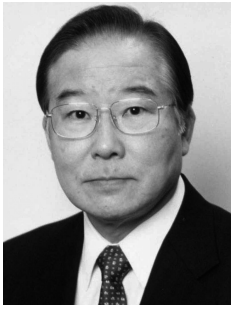
Japan Academy Prize to:



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for "Total Synthesis of Bioactive Natural Products using Carbohydrates"

Outline of the work:

Most natural products that show biological activities, contain asymmetric carbons. The importance of this aspect stems from the fact that similar activity is usually not found in their stereoisomers. Therefore in synthesizing these natural products, it is necessary to obtain the targeted natural products themselves, and not their stereoisomers.

Dr. Tatsuta has been playing a dominant role in the field of synthetic natural products chemistry through out his career, and he is recognized as an international leader. He has systematically and comprehensively developed synthetic methodologies and strategies for enantiospecific syntheses of bioactive natural products to study their structures as well as structure-activity relationship, using carbohydrates as readily available sources of asymmetric carbons. This strategy has resulted in total synthesis of 57 diverse bioactive natural products including representatives of the big four antibiotics, thereby paving the way for future related work. His major achievements are summarized as follows.

1. Total Synthesis of bioactive natural products using carbohydrates

Dr. Tatsuta was the first to succeed in the total synthesis of all representatives, such as kanamycin, thienamycin, tylosin and tetracycline, of the big four antibiotics (aminoglycoside, β-lactam, macrolide and tetracycline antibiotics) using carbohydrates. His tetracycline synthesis is particularly noteworthy, in that it was the first to be accomplished, occurring about fifty years after its structural determination.

Furthermore, more than 50 natural products have been synthesized, the structures of which include aromatic and/or heterocyclic as well as aliphatic motifs, proving that the methodology using carbohydrates is quite effective for the synthesis of complicated compounds with diverse structures. He has thus established the advantages of carbohydrate starting materials in synthetic organic chemistry as well as natural products chemistry.

2. Development of new organic reactions

Dr. Tatsuta has developed new methods for the synthesis of glycosides (glycosylation), and new rearrangement procedures, that have greatly increased the value of carbohydrates as starting materials. Stereoselective glycosylation has been notoriously difficult, but the Tatsuta methodologies provided practical solutions by which the highest levels of selectivity can be achieved. Thus both the 2-deoxy-α- and the 2-deoxy-β-series of *O*-glycosides can now be accessed efficiently using his newly developed reactions. These procedures have been effectively applied in the total syntheses of glycoside-containing natural products, including macrolide antibiotics.

He has developed skeletal rearrangement reactions of carbohydrates and other compounds, notably the one-step conversion of a pyranose ring to a furanose ring, that allows ready syntheses of thienamycin and rosmarinecine.

General methods for entry to carbasugars and cyclitols were also designed from carbohydrates, for example by using stereospecific intramolecular [3+2] cylcoaddition or aldol reactions, to synthesize cyclophellitol and validamine.

Furthermore, he has created new reagents to protect hydroxyls as the *O*-diethylisopropylsilyl group, which can be removed under hydrogenolysis conditions. This protecting group is now widely used by many researchers in their syntheses of natural products.

3. Structural determination of natural products by their total synthesis and clarification of their structure–activity relationships

Dr. Tatsuta has used total synthesis to determine or confirm the structures of many natural products. Especially noteworthy are complex molecules such as an antitubercular antibiotic, rifamycin W, and a tyrosine kinase inhibitor, herbimycin, whose absolute configurations have been determined by their enantiospecific total synthesis from carbohydrates. It has therefore been possible to associate their absolute structures with their bioactivities.

Thus, he has thoroughly investigated their structure–activity relationships. For example, by his total syntheses of glycosidase inhibitors, he has shown that glycosidase inhibitors act essentially as antagonists of the corresponding glycosides, thereby demonstrating the possibility of chemically creating inhibitors against all glycosidases and developing useful anti-diabetes agents.

The above-described extraordinary contributions of Dr. Tatsuta to organic chemistry as well as natural products chemistry, have gained worldwide recognition for a long time. For these achievements, he has received the Award of the Chemical Society of Japan, the Award of Synthetic Organic Chemistry, the National Medal with Purple Ribbon of Japan, and Fujihara Award. He has been visiting professor at several universities, including Cambridge, Paris VI and Oxford.