Connecting Rings: Architecture on a Nanometre Scale

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Imagine you are an architect, building beautiful buildings. You may first design the buildings, which you can be satisfied with, yet are constructable with current techniques, and later you are going to build the buildings. Organic chemists are doing almost the same thing, but on a nanometre scale, that is, 0.000000001 metre! They first design a molecule of interest, and then think about how to synthesize this molecule using the existing method. Finally, they synthesize molecules with its size of ca. 1 nanometre. Imagine how small they are. They are 10000000 times smaller than baseball, 10000 times smaller than your cells, and even 100 times smaller than a flu virus! Of course we cannot see such a small thing with our naked eye, but organic chemists can precisely control the structure of these tiny molecules, which are used everywhere in our daily lives.

One promising strategy for the design of interesting molecules is to take advantage of "aromaticity". When six carbon atoms are connected together to make a ring, there occurs a special stabilization due to an effect called "aromaticity". This carbon ring is called "aromatic rings". (This effect was named after "aroma," but to be honest, most aromatic rings are stinky!) This aromaticity also leads to changes in colour or reactivity, and such an effect can be further enhanced by connecting these aromatic rings together. In this sense, it is very important to develop a convenient reaction to connect the aromatic rings. However, such a good reaction has not existed, until the development of the "Suzuki-Miyaura coupling reaction" in 1979.

How can we connect two rings together? Organic chemists usually rely on the "electronic effect," i.e., the attraction force between positively charged atoms and negatively charged atoms. However, the aromatic rings are less likely to be charged, which means that we need another strategy to connect rings. A promising solution came out in the 1960s, which utilized transition metal atoms. Metal atoms are known to react with aromatic rings in a unique manner if a certain type of "hook" is installed in the ring. Taking advantage of this interesting reactivity, chemists have tried to develop a new reaction to connect aromatic rings. There had been so many reports on this topic, but they have several problems. For example, some reactions must be carried out in the complete absence of water or oxygen. Also, in some cases, the reagents used in the reaction are too reactive and might break the starting material itself in an unfavourable manner. Thus, the development of a convenient and moderate reaction was highly desired.

It was Professor Suzuki Akira and assistant professor Miyaura Norio at Hokkaido University that developed such a magical reaction in 1979. They discovered that palladium could work very well for this kind of reaction. Notably, this reaction can be conducted with oxygen and water (in fact, this reaction needs water). This reaction was so significant that Professor Suzuki was given an honour to be a Nobel Prize winner.

Let me explain the mechanism in more detail. This reaction consists of three steps. Firstly, one aromatic ring with a certain "hook" reacts with and bonds to palladium. Secondly, the other aromatic ring with another kind of "hook" bonds to palladium. And finally, these two rings are connected together to yield the desired product, while, at the same time, the palladium atom goes back to its original state and gets ready to react again, meaning that the very tiny amount of palladium would work fine. The installation of the "hook" to the aromatic rings is usually not so difficult, and this reaction proceeds selectively, without breaking any other parts of the materials. Considering these points, we can say that this Suzuki-Miyaura coupling reaction is a highly useful reaction for connecting aromatic rings.

This reaction was, and still is, very useful and has been widely used. Let's take a computer display for example. We can find displays everywhere in our lives in these days of the era of computers. The component of this display is liquid crystals, consisting of organic molecules. And, for the synthesis of this molecule, the Suzuki-Miyaura coupling reaction is used! Whenever we saw the computer screen – watching TV, playing games, or reading this essay on the computer, – we witness the child of the Suzuki-Miyaura coupling reaction. A recent development of much thinner displays, called OLED (organic light-emitting diodes), also exploits the usefulness of the Suzuki-Miyaura coupling.

Another example is medicine. Losartan, a drug for the treatment of high blood pressure, has a structure in which several aromatic rings are connected. Here, Suzuki-Miyaura coupling can connect rings to efficiently synthesize the drugs. This drug is the ninth sold drug in 2020 in the United States of America, with more than 10 million patients.

Suzuki-Miyaura coupling reaction originally starts from the academic interest, but it was so useful that this reaction now became very widely used. We are watching the display made by Suzuki-Miyaura coupling, taking a pill made with Suzuki-Miyaura coupling, etc... We are living in a world based on "connecting ring" chemistry, which Suzuki and Miyaura, and other researchers, have developed. And again, it is organic chemists that have made these things into real world. Doesn't it sound fun to literally "create" our world, using historical yet interesting reactions? (879 words)

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