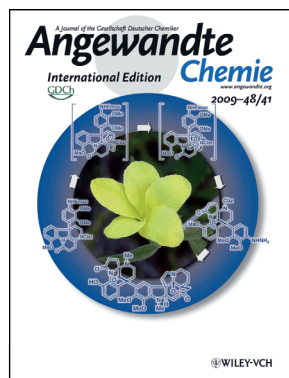


H. Tokuyama

The author presented on this page has recently published his **10th article** in *Angewandte Chemie* in the last 10 years:

“Total Synthesis of Actinophyllic Acid”: Y. Yoshii, H. Tokuyama, D. Y.-K. Chen, *Angew. Chem. Int. Ed.* **2017**, *56*, 12277; *Angew. Chem.* **2017**, *129*, 12445.



The work of H. Tokuyama has been featured on the inside cover of *Angewandte Chemie*:

“Total Synthesis of (+)-Haplophytine”: H. Ueda, H. Satoh, K. Matsumoto, K. Sugimoto, T. Fukuyama, H. Tokuyama, *Angew. Chem. Int. Ed.* **2009**, *48*, 7600; *Angew. Chem.* **2009**, *121*, 7736.

## Hidetoshi Tokuyama

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<b>Education:</b>	1990 BSc, Tokyo Institute of Technology 1992 MSc, Tokyo Institute of Technology 1994 PhD supervised by Professor Eiichi Nakamura, Tokyo Institute of Technology
<b>Awards:</b>	1994–1995 Postdoctoral research with Professor Amos B. Smith, III, University of Pennsylvania <b>2003</b> Pharmaceutical Society Japan (PSJ) Award for Young Scientists; <b>2007</b> Young Scientist's Prize, Commendation for Science and Technology by MEXT, Japan; <b>2014</b> PSJ Award for Divisional Scientific Promotion; <b>2015</b> Daiichi–Sankyo Award for Medicinal Organic Chemistry, SSOCJ; <b>2015</b> Alan R. Katritzky Junior Award in Heterocyclic Chemistry, International Society of Heterocyclic Chemistry
<b>Research:</b>	Total synthesis of natural products; development of new synthetic methodology
<b>Hobbies:</b>	Traveling; visiting art museums; skiing; gardening

**My favorite painters are** Wassily Kandinsky, Jean-François Millet, Maurice Utrillo, Johannes Vermeer, and Andrew Wyeth.

**My science “heroes” are** Teruaki Mukaiyama and R. B. Woodward.

**My favorite name reaction is** the Fischer Indole Synthesis. When I first learned this reaction, it was impressive for me as the reaction of simple hydrazines and ketones forms medically important indole derivatives quite easily.

**If I had one year of paid leave I would like to** travel around the world and visit art museums and world heritage sites, which I could not do when I was a student.

**My favorite composer is** Wolfgang Amadeus Mozart because I feel that his compositions bring an intellectual revitalization that leads to inspiration.

**When I was eighteen I wanted to be** a physicist, since I was impressed by the fact that all events can be explained clearly by formulas. Later, my interest moved toward chemistry because many chemical events can not be explained by simple mathematical expressions, which was more mysterious and attractive for me.

**Chemistry is fun because** we occasionally get results beyond our expectations, even if we are doing small experiments.

**Looking back over my career, I** am very happy since I received valuable guidance from brilliant three organic chemists, Professors Eiichi Nakamura, Amos B. Smith, III, and Tohru Fukuyama, each with a different style. Their education and way of thinking is still alive in my mind and continues to influence my present research in many ways.

**My first experiment was** a gram-scale preparation of methylene cyclopropanone acetal, which was developed as a precursor of trimethylene methane in the Nakamura Group.

**In a spare hour, I** enjoy walking around the medicinal botanical garden belonging to our department. We can enjoy the green trees and birdsong because Tohoku University is located on Aoba Mountain, a small peak in Sendai City.

**My favorite quote is** “Work pursuing a fashion is shed like a floating grass, but his original work is rooted in the bottom of the river forever” (Professor Teruaki Mukaiyama).

**I advise my students to** work as hard as they can for their own growth. The hardships endured and efforts made at an early age will lead to future success.

**My favorite way to spend my spare time is** shopping with my wife and daughter, or gardening.

**How has your approach to chemistry research changed since the start of your career?**

The internet continues to influence our approach to research in many ways. On the positive side, we no longer need to spend all day in the library to consult the chemical abstracts, and the publication of articles has become more rapid. Furthermore, collaborative research over long distances became easier. The negative aspect is that research topics tend to become more fragmented so as to obtain results as soon as possible, for example, small modifications of “hot” topics. Although it is quite difficult, I would like to carefully work on original research topics with more essential meanings.

**How do you think your field of research will evolve over the next 10 years?**

The integration of benchtop experiments on the bench and informatics based on big data (AI) is expected to progress in various research fields. Even in the field of total synthesis, it may soon become possible to plan synthetic pathways by AI, even for relatively complicated molecules. The key to success is to perform data mining from huge reaction data utilizing both successful and unsuccessful experimental results, the latter of which is now hidden in many cases. Reporting full articles, including negative data, should become more important. On the other hand, I am a bit pessimistic about whether we can continue to train skilled synthetic chemists who can implement the synthetic pathways planned by AI.

**My 5 top papers:**

1. “Photoinduced Biochemical Activity of Fullerene Carboxylic Acid”: H. Tokuyama, S. Yamago, E. Nakamura, T. Shiraki, Y. Sugiura, *J. Am. Chem. Soc.* **1993**, *115*, 7918.

This was my PhD project. I learned the excitement of scientific research in an effort to clarify the physiological activity of fullerene, which was not known at the time. We synthesized a water-miscible C<sub>60</sub> derivative through the [3+2]cycloaddition of a trimethylenemethane species and found for the first time that C<sub>60</sub> derivatives possessed antitumor activity only under irradiation of visible light. In addition, we clarified that the mechanism of action involved photoinduced singlet oxygen generation and DNA cleavage.

2. “Synthesis of Oxo- and Methylene-Bridged C<sub>60</sub> Dimers, the First Well-Characterized Species Containing Fullerene–Fullerene Bonds”: A. B. Smith III, H. Tokuyama, R. M. Strongin, G. T. Furst, W. J. Romanow, B. T. Chait, U. A. Mirza, I. Haller, *J. Am. Chem. Soc.* **1995**, *117*, 9359.

This was my postdoctoral research. This research was my first and last attempt to determine the structure of a compound, C<sub>120</sub>O, which can not be characterized by <sup>1</sup>H NMR spectroscopy. We synthesized <sup>13</sup>C-enriched C<sub>120</sub>O by reaction of <sup>13</sup>C-enriched C<sub>60</sub> and the C<sub>60</sub> epoxide, and determined its <sup>13</sup>C–<sup>13</sup>C INADEQUATE NMR spectrum.

3. “Stereocontrolled Total Synthesis of (+)-Vinblastine”: S. Yokoshima, T. Ueda, S. Kobayashi, A. Sato, T. Kuboyama, H. Tokuyama, T. Fukuyama, *J. Am. Chem. Soc.* **2002**, *124*, 2137.

By conducting synthetic studies on this historical vinca alkaloid, I learned a lot about indole chemistry and total synthesis. We accomplished the de novo total

synthesis by utilizing our original synthesis of 2,3-disubstituted indoles by radical cyclization of 2-alkenylthioanilides. The highlight of the synthesis was a coupling of two segments with complete stereochemical control.

4. “Total Synthesis of (+)-Haplophytine”: H. Ueda, H. Satoh, K. Matsumoto, K. Sugimoto, T. Fukuyama, H. Tokuyama, *Angew. Chem. Int. Ed.* **2009**, *48*, 7600; *Angew. Chem.* **2009**, *121*, 7736.

This was the first successful project after starting my independent group at Tohoku University. The first reported total synthesis of the structurally intriguing dimeric alkaloid (+)-haplophytine was both difficult and exciting. We enjoyed the construction of the unusual structure by the oxidative skeletal rearrangement of an easily accessible intermediate. After this first total synthesis, we continued our research to establish a more convergent and efficient total synthesis. Finally, we recently completed the ultimate bioinspired total synthesis of this compound involving the late-stage auto-oxidative skeletal rearrangement.

5. “Protecting-Group-Free Total Synthesis of (–)-Rhaznilam and (–)-Rhazinicine using a Gold-Catalyzed Cascade Cyclization”: K. Sugimoto, K. Toyoshima, S. Nonaka, K. Kotaki, H. Ueda, H. Tokuyama, *Angew. Chem. Int. Ed.* **2013**, *52*, 7168; *Angew. Chem.* **2013**, *125*, 7309.

Despite its relatively small size, rhaznilam inspired us and gave us an opportunity to develop a new cascade reaction. This was our most successful case where the development of new reactions and the total synthesis progressed cooperatively, and culminated the establishment of this protecting-group-free total synthesis.

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