Mendeleev, Menshutkin and Beilstein: A New Generation Takes Over

This year is the sesquicentennial of the publication of the periodic table,[1] and 2019 has been designated the International Year of the Periodic Table by UNESCO. Of equal (or more) importance to organic chemists, this year is also the sesquicentennial of the initial publication of Markovnikov's Rule, making 1869 a standout year for Russian chemistry. As a result, during this sesquicentennial year, the Name Reaction Bio columns will focus on Russian name reactions and rules.

The last third of the nineteenth century was a banner era in Russian organic chemistry.[2] In 1868, the Russian Chemical Society was founded during a meeting of the first Congress of Russian Naturalists and Physicians, making it one of the oldest chemical societies in Europe (Figure 1). During this time, Butlerov, Borodin, Markovnikov, Zaitsev, Wagner, Zelinskii, Beilstein, Reformatskii, Menshutkin and others had contributed greatly to the growth of the discipline.

In the sixteen weeks from October 18, 1906, to February 5, 1907, three of the founding members of the Society died: Friedrich Konrad (Fedor Fedorovich) Beilstein (1838–1906; d. October 18), Dmitrii Ivanovich Mendeleev (1834–1907; d. February 2) and Nikolai Aleksandrovich Menshutkin (1842–1907, d. February 5). Their deaths followed those of Borodin (d. February 27, 1887), Wagner (d. November 27, 1903) and Markovnikov (d. February 11, 1904). This brief period also signaled the end of an era in Russian chemistry. The last of the Russian organic chemists who had achieved their zenith during the 19th century, Aleksandr Mikhailovich Zaitsev (1841–1910), died by the end of the decade.

Figure 1 Founders of the Russian Chemical Society. Standing (left to right): F. R. Vreden, P. A. Lachinov, G. A. Schmidt, A. R. Shulyachenko, A. P. Borodin, **N. A. Menshutkin**, N. A. Sokovkin, **F. F. Beil'shtein** (**F. K. Beilstein**), K. I. Lisenko, **D. I. Mendeleev**, F. H. Savchenkov. Seated (left to right): R. Yu. Richter, S. I. Kovalevskii, N. P. Nechaev, V. V. Markovnikov, A. A. Voskresenskii, P. A. Il'enkov, P. P. Alekseev, A. N. Engel'gardt. Image courtesy of Lomonosov Moscow State University.

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Beilstein Mendeleev Menshutkin

Mendeleev

Mendeleev was born in Tobolsk, Siberia, the youngest surviving child of seventeen. His father died when Mendeleev was a child, leaving his mother to raise her children alone. She reopened the family glass factory after her husband's death and ran it until it burned down. With that, she took her family to Moscow where she hoped to gain her son entry into the university. He was not accepted, however, so she moved the family again, to St. Petersburg, where Mendeleev was accepted into the Main Pedagogical Institute (now St. Petersburg State University), graduating in 1856. He contracted tuberculosis shortly thereafter, which forced him to move to a drier climate – Simferopol, Crimea. There he became science master at the Gymnasium, but he quickly found that he was not cut out to be a secondary school teacher. In 1857, recovered, he returned to St. Petersburg to the Chair of Chemistry at the St. Petersburg Technological Institute. He was called to the Chair in General Chemistry at St. Petersburg University in 1867 and was succeeded at the Technological Institute by Beilstein. He moved to the University of St. Petersburg, where he remained as Professor of Chemistry until 1890; he was appointed director of the Bureau of Weights and Measures in 1893 and occupied this position until his death.

In 1861, Mendeleev wrote *Organic Chemistry*[3] in response to his perception that there was no modern textbook for his course in organic chemistry. He wrote the book, which won the Demidov Prize of the Russian Academy of Sciences, in just two months. It was based on Gerhardt's type theory,[4] which was being superseded as organic chemists moved to the structural theory of organic chemistry.[5] Butlerov's book, *Introduction to the complete study of organic chemistry*,[6] published in 1864 and based entirely on structural theory, soon displaced it. Mendeleev's *Principles of Chemistry*, published in 1868,[7] quickly eclipsed his *Organic Chemistry* and became a major textbook of chemistry. It was while writing it that he developed his periodic table. The title pages of Mendeleev's books are given in Figure 2.

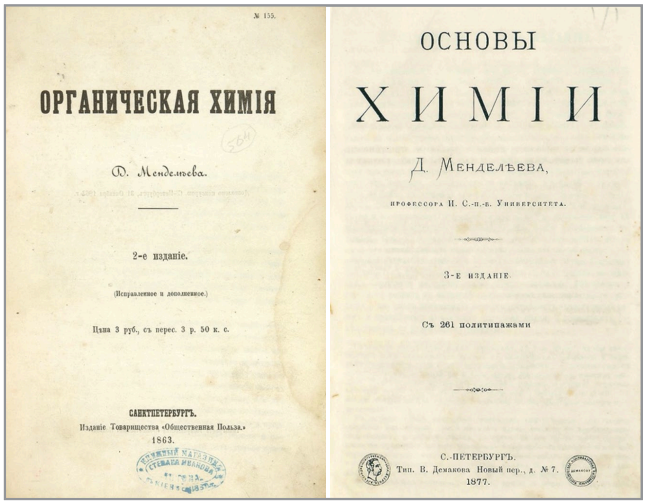


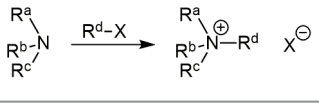
Figure 2 Title pages of Mendeleev's *Organic Chemistry* (left) and *Principles of Chemistry* (right)

His most lasting contribution to chemistry was his Periodic Law, during the development of which he proposed the existence of three then-unknown elements to fill gaps in his periodic table. Moreover, he asserted, on more than one occasion, that the accepted atomic weights for certain elements were incorrect because they did not correlate with periodic law; subsequent research proved him correct. Mendeleev did not present his proposals in person because he was absent from St. Petersburg on business for the Government Office of Weights and Measures. His paper[1] was read by his colleague and close friend, Menshutkin, and with Beilstein's encouragement, it was translated into German.[8] Mendeleev was elected a Corresponding Member of the Russian Academy of Sciences in 1876, but in 1880 he was denied the position of Professor of Technology in the Academy of Sciences by one vote (actually, an extraordinary majority was needed for election, but Mendeleev's supporters focused on the "just one vote").[9] He was awarded the Davy Medal of the Royal Society in 1882 (jointly with J. L. Meyer), and the Copley Medal of the Royal Society in 1905 for his work in elucidating the Periodic Law. In 1907 he missed a share of the Nobel Prize in Chemistry by a single vote (again!),[10] but the denial of the Professorship in the Russian Academy of Sciences was his most bitter defeat.

Menshutkin

Mendeleev's colleague and friend Nikolai Aleksandrovich Menshutkin was a pioneer in physical organic chemistry, though he is best known for his eponymous reaction, the quaternization of tertiary amines with alkyl halides (Scheme 1). This paper appeared first in Russian,[11a] and then in German,[11b]

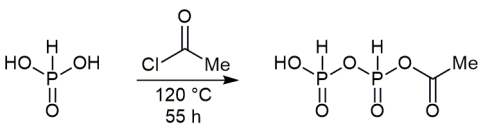
and although it has become primarily a synthetic paper, it was actually a far-reaching kinetic study of the rates of the quaternization reaction.



Scheme 1 The Menshutkin reaction: quaternization of tertiary amines with alkyl halides

Menshutkin was born to a wealthy merchant family in St. Petersburg and attended the German School there. He graduated first in his class 1857, at age 15, but because he was underage, he was prevented from entering the university until he had passed a comprehensive examination. At the university, he came under the mentorship of two distinguished elder statesmen of Russian chemistry: Aleksandr Abramovich Voskresenskii (1809–1880), from whom he learned analytical and physical chemistry, and Nikolai Nikolaevich Sokolov (1826–1877), from whom he learned organic chemistry. Sokolov was a dedicated pedagogue, and Menshutkin idolized him.

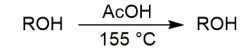
At this time, most Russian universities seldom had more than rudimentary laboratory facilities – the chemistry laboratory at St. Petersburg, for example, consisted of two small rooms[12] – so as soon as Menshutkin had graduated with the degree of *kandidat* in 1862, he set off on a three-year *komandirovka* (paid study leave) in Western Europe to learn practical chemistry. He spent these three years in the Tübingen laboratory of Adolph Strecker (1822–1871), the Paris laboratory of Adolphe Wurtz (1817–1884), and the Marburg laboratory of Hermann Kolbe (1818–1884). While in Paris, he began his studies on the phosphorous acid derivative formed by the reaction between phosphorous acid and acetyl chloride (Scheme 2).[13]



Scheme 2 Reaction of phosphorous acid and acetyl chloride

By the time of his return to St. Petersburg, he was ready to write up his dissertation for the degree of *Magistr Khimii*, based on his studies of phosphorous acid.[14] Immediately after his graduation, he became Privatdocent in chemistry, and was quickly appointed permanent Docent (Assistant Professor) in the Chair of Chemistry. Menshutkin taught analytical chemistry (both lecture and laboratory), and a special course on alcohols. He began the research for his *Dr. Khimii* degree at the same time, and presented his dissertation, *Synthesis and properties of ureides*, in April 1869.[15] The formal opponents of this dissertation were Mendeleev and Butlerov, who both noted the extraordinary experimental skill of its author. Menshutkin was immediately appointed Extraordinary (Associate) Professor of Chemistry, and in 1876 he became Ordinary (Full) Professor. Beginning in 1871, he served two terms as Secretary of the Physics–Mathematics Faculty, and this was followed in 1879 by his election as Dean. He held this position until 1887, when he returned to the faculty as Professor. In 1885, he had become Head of Organic Chemistry, and in 1891 he was appointed "Honored Professor." Two years later, in accord with the rules of the Ministry of Education, he retired from his Chair and became a "contingent" (i.e., Emeritus) Professor, but he retained his laboratory.

For much of his career, Menshutkin was an administrator, and his research output was fairly limited. He did serve as the Editor of the *Journal of the Russian Chemical Society* in 1869,



Primary alcohols

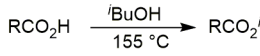
Alcohol	Initial velocity
MeOH	55.59
EtOH	46.81
^{n}PrOH	46.50
^{n}BuOH	46.85
$^{n}C_8H_{17}OH$	46.57
i-BuOH	44.36
H_2CCHCH_2OH	35.72
$HCCCH_2OH$	20.50
$PhCH_2OH$	38.64

Secondary alcohols

Alcohol	Initial velocity
^{i}PrOH	26.53
EtCH(Me)OH	22.59
^{i}PrCH(Me)OH	18.95
Et_2CHOH	16.93
^{i}BuCH(Et)OH	18.23
$^{n}C_6H_{13}CH(Me)OH$	21.19

Tertiary alcohols

Alcohol	Initial velocity
^{t}BuOH	1.43
$Me_2C(Et)OH$	0.81
$Et_2C(Me)OH$	1.04
$^{n}PrCMe_2OH$	2.15
$^{i}PrCMe_2OH$	0.86
$H_2C{=}CHCH_2CMe_2OH$	3.08



Acid	Initial velocity	Acid	Initial velocity
HCO_2H	61.69	$^{n}C_7H_{15}CO_2H$	30.86
$MeCO_2H$	44.36	$^{i}PrCO_2H$	29.03
$EtCO_2H$	41.16	$EtCH(Me)CO_2H$	21.50
$^{n}PrCO_2H$	33.25	$^{t}BuCO_2H$	8.28
$^{n}C_5H_{11}CO_2H$	33.08	$EtCMe_2CO_2H$	3.45

Figure 3 Menshutkin's investigations of uncatalyzed esterification reactions

and of its successor, the *Journal of the Russian Physical–Chemical Society* from 1870 to 1900, leaving a lasting mark on the course of organic chemistry in Russia.

We have already alluded to what we now know as the Menshutkin (Menschutkin) reaction, but he was actually one of the pioneers of physical organic chemistry. In both the Menshutkin reaction and his extensive studies of the effects of structure on the rates of uncatalyzed esterification reactions, he was able to show that the structure of the alkyl group of the acid and the alcohol both affect the rate of the esterification reaction. Figure 3 gives data from one of Menshutkin's studies in which equimolar quantities of the acid and alcohol were heated together at 155 °C without any catalyst. All the reactions were carried out to the same fraction of completion (approximately 70%).[16] Thus, Menshutkin was one of the pioneers in the study of what we call structure–reactivity relationships.

Beilstein

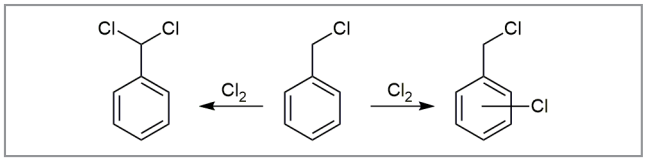
The third principal of this Name Reaction Bio is Fyodr Fyodrovich Beil'shtein, better known by the German form of his name, Friedrich Konrad Beilstein. To quote American historian Mark Gordin,[17] "Beilstein may be the best-known organic chemist that most organic chemists know nothing about." Most organic chemists are familiar with *Beilsteins Handbuch der organsichen Chemie*, which has gone through four supplements to the original *Hauptwerk*, and is now online (since 2009, the content has been maintained and distributed by Elsevier Information Systems in Frankfurt, under the product name "Reaxys"[18]).

Beilstein was born to an ethnic (Baltic) German family in St. Petersburg, but his parents decided that he should receive a German education. He began his education at the St. Petersburg German School, and then, in 1853, at the age of 15, his parents sent him to Germany to complete his education. He studied first with Bunsen at Heidelberg, then he moved to Berlin in 1855, where he worked with Jolly and attended lectures by Liebig. He met Hübner and Kekulé on his return to Heidelberg in 1856 and became firm friends with both. In 1857, he moved to Göttingen, where he received his Ph.D. two days before his 20th birthday.

Beilstein spent 1858 with Wurtz in Paris, and returned to Germany in 1859 as Assistant to Löwig in Breslau. However, Beilstein chafed under the rigid rules in Löwig's laboratory, so when Wöhler offered him a position at Göttingen in 1860, he eagerly returned to his alma mater. He remained at Göttingen until 1866, when he returned to St. Petersburg after the sudden death of his father. It is interesting that he had been made an offer by St. Petersburg University in 1865 and that this had been countered by an offer from Göttingen, but he returned to Russia to take up a position as Professor at the less prestigious St. Petersburg Technological Institute at a lower salary. A year after his return to Russia, he renounced his German citizenship to become a subject of the Tsar; at the time, this was a highly unusual action. Beilstein spent the remainder of his career at the Technological Institute.

Beilstein's research output was relatively scant (especially compared to his contemporaries, Menshutkin, Markovnikov and Butlerov), which may be surprising given the impact of his *magnum opus*. Unlike the University, the Technological Institute was not a research-focused institution, but was intended, instead, for the education of engineering students. Neither the students nor Beilstein's assistants had any interest in research, so his output rapidly dwindled to zero. This may, in fact, have been a blessing in disguise, because it gave him the time needed to write his *Handbuch der organischen Chemie*.

Beilstein's original research was involved with the preparation and reactions of organic halogen compounds. His study of the chlorination of benzyl chloride showed that the regiochemistry of the reaction was dependent on the exact reaction conditions. At low temperature, Beilstein obtained ring-substituted products, chlorobenzyl chlorides, and at high temperature, he observed the formation of the side-chain-chlorinated product, benzal chloride (Scheme 3).[19] During this same work, he developed the Beilstein test for halogens[20] (consisting of heating a copper wire in a Bunsen burner flame until all traces of blue or green were absent from the flame, cooling the wire, immersing the cold wire in the substance to be tested, and finally returning it to the flame; a green flame indicated the presence of halogen in the test material).



Scheme 3 Beilstein's investigations into the regiochemistry of the chlorination of benzyl chloride

Like Menshutkin, Beilstein served as Editor of a chemistry journal. In Beilstein's case, the journal was the *Zeitschrift für Chemie und Pharmacie*, which he co-edited with his friend, Hübner, and Rudolf Fittig. He continued editorship of the journal following his return to Russia, and there he successfully promoted the *Zeitschrift* as a German-language outlet for Russian chemists. It was Beilstein who persuaded Mendeleev to

publish his periodic law in the *Zeitschrift*, which was probably a critical step in obtaining its widespread acceptance.[21]

We cannot conclude this Name Reaction Bio without recounting the events of 1880, when Mendeleev was denied the Chair of Technology in the Academy of Sciences. This event literally tore the Russian chemical community apart. The "Russian" faction in the Academy, which included Aleksandr Mikhailovich Butlerov (1828–1886), viewed Mendeleev's rejection as a repudiation of Russian organic chemists in general. Butlerov led the major figures in writing a letter to the popular press in which they lambasted the Academy, but Beilstein did not sign the letter because he believed that the appropriate action was to censure the Academy in a lecture read before the Russian Physical–Chemical Society. This branded him as a member of the "German" faction (his actions in having become a naturalized subject of the Tsar thirteen years earlier notwithstanding) and shattered his long friendship with Butlerov. When Butlerov himself was elected to the Chair in 1882, he used the rules of the Academy to prevent Beilstein from being confirmed in that position: Beilstein became the Professor in the Chair of Chemical Technology only after Butlerov's death.

With the loss of these three chemists, the nineteenth century era of organic chemistry in Russia came to an end, and the torch was passed on to the next generation of Russian organic chemists. Among these were Markovnikov's students (Kizhner, Chichibabin and Dem'yanov), Zaitsev's students (Reformatskii and Arbuzov), as well as Butlerov's student (Favorskii) and Favorskii's student (Ipat'ev/Ipatieff), all of whom influenced the course of organic chemistry.

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