DOI: 10.1002/anie.201100215

# A. M. Zaitsev: Lasting Contributions of a Synthetic Virtuoso a Century after his Death

*David E. Lewis**

alcohols · history of chemistry · organic synthesis ·
sulfonium salts · Zaitsev, Aleksandr

The year 2010 marked the centenary of the death of Aleksandr Mikhailovich Zaitsev (Alexander Saytzeff, 1841–1910; Figure 1), Professor of Chemistry at Kazan University, and a pioneer in organosulfur and organozinc chemistry.[1] Zaitsev held the Chair of Chemistry at Kazan for 39 years, and in that time was responsible for the training of some of the most eminent organic chemists of the next generation, among them Egor Egorevich Vagner[2] (Georg Wagner, 1849–1903), Sergei Nikolaevich Reformatskii (1860–1934), and Aleksandr Ermingingel'dovich Arbuzov (1877–1968). In addition, he served two terms as the President of the Russian Physical-Chemical Society, and he was elected a Corresponding Member of the Russian Academy of Sciences. Today, Kazan is the capital of the Russian Republic of Tatarstan. It is located approximately 750 km east of Moscow on the Volga River, and is a city of approximately 1.2 million that is a major scientific and economic hub. In 1804, when the university there was founded, the population of Kazan was just over 40000; during Zaitsev's career, the population more than tripled from just over 60000 to more than 200000.

***Figure 1.*** Aleksandr Mikhailovich Zaitsev late in his career (estimated after 1900).

Zaitsev was born to Mikhail Savvich Zaitsev and his second wife, Nataliya Vasil'evna Lyapunova, the sister of the astronomer Mikhail Vasil'evich Lyapunov (1820–1868), who also served as Professor of Astronomy at Kazan University. Zaitsev's family had lived in the Kazan district since the time of Ivan the Terrible, and held a prominent place in the trading guilds (his grandfather, Savva Stepanovich Zaitsev had been an elder in the cathedral, and was one of the group directing the cathedral renovation during 1824–1825). Mikhail Zaitsev had determined that his son should follow him into the guilds, so when the time came for young Aleksandr to complete his education, it was only at the urging of his uncle that his father permitted him to enter the university, and then only so long as Aleksandr entered the Judicial-Economics faculty as a *cameralist*. It was Lyapunov who taught young Zaitsev the Latin he needed to enter the university.

As his father wished, Zaitsev entered Kazan University as a cameralist. The cameralisty were students in training to become government bureaucrats, and at the time that Zaitsev entered Kazan University, all cameralisty were required to study chemistry for two years. It was during these studies that he encountered one of the most influential Russian organic chemists of the nineteenth century: Aleksandr Mikhailovich Butlerov (1828–1886; Figure 2).[3]

At the time, Butlerov was Professor of Chemistry at Kazan. He had studied chemistry under Nikolai Nikolaevich Zinin (1812–1880), the discoverer of the reduction of nitrobenzene to aniline,[4] and Karl Karlovich Klaus (1796–1864), the discoverer of ruthenium,[5] but he had written his *kandidat* dissertation in entomology.[6] However, to meet the needs of the university, he was seconded to teaching chemistry, like his mentor, Zinin. He first became Klaus' assistant in chemistry and, after Klaus left for Dorpat, he assumed all instruction in chemistry. His *Magistr Khimii* (M. Chem.) dissertation[7] was largely a review of the literature, although it did contain the first report of the oxidation of alkenes with osmium tetroxide.[8] His dissertation for the degree of *Doktor Khimii* (Dr. Chem.), which was necessary before he could assume the Chair in Chemistry, was also largely a historical review. It is worthwhile noting that the faculty at Kazan did not approve Butlerov's dissertation for the degree of Dr. Chem., so he

---

[*] Prof. Dr. D. E. Lewis
Department of Chemistry
University of Wisconsin-Eau Claire
Eau Claire, WI 54702 (USA)
Fax: (+1) 715-836-4979
E-mail: lewisd@uwec.edu
Homepage: http://www.uwec.edu/lewisd/homepage/lewis.htm

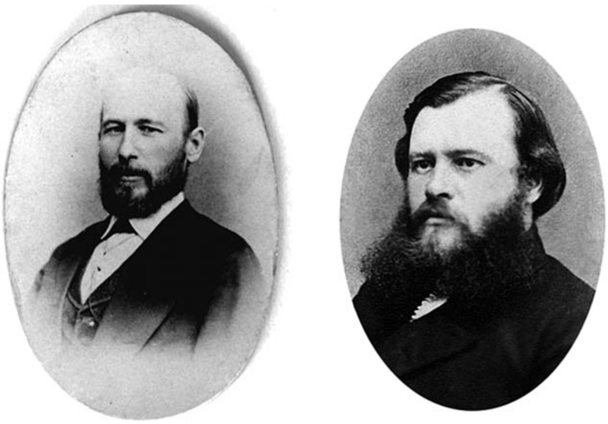


**Figure 2.** Left: Aleksandr Mikhailovich Butlerov as a professor at Kazan University (ca. 1867). Right: Vladimir Vasil'evich Markovnikov (ca. 1869)

defended it at Moscow University instead. Before he left Kazan for St. Petersburg in 1869, Butlerov had served two terms as Rector of the university; he spent the rest of his career at St. Petersburg. More complete reviews of his career can be found in references [3].

During his first study abroad (*komandirovka*) in western Europe (1857–1858), Butlerov spent time in the Paris laboratory of Adolphe Wurtz. While there, he carried out research with methylene derivatives, including methylene iodide and formaldehyde; these studies included the first synthesis of a saccharic substance ($\alpha$-acrose).[9] Butlerov's major contribution to organic chemistry was his work to clarify and simplify structural theory, which he incorporated into his lectures, and which he used to predict the existence of new isomers of organic compounds. In doing so, he also designed experiments to verify the existence of these compounds by synthesis, accomplishing the first designed syntheses of simple tertiary alcohols,[10] for example. In his address at the chemical section of the 36th *Versammlung deutscher Naturforscher und Ärzte* in Speyer, in September 1861, he first used and defined the term "chemical structure", and he set forth his version of structural theory.[11] His second *komandirovka* a decade later was spent in defending his claims to an important part in the development of structural theory. Soviet historians during the 1950s, especially, when politicization was rife, sought to give Butlerov credit for inventing the theory;[12] in doing so, they missed the decisive impact of his real contribution, which was to turn an esoteric theory into a truly useful predictive tool for organic chemists.

*David E. Lewis was born in South Australia and educated (BSc, PhD) at the University of Adelaide. Following postdoctoral study at Arkansas and Illinois, he joined the faculty of Baylor University as Assistant Professor in 1981. In 1989, he moved to South Dakota State University as Associate Professor, and, in 1997, to the University of Wisconsin-Eau Claire as Professor. He was Chair of the American Chemical Society's Division of the History of Chemistry from 2003 to 2004, and is a Fellow of the Royal Australian Chemical Institute.*

It is unclear whether Butlerov considered Zaitsev one of his disciples at this time, but it is clear that Zaitsev quickly became enamored of chemistry, even though he continued with his studies in the Judicial-Economics faculty. In 1862, he graduated with his *Diplom* in economics. His father had died shortly before his graduation, and the family business had been sold, so Zaitsev used his share of the proceeds to go to western Europe to study chemistry. He began by following his older brother, Konstantin Mikhailovich (born 1840) to the Marburg laboratory of Hermann Kolbe (1818–1884).[13] He spent four semesters studying with Kolbe and then moved to Paris, where he spent the next two semesters studying in Wurtz' laboratory. During his time in Paris, Zaitsev investigated the synthesis of diaminosalicylic acid and the reactions of chloroacetic ester with potassium cyanide.[14] In April 1865, he returned to Kolbe's Marburg laboratory for one last semester, but by this time, his funds were almost exhausted. In September 1865, his financial circumstances forced him to return to Russia; Zaitzev could not follow Kolbe to Leipzig when he took up the Chair of Chemistry there in October.

While at Marburg, young Zaitsev realized that his lack of a *kandidat* degree meant that he was not eligible for appointment to a salaried position at a university. In hope of avoiding this undesirable outcome, in February 1863 he submitted a hand-written dissertation[15] from Marburg to Kazan. The dissertation championed the position of Kolbe, structural theory's staunchest opponent, but it was examined by Butlerov, structural theory's most ardent proponent. Not surprisingly, it was an unmitigated disaster—Butlerov's unusually caustic comments pointed out its many inaccurate and unproven statements, and Butlerov described it as "a poor translation from the German." [16] Needless to say, Zaitsev did not receive the degree. And yet, less than three years later, it was Butlerov who enabled Zaitsev to return to Kazan University (by allowing him to join his research group as an unpaid laboratory assistant; Figure 3) and who encouraged him to write up his work on diaminosalicylic acid and its salts (work that he had carried out at Marburg) as his *kandidat* dissertation.[17] The degree of *kandidat* was awarded in 1865, and this allowed Zaitsev to be appointed to a salaried position as an assistant in Agronomy.

Zaitsev's ambition was to become a Professor of Chemistry, and to do this he needed the degree of Master of Chemistry (*Magistr Khimii*, M. Chem.), which was awarded by the Physics-Mathematics Faculty of the university. However, as a graduate in *cameral* science, he was not eligible to obtain the degree of M. Chem. from the Physics-Mathematics faculty.[18] He could, however, become eligible to pursue the degree of M. Chem. by obtaining a doctoral degree from a foreign university, so he submitted the results of his work at Marburg to Hermann Kolbe at Leipzig. Presumably with Kolbe's help (he is listed among Kolbe's *Praktikanten* at Marburg and is in the first list at Leipzig),[19] he was awarded the degree of Doctor of Philosophy by Leipzig University in 1866.[20] This gave him the needed qualifications to submit his work for the degree of M. Chem. at Kazan, but he still required Butlerov's help to obtain permission to submit for

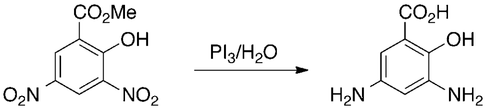
***Figure 3.*** Butlerov and a group of his students (1867—1868). Rear row: unidentified, A. N. Popov, A. M. Zaitsev, G. N. Glinskii. Front row: unidentified, unidentified, A. M. Butlerov, A. I. Loman, unidentified, unidentified.

the degree of M. Chem., which he did in 1867. The dissertation[21] described his work on the chemistry of sulfur compounds, and the degree was awarded in 1868.

On gaining his degree of M. Chem., Zaitsev was appointed to the faculty of Chemistry as an Extraordinary Professor in 1869. One year later, he received his Doctor of Chemistry degree for a dissertation[22] describing the reduction of fatty acid chlorides to the corresponding primary alcohols using sodium amalgam in diethyl ether buffered with acetic acid, and he was promoted to Ordinary Professor, becoming (briefly) the colleague of Vladimir Vasil'evich Markovnikov (1838–1904). He held this chair until 1910 (Figure 4). Markovnikov, with whom Zaitsev feuded most of his life,[23] had been appointed as one of the two formal opponents (examiners) of the dissertation, and his report was written as an overtly positive one, but meant to be read between the lines as a very negative one. Butlerov, who knew of the antipathy between the two young men, was able to convince the university faculty that the degree should be awarded; as it was, the vote to award the degree was split, 19: 12.

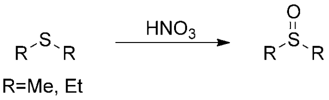
Zaitsev's time in Kolbe's laboratory was productive, and showcased the young man's impressive experimental skills, which were a hallmark of his long career. His synthesis of 3,5-diaminosalicylic acid,[14] a compound susceptible to extremely facile oxidation unless it is kept as its conjugate acid, and the study of its salts, led to the first papers from his work in Kolbe's laboratory, and attests – his experimental prowess (Scheme 1).

The first of his lasting chemical contributions from this time was his discovery of the oxidation of sulfides by nitric acid to give sulfoxides (Scheme 2).[24] Heretofore, this class of organic compounds had been unknown, and Zaitsev's synthesis and isolation of the sulfoxides made them easily available for study.



***Scheme 1.*** Zaitsev's synthesis of 3,5-diaminosalicylic acid.

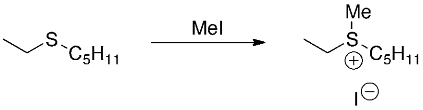
***Figure 4.*** Zaitsev lecturing to students in the Butlerov lecture room at Kazan University (late 1890s).



***Scheme 2.*** Zaitsev's synthesis of sulfoxides.

For many years sulfoxides were largely the province of a small group of organic chemists, but this situation changed in the 1960s and 1970s, when Corey began using the conjugate base of dimethyl sulfoxide, dimsyl sodium, as a base for preparing phosphonium ylides.[25] More recently, sulfoxides have become important synthetic intermediates in their own right, and there is a rich literature on the chemistry of these versatile compounds.[26]

At the same time that Zaitsev discovered the sulfoxides, he also discovered the sulfonium salts (Scheme 3).[27] These compounds, like the sulfoxides, languished for years as a curiosity. However, in the 1960s, Corey and Chaykovsky published their landmark paper on the synthesis and use of sulfonium ylides,[28] and these compounds, also, entered mainstream organic synthesis. The use of sulfonium ylides in cyclopropanation and epoxide formation has made these species invaluable in organic synthesis.[29] More recently, the application of chiral sulfonium ylides in the synthesis of epoxides and cyclopropanes has been explored.[30]



***Scheme 3.*** Zaitsev's synthesis of sulfonium salts.

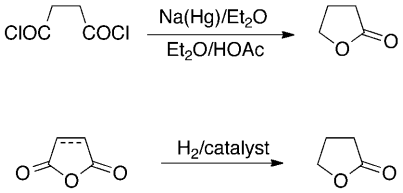
Zaitsev's Russian mentor had been Butlerov, and the influence of Butlerov is clear in the work that Zaitsev did as an independent researcher in the 1870s. In 1863, Butlerov had reported the first synthesis of a tertiary alcohol by the reaction between acetyl chloride and dimethylzinc.[10] Zaitsev took this reaction further, replacing the pyrophoric dimethylzinc with zinc metal and an alkyl iodide (which forms the alkylzinc iodide in situ; Scheme 4).[31] With his students, he was able to show that this facilitated the synthesis of tertiary 2-alkyl-2-propanols and 3-alkyl-3-pentanols; with his brother, he showed that when propyl iodide was used, the product of the reaction was the secondary alcohol rather than the expected 4-alkyl-4-heptanol. For a quarter of a century, the Zaitsev–Butlerov organozinc synthesis was the method of choice for preparing alcohols. However, the reaction did not work under all conditions, and in 1900, it was superseded when Victor Grignard (1871–1935) discovered the alkylmagnesium halides and the reaction that now bears his name.[32]

***Scheme 4.*** Zaitsev (top) and Zaitsev–Wagner (bottom) syntheses of alcohols.

In the 1980s, however, the synthesis of alcohols using organozinc reagents underwent a major revival when Noyori discovered the asymmetric synthesis of secondary alcohols by the reaction between an aldehyde and a dialkylzinc, catalyzed by a chiral β-aminoalcohol.[33] That Noyori shared the Nobel Prize in Chemistry for 2001 reflects the importance of organozinc nucleophiles in modern synthesis. This renaissance of organozinc chemistry has been continued by the work several research groups, as illustrated by the number of reviews in this area in the past two decades;[34] one may gauge how active this area of research is by the number of papers appearing in the last two years.

The original Zaitsev synthesis of alcohols using allyl iodide and zinc as the organometallic reagent (presumably allylzinc iodide) has itself been the subject of a major resurgence during the last twenty years, although the reaction has been incorrectly ascribed to Phillipe Antoine Barbier (1848–1922) rather than to Zaitsev. In particular, the use of propargyl halides and zinc or indium metal provides a version of the reaction that can be carried out in aqueous medium.[35]

As noted earlier, Zaitsev's Dr. Chem. dissertation described the reduction of acid chlorides by sodium amalgam in ether (Scheme 5).[36] The critical part of this work was Zaitsev's observation that the reduction reaction becomes exceptionally slow as the pH of the solution increases, and that buffering with acetic acid is necessary to obtain a good yield of the desired alcohol. In the course of this research, Zaitsev discovered γ-butyrolactone, which he prepared by the reduction of succinyl chloride.[37] Industrially, γ-butyrolactone is an important solvent with applications such as in de-inking. Its large-scale production today relies on the catalytic hydrogenation of succinic or maleic anhydride in the gas phase. This provides an interesting historical continuity with Zaitsev's original synthesis by reduction of a succinic acid derivative.



***Scheme 5.*** Zaitsev's synthesis of butyrolactone (top) may be contrasted with the modern large-scale synthesis from maleic or succinic anhydride (bottom).

The uses of γ-butyrolactone are not, however, all benign. Its use today as an illicit drug (the "date rape" drug[38]) has once again brought Zaitsev's work into the spotlight, albeit in a less-than-flattering light.

Zaitsev also examined, albeit briefly, oxidation reactions. In 1886, he described the oxidation of oleic and elaidic acids with aqueous potassium permanganate to give dihydroxystearic acids.[39] He did not pursue this reaction further, but his student, Wagner, did, with the result that the reaction became a method of choice for locating double bonds in alkene hydrocarbons, and became known as the "Wagner oxidation".

The reason that most organic chemists remember Zaitsev's name today is not, however, for his accomplishments in organosulfur chemistry or in the synthesis of alcohols. It is for a single paper in 1875, in which he first set forth the rule that now bears his name.[40] In this paper, which contains—unacknowledged, for some reason—elements of work by his students, Wagner and Grabovskii, as well as work done by another Butlerov student, Aleksandr Nikolaevich Popov (1840–1881), Zaitsev shows that the elimination of hydrogen halides from alkyl halides gives the alkene with the more substituted double bond, which means that elimination is not, in fact, the exact reverse of addition, as had been speculated by Markovnikov at the time he carried out his seminal studies on addition reactions. It has been suggested[23] that the feud between Zaitsev and Markovnikov may have been one factor behind the work that led to Zaitsev's Rule.

Just as Zaitsev's independent career and the course of his research program had been strongly influenced by his mentor, Butlerov, so one can trace the influence of Zaitsev himself on the careers of his own students. Three of his students, who have already been mentioned, attained positions of international eminence: Wagner, Reformatskii, and Arbuzov (Figure 5). The first of Wagner's contributions to synthetic chemistry, begun while he was a student at Kazan, was his extension of the Zaitsev–Butlerov synthesis of alcohols by using aldehydes and formate esters as the carbonyl partner, thus providing a reliable method for the synthesis of both symmetrical and unsymmetrical secondary alcohols. Although the early papers in the series were co-published with Zaitsev,[30a,e] later Wagner published his results under his own name, without Zaitsev as a coauthor.[41] This reaction, which became known as the Wagner–Zaitsev reaction, is now once again an important method for the synthesis of alcohols owing

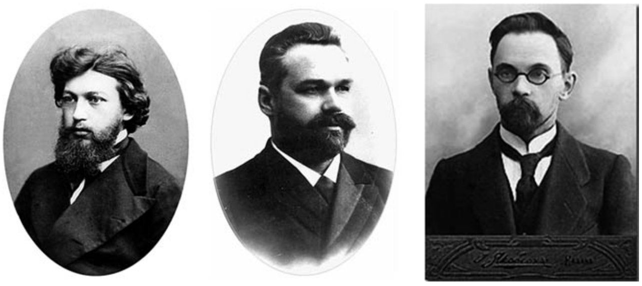
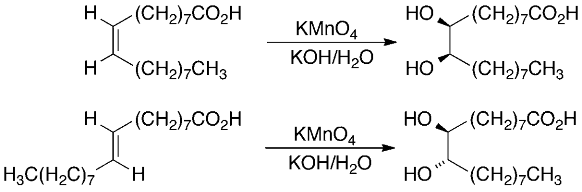


**Figure 5.** Zaitsev's students who themselves achieved eminence. Georg Wagner (1849–1903), Sergei Reformatskii (1860–1934), Aleksandr Arbuzov (1877–1968).

to the discoveries of Noyori, alluded to above, and with the development of organozinc chemistry as a viable alternative to other organometallic reactions. As has become apparent over the years, organozinc reagents do have the great advantage over organomagnesium and organolithium reagents of being tolerant to a wide range of functional groups.

Wagner later went on to become a pioneer in the oxidation of alkenes with permanganate; his important contribution[42] was to extend and systematize his mentor's work by determining the effects of permanganate concentration on the course of the reaction. He found that it is critical to keep the concentration of permanganate below 4 %, and to keep the pH of the solution basic if one wishes to avoid over-oxidation of the alkene. Under these conditions, however, good yields of the diol can often be obtained, and this remains an important oxidation reaction (Scheme 6).

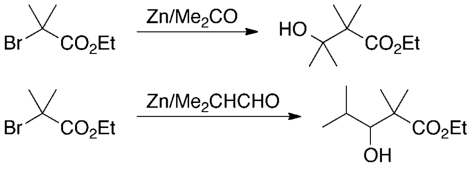


**Scheme 6.** Oxidations of oleic and elaidic acids studied by Zaitsev (1869) and Wagner (1888).

Most famously, Wagner introduced the concept of rearrangements[43] to the chemical community, work that was completed by Hans Leberecht Meerwein (1879–1965).

Reformatskii was the Zaitsev student whose independent work most closely mirrored that of his mentor. As a student in Zaitsev's laboratory, Reformatskii was encouraged to study the reactions of ketones with zinc metal and α-halocarbonyl compounds in an obvious extension of Zaitsev's discovery that allyl halides and zinc form an intermediate compound that adds to aldehydes and ketones to give homoallylic alcohols (Scheme 7). The one organozinc synthesis of alcohols that the Grignard reaction failed to displace was published by Reformatskii under his own name, without Zaitsev as a coauthor, in 1887.[44]

Having noted that allylic iodides reacted much better than their saturated counterparts in the synthesis of alcohols, Zaitsev may have suggested to his student, Refomatskii, that he try making organozinc reagents from the carbonyl analogue of an allylic halide. Reformatskii's discovery of this synthesis of β-hydroxyesters gave organic chemists a reaction that is still in use today, although it has been replaced somewhat since the late 1970s by the use of strong amide bases for the generation of lithium enolates.



**Scheme 7.** The Reformatskii reaction.

The last Zaitsev student to synthesize an alcohol by the organozinc route was Aleksandr Arbuzov. In 1900, just months before Grignard published his papers on the use of organomagnesium halides, Arbuzov completed the synthesis of 2-phenylpent-4-en-2-ol by the organozinc method, following this a year later by a synthesis by means of the Grignard procedure.[45] Of course, the Grignard reaction rendered his proposed dissertation topic obsolete, and he turned to what was to become both his life's work, and chemistry that led to his international reputation. Arbuzov's *kandidat* dissertation was on the unique hydrogen atom in phosphorus acid, and this started his over sixty years as an eminent phosphorus chemist, a career that included the discovery of the Arbuzov rearrangement.[46] In 1911, Arbuzov followed his mentor and assumed the Chair of Chemistry at Kazan University.

Aleksandr Zaitsev may have had the good fortune to live in an era when there was much to discover in organic chemistry, and he did, indeed, discover much. In addition, his students extended some of those discoveries to make them even more useful. His work has endured for over a century, and it is interesting to note that much of his chemistry has, in fact, undergone a renaissance since the last quarter of the twentieth century. What has not survived (unfairly, in my opinion) is the connection of Zaitsev's name to the very chemistry he pioneered.[47]

Received: January 11, 2011

---

[1] For biographies of Zaitsev in Russian, see: a) "*Biografiya Aleksandrovicha Zaitseva* [Biography of Aleksandr Mikhailovich Zaitsev]": A. N. Reformatskii, *Zh. Russ. Fiz.-Khim. O-va.* **1911**, *43*, abstract 6, p. 876; b) A. S. Klyuchevich, G. B. Bykov, *Aleksandr Mikhailovich Zaitsev (1841–1910)*, Science Publishing House, Moscow, **1980**; c) "Pamyati Prof. A. M. Zaitseva [Memories of Prof. A. M. Zaitsev]": S. N. Reformatskii, *Univ. Izv. Kiev*, **1910**, No. 11. *Pril.* 2. In *Protokol. Fiz.-Khim. O-va.*, p. 1; d) A. E. Arbuzov, *Kratkii ocherk razvitiya organicheskoi khimii v Rossii [A brief account of the development of organic chemistry in Russia]*, U.S.S.R. Academy of Science Publishers, Moscow, **1948**; e) A. M. Zaitsev provided autobiographical material in *Biograficheskii slovar' professorov i prepodavatelei Kazanskogo universiteta* (1804–1904) *[Biographical dictionary of the professors and teachers of Kazan university (1804–1904)]* (Ed.: N. P. Zagoskin), Kazan, **1904**, Part 1, 323–325; a list of his

works is included on pp. 325–332. Biographies in western European languages are less common: f) “Alexander Michola-jeff Saytzeff:” *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 2784; g) “Alexander Michajlowich Saytzeff,” *Pogg. biogr.-lit. Handwört. Gesch. exact. Wiss.*, Vol. III, p. 1176 (1898); Vol. IV, 1310 (1904); Vol. V, 1098 (1926); h) D. E. Lewis, *Bull. Hist. Chem.* **1995**, *17/18*, 21–30.

[2] Vagner was the grandson of a German immigrant to Russia. Both he and his father used the common Russian spelling, Egor, rather than the alternative form, Georgii, to emphasize the fact that they were Russian rather than German: see A. Sementsov, *Chymia* **1966**, *11*, 151–155. At the suggestion of a referee, the German transliteration of his name, Wagner, is used throughout this paper since he is best known under this form of the name.

[3] For biographies of Butlerov in Russian, see: a) “Vospominaniya i cherty ot zhizni i deyatel’nosti A. M. Butlerova [Memoires and features of the life and activities of A. M. Butlerov.]”: V. V. Markovnikov, *Zh. Russ. Fiz.-Khim. O-va.* **1887**, *19*, 69; b) “A. M. Butlerov. 1828–1928” (Akademiya Nauk SSSR: Leningrad, **1929**. This publication on the centenary of Butlerov’s birth contains chapters by V. E. Tishchenko, D. I. Konovalov, A. E. Favorskii, I. A. Kablukov, I. A. Gorbov, and A. E. Chichibabin. For biographies in English, see: c) H. M. Leicester, *J. Chem. Educ.* **1940**, *17*, 247; d) “Butlerov, Aleksandr Mikhailovich”: G. V. Bykov, in *Dictionary of Scientific Biography*, *Vol. II* (Ed.: C. C. Gillespie), Charles Scribners and Sons, New York, **1970**, p. 620; e) “Butlerov, Aleksandr Mikhailovich”: N. M. Brooks, *Complete Dictionary of Scientific Biography*, *Vol. 19*, Scribner’s Sons, Detroit, **2008**, pp. 465–468.

[4] a) N. N. Zinin, *Bull. Sci. Acad. Imp. Sci. St.-Petersbourg* **1843**, *10*, col. 273–285; b) N. Zinin, *Justus Liebigs Ann. Chem.* **1842**, *44*, 283–287; N. Zinin, *Justus Liebigs Ann. Chem.* **1844**, *52*, 361–362; N. Zinin, *J. Prakt. Chem.* **1842**, *27*, 140–153.

[5] C. Claus, *J. Prakt. Chem.* **1844**, *32*, 479–492; C. Claus, *Ann. Phys.* **1845**, *140*, 192–197; C. Claus, *Ann. Phys.* **1845**, *141*, 200–221.

[6] A. Butlerov, *Dnevnie babochki Volgo-Uralskoy fauny [Diurnal butterflies of the Volga-Ural region]*, Kand. Diss., Kazan, **1849**.

[7] A. M. Butlerov, *Ob okisleny organicheskikh soedineny [On the oxidation of organic compounds]*, M. Chem. Diss., Kazan, **1851**.

[8] a) A. M. Butlerov, *Ob efirnykh maslakh [On ethereal oils]*, Dr. Chem. Diss., Moscow, **1854**; b) A. Butlerow, *Justus Liebigs Ann. Chem.* **1852**, *84*, 278–280.

[9] a) A. Boutlerow, *C. R. Hebd. Seances Acad.* **1859**, *49*, 137–138; A. Boutlerow, *C. R. Hebd. Seances Acad.* **1861**, *46*, 595–597; A. Boutlerow, *C. R. Hebd. Seances Acad.* **1861**, *53*, 145–147; b) A. Butlerow, *Justus Liebigs Ann. Chem.* **1858**, *107*, 110–112; A. Butlerow, *Justus Liebigs Ann. Chem.* **1859**, *111*, 242–252.

[10] a) A. Boutlerow, *Bull. Soc. Chim. Paris* **1863**, *5*, 582; A. Boutlerow, *Bull. Soc. Chim. Paris* **1864**, *2*, 106–116; b) A. Butlerow, *Jahresb.* **1863**, 475; A. Butlerow, *Jahresb.* **1864**, 496; A. Butlerow, *Justus Liebigs Ann. Chem.* **1867**, *144*, 1–32. The synthesis of α-hydroxybutyric acid derivatives had been accomplished earlier by the reaction between dimethylzinc and oxalate esters [c) E. Frankland, *Justus Liebigs Ann. Chem.* **1863**, *126*, 109–113; d) E. Frankland, B. Duppa, *Justus Liebigs Ann. Chem.* **1865**, *135*, 25–29], but Butlerov’s synthesis was the first of simple tertiary alcohols.

[11] A. Butlerow, *Z. Chem. Pharm.* **1861**, *4*, 549–560.

[12] The propensity for Soviet historians of science to give Butlerov the credit for inventing the structural theory of organic chemistry rose to a peak during the politicization of the arguments over resonance theory in the 1950s: a) I. Hargittai in *Candid Science: Conversations with Famous Chemists* (Ed.: M. Hargittai), Imperial College Press, London, **2000**, pp. 8–13; b) *Sostoyanie teorii khimicheskogo stroeniya v organicheskoi khimii [The state of affairs of the theory of chemical structure in organic chemistry]*, Publishing House of the Soviet Academy of Sciences, Moscow, **1952**; c) A. J. Rocke, *Br. J. Hist. Sci.* **1981**, *14*, 27–57; d) *Atoms in Chemistry: From Dalton’s Predecessors to Complex Atoms and Beyond* (Ed.: C. J. Giunta): D. E. Lewis, *ACS Symp. Ser.* **2010**, *1044*, 35–57; e) I. Hargittai, *Struct. Chem.* **2011**, *22*, 247–251.

[13] K. M. Zaitsev was the first of a series of Butlerov students who worked with Kolbe at Marburg and then at Leipzig. On his return to Russia in 1863, after two semesters with Kolbe, he became a lecturer in analytical chemistry. In 1868, he was invited by the owners of the Krestovnikov soap factory to join the staff of the plant to organize the laboratory there. In 1872, he was appointed director of the laboratory, position he held for the next 35 years.

[14] A. Saytzeff, *Justus Liebigs Ann. Chem.* **1865**, *133*, 321–329; A. Saytzeff, *Bull. Soc. Chim. Paris* **1865**, *3*, 244–250. In these papers, Zaitsev reports that the colorless acid becomes a black mass, and that all attempts at preparing a nitrate salt—using an oxidizing acid—also gave a black mass.

[15] A. M. Zaitsev, *Teoreticheskie vzglyady Kol’be na ratsional’nuyu konstitutsiyu organicheskikh soedinenii i ikh svyaz’ s neorganicheskimi [The theoretical views of Kolbe on the rational constitution of organic compounds and their relationship with inorganic (compounds-DEL)]*. This dissertation is referred to in Ref. [1b].

[16] A. S. Klyuchevich, G. B. Bykov, *Aleksandr Mikhailovich Zaitsev (1841–1910)*, Science Publishing House, Moscow, **1980**, p. 12; A. S. Klyuchevich, G. B. Bykov, *Aleksandr Mikhailovich Zaitsev (1841–1910)*, Science Publishing House, Moscow, **1980**, pp. 65–66.

[17] A. Zaitsev, *O diamidosalitsilovnoi kislote* [Concerning diamidosalicylic acid], Kand. Diss., Kazan University, **1866**.

[18] Ref. [1b], p. 18.

[19] See A. J. Rocke, *The Quiet Revolution. Hermann Kolbe and the Science of Organic Chemistry*, University of California Press, Berkeley, **1993**, pp. 123, 284.

[20] A. Saytzeff, *Über eine neue Reihe organischer Schwefelverbindungen*. Ph.D. Diss., Leipzig University, **1866**.

[21] A. M. Zaitsev, *O deistvii azotnoi kisloty na nekotorye organicheskie soedineniya dvuatomnoi sery i o novom ryade organicheskikh sernistykh soedinenii pol’chennom pri etoi reaktsii prolozhenie [On the reactions of nitric acid with divalent sulfur compounds and on a new class of organic sulfur compounds obtained from this reaction]*, M. Chem. Diss., Kazan University, **1867**. The abstract of this dissertation also appeared in Student Writings of Kazan University, **1867**, *3*, 2; *Prilozhenie: Iz khimicheskoi laboratorii Kazanskogo universiteta.* s. 1–24 *[Appendix: From the chemical laboratories of Kazan University.* p. 1–24*]*.

[22] A. M. Zaitsev, *Novye sposob prevashcheniya zhirnykh kislot v sootvetstvuyushchie im alkogoli. Normal’nyi butil’nyi alkogol’ (propilkarbinol)i ego prevashchenie vo vtorichnyi butil’nyi alkogol’ (mefil-efil-karbinol) [A new method for converting a fatty acid into its corresponding alcohol. Normal butyl alcohol (propyl carbinol) and its conversion to secondary butyl alcohol (methyl-ethyl-carbinol)]*, Dr. Chem. Diss., Kazan University, **1870**. The work was also published under the same title: A. M. Zaitsev, *Zh. Russ. Fiz.-Khim. O-va.* **1870**, *2*, 292–310.

[23] For a commentary on the possible origins of this feud and its possible contribution to what is now known as Zaitsev’s Rule, see: D. E. Lewis, *Bull. Hist. Chem.* **2010**, *35*, 115–124.

[24] A. Saytzeff, *Justus Liebigs Ann. Chem.* **1866**, *139*, 354–364; A. Saytzeff, *Justus Liebigs Ann. Chem.* **1867**, *144*, 148–156.

[25] E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, *87*, 1345.

[26] Leading reviews: a) M. C. Carreno, *Chem. Rev.* **1995**, *95*, 1717–1760; b) I. Fernández, N. Khiar, *Chem. Rev.* **2003**, *103*, 3651–3706; c) E. Wojaczyńska, J. Wojaczyński, *Chem. Rev.* **2010**, *110*, 4303–4356.

[27] A. Saytzeff, *Justus Liebigs Ann. Chem.* **1867**, *144*, 145–148.

[28] E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, *87*, 1353.

[29] a) B. M. Trost, L. S. Melvin, Jr., *Sulfur Ylides*, Academic, New York, **1975**; b) A. W. Johnson, *Ylide Chemistry*, Academic, New York, **1966**; c) C. R. Johnson in *Comprehensive Organic Chemistry, Vol. 3* (Eds.: D. H. R. Barton, W. D. Ollis), Pergamon, Oxford, **1979**, p. 247–260; d) Yu. G. Gololobov, A. N. Nesmeyanov, V. P. Lysenko, I. E. Boldeskul, *Tetrahedron* **1987**, *43*, 2609–2651; e) A.-H. Li, L.-X. Dai, V. K. Aggarwal, *Chem. Rev.* **1997**, *97*, 2341–2372.

[30] a) V. K. Aggarwal, *Synlett* **1998**, 329–337; b) L. X. Dai, X. L. Hou, Y. G. Zhou, *Pure Appl. Chem.* **1999**, *71*, 369–376; c) V. K. Aggarwal, C. L. Winn, *Acc. Chem. Res.* **2004**, *37*, 611–620; d) S. L. Riches, C. Saha, N. Fontán Filgueira, E. Grange, E. M. McGarrigle, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 7626–7630, and references therein.

[31] a) G. Wagner, A. Saytzeff, *Justus Liebigs Ann. Chem.* **1875**, *175*, 351–374; G. Wagner, A. Saytzeff, *Justus Liebigs Ann. Chem.* **1875**, *179*, 302–313; b) J. Kanonnikoff, A. Saytzeff, *Justus Liebigs Ann. Chem.* **1875**, *175*, 374–378; J. Kanonnikoff, A. Saytzeff, *Justus Liebigs Ann. Chem.* **1877**, *185*, 148–150; c) M. Saytzeff, A. Saytzeff, *Justus Liebigs Ann. Chem.* **1877**, *185*, 151–169; d) A. Saytzeff, *Justus Liebigs Ann. Chem.* **1877**, *185*, 175–183; A. Saytzeff, *J. Prakt. Chem.* **1885**, *31*, 319–320; e) E. Vagner, A. Zaitsev, *Zh. Russ. Fiz.-Khim. O-va.* **1874**, *6*, 290–308; E. Vagner, A. Zaitsev, *Zh. Russ. Fiz.-Khim. O-va.* **1875**, *7*, 293–302; E. Vagner, A. Zaitsev, *Zh. Russ. Fiz.-Khim. O-va.* *Z***1875**, *7*, 302–312; E. Vagner, A. Zaitsev, *Zh. Russ. Khim. O-va. Fiz. O-va.* **1876**, *8*, 290–308; f) I. Kanonnikov, A. Zaitsev, *Zh. Russ. Fiz.-Khim. O-va.* **1874**, *6*, 308–312.

[32] a) V. Grignard, *C. R. Hebd. Seances Acad.* **1900**, *130*, 1322–1324; V. Grignard, *C. R. Hebd. Seances Acad.* **1901**, *132*, 336–338; V. Grignard, *C. R. Hebd. Seances Acad.* **1901**, *132*, 558–561; V. Grignard, *C. R. Hebd. Seances Acad.* **1902**, *134*, 849–851; V. Grignard, *Chem. Zentralbl.* **1901**, II, 622; V. Grignard, *Ann. Chim. Phys.* **1901**, *24 [vii]*, 433–490; b) V. Grignard, L. Tissier, *C. R. Hebd. Seances Acad.* **1901**, *132*, 835–837; V. Grignard, L. Tissier, *C. R. Hebd. Seances Acad.* **1902**, *134*, 107–108.

[33] M. Kitamura, S Suga, K. Kawai, R. Noyori, *J. Am. Chem. Soc.* **1986**, *108*, 6071–6072.

[34] Selected reviews: a) R. Noyori, M. Kitamura, *Angew. Chem.* **1991**, *103*, 34–55; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49–69; b) K. Soai, S. Niwa, *Chem. Rev.* **1992**, *92*, 833–856; c) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117–2188; d) *Organozinc Reagents: A Practical Approach* (Eds.: P. Knochel, P. Jones), Oxford University Press, Oxford, **1999**; e) P. Knochel, S. Vettel, C. Eisenberg, *Appl. Organomet. Chem.* **1995**, *9*, 175–188; f) P. Knochel, J. Almena, P. Jones, *Tetrahedron* **1998**, *54*, 8275–8319; g) E. Erdik, *Organozinc Reagents in Organic Synthesis*, CRC, Boca Raton, FL, **1996**; h) K. Soai, *Enantiomer* **1999**, *4*, 591–598; i) D. E. Frantz, R. Faessler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res.* **2000**, *33*, 373–381; j) A. Boudier, L. O. Bromm, M. Lotz, P. Knochel, *Angew. Chem.* **2000**, *112*, 4584–4606; *Angew. Chem. Int. Ed.* **2000**, *39*, 4414–4435; k) L. Pu, H.-B. Yu, *Chem. Rev.* **2001**, *101*, 757–824; l) P. Knochel, N. Millot, A. L. Rodriguez, C. A. Tucker, *Org. React.* **2001**, *58*, 417–731; m) P. Knochel, *Science of Synthesis*, *Vol. 3*, Georg Thieme, Stuttgart, **2004**, p. 5–90. For recent examples of the use of organozinc reagents in synthesis by one of the leading research groups in this area, see: n) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1102–1110; o) S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2007**, *119*, 7829–7832; *Angew. Chem. Int. Ed.* **2007**, *46*, 7685–7688; p) S. H. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705–4707; q) Z. Dong, F. Piller, P. Knochel, *Chem. Eur. J.* **2008**, *15*, 457–468; r) A. Metzger, F. Piller, P. Knochel, *Chem. Commun.* **2008**, 5824–5826; s) A. Metzger, L. Melzig, P. Knochel, *Synthesis* **2010**, 2853–2858; t) M. A. Schade, G. Manolikakes, P. Knochel, *Org. Lett.* **2010**, *12*, 3648–3650.

[35] a) C. J. Li, *Tetrahedron* **1996**, *52*, 5643–5668; b) Y. S. Cho, J. E. Lee, A. N. Pae, K. I. Choi, H. Y. Koh, *Tetrahedron Lett.* **1999**, *40*, 1725–1728; c) S. H. Kim, E. H. Han, *Tetrahedron Lett.* **2000**, *41*, 6479–6482.

[36] A. Saytzeff, *Z. Chem. N. F.* **1869**, *5*, 551–552; A. Saytzeff, *Z. Chem. N. F.* **1870**, *6*, 105–108; A. Saytzeff, *J. Prakt. Chem.* **1871**, *3*, 76–88, 427.

[37] A. Saytzeff, *Justus Liebigs Ann. Chem.* **1874**, *171*, 258–290; A. Saytzeff, *J. Prakt. Chem.* **1882**, *25*, 61–72.

[38] M. A. ElSohly, S. J. Salamone, *J. Anal. Toxicol.* **1999**, *23*, 141–146.

[39] A. Saytzeff, *J. Prakt. Chem.* **1885**, *31*, 541–542; A. Saytzeff, *J. Prakt. Chem.* **1886**, *33*, 300–318.

[40] A. Saytzeff, *Justus Liebigs Ann. Chem.* **1875**, *179*, 296–301.

[41] a) E. Vagner, *Zh. Russ. Khim. O-va. Fiz. O-va.* **1876**, *8*, 37–40; E. Vagner, *Zh. Russ. Fiz.-Khim. O-va.* **1884**, *16*, 283–353; b) G. Wagner, *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 2434–2439.

[42] G. Wagner, *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 1230–1240, 3343–3346; G. Wagner, *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 3347–3355; G. Wagner, *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 3356–3360.

[43] a) G. Wagner, W. Brickner, *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 2302–2325; b) G. Wagner, W. Brykner, *Ber. Dtsch. Chem. Ges.* **1900**, *33*, 2121–2125; c) E. E. Vagner, V. O. Brykner, *Zh. Russ. Fiz.-Khim. O-va.* **1903**, *35*, 534–537, 537–538.

[44] a) S. Reformatsky, *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 1210–1211; S. Reformatsky, *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 2842–2847; S. Reformatsky, *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 3262–3265; b) S. Reformatsky, B. Plesconossoff, *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 2838–2841.

[45] A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. O-va.* **1900**, *32*, 753; A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. O-va.* **1901**, *33*, 38–45.

[46] a) A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. O-va.* **1906**, *38*, 687; A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. O-va.* **1910**, *42*, 395, 549; b) A. Arbuzow, *Chem. Zentralbl.* **1906**, II, 1639; A. Arbuzow, *Chem. Zentralbl.* **1910**, II, 453.

[47] All photographs are reproduced from the web site of the Museum of the Kasan School of Chemistry, Kandidat Tamara Dmitrievna Sorokina, Director: URL http://www.ksu.ru/museums/chmku/eng/index.htm. Names and book/monograph titles in the references are transliterated from the Cyrillic for articles and books in Russian, and are rendered as written in articles and books in French, German and English. The soft sign (ь) is transliterated as an apostrophe ('), and is omitted at the end of the name Kazan; the vowels й, ю, and я are transliterated as i, yu, and ya, respectively; the consonants х and ч are transliterated as kh and ch, respectively. English translations of Russian titles appear in square brackets following the transliterated Russian.