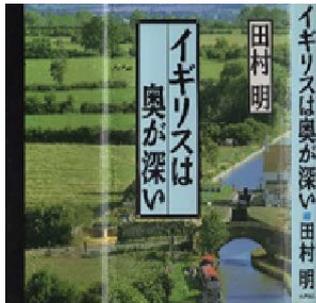
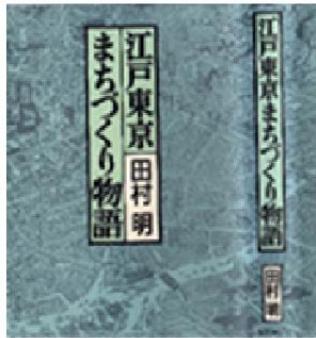
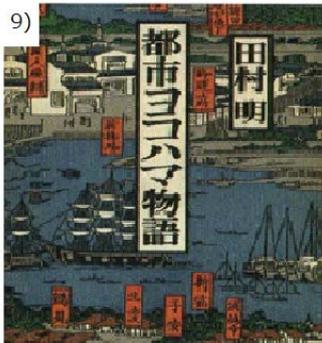
book was translated into English, but not-for-sale only as gift books important foreigners visiting Osaka city in 1987. A sub title of “A Personal Appraisal of Its Plebeian Origins”. Shiba wrote in the preliminary session, contrast between the soil of Tokyo and the soil of Osaka which was cleverly conceived. He experienced that when he ate eggplants in Tokyo, it

8) had not good taste at all. This incident recognized him as Osaka born. The reason why it had no taste of egg plant was because the soil of Tokyo area consisted of volcanic ash from Mt. Fuji and/or Mt. Asama. Therefore, constituents of the soil were simple and not nutritious. Through this observation by Shiba, Yoshiya was brought back to the past and called “red soil! red soil!” when he was young and played around in the field.

9) Representative writings of Akira with Yoshiya’s binding were following four.

“Toshi Yokohama Monogatari”, meant “The story of City Yokohama”, “Edo Tokyo Machizukuri Monogatari” means “The story of Edo-Tokyo Town Making”, “Igirisu wa Yutakanari” means “Britain is Really Rich (To Enrich Society)” and “Igirisu wa Okugafukai” meant “Britain has a deep interiorly”. These double twin books were conspicuous in designing that have a gentle nature fitted to Akira’s daily attitude.

When Yoshiya passed away in 2003, Akira was deeply regret to say “I really wanted to write books more by Yoshiya’s bookbinding”



Yoshiya married Kumiko Oshima in 1967 and had two boys named Yoshitami and Michiya. Kumiko loved and respected exceedingly her mother-in-law, Tadako, that she lived within her residence one year to understand and to learn the manner of her mother-in-law. We, Akira and Chihiro, talked about Kumiko that she is a wonderful sister-in-law for our mother as she tried to know about our mother. After they married, Yoshiya gradually opened his mind to all our family

and became more talkative to us. There was an episode that since she was a pianist, piano lesson was very hard. One day, our mother felt the lesson was little noisy, she said “I never imagined that a piano can be noisy sometimes”.

4-3 Chihiro (Author, describe as a third person)



Chihiro was two years old. His mother wanted to have a girl, she made her own pink baby clothes. At that time, all western baby clothes were imported and very expensive.

4-3-1 His Childhood

Chihiro was born at the Red-Cross hospital Shibuya in 11th July 1930. Our parents expected a girl since they had three boys before, so the name “Chihiro” was ready for either a boy or a girl. At the beginning of the Japanese-Chinese War in 1937, he had to enter the usual town public school. When he was in fifth grade of primary school, World War II had begun. He entered Aoyamagakuin middle school. All students worked to make certain weapons for the military, he worked as a lathe operator on special stainless steel for making test pieces. His ability as a lathe operator was high that his boss recommended him to become an engineer in the future.

We never forgot about the Great Tokyo Air Raids that a number of people and several of his friends at

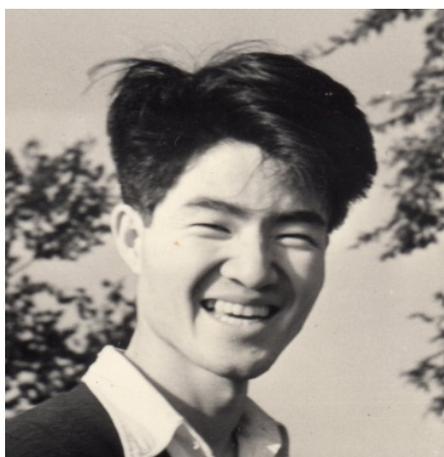


When he lived in Aoyama, he suffered from a dysentery. There was no medicine for this illness at that time, he was in a serious situation. His mother was also infected, both were hospitalized for two weeks

school were killed. Most of down town Tokyo was burnt down see on page 11. Furthermore, the atomic bombing of Hiroshima and Nagasaki, no one could imagine how gruesome was the landscape. In 1945, 15th August the War ended. After that there was not only no more fear of bombing but also no obligation to do military service. From that moment, people could sleep well with the peaceful mind.

However, due to the end of the war starvation was at its worst. Chihiro was 15 years old, at the time, he felt that anything was edible, to put in his mouth to fill his stomach. These were frogs, snails, and wild grass, etc.

4-3-2 His Life as a Student



Chihiro entered Tokyo Metropolitan University at the age of 19. He grew to 177cm in height and was the tallest young man among all the relatives. It was unusual because he grew up during the starvation time.

He decided to choose to study in the field of organic chemistry which seemed over all to have wide range possibilities in the future. It was a remarkable experience, that even through the chemical experiment he understood the molecules were tangible and one can change their structures to any direction with synthetic techniques.

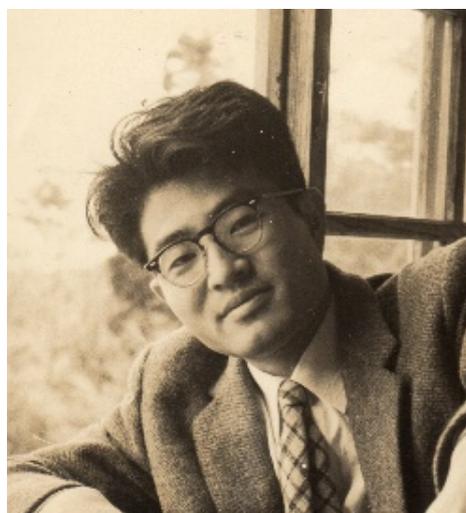
His two elder brothers were a little different from younger ones, they could make small money to eat by getting a job. Even though, it was remarkable that during the World-War II and afterwards, in this food crises no one died from our family and relatives. There was news going around that an authorized judge, Mr. Yoshitada Yamaguchi, died of starvation, because he never had an illegal rice supply, and was faithful in his job as a judge.

The most painful situation for our father was he lost his job after the War. He desperately searched for a job in Tokyo, and found it at the Civil Censorship Detachment in GHQ. Our father said to Chihiro “Where there is a will, there is a way” which was the first English proverb that he knew. However, later, this activity has been criticized by several people and organizations even though the USA was the winner of the war. The action of censorship should be allowed due to the freedom of speech has been unenthusiastic about democratic nations.

Chihiro knew the situation the economy of our

family was very tight, our parents barely managed to have one meal a day. He wanted to work in society as soon as he graduated Middle School. at his father admonished him “You should further your studies in a certain college, since society from now, might not accept you at this stage of your ability”. He obeyed his father’s suggestion and he entered Tokyo Municipal College to study engineering. Two years later, his father had been reinstated to his former position at the Company of NCR. His father asked Chihiro, “If you want to study more, you would better to go to a certain University”. During his study in college, he wanted to learn more about the nature in the field of chemistry. He took the entrance examination and passed and he was admitted to Tokyo Metropolitan University Faculty of Science and the field of Chemistry. He started his University life under a new mixed genders school system. Before the World-War II the government forbade this system because of an idea of Confucianism. He had never experienced female companionship around him because he had no sisters and no occasion to have fun with girls in his past life. He was expected something to happen, however, it was difficult to talk with girls when the situation arose. Society calmed down and was peaceful and the food situation rapidly improved in 1953. One of his hobbies was playing piano which he started at fourth grade in primary school his Uncle Nobu who studied at Julliard school was his teacher. But, because of World-War II, all such pleasure stopped. After three years of the War, he wanted to start again to practice piano with Uncle Nobu. It was however, one year later again he felt the urge to quit because of experiments in chemistry study needed more time. He regretted to quit the piano lesson again.

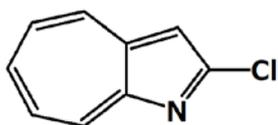
4-3-3 His life as a researcher in the beginning and Marriage



Around the time of 1957, he entered Laboratory of Sankyo Co. Director Mr. Soshun Matsui expressed to all researchers "Please study chemistry, and more biology, and biologists' study more medical science. Since we did not have any medical scientists at that time. This was urgent requirement in our laboratory. He realized that medicinal chemistry was part of studying biochemistry. Chihiro gradually made progress to learn more about the state of biological science. His target gradually changed to study the subject of life science and how the chemical structure were concerned with it.

In 1955, ten years after World War II, Chihiro graduated from University. He entered Nikken Chemistry Co. and he was in charge of a chemical testing Section. However, a few

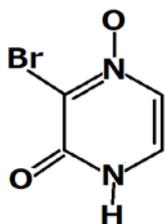
months later, the company lost the dispute concern of the patent and started to be in a slump in business. He could get a position of Research Laboratory of Sankyo Pharmaceutical Company with an introduction of his father. Mr. Matsui who was the director of the research laboratory gave him the condition which was to study and get the technique of X-ray crystallographic analysis. He became a member of Prof. Nitta's laboratory in Osaka University as a research student. Dr. Sasada undertook the guidance of the X-ray crystallography for Chihiro. He said "I will give you one crystal, chloro-aza-azulene if you could solve its crystal structure with me, then you may find



Chloro-aza-azulene: The chemical structure was already known. The main purpose of this work was to understand the diffraction of X-ray and how can we solve the crystal structure.

easy to challenge the next one". It took about one year to solve that crystal successfully and Dr. Sasada praised Chihiro "no one got success in one-year of study, but you did it, please you keep this technique for further studies when you go back home". However, he felt this technique may be restricted for solving the structure of general organic compounds, because of that too many calculations would be needed to do by hand. After he returned to his laboratory of Sankyo Co., his boss gave him a theme which was "To find some relation between organic compounds and X-ray diffraction patterns". But Chihiro could see ahead that

those two factors may not have any relation so called as organic functions and he showed it to him through experiments. The next theme from the boss was to find the cause of Chloramphenicol-palmitate, an antibiotic substance, which after certain time span it was observed and changed into scaly phenomenon from dry syrup. If it occurred, the medicinal activity was considerably weakened. He could find the cause of this phenomenon was due to the polymorphism of Chloramphenicol-palmitate. Through these two experiments, he could find some interesting phenomena about the crystallization processes in organic compounds. And furthermore, about the interaction mechanisms between more than two compounds.



In all laboratories of Japanese pharmaceutical companies, bromoemimycin became the first trial to determine a chemical structure of natural substance by X-ray crystallographic analysis. The structure was very simple but at this time, an elemental analysis was the basic instrument to determine a chemical structure. And there was a few other analytical instruments available such as *infrared* and ultra violet spectrums. But, these instruments was limited to give definite structural information.

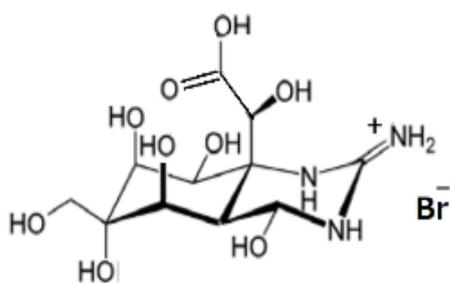
Chihiro was anxious about his technique which he learned from Dr. Sasada that there was nothing to use or to refrain of it. He got to know by chance that Mr. Terao, another

research group member, had encountered a difficulty on solving the structure of antibiotics, emimycin. He was dealing with this chemical substance for about four years but could not see the future of it. When Chihiro asked precisely about this substance, it seemed suitable for X-ray analysis. As far as until that time, there was no computing system like today, he had to work everything with his brain and a slide rule for in his studies. Two months later, the structure of emimycin could be solved with reasonable chemical characters. This result impressed researchers in our laboratories that a new period of scientific approach for the future was started.

Chihiro got married with Yoshiko Nagaki who worked as a private secretary of Prof. Nitta in Osaka University. As he attended the non-church Bible meeting promoted by Prof. Yanaihara who was the President of Tokyo University, Chihi asked him to preside for their wedding. Prof. Yanaihara gave a requirement to Yoshiko which was "To read the Bible and send letters to me every month how you could become a believer in God". She sent letters every month and a half year later, Prof. Yanaihara gave her permission to marry Chihiro. However, just after the marriage was permitted, she was found to have pulmonary tuberculosis, which was a big ordeal for this marriage. She needed to recover from this illness for a period of year. Prof. Yanaihara held a wedding ceremony for them and it was the same year that Akira and Makiko got married. Regretfully our father died next year but he knew we were expecting a baby and he left a name for our first son, "Hiroshi"

4-3-3 Puffer Fish-Toxin, Tetrodotoxin

From prehistoric times, Japanese people ate pufferfish in spite of a big danger of its toxic substances. Research for this toxin started around the end of the 18th century. Dr. Tahara extracted powder from the organs of a pufferfish, which 4.1 micro-gram had killed a mouse and the toxin was named Tetrodotoxin.

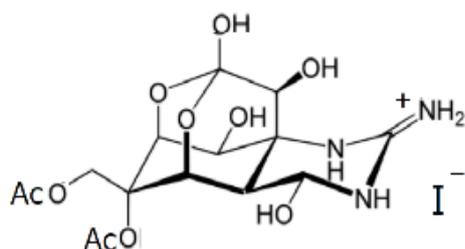


The structure of Tetrodonic acid Crystal structure was solved using IBM-7090 electronic computer with a first trial of three-dimensional data collection. All programs were written by Fortran, a programming language. The processes were the battle against time, a fault in programming was serious which no one could help it.

His idea was proposed to Sankyo Co. to use as medicine for neuralgic diseases like gout and Sankyo sold it for this specific disease in early 1930s. Unfortunately, all research activities were stopped during period of World War II. In early 1950s, Mr. Kawamura started purification of the toxin and also directed to solve chemical structures. One success was that producing quinazoline derivatives from alkaline degradation product from

tetrodotoxin which was succeeded by old synthetic approaches. However, at that time, this substance was severely difficult to solve, with a knowledge of chemical methods. After further studies they couldn't find clues to reveal the structure. On the other hand, as competitors to us, Prof. Hirata and his colleagues of Nagoya University started to study a structure determination of this toxin. He was a famous Japanese chemist of natural products. Afterwards Chihiro succeeded to solve the structure of emimycin, Mr. Matsui the director gave an order to him to collaborate with the tetrodotoxin study group.

There was an announcement, which was "International Symposium of the Chemistry of Natural Products would be held in Kyoto in 1964". This was the first occasion in Japan, where a big conference was held regarding the chemical research activity. All Japanese chemists were excited to attend this Symposium especially researchers who wanted to have an opportunity to speak at the World Conference. In that situation, Dr. Sasada told Chihiro astonishing news which was that Prof. Hirata asked to have Prof. Nitta's reinforcement in the X-ray analysis. He had to compete against a top leader of X-ray chemists whom he had studied under, four years ago. Furthermore, Prof. Woodward of Harvard University entered this race. He was also a very famous chemist in the field of natural products and he won the Nobel prize in Chemistry Laurence two years later. Good news was that IBM started to open IBM7090 electronic computing system for city market users. Chihiro thought "As we have a computer now, this is the time for X-ray analysis to be applied to the chemistry world".



Tetrodotoxin-diacetate by means of X-ray crystal structure analysis. The final structure was that the one which Hirata's proposed as in a low possibility. Regrettably, in our group it did not include this structure. During the process of time, a fault in programming was serious where no one could help it.

It was difficult to obtain a good crystal of tetrodotoxin itself. Mr. Kawamura supplied a crystal named tetrodonic acid which was treated with diluted hydrochloric acid to tetrodotoxin. Chihiro started to study the development of the electronic language of "Fortran" which was the usage rule for electronic computing system. There was no soft-ware in the market, people needed to make all programs for certain purposes, also people who worked with computers such as IBM workers had little knowledge about this language. It took about 9 months to elucidate the crystal structure. However, the solution of this compound was not sufficient to give a definite final structure of

tetrodotoxin itself. The reason was when treating acid with tetrodotoxin, a migration reaction would take place. Therefore, three or four proposal structures were submitted with uncertainty.

Mr. Kawamura had made another derivative of tetrodotoxin acetate which was treated with acetic acid to tetrodotoxin, this substance had a little toxicity which was thought to be in a close resemblance to the structure of tetrodotoxin as the main part. We only had a half year left till the Conference. Chihiro conducted himself at all times with power and concentration, however, he met several unexpected matters at work. Paying for a pile of white sheets of papers by the missing programming, even though a cost of computing for one minute was almost equal to his monthly salary. He got tired at work and sometimes slept on a commuter train till the last stop, because of this, there was no train to come back.

Chihiro had made the process of atoms connected to the space of Fourier synthesis. Some atoms were considerably crowded at a certain space, which seemed to be very unusual. He was anxious about any existing mistakes in the programming. However, there was no fault, he verified the structure through chemical knowledge. Yes, he got the final answer of tetrodotoxin at that time, it was definitely a determined effort. The structure of tetrodotoxin-diacetate was found in the middle of February, which was 40 days before the conference. The ortho-acid structure of tetrodotoxin was the first observed in nature and its basic skeleton would be a diamond if it was made from all carbon atoms.

At the conference in Kyoto, in April, three groups for tetrodotoxin structure researchers gave the same structure as in the figure in which two Ac(acetyl) groups exchanged to hydrogen atoms. In the conference, there was a remarkable presentation regarding this toxin. Prof. Mosher reported that *Tarica torosa* in California had the same toxin which meant that this toxin was not only in pufferfish.

Thereafter, the investigation for tetrodotoxin in nature was remarkably developed. It was investigated that toxin produced by microbes of *Vibrio alginolyticus* and through certain food chain systems of marine life accumulated to pufferfish. The reason of this toxin accumulated especially in ovaries was when eggs came out to the outside world, they would be protected from predators in the sea. However, it is still difficult to explain how those microbes found in the toxin and inserted into the DNA system. Three Professors Nitta, Hirata and Tsuda were awarded prize from Asahi newspaper company but no attention to Sankyo Research members. Chihiro saw the power in the academics of this country through this evidence.

4-3-3 Post doctorate Life in University of Illinois

Chihiro made his application to Prof. G.A.Sim in Illinois University as his post-doctorate study. He wanted to study the technique of further computer programming in the computer developing country of USA. From 1965 Prof Sim accepted his proposal for two years when Japan had shown barely signs of revival. Ratification has been made by the personnel section in the Laboratory. As there was no Jet only propeller air plane, it took about 8 hours to Hawaii. He saw and felt the island of Hawaii from the sky, where beautiful green grass and red roofing tiles were dotted like seeing a fairy-tale even in the winter season. He had pleasing time talking with his relatives while he visited Hawaii and Los-Angeles for a few-days.

It was snowy and ice cold in Chicago in that winter. A dramatic change from tropical Hawaii and Los-Angeles was not only due to his mental state that carrying young family and also holding communication with American people with using his limited English skill at that time. The O'Hare airport was a transit for Champaign-Urbana, because of its size it was difficult to find the correct port terminal, just in time they got the last small air plane which flew to the final towns. It was snowing and very cold and temperature was below 0 ° F even though they were welcomed by several chemistry members.

The theme, which Prof. Sim gave Chihiro was natural product of Lunarine, he got as a result in a few months. Because of the conformational interest in the structure the Next theme was a synthetic cyclic compound. He assured that the X-ray analysis would become a common tool for fields of chemical and biological in wider subjects. Using the Computing facility of the University went very well using IBM 7090 and its fee was low for University rates. Chihiro could make programs to enable applications and he experienced various trials regarding logics. His monthly salary was \$750 which was not bad as usual Post doctorate. He bought a car, Ford Galaxy 1962 model, apart from studying in University he enjoyed driving in such a big continent.

One day, Prof. Sim talked to Chihiro, "I will return to UK in August, I have stayed here two years, my wife and I were bored about seeing these huge corn fields apart from city cultures, I'm going to the University of Sussex, if you want, you can work with me there". Chihiro decided to stay in Illinois about three months for remaining arrangements.

4-3-4 Chemical Structure and its biological significance

4-3-4-1 Hydrogen bonding study

In 1962, the Nobel committee announced that the two molecular level works by using X-ray techniques were awarded the Nobel Prize. Since those days, we understood that peptide, DNA and all biological materials were known as visible substances in atomic or molecular levels. The interaction of living cells and/or tissues are complicated, but if we see them as molecules, the hydrogen bonding would be one of the most important phenomena. He was interested in those of molecular level interactions and add more examples in this field of study. He tried about 100 compounds whether these compounds would be formed as molecular complexes with each of cytosine, adenine and thymine as simple nucleotide bases. He found that a functional group of carboxylic acid was important to make complex crystals with cytosine and adenine. Through these series of experiments, he found certain suggestive facts regarding to cleavages and/or reconstructions in the helix of the DNA molecules. Three complexes will be shown which are cytosine \leftrightarrow resorcilic acid, adenine \leftrightarrow bromobenzoic acid and cytosine \leftrightarrow uracil. The fact that a proton atom of carboxy group acts as a sensitive mediator between two molecules to form complexes. The proton moves to nucleotide base forming plus nucleotide⁻ and minus acid⁻ ionic structures, which resulted in electromagnetic attracting force to stabilize both molecules. At that time, showing biophysical interest about the processes of the peptide synthesis, there should have been some intermolecular interaction between amino-acids and DNA molecules. However, with the bases of nucleotide never form complex with amino-acids. He supposed that due to the carboxyl group in amino-acid, which formed self zwitter-ion form of amino-acid structure, then he tried acylated amino-acid with those bases of nucleotide. The most of acylated amino-acids were interacted to form complexes. The mechanism of the nucleic acid and peptide in nature was exquisite phenomena. From this observation, he assumed that in the initiating process of the peptide synthesis, acylated amino-acid would be important step for this reaction and the most of a biggest sized enzyme known to be started from acyl-methionine.

4-3-4-2 Natural products

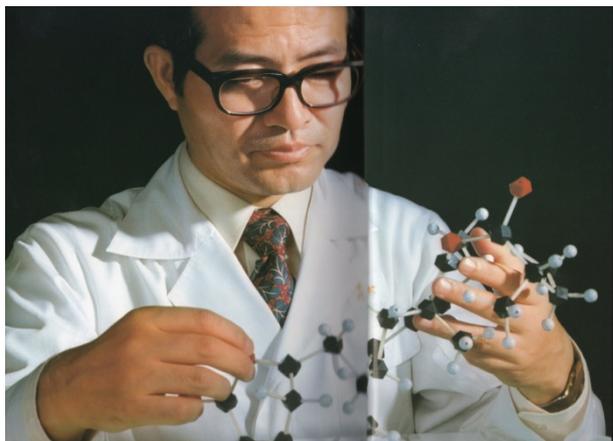
Since he had been an X-ray chemist, more than 20 natural compounds had succeeded to solve their structures. In the early stage, it was needed to have huge amount of collecting measurement and calculation time but it was all together boring. The end of 1970s, computer facilities were considerably developed, and an automated X-ray data collection machine appeared in the market. Also, each organization was able to have its own big computer system to handle data. Furthermore, the direct

phase solving system of MULTAN, developed by H. Hauptman,⁷⁾ was unique and powerful. Since this time, one who had a single crystal of a natural product, it would be able to solve its structure without chemical knowledge.

In such circumstances, there was a higher possibility of developing for hyperlipidemia which was upstream in early 1970s. One of Chihiro's colleagues Dr. Endo, asked about structure determination of a compound, ML-236, which was active to reduce cholesterol and homo-cysteine level in experimental animals. The MULTAN program was just launched in time to be able to be in use it became the first trial for a natural compound to attack its structure determination. Surprisingly, in a few weeks from the beginning, this structure was visible in sight. However, during the trial of the long-term of this compound, there would show a higher list of carcinogenesis, shown as a medicine, there was a big story covering of the development of this compound. After that, it became a long story to develop a safe level medicine took about a quarter century. The long-term toxicity trials of this compound showed a higher list of carcinogenesis which meant this substance would not be utilized as medicine. The top of research Headquarters was considerably disappointed, since this was a big loss of time and money. However, Nishigaki continued to study about metabolic substances of ML-236B because he wanted to obtain a title of Ph.D studying with this theme. By chance, he found a more active substance in urine of a dog which would be a metabolite of ML-236B. All laboratory members again restarted for this particular strong metabolite that how its structure was changed to more active one. This work was proceeded by NMR and MASS chemical instruments and made it in a few months. In order to develop this small amount of metabolite to be a medicine, there was a question, how to produce a large amount of it for animal experiments. This had been succeeded by action of microorganisms which could be found in Australian soil. After clearing this problem, development process had made it steady. Including phase-3 investigative treatment, and a candidate (drop testing candating) through this all members were successful. In 2004, Sankyo sold ¥200 billion a year by this medicine.

4-3-4 Chemical Structure and its biological significance

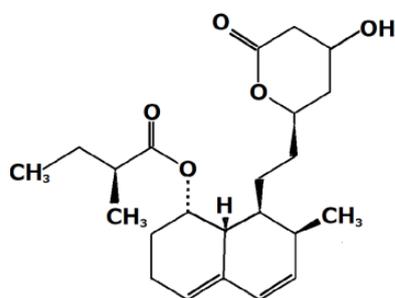
4-3-4-1 Natural products



He likes to handle with a molecular model, this is ML-236-B. Amazing that handling with model, we can image just as in minimal world which might connect to this real visible world.

Since he had been an X-ray chemist, more than 20 natural compounds had succeeded to solve their structures. In the early stage, it was needed to have huge amounts of collecting measurement and calculation time but it was totally boring. The end of 1970s, computer facilities were considerably developed, and automated X-ray data collection machines appeared in the market. Also, each organization was able to have its own big computer system to handle data. Furthermore, the direct phase solving system of MULTAN, developed by H.Hauptman,⁷⁾ was unique and powerful. Since this time, one who had a single crystal from a natural product, would be able to solve its structure without chemical knowledge.

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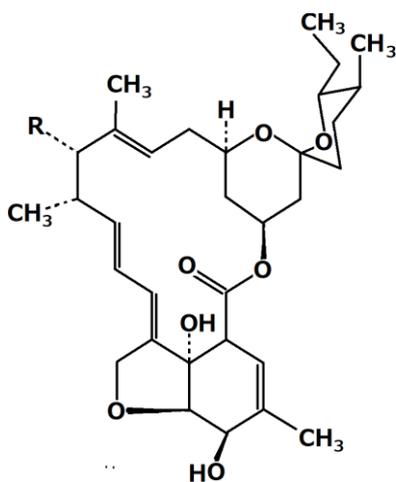


ML236B was produced in the course of biochemical screening to discover inhibitor of cholesterol synthesis.

An Independent research group isolated from the culture broth of *P. brevicompacum* as an antibiotic named compactin.

A.Endo, asked about possibility of structure determination for a compound, ML-236, which was active to reduce cholesterol and homo-cysteine level in experimental animals. The MULTAN program was just launched in time for use and it became the first trial for a natural compound to attack its structure determination. Surprisingly, in a few weeks from the beginning, this structure was visible in sight. However, in the long-term trial of this compound, there would show a higher list of carcinogenesis, shown as a medicine, there was a big story concerning the development of this compound. After that, this became a long story to develop a safe level medicine took about a quarter century. The long-term toxicity trials of this compound showed a higher list of

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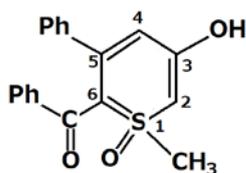


Milbemycin was originally produced in laboratory of Hokkai-Sankyo Co.

of research headquarters was disappointed considerably, since this was a big loss of time and money. However, Mr. Nishigaki continued to study about metabolic substances of ML-236B because he wanted to have a Ph.D title studying with this theme. He found by chance a more active substance in the urine of a dog which would be a metabolite of ML-236B. All laboratory members again started to have this particular strong metabolite that its structure was changed to more active one. This work was proceeded by NMR and MASS chemical instruments and made it in a few months. In order to develop this small amount of metabolite to be a medicine, it was necessary to produce a large amount of it for animal experiments. This had been succeeded by action of microorganisms which was found in Australian soil. After this problem was cleared, development process was made steady. Including phase-3 investigative treatment, and candidates to be tested upon with drugs through this all members were successful. In 2004, Sankyo was able to sell this medicine for ¥200 billion.

Metabolites, produced by *Streptomyces* B41-146 strain, were a mixture of macrolides, designated as Milbemycin which exhibited a remarkable pesticidal activity against mites, such as two-spotted spider mites and citrus red mites, and insects such as rice leaf beetles and tent caterpillars, without any phytotoxicity towards many varieties of crops at effective dosages. A good crystal was obtained as a reactional product of p-bromo- phenylisocyanate. Including two other products, Milbemycin, which was performed to determine the structure of these compounds with his colleague called Mr. S. Sato. However, an unfair management division had a control on sending a Presidential prize to the other person Mr. M. The Nobel Prize in Physiology or Medicine in 2015 was divided, equally in two halves to William C. Campbell and Satoshi Ōmura "for their discoveries concerning a high-level therapy against infections caused by roundworm parasites". Discovered work of professor. Omurawas very close to Milbemycin which the function of R was a kind of bounded sugar group. Because of that, his path to work for structure determination, he walked in close proximity to the person who shared the Nobel Prize.

4-3-4-2 Compounds containing Sulfur



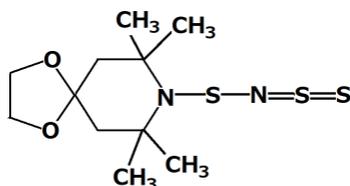
Many Organic chemists were interested in thiabenzene which was a sulfur atom included in the six membered ring system.

When Chihiro returned to Japan in 1966, the method of the heavy atom was only the way for the X-ray crystal structure determination. He expected the sulfur atom could be used for a heavy atom because there were many biological and medicinal substances which had sulfur atom in it. Many organic chemists also paid attention to sulfur containing compounds for medicinal chemistry. At that time, a few numbers of bond distances and angles regarding to sulfurs were reported. Therefore, studying sulfur atoms seemed to be a good theme to him at that time. Furthermore, in organic chemistry, synthetic techniques were considerably developed and many

interesting and rare compounds came out.

Dr. Junya Ide made a thiabenzene which had sulfur and contained a semi benzenoid structure. The question had arisen whether the sulfur containing six membered ring systems could be as plain like benzene or not. The sulfur atom deviated about 0.6 \AA from the least-square plane which consisted of rest of five carbon atoms. The length of carbon atoms in this ring system varied from 1.33 to 1.42 \AA which was close to a benzenoid character but deviations of the length were remarkably large. These facts showed that thiabenzene is not a benzenoid group. The sulfur was found to be a good marker for heavy atom method.

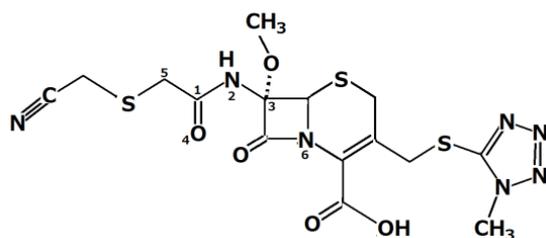
Dr. Takao Yoshioka synthesized 7,7,9,9-Tetra-methyl-8-thiosulphinyl-amino-thio-1,4-dioxa-8-azaspiro [4,5]decane. The bond system of $-\text{S}-\text{N}=\text{S}=\text{S}$ was new in the world and the X-ray



7,7,9,9-Tetramethyl-8-thiosulphinyl-amino-thio-1,4-dioxa-8-azaspiro[4,5] decane. A few numbers of atomic dimensions of sulfur were reported at that time.

technique was only the way to reveal its structure. The obtained S=S bond length of 1.912 \AA was shorter than known S-S bond of 2 \AA but difference is not so large since in the case of C=C and C-C which are 1.54 \AA and 1.34 \AA . This might be due to the flexibility of the movement of d-orbital electrons.

As for a medicinal world, sulfur was also worthwhile for antimicrobial and diuretic drugs especially before the antibiotic's era. Antibiotics especially penicillin and/or cephalosporin included a sulfur atom and those semi synthetic products were produced in Japanese pharmaceutical companies.



In the battle against bacteria, we were faced against drug resistant strains of bacteria. Some of the pharmaceutical companies which were on the stage of competitiveness to have priority of its own activity. There was a certain design of medicine to get more active compounds to find. However, most of the case, organic chemist continued experiments by trial and error method without any logical reasons.

being a $\overset{\ominus}{\text{O}}=\overset{\oplus}{\text{N}}\text{H}$ ion-oriented structure. This large contribution of the dipole structure may be due to the functional group of $\text{N}\equiv\text{C}-\text{CH}_2\text{S}-\text{CH}_2-$ in the left side of the molecule, but not the central $\text{CH}_3\text{O}-$. Such large dipole structure may act for large sterilization. Another characteristic of this molecule is observed at the functional group of thiotetrazole moiety in the right side of the molecule. He discussed about the N(6) atom relating to the structure of carbapenem. In the future, medicinal chemistry would be designed by atomic level construction or bond formation in highly sophisticated manner.

4-3-4-1 Study of complex formation between nucleotide bases and organic compounds

Figure GC

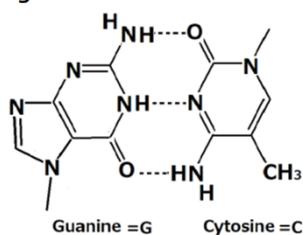
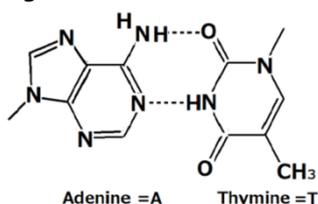


Figure AT



These figures were not result of Chihiro's achievement however, the model of DNA hydrogen bond system which was reported by Watson and Crick inspired him a lot. A short story of this Nobel Prize work is as follows: The amount molecules in DNA, A equal to T and C equal to G were realized by Shargaff. Watson and Crick's work were combined with the work of X-ray crystallography by R. Franklin and M. Wilkins, which derived the three-dimensional double-helical model as the structure of DNA

Dr. Hideo Nakao developed Cefmetazole in the market which was one of the most active cephalosporine derivative at that time. The bond distance of $\text{C}(1)-\text{O}(4)=1.27\text{\AA}$ is comparatively long instead that of $\text{C}(1)-\text{N}(2)=1.319\text{\AA}$ is short. Also the bond angles of $\text{C}(3)-\text{N}(2)-\text{C}(1)=124.1^\circ$ is comparatively large but $\text{N}(2)-\text{C}(1)-\text{C}(5)=121.1^\circ$. These facts indicated that this molecule has a strong tendency of dipole system as

Using X-ray techniques, one Nobel prize for Chemistry and one for Physiology or medicine were awarded in 1962. The first one was awarded to Kendrew and Perutz who successfully analyzed the X-ray crystal structure determination of Myoglobin and Hemoglobin. The second was awarded to Watson and Crick who submitted the structure of DNA which was done by a very carefully built up

model. About a half century ago, the messages of these prizes were presented so, now

we could see the molecular level interactions in biological significances. At that time, biology was going to be explained by the field of chemistry.

	p-amino benzoic acid	p-amino benzoic acid	p-amino benzoic acid
Adenine	+	+	+
Cytosine	-	-	-
	iso-nicotinic acid	nicotinic acid	picolic acid
Adenine	-	+	+
Cytosine	+	+	+

Complex formation ability for adenine and cytosine with compounds containing carboxylic acid and nitrogen gave unique behaviors. Three types of aminobenzoic acid did not form complex with cytosine but formed with adenine. Instead, carboxylic pyridine with cytosine or adenine except iso-nicotinic acid.

observed with uracil. The topics of this experiment was a six-membered ring system with a nitrogen atom. Adenine was formed with all amino-benzoic acid, but cytosine was not. However, iso-nicotinic-, nicotinic-, picolic acids formed a complex with cytosine and adenine, except picolic acid with adenine as shown in this diagram.

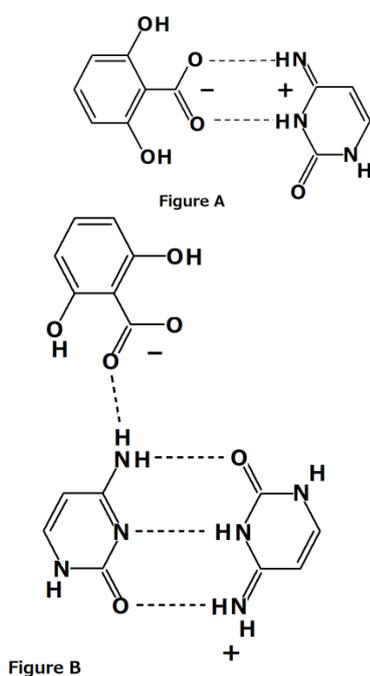


Figure A shows a complex between resorcillic acid and cytosine. The portions of the two pairs carboxylic acid in resorcillic acid and amidine in cytosine are important to form complex crystals. This is a standard hydrogen bond style which a proton at resorcillic acid moved to cytosine to form a stable ionic structure.

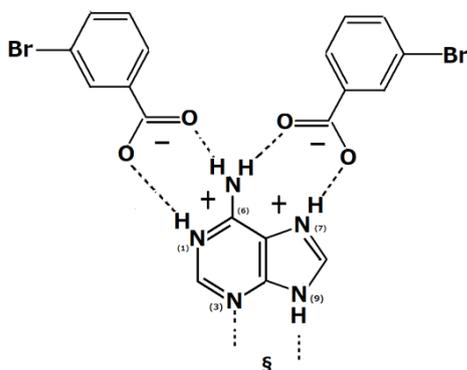
Figure B shows a complex of two cytosine molecules bound to make triple hydrogen bonds which is very similar to hydrogen bond relations between guanosine and cytosine.

Chihiro was interested in the molecular interaction between any molecules especially nucleotide bases and some other organic compounds. It was expected that there would be shown some specific partial structures which would play a role as formed complex crystals. The X-ray powder method was applied to do a survey on complexes formation ability of 134 compounds.

92% of the carboxylic acids which were examined could form complexes with adenine and 78%, with cytosine but no reaction was

The crystal structures of molecular complexes were analyzed in several combinations. Here the two styles of complex crystals with resorcillic acid and cytosine were shown in the Fig. A and B. In both cases the proton in carboxylic acid changed to cytosine to form a stable hydrogen bond plus an ionic structure. Number of reports of Fig. A, were observed in the later examinations which meant this is the fundamental complex formation style. Another hydrogen bond style with the same components were observed as shown in

Fig. B. A proton at resorcillic acid moved to cytosine forming ionic structure as well, then this cytosine changed to a molecular orbital to form with triple hydrogen bonds with another cytosine molecule.



There was another same style of complex which was positioned under the figure with rotational positioning at the mark §. Thus, the complex system was consisted with two adenines and four m-bromo- benzoic acids. It was interesting to note that this big size of complex was stacked on the same vertical direction with a stacking in the mirror image...

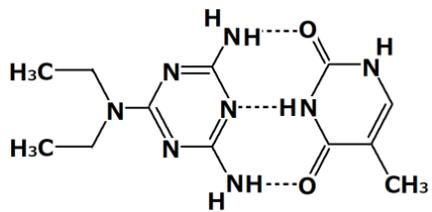
Also, Amidine moiety in adenine formed a complex with carboxylic acid. Two adenine molecules positioned at N (3) and NH (9) were bound to form a dimer and four m-Bromobenzoic acids were made into a complex as shown in the figure.

Further studies for essential amino acids have continued but all 20 amino acids could not form a complex with adenine, cytosine, and uracil. As we have known that all peptides were synthesized from amino-acids under the triplet information of the DNA or RNA. Therefore, between these molecules there must have been some interaction scheme. He supposed that the proton in a carboxylic acid

group which was moved to an intra molecular amino group to form a stable zwitter ion which might lose inter molecular interaction ability. Thus, if the amino-group was suppressed by an acyl-function, they might appear a basic character and to form a complex with carboxylic acid. To realize this expectation, a total of 144 compounds of N-formyl, N-acetyl, N-benzoyl and N-benzyoxy-amino acids were tested for complex forming ability with adenine and cytosine. Most of amino acids formed a complex except arginine and histidine which are in the same group of basic amino acids since these compounds form zwitter ion with rest of the amino group.

A carboxyl group of m-bromobenzoic acid hydrogen bond to an amidine group in which the scheme is same as that of cytosine and resorcillic acid in figure A. Another carboxyl group of m-bromobenzoic acid hydrogen bonded to an amino group and nitrogen at a position of No.7. Both acids donated a proton to adenine, forming an ionic structure reinforcing hydrogen bond. This scheme might play a role in biological tissues especially activating mechanism in DNA.

Note that, thimine molecule did not form with carboxylic acid containing molecules but melamine was associated to form a complex with it. The pairing of adenine and thimine and the pairing of cytosine and guanosine are definite biological sets of the scheme were two carboxyl amide groups and two amidine groups



which made three hydrogen bonds. This was a three-hydrogen bond system which would be evoked into the DNA model in Figure GC.