林民生教授 (Tamio Hayashi)

Yushan Fellow Program

Performance Report

Assessment of effectiveness of tangible work (The implementation results can be presented cumulatively, including the annual performance report of the second year, which can include the results of the first year and the second year)

Main points of assessment	The anticipated goals	Concrete work achievements or results	Supporting documents
1. Chief content of the Yushan (Young) Fellows' research work and overview of full research process.	Professor Hayashi's main research subject is to develop novel types of catalytic asymmetric reactions, which is one of the most important research area in producing enantioenriched chemical compounds such as pharmaceutical products with highest efficiency. This research is based on Hayashi's research proposals and experiments of organic synthesis performed by graduate students. To be a world leader in this research area, it is essential to have the proposals of high creativity and the experiments of high reliability.	Professor Hayashi has been successful in realizing his research project "Novel Types of Rhodium-Catalyzed Asymmetric Arylation Reactions". During the first two years, he has published his achievements in Tier 1 journals, and he has some preliminary results which will be reported in the third year. The details are shown in the next Section.	Appendix No.
2. The link between Yushan (Young) Fellows' future research topics and the university's development and the anticipated benefits (including Higher Education SPROUT Project): (1)Fellows' research plan and goals (2)The link between scholars' research content and the	(1) Fellows' research plan and goals Professor Hayashi proposes "Novel Types of Rhodium-Catalyzed Asymmetric Arylation Reactions" as a main research project performed as a Yushan Scholar in National Tsing Hua University. The objective of this research project is to develop new types of catalytic asymmetric carbon–carbon	As described in the research plan, Professor Hayashi has concentrated his research on "Novel Types of Rhodium-Catalyzed Asymmetric Arylation Reactions" during the last two years. He has successfully developed new asymmetric carbon-carbon bond forming reactions using aryl- and alkyl-zinc reagents in the presence of rhodium catalysts coordinated with a chiral diene	

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university's development (3)Specific work performance or achievements, please include the mid-term progress report of the particular research plan (4)Anticipated goals (including qualitative or quantitative working performance or results) ※ If there is a quantitative work achievements, please fill out "Quantitative Assessment Form"	bond forming reactions based on the asymmetric conjugate arylation and alkenylation reactions catalyzed by chiral rhodium complexes, which we have recently developed successfully. The rhodium-catalyzed asymmetric conjugate addition reaction has been recognized to be one of the most efficient and reliable methods of forming benzylic and allylic stereogenic carbon centers and has been called worldwide "Hayashi-Miyaura Reaction" based on the authors of the first publication. This project is focused particularly on the reactions in aprotic media. The rhodium-catalyzed asymmetric conjugate arylation has been reported, in most cases, for the reaction of aryl- and alkenyl-boronic acids in protic solvents, typically in a mixed solvent consisting of 1,4-dioxane and water. Those reactions in the protic solvent systems produce the arylation products as "hydro-arylation products". This is because the final step in the catalytic cycle is protonolysis of an alkyl-rhodium intermediate. The reactions under aprotic conditions would provide us with chances to find many other types of catalytic reactions, some of which must be of scientific interest and of practical use. Under the aprotic conditions, we can use a wide	ligand. One of the most important achievements is "Asymmetric Synthesis of Alkylzincs by Rhodium-Catalyzed Enantioselective Arylative Cyclization of 1,6-Enynes with Arylzincs", which has been published in *Angew. Chem. Int. Ed.* **2020**, *59*, 18510–18514. A chiral diene–rhodium complex was found to catalyze the reaction of 1,6-enynes with ArZnCl to give high yields of 2-(alkylidene)cyclopentylmethylzincs with high enantioselectivity (95–99% ee). The enantioenriched alkylzincs were readily converted in one-pot into a wide variety of functionalized products by taking advantages of their unique reactivity. The catalytic cylcle involves arylrhodation of alkyne, intramolecular alkenylrhodation of alkene, and transmetalation of the alkyl-rhodium intermediate into alkylzinc. Another important achievement is "Asymmetric Synthesis of Fluorinated Allenes by Rhodium-Catalyzed Enantioselective Alkylation/Defluorination of Propargyl Difluorides with Alkylzincs", which has been published in *Angew. Chem. Int. Ed.* **2021**, *60*, 20771–20775. The reaction of propargyl difluorides $R^1CF_2C{\equiv}CR^2$ with alkylzincs R^3ZnCl giving axially chiral fluorinated allenes $R^1FC{=}C{=}CR^2R^3$ with	Appendix #1 Chen, J.; Hayashi, T. *Angew. Chem. Int. Ed.* **2020**, *59*, 18510–18514. DOI: 10.1002/anie.202008770 and 10.1002/ange. 202008770. Appendix #2 Ng. J. S.; Hayashi, T. *Angew. Chem. Int. Ed.* **2021**, *60*, 20771–20775. DOI: org/10.1002/anie.202109290 and org/10.1002/ange.202109290

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	variety of organometallic reagents which are not stable in protic solvent. They are, for examples, organomagnesium, lithium, zinc, titanium, and so on. The purpose of this project is to find and develop new reactions which are based on the rhodium–catalyzed addition reactions and are useful for practical synthesis of biologically active molecules such as medicines.	high enantioselectivity (up to 99% ee) was found to be catalyzed by a chiral diene/rhodium complex. A key step in the catalytic cycle is selective elimination of one of the enantiotopic fluorides at β-position of an alkenyl–Rh intermediate which is generated by regioselective addition of R^3–Rh onto the triple bond of the starting difluorides. In addition to the two reports described above, both of which are concerned with development of new reactions, Professor Hayashi also reported application of one of his rhodium-catalyzed asymmetric reactions to the synthesis of new chiral diene ligands. Professor Hayashi has written a review article in *Chem. Rev.* (impact factor 72.084) entitled "Chiral Diene Ligands in Asymmetric Catalysis" which summarizes all the catalytic asymmetric reactions using chiral dienes as ligands. It has been highly evaluated as a review on this research field. He is one of the corresponding authors of publication in *Angew. Chem. Int. Ed.* on iridium-catalyzed asymmetric allylic phosphination reactions, which produces chiral allylic phosphines with high enantioselectivity. This new asymmetric	Appendix #3 Sun, C.; Meng, H.; Chen, C.; Wei, H.; Ming, J.; Hayashi, T. *Org. Lett.* **2021***, 23,* 6311–6315. DOI: org/10.1021/acs.orglett.1c02088 Appendix #4 Huang, Y.; Hayashi, T. *Chem. Rev.* **2022***, 122,* 14346–14404. DOI: org/10.1021/acs.chemrev.2c00218 Appendix #5 Wu Z.-H.; Wang, H.-Y.; Yang, H.-L.; Wei, L.-H.; Hayashi, H.; Duan W.-L. *Angew. Chem. Int. Ed.* **2022**, *61*, e202213904. DOI:org/10.1002/anie.202213904

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		reaction was realized by collaboration with researchers in Shaanxi Normal University, China.	
	(2) The link between scholars' research content and the university's development Hayashi is devoted to the development of metal-catalyzed asymmetric synthesis. This research area is very important to develop modern technology in pharmaceutical companies. The reactions in this research project are categorized into two types according to the reaction manner of alkyl-rhodium intermediates in the catalytic cycle. This includes (1) Rhodium-catalyzed asymmetric arylation/ß-elimination and (2) Rhodium-catalyzed asymmetric arylation/electrophilic functionalization reactions. Both of these two reactions are the novel catalytic reactions that are very difficult to be realized in protic solvent systems. This research proposal also involves (3) Application of the present asymmetric reactions to practical synthesis of industrially important compounds. The development of new synthetic organic reactions such as those	Professor Hayashi is an expert of the research on organic synthesis, particularly on asymmetric reactions catalyzed by chiral transition metal complexes. This research subject is connected with several fields of science and technology including organic chemistry, organometallic chemistry, catalysis, and organic synthesis. For his research on this subject to be developed, he has had collaborations with research groups in NTHU and National Taiwan Normal University (NTNU). The experiments to realize development of new types of catalytic asymmetric reactions have been performed mainly by the students in his own research group and partly by those in other research groups in NTHU and NTNU. Through the studies on the development of new types of catalytic asymmetric reactions, Hayashi has shown these students in NTHU and NTNU what the studies of high originality and creativity are and how they can join the research projects, which are running top in the world, as graduate students. His achievements in his research have been attracting interests of the members who have been working in related fields	

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	proposed by Hayashi is a fundamental research project which may attract interests of many of the members of Department of Chemistry and will activate collaborations in the department. (3) Specific work performance or achievements, please include the mid-term progress report of the particular research plan Professor Hayashi will be offered a three-year an appointment; he will have a new laboratory in National Tsing-Hua university. He will offer two courses during this period. His research proposal addresses a crucial and fundamental challenge in catalysis and synthetic organic chemistry. Development of novel synthetic reactions by means of catalysis has always been a key and challenging research project for producing important chemicals for our life including medicines. From a scientific viewpoint, the novel types of rhodium-catalyzed asymmetric carbon–carbon bond forming reactions, where the alkyl-rhodium intermediates in the catalytic cycle undergo electrophilic substitutions or β-elimination reactions, may have enormous implications and applications in synthetic organic	in NTHU and other universities in Taiwan. At his application to Yushan Fellow Program, Professor Hayashi proposed a research project “Novel Types of Rhodium-Catalyzed Asymmetric Arylation Reactions”, which involves (1) Rhodium-catalyzed asymmetric arylation/ß-elimination, (2) Rhodium-catalyzed asymmetric arylation/electrophilic functionalization reactions, and (3) Application of the present asymmetric reactions to practical synthesis of industrially important compounds. The first two reactions (1) and (2) have been successfully developed, and their results have been published from National Tsing Hua University (NTHU) in *Angew. Chem. Int. Ed*. (impact factor 15.336). More detailed contents of the results are described above in the section of Fellows' research plan and goals. The application of the asymmetric reactions to practical synthesis of industrially important compounds shown in (3) has not been realized yet. Although they are not industrially important compounds, chiral dienes, which are useful as chiral ligands for asymmetric	

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	chemistry. This project also has great practical applications, both in academic and industrial settings. Professor Hayashi is among the first few researchers in the world to develop novel types of catalytic asymmetric carbon–carbon bond forming reactions, particularly rhodium-catalyzed reactions. The first example of the rhodium-catalyzed asymmetric conjugate arylation/alkenylation was reported for α,β-unsaturated ketones by Hayashi himself in 1998, and the reaction has been extended to a various kinds of electron-deficient alkenes and alkynes. It is remarkable that the feasibilities of approaches described in this research proposal are well supported by his preliminary studies. (4)Anticipated goals (including qualitative or quantitative working performance or results) Professor Hayashi is very high in terms of his research ability, as it is shown by his publications in Tier-1 journals and the high citation numbers of his publications. It is anticipated that he keeps publishing his research results in Tier-1 journals and he initiates collaborations with other members in Department of Chemistry, which will	reactions, have been synthesized by application of one of the rhodium-catalyzed asymmetric carbon-carbon bond forming reactions, and it has been published in *Org. Lett*. (impact factor 5.61). For further development in a wider research area he has started collaborations with the professors of NTHU and other universities in Taiwan. He has already discovered some interesting and promising results, which will be reported in Tier 1 journals in the near future. Professor Hayashi has kept his research activity and productivity high during the last two years since he started his position as a Yushan Fellow. He has already discovered several new types of catalytic asymmetric reactions and some of the results have been published in *Angew. Chem. Int. Ed*., which is one of the Tier-1 journals. The quality of his research is very high with high originality and creativity, which is demonstrated by his publication list. He has started collaborations with professors in NTHU and NTNU, and the collaborations will	

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	eventually contribute to the higher activity and productivity of the department. Because of his enthusiasm and creativity, he will contribute to the publications of top journals with NTHU.	accelerate his research productivity, which is expected to enhance his contribution to higher reputation of NTHU and universities in Taiwan.	
3. Support provided by the university and the project's original goals (please specify the type of support or funds provided by the university to assist in research, such as research equipment and funds, research assistant personnel expenses, accommodation, relocation, children's education assistance, etc.)	a. Overall package of supportive measures and arrangements the university will provide: I. National Tsing Hua University Newly-Recruited Faculty Academic Research Subsidy (start-up subsidy) NTHU provides the Academic Research Subsidy (start-up subsidy) to help the newly-recruited faculties build up their research labs and facilities, and encourage them concentrate on research. Within six months after reporting, the newly-recruited faculties can apply for the subsidy. After approval, in principle every applicant can obtain NTD$ 1.5 million at most provided together by department, college and university. II. Guest House and accommodation subsidy i. Guest House In principle the newly-recruited faculties have the priority to apply to live in Guest House Ⅲ, single room or double room. Besides, the newly-recruited faculties also can apply to	The research by Professor Tamio Hayashi has been well supported by the subsidy from National Tsing Hua University and Ministry of Education, Taiwan. The funding for research has been used for the salary of Master course students (total 7 students) and purchase of consumables, typically chemicals, solvents, metal complexes, and glassware for the experiments, which are necessary for his research. In addition, a set of HPLC machine (High Performance Liquid Chromatography) was purchased, which is frequently used for determination of the enantiomeric excess (% ee) of the chiral products obtained by his research on catalytic asymmetric reactions.	

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	live in Guest House Ⅰ or Guest House Ⅱ. Further information please refer to http://affairs.web.nthu.edu.tw/files/13-1011-44868.php. ii. Accommodation subsidy If it conforms to the regulation of the accommodation subsidy in NTHU, the newly-recruited full-time faculties have the option to apply for the accommodation subsidy (up to NTD$10,000 per month) for a duration of three years. III. Education of children i. Children of the newly-recruited full-time faculties have the priority to apply to study in the Affiliated Kindergarten or Affiliated Experimental Elementary School of National Tsing Hua University. ii. Children's education subsidy： Further information please refer to http://person.web.nthu.edu.tw/files/14-1138-12001,r940-1.php. IV. Others i. Birthday vouchers：Every full-time faculty member will receive the birthday vouchers NTD$ 1000 every year. ii. Health-check subsidy：Every full-time faculty member over 40-year-old can apply for the health-check subsidy NTD$ 3500 once every two years.		

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	iii. Group insurance at one's own expense b. Overall package of supportive measures and arrangements the college/Department will provide (1) A totally 66-square-meter laboratory located on the fifth floor and the sixth floor in the Chemistry Building will be provided. (2) The subsidy of master student stipends and post-doctoral researchers will be provided. The subsidy will be partially supported by NTHU Frontier Research Center on Fundamental and Applied Sciences of Matters. (3) The subsidy of research funding & facilities 500,000 NTD will be provided, which is shared by the College of Science, the Department of Chemistry and NTHU.		
4. Yushan Fellows ' team cooperation (please list team members and cooperation methods) (Yushan Young Fellows don't need to fill in this)	The college of science at National Tsing-Hua University has been funded with a frontier research center by the two institutes of Taiwan governments. The focus is to develop fundamental and Appied Science of Matters; the chief PI is profeesor Liu, Rai-Shung.. This research center carries an annual budget of NT 55 million/year, the main themes include catalytic science and technology, development of new	Professor Hayashi has started his research cooperations with Professor C.-T. Chen to develop a new technology to synthesize chiral molecules, and the cooperation team has obtained a promising result on asymmetric cyclization reactions catalyzed by chiral phosphine-palladium and rhodium complexes. Collaboration with Professor S.-L. Wu of National Taiwan Normal University has been successful in developing several	

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	technology of biomaterials and applied science of nanomaterials and semiconductors. In the aspect of catalytic science, there are Professor Liu, R.-S.; Cheng C.-H., Chen C.-T. Hwu J.-R., Hwang K.-C.; PengC.-H.; we plan to form a research team with Professor Hayash. One newly appointed young faculty will join this research group. We seek research cooperation with professor Hayashi and to employ his new method to develop new chiral molecules, further a mass production of new chiral drugs. Such a high technology in chiral science will be very desirable in Taiwan biotechnology. a. Planning to collaboratively establish a team We will plan three directions in this research cooperations: (1) New technology to make chiral intermediates: members include Prof. Hayashi T. and Cheng, C.-T. (2) Access to complex molecules and bioactive materials, including Liu, R.-S., Cheng, C.-H.; Hwu, J.-R. and Peng C.-H. (3) Synthesis of bioactive molecules including Prof. Cheng, C.-H. and Hwang Y.-W. (assistant professor)	types of new catalytic asymmetric reactions. The results will be published in the near future.	

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<tr><th>Main points of assessment</th><th>The anticipated goals</th><th>Concrete work achievements or results</th><th>Supporting documents</th></tr>
<tr><td></td><td>b. List of team members
<table>
<tr><th>Name</th><th>Unit</th><th>Job title</th></tr>
<tr><td>Tamio Hayashi</td><td>Dept. of Chemistry</td><td>Visiting Professor</td></tr>
<tr><td>Rai-Shung Liu</td><td>Dept. of Chemistry</td><td>Professor</td></tr>
<tr><td>Chien-Hong Cheng</td><td>Dept. of Chemistry</td><td>Professor</td></tr>
<tr><td>Chien-Tien Chen</td><td>Dept. of Chemistry</td><td>Professor</td></tr>
<tr><td>Jih-Ru Hwu</td><td>Dept. of Chemistry</td><td>Professor</td></tr>
<tr><td>Peng Chi-Haw</td><td>Dept. of Chemistry</td><td>Associate Professor</td></tr>
<tr><td>Yu-Wen Huang</td><td>Dept. of Chemistry</td><td>Assistant Professor</td></tr>
</table></td><td></td><td></td></tr>
<tr><td>5. Yushan (Young) Fellow should aim to cooperate and exchange foreign academic resources, which should be linked to university development. It's suggested to make good use of these global academic network resources to assist the internationalization of the host university and promote international exchanges and cooperation, including teachers and students exchange activity between universities, international research collaborations, dual degree programs and so on.</td><td></td><td>Hayashi originally planned to have an international exchange program with universities in Singapore and Japan. However, unfortunately, the corona virus pandemic problems made the exchange of teachers and students made difficult and unrealistic. If the situation turns better, the exchange program will be started.</td><td></td></tr>
</table>

Appendix 1

Quantitative Assessment Form

Item		Results and concrete work performance	Explanation
1. Manpower training		Doctoral courses:_____ Graduate courses:_____ Undergraduate courses:_____ Doctoral students:_____0_____ persons Master's students:_____7_____ persons Undergraduate students:____0____ persons Others:____0____ persons	
2. Papers and research works	Domestic	Journal papers:_____ Academic books and papers in books:_____ Conference papers:____1____ Technical reports:_____ Others:_____	
	Overseas	Journal papers:_____5_____ Academic books and papers in books:__0____ Conference papers: ___0_____ Technical reports:____0_____ Others:_____	Appendix #1, 2, 3, 4, and 5
3. Keynote speaker		___1____panels /sessions	At CSS annual meeting in 2021
4. Patents （including patents pending）	Domestic	Quantity:_____	
	Overseas	Quantity:_____	
	☐✓ N/A		
5. Industry-Academia Cooperation		Number of partnered enterprises :_____	
		Number of industry-academia research projects:_____	
6. Technology licensing		Technology licensing cases:_____	
		Total technology licensing royalties （amount）NT$_____	
		☐✓ N/A	
7. Others			