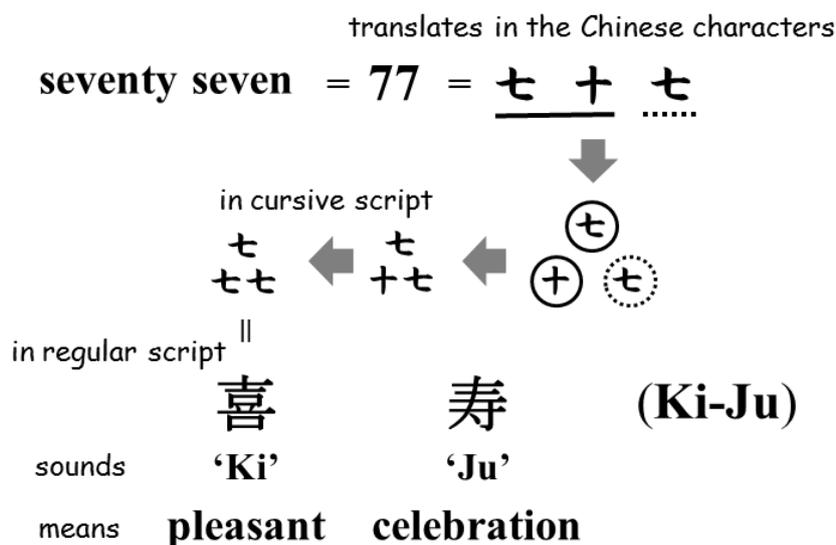


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CONGRATULATIONS TO PROFESSOR EI-ICHI NEGISHI ON HIS KI-JU (77TH BIRTHDAY)

It is my great honor to deliver this message to Professor Ei-ichi Negishi on the occasion of his 'Ki-Ju', his 77th birthday.

Seventy-seven is written in Chinese using three numerical characters; '七 + (seventy)' and '七 (seven)'. A combination of these three characters in a triangle direction produces a new one, '喜', read 'Ki', in cursive script, which means "pleasant". The other Chinese character, '寿', read 'Ju', means celebration. Thus, 'Ki-Ju' in essence is a celebration of a long pleasant and happy life that is seventy-seven years, in good health.



In 1986, Professor Negishi visited one of his best friends, Professor Yoshinori Yamamoto, in Sendai. As most readers of this message know, Professors Negishi and Yamamoto both spent the early 1970s in Professor Brown's laboratory at Purdue University. At that time, Professor Negishi gave a lecture about the zirconocene-mediated carboalumination of alkynes and alkenes.¹ I was a graduate student then and attended his lecture. After his lecture, I was impressed by a couple of points he mentioned in his lecture. Although carboalumination was then known in polymer chemistry typically as the Ziegler-Natta polymerization of alkenes, controlled reactions, especially the synthesis of simple monomers, were not known yet. Professor Negishi switched the catalyst from titanium to zirconium and performed this

carboalumination to introduce alkyl groups into simple alkynes. This achievement, particularly the introduction of a methyl group into alkynes in a stereoselective manner, led to a useful tool for the synthesis of isoprenoid natural products. Although the outcomes in the cases of alkyl groups being introduced into alkynes look the same, the reaction mechanisms differ between the methyl and other alkyl cases. Methylalumination proceeds *via* a direct pathway as in hydroboration,^{2,3} and the introduction of other alkyl groups is carried out *via* both the direct pathway and the formation of alumina- and/or zircona-cyclopentenes.^{4,5} In addition, it seemed to be ‘magical’ for me to be able to change the solvent step by step in an operating reaction. Dichloromethane is used in the beginning for carboalumination followed by evaporation, and *n*-hexane is used for the extraction of the resulting alkenylaluminums. Finally, THF is used for further alkylation of the alkenylaluminums.³ When the solvent is replaced with other solvents, the desired reaction does not proceed successfully. Therefore, the proper choice of solvent is important and this seemed like ‘solvent magic’.

The palladium-catalyzed cross-coupling reaction of organozinc compounds with organic halides is well known as the ‘Negishi coupling reaction’ and has been widely used for the synthesis of many types of compound with various functions including natural products. This reaction is fast and widely applicable. The reaction is usually carried out in tetrahydrofuran, benzene, toluene, and *N,N*-dimethylformamide as the solvents. However, *N,N*-dimethylformamide may react with certain nucleophiles such as organozinc compounds. Therefore, this solvent is usually avoided when the coupling reaction of organozinc compounds is carried out. Professor Negishi knew from his experiences that organozinc compounds do not react easily with amides, which do not have an active hydrogen, and decided to use them as the solvents. Actually, the coupling reaction in *N,N*-dimethylformamide is usually clean and fast, giving the desired compounds in excellent yields.⁶

The palladium-catalyzed carbonylation reaction is also an important research area developed by Professor Negishi. The oxidative addition of palladium complexes to organic halides followed by the insertion of carbon monoxide produces acylpalladium intermediates, which are transformed into organic carbonyl compounds by reacting with nucleophiles. The intramolecular reaction is usually a thousand to a million times faster than the intermolecular reaction. Hydrophobic compounds are known to aggregate in hydrophilic media to minimize their surface area. Professor Negishi exploited these features and synthesized a polycyclic conjugated ester in methanol from polyalkyne alcohol, which was the so-called deferred carbonylative esterification in the carbopalladation and carbonylation cascades.⁷

Professor Negishi also introduced many new, convenient, efficient, and interesting tools for the synthesis of organic molecules with various functions. As a result of all his works, Professor Negishi was awarded the 2010 Nobel Prize in Chemistry jointly with Professors Akira Suzuki and Richard F. Heck.

This issue of HETEROCYCLES is dedicated to Professor Ei-ichi Negishi on the occasion of his 'Ki-Ju'. It is with deepest respect and admiration to share with you these remarks about his unique impact on Synthetic Organic Chemistry. We are wishing him and his wife, Sumire, more enjoyable years of a fulfilled life in their 'pursuit of happiness with eternal optimism'.

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Professor Takumichi Sugihara
Faculty of Pharmaceutical Sciences
Niigata University of Pharmacy and Applied Life Sciences
Niigata, Japan



Takumichi Sugihara was born in Toyohashi, Japan in 1962. He graduated from Faculty of Pharmaceutical Sciences, Tohoku University in 1986, and received Ph. D. in 1991 from Graduate School of Tohoku University under the supervision of Professors Seiichi Takano and Kunio Ogasawara. After joining Professor Ei-ichi Negishi's group as a post-doctoral fellow for two years, he promoted to assistant professor at Faculty of Pharmaceutical Sciences, Tohoku University (1994-1998), associate professor at Faculty of Pharmaceutical Sciences, Tokushima Bunri University (1998-2004), and full professor at Faculty of Pharmaceutical Sciences, Niigata University of Pharmacy and Applied Life Sciences (2004~), and now becomes the Dean & Director of School of Pharmacy (2012~). His research interest is development of new and efficient reactions including cobalt and molybdenum chemistry and fixation of nitrogen oxides into organic molecules.