

Arthur Michael (1853–1942): The Michael Addition Reaction

The Michael reaction is now 130 years old,¹ and its use has continued unabated since.² As is so often the case, the chemist behind the reaction is not nearly as well known to chemists as the reaction itself. Despite several useful biographies of Michael,³ most organic chemists have little knowledge of his far-reaching work, or of the razor-sharp intellect that he used to great effect in criticizing the science of his contemporaries.



Arthur Michael (1853–1942) in 1886
(image courtesy of Tufts University archives)

Michael was born in Buffalo, New York, and attended classical school there, where he received private instruction in chemistry. His father, a well-off real-estate investor, encouraged his son's early love for chemistry, setting up a home laboratory for him and allowing him to conduct his own experiments there. However, toward the end of his teens he suffered a serious illness (brain fever, possibly scarlet fever), which eliminated his chances of entering Harvard College but allowed him to dabble in art and literature before returning to chemistry.

In 1871, he was admitted to Berlin University, where he studied in August Wilhelm von Hofmann's laboratory – despite not having the required chemistry background. After a year in Hofmann's laboratory, Michael continued his studies under Robert Bunsen at Heidelberg, where he strengthened his practical training. During this year Michael became the first to synthesize a natural glucoside, helicin.⁴ The method he used would become the standard synthetic route for this class of natural products.

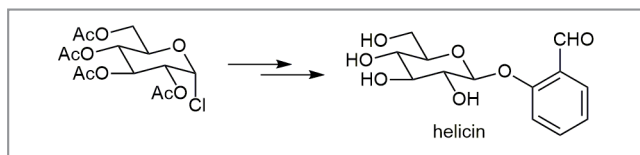


Figure 1

Two years later, he rejoined Hofmann at Berlin and continued his work there from 1875 to 1878. In 1879, Michael conducted research in Paris with Charles-Adolphe Wurtz, as well as in St. Petersburg with Mendeleev.

Michael returned to the United States in 1880, with considerable experience, but no formal degree. Even so, just as he had first been appointed to Hofmann's group without having satisfied all the requirements, he was appointed as an assistant in the chemical laboratory at Tufts College for a year before being appointed Professor of Chemistry there. He was awarded two honorary degrees from Tufts: the A. M. in 1882, and the Ph.D. in 1890.

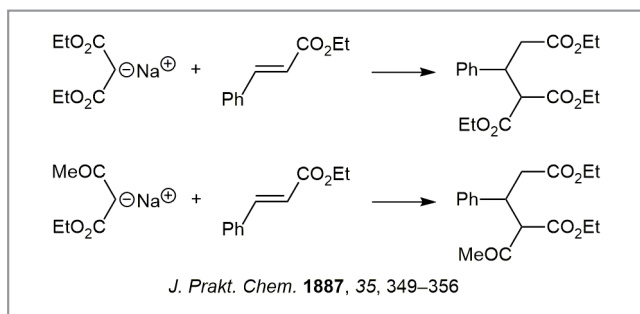


Helen Abbott Michael (1857–1904);
Frontispiece to Studies in Plant and Organic Chemistry: And Literary Papers

In 1889, Michael married his student, Helen Cecilia DeSilver Abbott (1857–1904), an organic chemist herself, and one of the few women in the field. In addition, she was fully Michael's intellectual equal. After their marriage, the couple spent 18 months traveling around the world. Michael was an enthusiastic mountaineer, and climbed several alpine peaks, including the Matterhorn. After their return to the United States, Michael accepted the position of Head of the Chemical Laboratory at Clark University in Worcester, Massachusetts – a position he had originally declined. After just one year at Clark, Michael moved to the Isle of Wight, where he set up a private laboratory. He worked in this laboratory for three years. He resumed his professorship at Tufts in 1894, and held this position until his retirement in 1907. Following his retirement, Michael set up a new private laboratory near Boston. In 1912, he was appointed Professor, without lecturing duties, at Harvard University. He retired from this position in 1936.

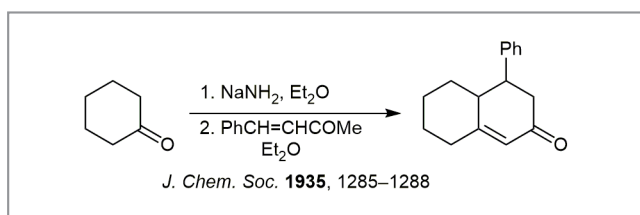
In 1887 Michael published the first of four papers with the title "Ueber die Addition von Natriumacetessig- und Natriummalsäureäthern zu den Aethern ungesättigter Säuren." In this first report of what is now his eponymous reaction, Michael reported the addition of diethyl sodiomalonate and

ethyl sodioacetatoacetate to ethyl cinnamate. Over the course of the next seven years, Michael and his students extended the reaction to a wide range of conjugated esters, including acetylenic esters.^{1d}



Scheme 1

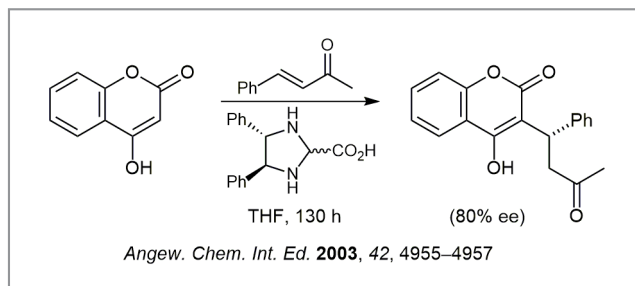
The power of this relatively simple reaction has been demonstrated repeatedly since its discovery. In 1935, Rapson and Robinson demonstrated an extremely useful tandem Michael reaction, now known as the Robinson annulation (or annelation).⁵



Scheme 2

More recently, research on the Michael reaction has been focused on controlling stereochemistry in both the relative and the absolute sense,^{2g-i} especially using chiral catalysts. The use of a chiral organocatalyst is nicely illustrated by Jørgensen's synthesis of (*S*)-warfarin using a *C*₂-pseudosymmetric chiral diamino acid, where the carboxy group is attached to the ring as either an *r* or an *s* pseudocenter of chirality.⁶

Although he is best remembered for the Michael addition reaction and its many derivatives, Michael's primary focus was actually the role of theory in organic chemistry. Working just after the great advances in organic structure and stereochemistry, he became a pioneer in physical chemistry and physical organic chemistry. As such, many of his most important contributions were as a critic of others' scientific work. He was highly respected as a very intuitive critic, if often ex-



Scheme 3

cessively blunt in his criticism. His criticisms were usually so cogent that he was hard for others to ignore. When Kolbe, Lossen, Claus, and Fittig all raised questions about the first version of van't Hoff's theory, their critiques were not taken completely seriously, especially following Kolbe's infamous diatribe.⁷

Michael often took the persona of an outsider arguing with the mainstream ideas. He was never afraid to take a stance at odds with the rest of the chemical community. He had great confidence in his work and had no problem disagreeing with others. He helped to broaden the field of structural theory through his criticisms and research.

Michael's Harvard colleagues described him as "a powerful theorist, a keen critic, and a consummate experimentalist." His criticisms of van't Hoff's stereochemical theory, for example, were taken seriously – such an extensive, multi-part critique could not be so easily dismissed.⁸ Michael's cogent arguments helped establish stereochemistry in organic chemistry. He also saw weakness in Wislicenus's theory that additions to unsaturated substances necessarily precede *cis*. Michael was driven by his general dislike of the mechanical aspects of stereochemical theory.

He lost his wife, Helen, to the influenza virus in 1904. He then retired from Tufts but continued to work in a private laboratory in Boston. In 1912 he was asked back to Harvard where he supervised graduate work until 1936 when he became emeritus. His love for research lasted until the day he died and with age he grew to enjoy gardening, a love for plants was something he and Helen both shared, as well as golf. He passed away at almost ninety years old in 1942 while wintering in Florida.

Throughout his life, Michael was an avid art collector; he was especially fond of ancient and medieval art. His collection grew over the course of the years to contain thousands of rare art pieces and objects. The friendship he developed with Ernest Fenollosa, an American art historian who specialized in Japanese art, led him to become fascinated with oriental art.

Much of his collection was objects and pieces from the Orient. Upon his passing he donated his large collection of American silver to the Smithsonian Institution and the remainder of his collection to the Albright Art Gallery located in his hometown of Buffalo. Even though he loved children he never had any of his own and therefore gave the remainder of his sizable estate to Buffalo Institutes that cared for crippled, blind, and needy children.

He also had a great love for hiking and climbing mountains, taking a majority of his vacations among mountain ranges like the Alps, the Canadian Rockies, and the Selkirks. He was among the first group to ascend both Mount Lefroy and Mount Victoria between Alberta and British Columbia's borders. He was an alert, artistic, and brilliant person but he was also intensely private. Michael resented publicity of any kind, even denying awards due to the publicity they would draw. It can be believed that he never received the credit he was due but many that knew him believed he wouldn't have appreciated the attention. His intense dedication to organic chemistry was not done for accolades but for his love of organic chemistry. His career spanned the length of almost seven decades; he first became published at the age of twenty-three and had a great number of publications throughout his life, with his final publication appearing a few months after his death.

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