

ALEKSANDR MIKHAILOVICH ZAITSEV (1841-1910)

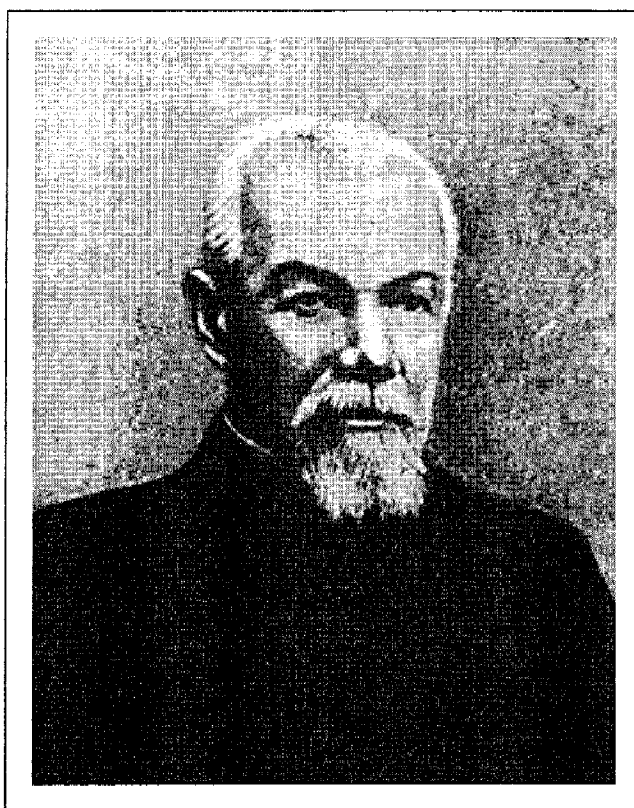
Markovnikov's Conservative Contemporary

David E. Lewis, South Dakota State University

Most students in organic chemistry today are familiar with Saytzeff's Rule for elimination reactions, although few, if any are aware of the Russian chemist, Aleksandr Mikhailovich Zaitsev (1841-1910), for whom it is named. In part, this may be due to the lack of western sources concerning his life. All the biographical material available on Zaitsev is in Russian (1, 2) with the exception of two German sources—the brief death notice in *Berichte* (3a) and the minimal information in *Poggendorff's* biographical bibliography (3b)—and two brief surveys of his work in English—the recent thesis by Brooks (3c) and a survey paper in *J. Chem. Educ.* (3d).

Zaitsev was born in Kazan' to a mercantile family that had lived in the region since the time of Ivan the Terrible (1533-1584), and there is evidence that the Zaitsev family had been agents of commerce between the Russian Empire and the Orient since that time. His father, Mikhail Savvich Zaitsev, had two sons by his first wife and three sons, of whom Aleksandr was the middle one, by his second wife, Natalie Vasil'evna Lyapunova. A merchant with control over the tea and sugar trade, Mikhail Savvich Zaitsev resolved early that his son should join the mercantile guilds and follow in his footsteps. However, Zaitsev's maternal uncle, the astronomer Mikhail Vasil'evich Lyapunov (later Professor of Astronomy at Kazan' University), persuaded his brother-in-law that young Aleksandr should attend the university, instead. Accordingly, Aleksandr was enrolled in the Gymnasium.

Founded in 1804, Kazan' University was the easternmost outpost of Russian higher education during the nineteenth century, and yet by the middle of the nineteenth century it had assumed a pre-eminent position in



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Russian organic chemistry despite its provincial location and status. This ascendancy of the chemistry department of Kazan' University was achieved under the guidance of such luminaries as Nikolai Nikolaevich Zinin (1812-1880), Karl Karlovich Klaus (1796-1864), and Aleksandr Mikhailovich Butlerov (1828-1886), and it was maintained under such renowned chemists as

Vladimir Vasil'evich Markovnikov (1838-1904), Zaitsev himself, and Aleksandr Erminingel'dovich Arbuzov (1877-1968).

In 1858, following his graduation from the Gymnasium, Zaitsev entered Kazan' University as a student in economic science in the Faculty of Law. At that time, all students entering the Faculty of Law were required to pass a qualifying examination in Latin. Because there were no classes in Latin at the Gymnasium, Lyapunov himself had taught the young Aleksandr the Latin which he needed to pass the entrance examinations. At that time, also, all students in the Faculty of Law were required to pass two years of chemistry in order to graduate. It was while taking these required chemistry courses that the young Zaitsev came under the influence of one of the greatest organic chemists produced by Russia — Aleksandr Mikhailovich Butlerov. By the time that he had graduated, Zaitsev was no longer an economist, but a committed chemist. Zaitsev graduated with his degree in economic science in 1862.

Up to this time Russian tradition prescribed a fairly rigid course of action following graduation.

The most immediate concern for most students was to remain in Russia to write the dissertation for the degree of Kandidat, without which one could not obtain a salaried position as a laboratory assistant. Today, the degree of Kandidat at most Russian universities is the approximate equivalent of the Ph.D.; in the nineteenth century, however, it was somewhere between a modern master's degree and a modern Ph.D. Following graduation with the degree of Kandidat, most students studied abroad for two to three years, then returned to Russia to submit a dissertation for the degree of Master of Chemistry (the minimum qualification for obtaining a teaching post at a university). In order to obtain the rank of Professor at a university, one needed the degree of Doctor of Chemistry, which necessitated

the submission and defense of a dissertation, as well as passing an examination over every area of chemistry.

For whatever reason, whether from impatience and a desire to study under the best in Europe or simply because he did not think ahead about his financial security on his return to Russia, Zaitsev chose to ignore these traditions; this very nearly proved to be a fatal mistake. Immediately after his graduation from Kazan' University he left for Germany, where he entered the laboratory of Hermann Kolbe at the University of Marburg. In 1863, after his first year with Kolbe, Zaitsev submitted a dissertation to Kazan' University for the degree of

Kandidat. This 76-page hand-written dissertation was entitled, "The Theoretical Views of Kolbe on the Rational Constitution of Organic Compounds and Their Relationship with Inorganic Compounds." It contained an overview of Kolbe's version of structural theory (Kolbe viewed the term "chemical structure" as specious, and he eschewed it in favor of "rational constitution") that had led him to predict the ex-



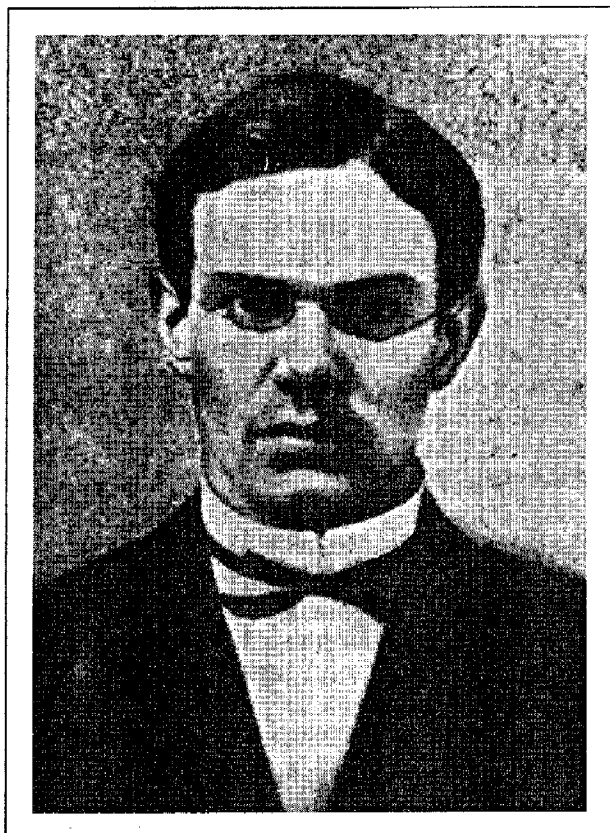
Kazan University Chemical Laboratory in Zaitsev's time

istence of, among other compounds, the tertiary alcohols. Ironically, it was Butlerov who was the primary examiner of this dissertation. As one of the developers of the modern structural theory of organic chemistry, and as the chemist who first synthesized *tert*-butyl alcohol (4), thus confirming Kolbe's predictions, Butlerov was intimately acquainted with Kolbe's views (and opposed to them). Unfortunately for Zaitsev, the dissertation was neither well written nor novel — Butlerov characterized it as "a poor rendering of the German" — and the degree was not awarded.

Zaitsev's studies continued uninterrupted at Marburg until August, 1864. At Marburg, he studied the chemistry of organic sulfur compounds. He made the first of his major discoveries — the sulfoxides, whose

existence and formation he reported in a series of papers (5) during the last half of the 1860's—while studying the oxidation of organic sulfides by nitric acid. During the 1864-1865 academic year (August 1864-April 1865), Zaitsev moved to Paris, where he studied under Charles Adolphe Wurtz at the Université de Paris. His work at Paris, primarily concerned with the reactions of carboxylic acid derivatives (6, 7), was subsequently the basis of his successful dissertation for the degree of Kandidat (8).

In May, 1865, Zaitsev returned to Marburg to be greeted by the news that Kolbe had accepted the Chair



Zaitsev as Laboratory Assistant (1871)

of Chemistry at the University of Leipzig. Choosing not to follow his mentor to his new post, Zaitsev returned to Russia. Here he was unable to work as a salaried laboratory assistant because he lacked the degree of Kandidat. This did not deter Zaitsev, who immediately offered his services "as a private individual"—an unpaid, unofficial laboratory assistant—to Butlerov. He quickly impressed his mentor, who urged him to write his dissertation for the degree of Kandidat. In 1865, he submitted his dissertation, "Concerning Diamidosalicic Acid," based on the results of his two semesters of work in Wurtz' laboratory. The papers de-

scribing this work appeared in both French and German the same year (6). The degree was awarded and, thanks to the support of Butlerov, Zaitsev obtained a position as laboratory assistant in agronomy in 1866. The university also committed the direction of the laboratories in agronomic chemistry to him.

In order to teach at Kazan', Zaitsev needed a degree beyond the Kandidat. The expected degree was the Master of Chemistry degree, but it would require two years of study beyond the Kandidat before he could submit a Master's dissertation. Therefore, once again in defiance of Russian tradition, he wrote up the results of his Marburg work and sent them to Kolbe at Leipzig in the form of a Ph.D. dissertation (9). In 1866 he was granted the degree of Ph.D. by the University of Leipzig (one may speculate on the extent to which Kolbe's influence affected this outcome). Herein may also lie some of the origins of the disdain of Markovnikov, Butlerov's student and successor at Kazan', towards Zaitsev. When Zaitsev submitted his Ph.D. dissertation to the University of Leipzig, Markovnikov, who was an ardently nationalistic Russian, was a senior student in Kolbe's laboratories, and probably privy to the fact that Zaitsev had once again flouted Russian tradition by applying for a doctoral degree from a foreign university.

The work for which Zaitsev was awarded the Ph.D. by Leipzig appeared the same year as a paper in *Liebigs Annalen* with the same title, "Ueber eine neue Reihe organischer Schwefelverbindungen." He completed his dissertation for the degree of Master of Chemistry, "On the Action of Nitric Acid on Certain Organic Compounds of Divalent Sulfur and on a New Series of Organic Sulfur Compounds Obtained from this Reaction," in the first half of 1867 (10). Initially, several members of the faculty of the University did not want to permit Zaitsev to submit the dissertation because he already held a doctoral degree from a foreign university (despite the fact that foreign doctoral degrees were not recognized in Russia at the time); it was only because of Butlerov's intervention that he was permitted to do so. He successfully defended the dissertation in October, 1868, and was awarded the degree that December.

In May, 1868, Butlerov accepted the chair of Chemistry at St. Petersburg University. However, he asked for and received permission to delay his departure from Kazan' until January, 1869, to permit a smooth transition of the chair to his successor and student, Markovnikov. This delay proved to be critical for Zaitsev's career. Since its earliest days, Kazan' University had two chairs, one in chemistry and one in chemical technology. In the 1840's these two chairs were occupied by Zinin, who discovered the first method for the reduction of nitrobenzene to aniline,

and Klaus, the discoverer of ruthenium; when Zinin moved to St. Petersburg, his chair remained vacant. When Klaus also left Kazan', Butlerov was appointed as his sole successor.

Of course, when Butlerov announced that he was to become the Professor of Chemistry at St. Petersburg, Markovnikov (who had already substituted for his mentor while Butlerov was abroad defending his claims of priority in developing the structural theory of organic chemistry) quite rightly expected that he would become the sole Professor of Chemistry at Kazan'. However, Markovnikov was an irascible and prickly individual whose politically progressive ideas did not sit well with a conservative administration. Consequently, the administration delayed his inevitable appointment to the Chair of Chemistry as long as possible. Indeed, there was sufficient opposition to Markovnikov's appointment as Butlerov's sole successor that the University decided that both chairs of chemistry should be filled when Butlerov left. Their first choice for the second chair was another Butlerov student, Aleksandr Nikolaevich Popov (1840-1881), who had written a brilliant master's dissertation on structural theory under Markovnikov's direction. The university administration may have viewed Popov's friendship with Markovnikov as a potential buffer between themselves and Markovnikov. In 1869, however, Popov accepted the Chair of Chemistry at the University of Warsaw and moved to Bonn for advanced study under Kekulé in preparation to take up his new post. This may actually have been fortunate for Kazan' University for Popov's health was not robust, and he died before achieving anything further of note (or for which he was given the appropriate recognition, at least, as we shall see later).

This left Zaitsev, for whom Markovnikov had little regard, as the next logical choice. As a political conservative, Zaitsev had the support of the dean and the administration, especially in the light of the very strong recommendation which Butlerov wrote for him. In January, 1869, Zaitsev was elected unanimously to the Council of Docents and appointed to the second chair of chemistry. Following his appointment, Zaitsev taught the public courses in organic and inorganic chemistry, and the practicum in organic and analytical chemistry. Markovnikov taught the special course in organic chemistry and the analytical and organic chemistry practicum to his students.

Zaitsev quickly gathered a number of laboratory assistants (although never as many as Markovnikov). In September, 1870, he defended his doctoral dissertation, a two-part study entitled, "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) (11)." Markovnikov—who had defended his own dissertation in April, 1869, and had been appointed Extraordinary (May, 1869) and then Ordinary (spring, 1870) Professor of Chemistry—was the primary reviewer of the dissertation. Overtly positive, albeit with a very condescending tone towards the author, Markovnikov's review of Zaitsev's dissertation was meant to be read between the lines. This is in marked contrast to Zaitsev's review of Markovnikov's own dissertation, which contained high praise. Fortunately, the faculty was aware of Markovnikov's antipathy towards Zaitsev and of Butlerov's high opinion of him; so, Markovnikov notwithstanding, Zaitsev was awarded the doctor's degree and was appointed Extraordinary Professor of Chemistry in November, 1870. One year later, the dean nominated Zaitsev as a candidate for the rank of Ordinary Professor of Chemistry, a post to which he was elected in November, 1871, in a 19-12 split vote.

It is very possible that Zaitsev's appointment as professor—which Markovnikov had tried to prevent—was one of the precipitating factors that led to Markovnikov's rancorous departure from Kazan' University less than six weeks later. Certainly, Zaitsev's 1869 appointment as his colleague had infuriated Markovnikov, who refused to speak to his new colleague (in October, 1869, he wrote to Butlerov, "With the departure of Popov I am determined to speak to nobody. I see Zaitsev only before his lectures...") (12). After Markovnikov's departure, Zaitsev assumed the direction of the chemistry laboratories at Kazan' as Professor of Chemistry. It was not until 1884 that Zaitsev obtained a colleague with Professorial rank, when Flavian Mikhailovich Flavitskii (1848-1917)—another Butlerov student—was appointed to the vacant second chair of chemistry at Kazan' as Professor of Inorganic Chemistry.

Most of Zaitsev's independent scientific work is characterized by the extension of and continued development of the ideas of his mentors, especially Butlerov; and his career is usually associated with the continued development of the Butlerov school at Kazan'. His earliest independent work, however, owed more to the influence of Kolbe on his professional development. It was a continuation of the work he had begun while a student at Marburg, where he had discovered the sulfoxides during his studies of the oxidation of thioethers. Had the usefulness and versatility of these sulfur compounds as synthetic intermediates been recognized during the nineteenth century, Zaitsev's reputation may well have flowered like that of Markovnikov, but it was to be nearly 100 years before the full potential of sulfoxides and sulfonium salts in organic synthesis was realized. Today it is difficult to imagine modern organic synthesis without methods based on the chemistry of the sul-

foxides and sulfur ylides that have been developed since the 1960's (13).

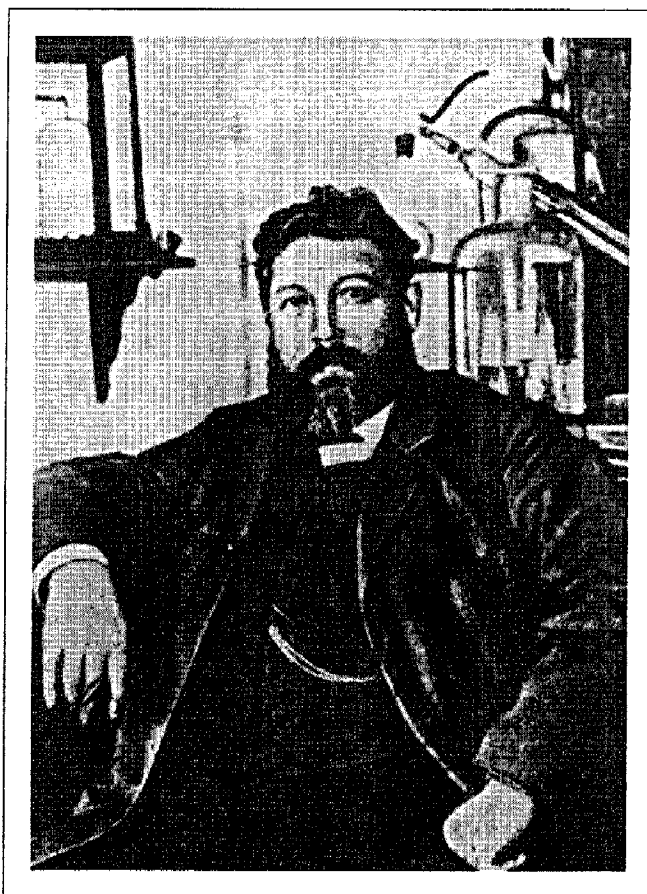
It is clear from Butlerov's writings that he rated Zaitsev's graduate research in sulfur chemistry far above the work he had done in Paris, and it was the papers describing the work that Zaitsev had carried out in Kolbe's laboratories that Butlerov cited in several glowing recommendation letters that he wrote for him. Indeed, it is not inconceivable that Butlerov himself may have advised his protégé to continue his work in this area. Whatever the underlying reasons, Zaitsev continued to study the chemistry of organic sulfur compounds after his return to Russia, at least until after his appointment as Professor of Chemistry at Kazan'.

By the early 1870's, Zaitsev had begun to publish papers describing the synthesis and transformations of alcohols, and by far the majority of his scientific papers are concerned with this field of study, where he did much to further Butlerov's influence on the development of Russian organic chemistry. His first independent contribution was the discovery that carboxylic acid chlorides could be reduced cleanly to the corresponding primary alcohols with 3% sodium amalgam in dry ether with acetic acid as a buffering agent and hydrogen source (14). Zaitsev applied this reaction to several acid chlorides, including succinyl chloride. During the reduction of succinyl chloride with sodium amalgam he discovered a new product whose analysis agreed with its formulation as succinaldehyde, and which would thus provide evidence of aldehydes as intermediates in his acid chloride reduction; with further work, however, he proved the structure to be that of γ -butyrolactone; this constituted the first synthesis of this compound (15).

Butlerov's influence pervades most of Zaitsev's scientific work, but nowhere is it more apparent than in his work with dialkylzinc reagents. In 1864, Butlerov had prepared *tert*-butyl alcohol by the reaction between phosgene and dimethylzinc, a method he subsequently extended to the reaction between acid chlorides, in general, and a dialkylzinc (4). The report of this result confirmed the existence of tertiary alcohols, a possibility that had been predicted from a theoretical standpoint four years earlier by Kolbe. As a Butlerov student working under Kolbe's direction when the synthesis of *tert*-butyl alcohol was reported, Zaitsev must have been under intense pressure to acquire an interest in the synthesis of alcohols by means of dialkylzinc reagents. Certainly, Zaitsev's major contribution to organic synthesis was to extend the work of Butlerov in the applications of dialkylzinc reagents in organic synthesis. Zaitsev extended the Butlerov reaction to other carbonyl compounds, including ketones and other acid derivatives; he showed that the reaction between dimethylzinc or

diethylzinc and an ester or ketone would afford the tertiary alcohol (16). At this time, also, his brother and student, Mikhail Mikhailovich, showed that the reaction between a dialkylzinc and an anhydride would give a ketone (17). Zaitsev also showed that the reaction between a dialkylzinc reagent and a ketone may, like the Grignard reaction, give reduction rather than addition: the reaction between 4-heptanone and dipropylzinc fails to give the tertiary alcohol, and the secondary alcohol obtained by reduction of the ketone is the major product of this reaction (18). In many ways, it was Zaitsev rather than his mentor who pioneered the use of dialkylzinc reagents for the synthesis of alcohols.

In addition to his own work, Zaitsev further influenced the development of organic chemistry—especially organozinc chemistry—through his students, several of whom founded their own schools. One of the most brilliant and highly regarded of Zaitsev's students was Egor Egorevich Vagner (or Wagner) (1849-1903), later Professor of Chemistry at the University of Warsaw. As a student under Zaitsev between 1870 and 1875, Vagner developed the first general synthesis of secondary alcohols by the reaction between dialkylzincs and



E. E. Vagner

ethyl formate (19), a reaction which he later extended to the reaction between dialkylzinc reagents and aldehydes (20). Until the advent of the Grignard reaction some thirty years later, this route was the method of choice for the formation of secondary alcohols. It is also interesting to note that the Grignard reaction itself was developed in an effort to improve the yield of the Zaitsev-Vagner synthesis by replacing the zinc atom with a more reactive divalent metal. The Zaitsev-Vagner synthesis of alcohols was rapidly eclipsed by the Grignard synthesis, which was simpler to carry out, and within twelve months the Zaitsev-Vagner synthesis had been relegated to a position of historical interest only. However, the advent of asymmetric synthesis has added a touch of irony to the story: whereas the Grignard addition reaction has proved to be difficult to carry out with high levels of asymmetric induction, Noyori (21) has found that the Zaitsev-Vagner addition is amenable to chiral catalysis to give very high levels of asymmetric induction in the adduct.

Another of Zaitsev's students whose name is associated with synthetic applications of organozinc reagents is Sergei Nikolaevich Reformatskii (Reformatsky) (1860-1934), later Professor of Chemistry at the Uni-



S. N. Reformatskii

versity of Kiev. In his own work, Zaitsev had shown that allylzinc reagents are particularly easy to prepare, and the extension of the concept to α -halocarbonyl compounds must have been a logical one. Certainly, it was Zaitsev who suggested to Reformatskii that he should study the formation and addition reactions of organozinc reagents from α -bromocarboxylic esters. The reaction was first carried out at Kazan' in 1887, so the reaction now known under Reformatskii's name (22) was actually discovered in Zaitsev's laboratory. Until the development of the strong lithium amide bases in the 1970's made preformed lithium enolates routinely available, and the subsequent resurgence of the aldol addition reaction as a method for carbon-carbon bond formation (23), the Reformatskii reaction was the only major synthetic method which could be used to prepare β -hydroxycarbonyl compounds from aldehydes and ketones without significant dehydration.

Zaitsev's master's dissertation described the oxidation of sulfides, and during his doctoral work he began to study the oxidation of unsaturated organic compounds. His interest in oxidation reactions continued for many years after his doctoral studies, and he pioneered the use of alkaline potassium permanganate for the oxidation of fatty acids (24). However, it remained for his student Vagner to realize that this reaction could be applied generally to the oxidation of unsaturated compounds to the corresponding 1,2-diols (25), thus providing a method for fixing the location of double bonds in a molecule. In this form the reaction was widely applied to structural problems in terpene chemistry as the Wagner oxidation.

The third of Zaitsev's students to have a significant impact on the development of modern organic chemistry was Aleksandr Erminingel'dovich Arbuzov, who succeeded his mentor as Professor of Chemistry at Kazan'. Arbuzov was to achieve eminence as an organophosphorus chemist, and he carried out pioneering research into the chemistry of organic phosphorus compounds. As a graduate student under Zaitsev, Arbuzov had begun his studies by carrying out the synthesis of allyl methyl phenyl carbinol, which was published in Russian in 1901 (26). However, the advent of Grignard reagents quickly rendered Arbuzov's initial studies rather moot; the Grignard reagents were easier to make and handle, and the Grignard reaction gave higher yields. For his master's dissertation, he submitted a thesis on phosphorous acid (27), on the chemistry of which he built an eminent career. Arbuzov's impact on modern synthetic organic chemistry is somewhat indirect: the phosphonate esters produced by the Arbuzov-Michaelis rearrangement (28) are the source of the phosphonate anions that are the key reagents in the Wadsworth-Emmons olefination reaction (29).



A. E. Arbuzov

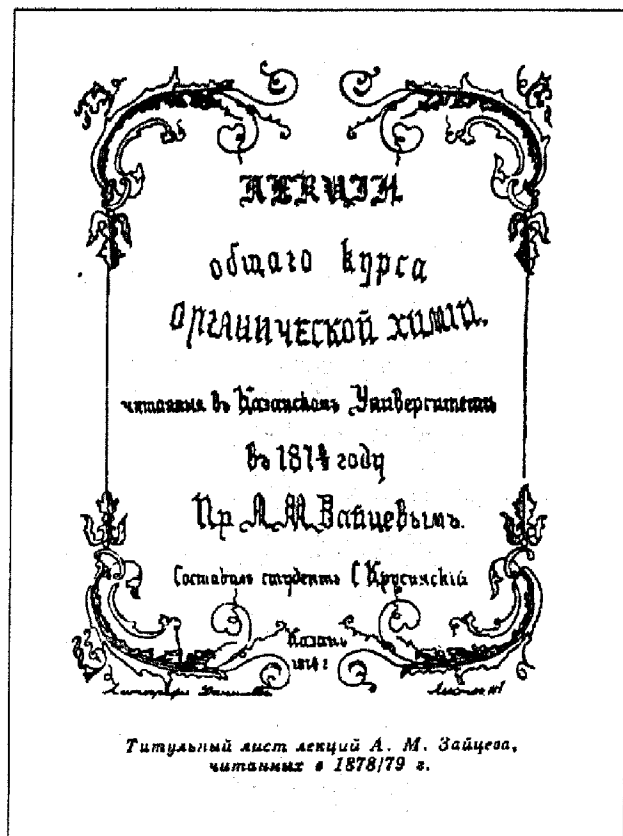
The paper for which Zaitsev's name is included in most organic chemistry textbooks—the paper in which he first expounded the empirical rule for elimination reactions now associated with his name—appeared in *Liebigs Annalen der Chemie und Pharmazie* in 1875 (30). Oddly enough, this paper was often quoted during the ensuing century, but it was not until the 1960's that Zaitsev's name was attached to his rule in most undergraduate textbooks. Even more diagnostic of the changing emphases in organic chemistry: although undergraduate organic chemistry textbooks published during the 1990's still include extensive discussion of the Saytzeff Rule and the underlying reasons for Saytzeff orientation in elimination reactions, they now specify his discovery of the sulfoxides as Zaitsev's major contribution to the development of modern organic chemistry.

Much of the impetus behind the work that led to the Saytzeff Rule, as it is usually spelled in textbooks, was provided by Markovnikov's doctoral dissertation, where it was implied that elimination should be the opposite of addition: that elimination should follow what we now call the Hofmann route instead of the Zaitsev route. It is fairly clear that Zaitsev formulated

his rule largely on the basis of published data, as well as those of his students Grabovskii and Vagner, and that it was published strictly as an empirical rule for predicting the regiochemistry of the dehydrohalogenation reactions of alkyl iodides. What has not been well publicized, however, is the fact that Popov (then a student in Kekulé's laboratory in Bonn) had proposed the possibility of a similar empirical rule in December, 1871, in a letter describing his proposed scheme for the oxidation of *tert*-amyl alcohol to his mentor, Butlerov. In 1872 Popov published a paper on the oxidation of ketones with chromic acid, in which he raised the possibility of the elimination of 3-methyl-2-butanol to the trisubstituted alkene as a possible first step in the cleavage reaction to acetone and acetic acid (31). In 1873, he presented the same view of elimination, illustrating it with the same oxidation reactions, at a chemical conference in Kazan'. In this presentation, he also postulated that proposals made for dehydration reactions might equally be extended to dehydrohalogenation reactions (32). Although it is likely that Zaitsev was unaware of Popov's letter to Butlerov, he was certainly aware of Popov's views on oxidation reactions: in his first paper with Vagner (19) he cites Popov's paper in *Liebigs Annalen*. Nevertheless, in the paper describing Zaitsev's Rule, he gives credit only to Vagner and Grabovskii. The reasons for this are not clear, but after a reading of Popov's *Annalen* paper it is difficult to see just how this work, at least, would have impacted Zaitsev's thinking in more than a peripheral way (certainly, this author would not have felt obligated to quote the Popov paper had he been writing Zaitsev's paper).

Zaitsev spent his entire academic career at Kazan' University, teaching and carrying out research in the tradition of Butlerov before him. In 1878, he wrote a 477-page textbook of organic chemistry (with a 42-page preface); in 1890 it was superseded by a larger, 873-page edition which was used until 1902. Although not a founding member, Zaitsev was among the first to join the Russian Physical Chemical Society, serving as its president in 1905, 1908, and 1909 and as its Vice-President in 1903 and 1910. In 1885 he was appointed a corresponding member of the Academy of Sciences, and in 1903 he was made an honorary member of Kiev University. As a teacher, Zaitsev followed the traditions of his own mentors, Butlerov and Kolbe. Like his mentors, Zaitsev was a "hands-on" teacher, known for his frequent appearances in the laboratory, and he inspired both respect and loyalty in his students.

When viewed as a body, Zaitsev's seventy-five scientific papers are characterized by the same empiricism that pervades most nineteenth-century organic chemistry: Zaitsev's Rule is an empirical statement which was couched in empirical terms; many of his observations



Title Page of 1878/1879 Text by Zaitsev

of the reactivity of dialkylzinc reagents with carbonyl compounds are couched in empirical terms. In none of his papers do we find any of the mechanistic discussions which characterize more modern papers. Nevertheless, when viewed from the perspective of the last decade of the twentieth century, Zaitsev's contributions were widespread and seminal. Unfortunately for Zaitsev, however, much of their importance was not recognized until many decades after his death.

In many ways, Zaitsev was fortunate to live at the time he did. During his lifetime, Russian organic chemistry was characterized by an inventiveness and a vibrancy which it has seldom achieved since, with the frontiers of the science being thrust forward by such luminaries as Butlerov, Vagner, Favorskii, Zelinskii, and Markovnikov. Perhaps it was his misfortune, also. In the absence of such company, perhaps his own contributions to the science would have been recognized earlier, and his own star would have shone more brightly.

ACKNOWLEDGMENT

It is a pleasure to acknowledge the help of Dr. Nathan M. Brooks of New Mexico State University through

several telephone conversations during the preparation of this manuscript. *Credit:* The photographs of Zaitsev (1867), the Kazan' Chemical Laboratory, and the title page of Zaitsev's text are taken from the biography by Klyucheich and Bykov, Ref. 2b.

REFERENCES AND NOTES

- Zaitsev's name is generally spelled two ways in this manuscript: In the references to journal articles in German and French his name is spelled exactly as it appears in the journal (Saytzeff), and it is transliterated from the Cyrillic as Zaitsev for journal articles in Russian. The same treatment has been applied to the journal articles of other Russian chemists. Russian-language sources are indicated by [Russ.] after the complete citation. Most of Zaitsev's papers appeared in both Russian (in *Zh. Russ. Phys.-Khim. Obshch.* quoted below as *J. Russ. Phys. Chem. Soc.*, or in *Zh. Russ. Khim. Obshch.*, quoted as *J. Russ. Chem. Soc.*), and German or French. Because of the limited accessibility of the Russian sources, the German or French references are quoted in the list below wherever possible.
- There are several Russian-language biographies of Zaitsev: (a) A.N. Reformatskii, "Biography of Aleksandr Mikhailovich Zaitsev," *J. Russ. Phys. Chem. Soc.*, **1911**, 43, abstract 6, p. 876. (b) A.S. Klyucheich and G.B. Bykov, "Aleksandr Mikhailovich Zaitsev," Science Publishing House, Moscow, 1980. (c) S.N. Reformatskii, "A Memorial of Professor A.M. Zaitsev," *University News*, Kiev, 1910, No. 11. Supplement 2 in *Reports of the Physical-Chemical Society*, p. 1-7. (d) A.E. Arbuzov, "A Brief Description 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 N.P. Zagoskin, Ed., *A Biographical Dictionary of the Professors and Lecturers of Kazan' University (1804-1904) in Two Parts*, Kazan', 1904, Part 1, pp. 323-325; a list of his works is included: pp. 325-332.
- (a) "Alexander Micholajeff Saytzeff," *Ber. Dtsch. Chem. Ges.*, **1910**, 43, 2784; (b) "Alexander Michajlowich Saytzeff," *Poggendorffs biographisch-literarisches Handwörterbuch zur Geschichte der exacten Wissenschaften*, Vol. III, p. 1176 (1898); Vol. IV, p. 1310 (1904); Vol. V, p. 1098 (1926); (c) N.M. Brooks, "The Formation of a Community of Chemists in Russia, 1700-1870," Ph.D. Thesis, Columbia University, 1989; (d) D.E. Lewis, "The University of Kazan—Provincial Cradle of Russian Organic Chemistry. Part II: Aleksandr Zaitsev and his Students." *J. Chem. Educ.*, **1994**, 71, 93-97.
- (a) A. Butlerow, "Ueber die Derivate-von Trimethylcarbinol (von tertiarem Pseudobutylalkohol). Isomerie der gesättigsten Kohlenwasserstoffe C_4H_{10} und der Butylene C_4H_8 . Isobutylalkohol (der primäre Pseudobutylalkohol oder Pseudopropylcarbinol)." *Ann.*

- Chem. Pharm.*, **1867**, *144*, 1-32; (b) A. Butlerow, "Studieren über die einfachsten Verbindungen der organischen Chemie," *Chem. Zentr.*, **1864**, *35*, 417-420; (c) A. Butlerow, "Ueber die tertiären Pseudobutyl- oder dreifach methylirten Methylalkohol," *Chem. Zentr.*, **1865**, *36*, 168-173. This paper cites: A. Butlerow, *Bull. Soc. Chim.*, **1863**, 587; *Bull. Soc. Chim. Paris, Nouv. Sér., II*, 106, Août 1864. See also, A. Butlerow, *Jahresb.*, **1863**, 475; 1864, 496.
5. a) A. Saytzeff, "Ueber eine neue Reihe organischer Schwefelverbindungen," *Ann. Chem. Pharm.*, **1866**, *139*, 354-364; (b) A. Saytzeff, "Ueber die Einwirkung von Jodmethyl auf Schwefelamyläthyl." *Ann. Chem. Pharm.*, **1867**, *144*, 145-148; (c) A. Saytzeff, "Ueber die Einwirkung von Salpetersäure auf Schwefelmethyl und Schwefeläthyl." *Ann. Chem. Pharm.*, **1867**, *144*, 148-156; (d) N. Grabowsky and A. Saytzeff, "Ueber einige Schwefelderivate der primären Butylalkohole," *Ann. Chem. Pharm.*, **1874**, *171*, 251-258.
 6. (a) A. Saytzeff, "Ueber die Einwirkung von cyansaurem Kali auf Monochloressigsäther." *Ann. Chem. Pharm.*, **1865**, *133*, 329-355; *135*, 229-236; (b) A. Saytzeff, "Action du cyanate de potasse sur l'ether monochloroacetique," *C. R. Acad. Sci.*, **1865**, *60*, 671-673; *Bull. Soc. Chim. Paris*, **1865**, *3*, 350-356.
 7. a) A. Saytzeff, "Ueber Diamidosalicylsäure." *Ann. Chem. Pharm.*, **1865**, *133*, 321-329; (b) A. Saytzeff, "Sur l'acide diamidosalicylique et sur ses combinaisons avec les acides," *Bull. Soc. Chim. Paris*, **1865**, *3*, 244-250.
 8. A.M. Zaitsev, "Concerning diamidosalicylic acid." Dissertation for the degree of kandidat in economic science, Kazan' University, 1865. [Russ.]
 9. A. Saytzeff, "Ueber eine neue Reihe organischer Schwefelverbindungen." Dissertation for the degree of Ph. D., Leipzig University, 1866.
 10. A.M. Zaitsev, "On the action of nitric acid on certain organic compounds of divalent sulfur and on a new series of organic sulfur compounds obtained from this reaction," Dissertation for the degree of M. Chem., Kazan' University, 1867. The abstract of this dissertation also appeared in *Student Writings of Kazan' University*, 1867, 3. [Russ.]
 11. A.M. Zaitsev, "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)." Dissertation for the degree of Dr. Chem., Kazan' University, 1870. The work was also published under the same title: *Zh. Russ. Khim. Obshch.*, **1870**, *2*, 292-310. [Russ.]
 12. This letter can be found in "Letters of Russian Chemists to A.M. Butlerov," *Scientific Heritage, U.S.S.R. Academy of Sciences Publishers*, Moscow, 1961, Vol. 4, p. 257. [Russ.] It is quoted in Ref. 2(b), p. 22.
 13. The impact of sulfoxide chemistry on modern organic synthesis may be gauged from the following reviews: (a) T. Durst, "Sulphoxides" in D.H.R. Barton and W.D. Ollis, Eds., *Comprehensive Organic Chemistry*, Pergamon Press, Oxford, 1979, Vol. 3, pp. 121-156; (b) T. Durst, "Polyfunctional Sulphoxides" in D.H.R. Barton and W.D. Ollis, Eds., *Comprehensive Organic Chemistry*, Pergamon Press, Oxford, 1979, Vol. 3, pp. 157-170; (c) A. Krief, "Alkylations of Sulfur and Selenium-Containing Carbanions" in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 3, pp. 85-191; (d) T.T. Tidwell, "Oxidations of Alcohols to Carbonyl Compounds via Alkoxysulfonium Ylides: The Moffatt, Swern, and Related Oxidations," *Org. React.*, **1990**, *39*, 297-572; (e) O. de Lucci, U. Motti, and G. Modena, "The Pummerer Reaction of Sulfinyl Compounds," *Org. React.*, **1991**, *40*, 157-405; (f) G. Solladié, "Asymmetric Synthesis Using Nucleophilic Reagents Containing a Chiral Sulfoxide Group," *Synthesis*, **1981**, 185-196.
 14. (a) A. Saytzeff, "Eine neue Methode Fettsäuren in entsprechende Alkohole umzuwandeln." *Z. Chem.*, N.F., **1869**, *5*, 551-552; (b) A. Saytzeff, "Neues Verfahren zur Umwandlung der Fettsäuren in deren Alkohole.— Synthese des normalen Butylalkohols." *Z. Chem.*, N.F., **1870**, *6*, 105-108; (c) A. Saytzeff, "Ein neues Verfahren, die Fettsäuren in die entsprechende Alkohole umzuwandeln." *J. Prakt. Chem.*, N.F., **1871**, *3*, 76-88; (d) A. Saytzeff, "Umwandlung der Bernsteinsäure in den entsprechenden zwei-atomigen Alkohol—Vorläufige Mittheilung." *J. Prakt. Chem.*, N.F., **1871**, *3*, 427.
 15. A. Saytzeff, "Ueber die Reduction des Succinylchlorids." *Ann. Chem. Pharm.*, **1874**, *171*, 258-290.
 16. G. Wagner and A. Saytzeff, "Synthese des Diäthylcarbinols, eines neuen Isomeren des Amylalkohols." *Ann. Chem. Pharm.*, **1875**, *175*, 351-374.
 17. (a) M.M. Zaitsev, "On the action of zinc-sodium on a mixture of ethyl and methyl iodide with acetic anhydride." *J. Russ. Chem. Soc.*, **1870**, *2*, 374-378; (b) J. Kanonnikoff and M. Saytzeff, "Zur Darstellung des Jodallyls und des Essigsäureanhydrids." *Ann. Chem. Pharm.*, **1877**, *185*, 191-192.
 18. D. Ustinoff and A. Saytzeff, "Ueber die Einwirkung von Jodpropyl und Zink auf Butyron. Bildungsweise des Dipropylcarbinols," *J. Prakt. Chem.*, **1886**, *34*, 468-472.
 19. (a) J. Kanonnikoff and A. Saytzeff, "Neue Synthese des secundären Butylalkohols." *Ann. Chem. Pharm.*, **1875**, *175*, 374-378. (b) J. Kanonnikoff and A. Saytzeff, "Ueber Einwirkung eines Gemisches von Jodallyl mit Jodäthyl und Zink auf das Ameisensäure Äthyl." *Ann. Chem. Pharm.*, **1877**, *185*, 148-150; (c) M. Saytzeff and A. Saytzeff, "Synthese des Allyldimethylcarbinols." *Ann. Chem. Pharm.*, **1877**, *185*, 151-169; (d) A. Saytzeff, "Synthese der tertiären gesättigten Alkohole aus den Ketonen; Vorläufige Mittheilung." *J. Prakt. Chem.*, **1885**, *31*, 319-320; (e) A. Saytzeff, "Bemerkung über Bildung und Eigenschaften der in den vorhergehende, Abhandlungen beschriebenen ungesättigten Alkohole," *Ann. Chem. Pharm.*, **1877**, *185*, 175-183.

20. G. Wagner, "Einwirkung von Zinkäthyl auf Acetaldehyde." *Ann. Chem. Pharm.*, **1876**, 181, 261-264.
21. Review: R. Noyori, "Chiral Metal Complexes as Discriminating Molecular Catalysts," *Science*, **1990**, 248, 1194-1199.
22. (a) S. Reformatsky, "Neue Synthesen zweiatomiger einbasischer Säuren aus den Ketonen," *Ber. Dtsch. Chem. Ges.*, **1887**, 20, 1210-1211; (b) S. Reformatsky and B. Plesconossoff, "Die Einwirkung eines Gemenges von Zink und Bromisobuttersäureester auf Aceton. Synthese der Tetramethyläthylmilchsäure," *Ber. Dtsch. Chem. Ges.*, **1895**, 28, 2838-2841; (c) S. Reformatsky, "Die Einwirkung eines Gemenges von Zink und Bromisobuttersäureester auf Isobutyraldehyd. Synthese der sekundären β -Oxysäuren." *Ber. Dtsch. Chem. Ges.*, **1895**, 28, 2842-2847. (d) S. Reformatsky, "Neue Darstellungsmethode der α,α -Dimethylglutarsäure aus der entsprechende Oxysäure," *Ber. Dtsch. Chem. Ges.*, **1895**, 28, 3262-3265; (e) S.N. Reformatskii, "Reaction of the Mixture of Zinc and Ethyl Monochloroacetate with Ketones and Aldehydes (Synthesis of Tertiary β -Hydroxyacids)," Dissertation for the degree of Dr. Chem., Warsaw, 1890.
23. Reviews: (a) H.B. Meikelburger and C.S. Wilcox, "Formation of Enolates," in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 2, pp. 99-131; (b) C.H. Heathcock, "The Aldol Reaction: Acid and General Base Catalysis," in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 2, pp. 133-179; (c) C.H. Heathcock, "The Aldol Reaction: Group I and Group II Enolates" in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 2, pp. 181-238; (d) B.M. Kim, S.F. Williams, and S. Masamune, "The Aldol Reaction: Group III Enolates," in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 2, pp. 239-275; (e) M.W. Rathke and P. Weipert, "Zinc Enolates: The Reformatsky and Blaise Reactions," in B.M. Trost and I. Fleming, Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford, 1991, Vol. 2, pp. 277-299.
24. (a) A. Saytzeff, "Ueber die Oxydation der Oelsäure mit Kaliumpermanganat in alkalischer Lösung." *J. Prakt. Chem.*, **1885**, 31, 541-542; (b) A. Saytzerff, "Ueber die Oxydation der Oel- und Elaidinsäure mit Kaliumpermanganat in alkalischer Lösung." *J. Prakt. Chem.*, **1886**, 33, 300-318.
25. (a) G. Wagner, "Ueber die Oxydation der Olefine und der Alkohole der Alkylalkoholreihe." *Ber. Dtsch. Chem. Ges.*, **1888**, 21, 1230-1240; (b) G. Wagner, "Ueber die Oxydation der Kohlenwasserstoffe, C_nH_{2n-2} ." *Ber. Dtsch. Chem. Ges.*, **1888**, 21, 3343-3346. (c) G. Wagner, "Zur Oxydation ungesättigter Verbindungen." *Ber. Dtsch. Chem. Ges.*, **1888**, 21, 3347-3355; (d) G. Wagner, "Zur Frage über die Betheiligung des Wassers an der Oxydation ungesättigter Verbindungen." *Ber. Dtsch. Chem. Ges.*, **1888**, 21, 3356-3360.
26. A.E. Arbuzov, "On Allylmethylphenylcarbinol," *J. Russ. Phys. Chem. Soc.*, **1901**, 33, 38-45. [Russ.]
27. A. Arbuzov, "The Structure of Phosphorous Acid and its Derivatives," Dissertation for the degree of M. Chem., Kazan', 1905. [Russ.]
28. (a) K. Michaelis and R. Kaehne, "Ueber das Verhalten der Jodalkyls gegen die sogen. Phosphorigsäureaether oder O-Phosphine." *Ber. Dtsch. Chem. Ges.*, **1898**, 31, 1048-1055; (b) A. Arbusow, "Über Isomerationsvorgänge bei einige Phosphorverbindungen." *Chem. Zentr.*, **1910**, II, 453-454; this paper cites *J. Russ. Phys. Chem. Soc.*, **1910**, 42, 395-420.
29. Review: W.S. Wadsworth, Jr., "Synthetic Applications of Phosphoryl-Stabilized Anions," *Org. React.*, **1977**, 25, 74-253.
30. A. Saytzeff, "Zur Kenntnis der Reihenfolge der Anlagerung und Ausscheidung der Jodwasserstoffelemente in organischen Verbindungen." *Ann. Chem. Pharm.*, **1875**, 179, 296-301.
31. A. Popoff, "Die Oxydation der Ketone als Mittel zu Bestimmung der Constitution der fetten Säuren und der Alkohole." *Ann. Chem. Pharm.*, **1872**, 162, 151-160. This paper also carries the following citation for Popov's earlier work in the Russian language: "Ueber die Oxydation der Ketone mit einem Carbonyl." Kasan 1869.
32. This paper is alluded to in ref. 2(b), p. 88.

ABOUT THE AUTHOR

David E. Lewis is Professor of Chemistry at South Dakota State University. His major interests in the history of chemistry are the contributions of Russian organic chemists to the development of the discipline.