FEUDING RULE MAKERS: ALEKSANDR MIKHAILOVICH ZAITSEV (1841-1910) AND VLADIMIR VASIL'EVICH MARKOVNIKOV (1838-1904). A COMMENTARY ON THE ORIGINS OF ZAITSEV'S RULE

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Two of the most widely known examples of empirical rules for predicting the outcomes of organic reactions are named for the Russian* chemists Aleksandr Mikhailovich Zaitsev (1841-1910) (1) and Vladimir Vasil'evich Markovnikov (1838-1904) (2). Today most students in organic chemistry are familiar with the empirical rules devised by these two chemists: Zaitsev's (Saytzeff's) Rule for predicting the regiochemistry of base-promoted β-elimination from alkyl halides (3) and Markovnikov's (Markownikoff's) Rule for predicting the regiochemistry of the addition of unsymmetrical electrophiles to unsymmetrical olefins (4). Indeed, Markovnikov's name (though not, generally speaking, his rule) is one of the few remembered by students in organic chemistry years after they have completed the course. What is less well known is the fact that these two chemists were well acquainted with each other, having been students at Kazan' University, a frontier outpost that developed into one of Russia's finest universities with the pre-eminent chemistry school in the nation (5), and that they carried on a long standing feud that lasted their entire careers.

Zinin

As students at Kazan', Markovnikov and Zaitsev were the recipients of a chemical education that was one of the best in Europe at the time. During the middle third of the nineteenth century, Kazan' University boasted some of the most productive, perceptive, and creative organic chemists practising the science, as well as some of the most enlightened administration of the time. The mathematician Nikolai Ivanovich Lobachevskii (1792-1856), developer of non-Euclidean geometry, served as rector from 1827-1846. During 1834-1837, Lobachevskii supervised the construction of a new science building, with the chemistry floor modeled on the Giessen laboratory (6).

The rise to eminence of the chemistry school at Kazan' is usually traced to Nikolai Nikolaevich Zinin (1812-1880) (7), although his colleague at Kazan', Karl Karlovich Klaus (1796-1864) (8) may well have played an equally important part in its development. The organic chemist Zinin actually spent a relatively short time at Kazan', but Russian historians, in particular,

cite his contributions as the catalyst forming the "Kazan' School" of chemistry. After graduating with a degree in physics and mathematics, Zinin was appointed as adjunct in those disciplines. However, the Ministry of Education had other plans for the young man and, despite his lack of knowledge in chemistry, he was appointed to teach chemistry after the dismissal of the "undistinguished" (5a) professor of chemistry Dunaev. It was common practice at this time for professors to be appointed with a view to the students receiving lectures in the requisite subjects without necessarily considering the qualifications of the instructor in the subject (5b). As part of his training for the professoriate, Zinin was sent on a *komandirovka* (study leave abroad) to attend lectures by eminent western chemists. This was not intended as a research trip, but Zinin nevertheless spent time in the Giessen laboratory of Justus von Liebig, where he discovered the benzoin condensation (9). How this reaction was discovered is not known, but the condensation of benzaldehyde to benzoin is catalyzed by cyanide anion, and it is also known that Zinin was in Liebig's laboratory during the period when Liebig and Wöhler were carrying out their seminal researches on benzoyl compounds. The synthesis of mandelonitrile (benzaldehyde cynohydrin) by addition of hydrogen cyanide to benzaldehyde fails to give the desired product if the cyanide salt is added too slowly. So, under conditions where, for example, the cyanide salt is added to the aldehyde too slowly or insufficient cyanide is used, the product isolated from the reaction becomes benzoin. Is it possible that Zinin's experimental technique was very tentative because of a lack of experience, and that this then led to the discovery of a new reaction? My experience in organic synthesis leads me to believe so, but this cannot be proven beyond doubt. On his return to Kazan' in 1841, Zinin was appointed to the Chair of Technology (Klaus had been appointed to the Chair of Chemistry during Zinin's absence), and he began the studies with nitroaromatic compounds that led to the monumental discovery of the reduction of nitroaromatic compounds to anilines (10) and to the synthesis of azobenzene, azoxybenzene, and benzidine (11). In 1847 Zinin left Kazan' to take up the Chair of Chemistry at the Medical-Surgical Kazan' University of the University of St. Petersburg, where he later became mentor to the chemist-composer Aleksandr Porfir'evich Borodin (1834-1887).

Klaus

In contrast to his colleague, Klaus' contributions are frequently overlooked by historians of organic chemistry because of his general preference for work in pharmacy. After he had obtained his master's degree in chemistry from Dorpat University (now Tartu, in Estonia), he applied for the vacant chair in pharmacy at Kazan' but received, instead, an appointment in chemistry. On graduating with his doctoral degree in pharmacy in 1839, he was promoted to Extraordinary Professor of Chemistry, and, in 1844 (the same year as his discovery of ruthenium), he was promoted to Ordinary Professor. When he left Kazan' in 1852, it was to take up the newly-created Chair of Pharmacy at his alma mater.

Klaus' predilection towards pharmacy and his conservative chemical views (he was an adherent of the dualistic theories of Berzelius) may have deterred later biographers from recognizing his real impact on the careers of chemists who studied under him. Oddly enough, his place in history is not as a pharmacist, but as the discoverer of ruthenium, a result of work begun in the chemistry of the platinum metals at the instigation of a friend who worked at the mint (Russia used platinum as a coinage metal in addition to silver and gold). Klaus' discovery of ruthenium capped an impressive body of work in the chemistry of the platinum metals, and he also directed research students in the chemistry of these metals. Butlerov studied the chemistry of osmium under Klaus. An objective examination of Klaus' research record would suggest that his contributions to the development of the science itself, as well as his effects on the subsequent career choices of his students, were more important than is usually allowed by more chemistry- (and especially organic chemistry-) oriented biographers.

Between them, Zinin and Klaus were responsible for the chemical education of the man who was to become the most influential Russian organic chemist of his day: Aleksandr Mikhailovich Butlerov (1828-1886) (12), after whom the Butlerov Prize is named.

Butlerov's entry into chemistry was hardly auspicious: he was apparently electrified by the lectures of Zinin, but after Zinin's departure for St. Petersburg, Butlerov chose to remain in Kazan'. Here he continued his study of chemistry under Klaus, becoming the first person to observe the oxidation of organic compounds by osmic acid (osmium tetroxide) (13). Nevertheless, the young Butlerov was not as enamored with chemistry as one might have expected, given his enormous impact on the later development of the science in Russia. In fact, he wrote his *kandidat* dissertation on the diurnal butterflies of the Volga region (14)! Furthermore, his master's and doctoral dissertations (15) were largely reviews of known chemistry, with little evidence of the piercing intellect and creativity that he would later display. Despite his apparent lack of interest in and commitment to chemistry, it was to Butlerov that the University entrusted the teaching of chemistry following the departure of Zinin to St. Petersburg and Klaus to Dorpat.

Butlerov

One of the first things the University did was to send Butlerov abroad on a *komandirovka* to study chemistry, and Butlerov made the most of his opportunity. The timing of the trip could hardly have been more auspicious: the year 1858 was a nexus in the development of organic chemistry, with the new ideas of organic structure and reactivity being developed by the younger generation of chemists exemplified by Kekulé and Erlenmeyer in the face of (often vitriolic) opposition by the conservative Kolbe and his adherents (16). During his trip, Butlerov generally associated with the younger, more progressive chemists. He met Kekulé, who became a life-long friend, and he spent close to a year in Paris in the laboratories of Charles Adolphe Wurtz, where he almost certainly had the opportunity to meet and interact with Archibald Scott Couper. By the end of his trip, Butlerov had been inculcated with the views of the modernists. One of the first to appreciate the true power of the new structural theory of organic chemistry, he was one of the first to use it in the classroom and to predict the existence of new organic compounds. By 1860, Butlerov had incorporated his own version into his lectures and had become one of its most influential and ardent advocates. Butlerov's contributions have only recently been given their due place in discussions of the development of organic chemistry by western scientists, and he is now accorded a place alongside Kekulé and Couper as one of the important founders of the structural theory of organic chemistry. Over the next quarter century, Butlerov was to become one of the most influential Russian chemists of all time. It is rather ironic that Butlerov, a strong proponent of structural theory at this pivotal time in its development, sent two of his brightest students to study with Hermann Kolbe—its most resolute opponent—when they left Kazan'.

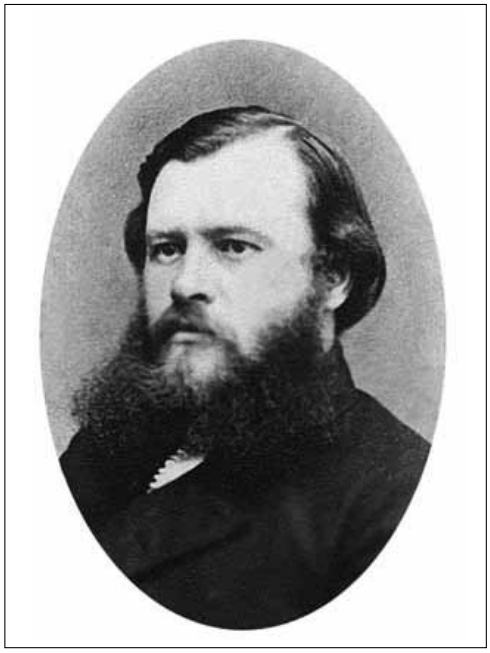
The subjects of this paper, Zaitsev and Markovnikov, had both entered Kazan' University as students in economics—*cameralisty*—and both came under the influence of Butlerov, who inspired them to become chemists. Unlike Zaitsev's student, E. E. Vagner (1849-1903), both students remained *cameralisty* through graduation. Of the two young chemists, it appears that Markovnikov, the older of the two, may have been the more theoretically inclined; certainly, it was Markovnikov who continued his mentor's work in structural theory as part of his master's degree. In contrast, Zaitsev appears to have been much more at home in the role of an experimentalist, and this is the nature of most of his contributions to organic chemistry.

One might have expected that being students of the great Butlerov, at the very time when he was making seminal contributions to the development of organic structural theory, would have cemented a friendship between the two young chemists. It actually appears that nothing could be further from the truth, and it is fascinating to speculate on the origins of this animosity, as well as on its importance in the development of organic chemistry as a whole.

Markovnikov graduated with a degree in economics in 1859. Following his graduation, Markovnikov began studies with Butlerov and wrote both *kandidat* (1860) and Master's (1865) dissertations under his direction. His *Magistr Khimii* (M. Chem.) dissertation, "On the Isomerism of Organic Compounds" (17), gave an incisive analysis of the state of organic structural theory and its

development, and was critical of Kekulé's overweening claims for his version of the theory and priority in its development. His doctoral dissertation, "On the Reciprocal Influences of Atoms in Chemical Compounds" (18), submitted four years later, was a brilliant theoretical exposition on the influence of structure on chemical reactivity. What we now know as Markovnikov's Rule—that the addition of hydrogen halides to unsymmetrical alkenes proceeds such that the major product obtained has the hydrogen bonded to the less substituted carbon atom—came out of this dissertation. The rule was published in both German (4a) and French (4b); but despite Butlerov's urgings that he publish the findings of his dissertation in German, it appeared as a complete entity only in Russian.

In the dissertation, Markovnikov not only gave a rationale of the regiochemistry of addition, but he went so far as to suggest that one should be able to predict the major product of an elimination, since this reaction would simply be the reverse of the addition reaction leading to it. In some ways, this prediction foreshadowed what we now know as the Principle of Microscopic Reversibility. Regardless, the application of this principle, as defined by Markovnikov, leads to the conclusion that since hydrogen iodide adds to 1-butene to give 2-iodobutane as the major product, elimination of hydrogen iodide from 2-iodobutane should give 1-butene as the major product.



Markovnikov

Markovnikov was an intuitively brilliant chemist whose theoretical insights earned him a place as one of the few Russian chemists to attain eminence outside Russia during his lifetime. However, he was also a prickly individual: a stubborn idealist whose character is perhaps best defined as a mix of jingoistic Russian, modernist rebel, and political *naïf*. Thus, despite the higher visibility and better reputation of the German journals, Markovnikov published some of his most important work only in Russian journals, in an attempt (ultimately futile) to raise western consciousness of Russian chemistry. At the same time, this loyal subject of the Tsar appears to have had a healthy disrespect for authority in all its personifications—except, of course, for his revered Butlerov. And finally, he seldom appears to have tempered his willingness to take a stand on controversial issues with a real appreciation of the potential consequences of doing so. Certainly, scientific eminence abroad and at home did not protect Markovnikov from his political enemies as it had protected Mendeleev.

This rather incongruous mix of characteristics, which resulted in Markovnikov's inspiring both fanatical loyalty and equally committed enmity, may explain some of his checkered career, which is illustrated by the mechanism of his removal from his Chair at Moscow. In 1881 the freedom that had been enjoyed by universities under the reforms of Aleksandr II were severely curtailed, and professors could, by vote of the faculty, be forcibly retired 25 years after their first appointment to an academic position. Markovnikov's appointment as Extraordinary Professor at Kazan' occurred in 1868. Thus, in 1893, his political opponents were able to use the arcane regulations of the Ministry of Education to orchestrate his ouster from the Chair of organic chemistry while Markovnikov and his supporters were absent from the University; and he was forced to turn over his chair to Nikolai Dmitrievich Zelinskii (1861-1953). The supervision of his doctoral student, Aleksei Evgen'evich Chichibabin (1871-1945), was left to his assistant, Konovalov, since Zelinskii did not want anything to do with the students of his predecessor.

After his graduation, Markovnikov took a *komandirovka* in western Europe, spending 1865 and 1866 with Kolbe in Leipzig. It is interesting to note that Markovnikov, the older student, actually followed the younger, Zaitsev, into Kolbe's laboratory. Markovnikov's adherence to the modern structural ideas of Butlerov led to more than one interesting discussion with Kolbe, who eschewed the term, "chemical structure," in favor of the term, "rational constitution," even though his theory was much closer to the more modern view held by Butlerov and Erlenmeyer than he would like to admit. Despite their occasional scientific differences, it is clear that Markovnikov both liked and respected his German mentor.

On his return to Russia, Markovnikov became *docent* at Kazan' University; and, thanks to the efforts of Butlerov, he was appointed as Extraordinary Professor (Associate Professor) of Chemistry. This is a critical

example of how Butlerov, who had already served two terms as Rector of the University, promoted his students by making the case that students in the cameral sciences at Kazan' were well prepared for careers as *scientists*, not just as members of the government bureaucracy. Butlerov's support—and his vigorous championing of students in cameral science as being as well qualified for careers in science as students in the Mathematical-Physical Faculty—was critical in the careers of Markovnikov and Zaitsev, both of whom had graduated in cameral science. Markovnikov was promoted to Ordinary (Full) Professor of Chemistry at Kazan' in 1869, succeeding his mentor. In 1871 he left the University and took up the post of Professor of Chemistry at Odessa; two years later, he took up his final position as Professor of Chemistry at the University of Moscow.

In contrast to his older contemporary, Zaitsev appears to have been much more astute politically. The son of a tea merchant, Mikhail Savvich Zaitsev, Aleksandr Zaitsev had—with the help of his uncle, the astronomer, Lyapunov—persuaded his father to allow him to study at Kazan' University, although his father imposed the condition that he study economics as a prelude to entering business. The death of his father shortly before his graduation and the sale of the family business and distribution of the proceeds among the sons immediately thereafter freed Zaitsev from the specter of a life spent in the mercantile guilds and eliminated his financial worries for a while.

While a student in economics at Kazan', Zaitsev had also fallen under the spell of Butlerov, and he had begun to work with him. While the Russian biographical literature, at least, implies that Butlerov claimed Zaitsev as a disciple from the beginning of their relationship, a reviewer has suggested that it is not really legitimate to call Zaitsev a disciple of Butlerov at this time, at least not in the reciprocal sense. He maintains that it should be stressed, instead, that while Zaitsev might have considered himself a Butlerov disciple, he was not close enough to Butlerov at this time to be counted as one of his disciples.

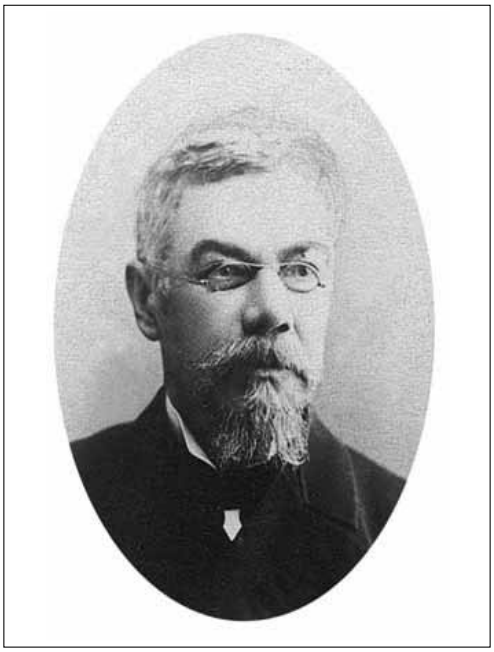
The removal of his financial worries (for a while, at least) and the elimination of his father's control over his future allowed Zaitsev to take the very risky and unconventional step of leaving Russia, as soon as he had graduated with his *Diplom*, to study in Western Europe with Kolbe, then the most influential organic chemist in western Europe. In studying with Kolbe, Zaitsev may have been influenced by his older brother, Konstantin Mikhailovich, who, in 1862, had become the first of a series of Kazan' students to study at Marburg. Rocke (19) has suggested that the steady stream of students from Kazan' to Marburg may have been at Butlerov's instigation, which would mean that Zaitsev's choice may still have been influenced by Butlerov.

While studying in Kolbe's laboratory, Zaitsev probably had time to consider the potentially serious consequences of his actions in leaving Kazan' before obtaining the degree of *kandidat*. At that time, the degree of *kandidat* was the minimum required qualification to be appointed to a salaried position as a laboratory assistant in Russian universities; and Zaitsev may have realized that his rather precipitous departure might have compromised his future. Thus, in 1863, after his first year with Kolbe, Zaitsev submitted a 76-page hand-written dissertation, "The Theoretical Views of Kolbe on the Rational Constitution of Organic Compounds and their Relationship with Inorganic Compounds" (20), for the degree of *kandidat*. The move could hardly have been more ill-considered. Not only did this dissertation expound favorably on the views of Kolbe, structural theory's most ardent opponent, but it was examined by Butlerov, structural theory's most ardent champion. Butlerov's evaluation of this dissertation was unusually acerbic. At one point he characterizes it as "a poor rendering of the German" and in other places mercilessly criticizes lapses in logic. Needless to say, the degree was not awarded.

Zaitsev remained abroad until his money was nearly depleted; and then, lacking the funds to follow Kolbe to Leipzig, he returned to Russia to seek a position. Now surfaced the first of his problems: without the *kandidat* degree, he was not qualified for a salaried position as a laboratory assistant. What he did to overcome this problem was characteristic of the man: he realized that there was but one individual who could restore him to the good graces of the administration of Kazan' University: Butlerov. So he offered him his services as an unpaid assistant. Why Butlerov bothered to help Zaitsev is something of a puzzle, since he had no compelling reason to do so. At Mendeleev's urging, Butlerov was already in negotiation with St. Petersburg University for the chair of Chemistry, and he had more than enough students wanting to work with him. But, by this time, Zaitsev's record in the laboratory of Kolbe, where he discovered the sulfoxides and the sulfonium salts (21), and his work with Wurtz, which had led to a series of five publications on the reactions of carboxylic acid derivatives (22), had marked him as a gifted experimentalist. Zaitsev's level of productivity in his three years abroad was clearly appreciated by Butlerov, whose actions permit one to

deduce that he recognized his skill and determined to preserve it for Russian chemistry (23). The impressive body of synthetic chemistry centered around zinc alkyls—notoriously air-sensitive and difficult reagents to work with—developed by Zaitsev and his students over the next three decades tends to affirm Butlerov's wisdom in helping Zaitsev re-enter the academic mainstream in Russia.

Immediately on his return to Russia, Zaitsev was shepherded by Butlerov through the process of writing his *kandidat* dissertation, describing the work he had done while a student in Wurtz' laboratory in Paris (24). As soon as he had obtained his degree, Zaitsev was appointed laboratory assistant in agronomy, and the direction of the agronomy laboratories was given over to him. At this stage, Zaitsev had re-entered the career mainstream. However, he had his sights set on a professorship in chemistry, and the only way to obtain a professorship was by holding the degree of Master of Chemistry or Doctor of Chemistry.



Zaitsev

This time it was not entirely Zaitsev's fault that his career nearly ended in ruins. His *kandidat* degree was in *cameral* science, and this meant that he was not formally eligible to receive the degree of *Magistr* in the Mathematical-Physical Faculty. Even here, his response to the problem was typical of the man: instead of waiting for his mentor Butlerov to plead his case, as he had done for Markovnikov before him, Zaitsev sought his own—legalistic—solution. Finding that a doctoral degree from a foreign university would satisfy the requirements, Zaitsev submitted a dissertation for the doctoral degree in chemistry to Kolbe at Leipzig (25). There, thanks to the influence of his former mentor (which suggests that Kolbe had fond memories of his Russian student), he was awarded the degree of D. Phil. in 1866 *in absentia*. Even with this degree in hand, however, there were some who were opposed to granting the exception that would allow him to submit for the master of Chemistry degree, and it was Butlerov who, again, came to the aid of his student by making the case very strongly for this graduate in cameral science.

At Butlerov's suggestion, Zaitsev submitted the work detailing his discovery of the sulfoxides at Marburg, for the degree of Master of Chemistry at Kazan' in 1867 (26). In 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)" (27).

With Butlerov's impending departure for St. Petersburg, Markovnikov was the obvious choice for his replacement, having substituted for him while Butlerov was abroad in the west making his case for priority in the development of the structural theory of organic chemistry. However, Markovnikov's temperament was such that the University administration was determined that he would not occupy the chair alone; unlike Butlerov, who was universally loved and admired, Markovnikov as the sole occupant of the chair in chemistry raised a specter that the University administration did not want to face. Another Butlerov student, Aleksandr Nikolaevich Popov (1840-1881), who had written a brilliant master's dissertation on structural theory under Markovnikov, was the first choice to occupy the second chair at Kazan'. However, before he could be formally offered that chair, he accepted the invitation of the chair of chemistry at Warsaw University and departed for Bonn to study under Kekulé prior to taking his new appointment. This left Zaitsev as the logical choice for the vacant chair at Kazan'.

Markovnikov's disdain for Zaitsev was very poorly disguised, and Zaitsev's appointment as Extraordinary Professor in May, 1869, left Markovnikov so chagrined that he wrote in a letter to Butlerov in October, 1869 (28):

> With the departure of Popov I am determined to speak to nobody. I see Zaitsev only before his lectures...

Further evidence of Markovnikov's contempt for his new colleague arose when Zaitsev submitted his doctoral dissertation. Markovnikov, appointed as the primary examiner of the dissertation, wrote an overtly positive review that was filled with negative innuendo. This attempt to derail Zaitsev's promotion to Ordinary Professor

failed because Butlerov and the university faculty were well aware of Markovnikov's personal animus towards Zaitsev; and so, on the strength of Butlerov's positive recommendation, he was awarded his doctoral degree and promoted to Ordinary Professor by a 19-12 split vote in November, 1871. Although the primary reason for Markovnikov's rancorous departure for Odessa is universally accepted as the dismissal of the popular Rector, Pyotr Frantsevich Lesgaft (1837-1909), Zaitsev's appointment as Ordinary Professor must have been a factor. Markovnikov left less than six weeks after Zaitsev's election.

The origins of the bad blood between Zaitsev and Markovnikov are not known explicitly, so some degree of inference (even speculation) is required to provide a plausible reason for their mutual antipathy. There are two plausible causes for the mutual dislike, and while the evidence for each individually is not especially strong, I submit that the combination of the two provides a reasonable rationale for the origins of the feud.

The first potential cause of the feud is Zaitsev's failed *kandidat* dissertation. At the time that Zaitsev submitted the dissertation, Markovnikov was completing his master's degree with Butlerov at Kazan'. Given that Butlerov later recommended Markovnikov as one of the formal opponents (i.e. examiners) of Zaitsev's doctoral dissertation, I suggest that Butlerov might also have shared this early dissertation with Markovnikov, especially in light of the latter's work with structural theory. Were this to be the case, the apparent apostasy of Zaitsev, another student who had received instruction from his revered Butlerov, would undoubtedly have been viewed by the very nationalistic Markovnikov as nothing less than an idealogical betrayal of Russia and Russian chemistry.

The second potential cause may be Kolbe himself, who may have (unwittingly) negatively affected the relationship between his two young Russian students. To what extent he compared the gifted theoretician Markovnikov with the talented experimentalist Zaitsev is not clear. However, given his practical turn of mind and the evidence of his support for Zaitsev's doctoral dissertation *in absentia*, it is probable that Kolbe had fond memories of Mr. Zaitsev. Consequently, Markovnikov may have occasionally found himself compared to his younger colleague by the Herr Dr. Professor. Such comparisons would have prompted a terrible dilemma for Markovnikov, given that any praise of Zaitsev by Kolbe would, of necessity, have meant praise for a Russian chemist trained by Butlerov …but at the price of having been compared to an apostate who had flouted Russian customs.

Unlike that of his demonstrative colleague, Zaitsev's career was not colored by outbursts that provide a window into his character, which means that one must use inference to divine his opinions. His career, as we have already pointed out, suggests that Zaitsev was far from being a political *naïf*, although, as a young man, he did suffer from an impetuousness and lack of foresight that almost derailed his career before it had begun. But Zaitsev always seemed to know how to fix the problems caused by his impatience: he appreciated who it was he needed to cultivate, and when. He seems to have been aware of Butlerov's feelings about building a Russian professoriate in Russian universities, and his appeal to Butlerov as an unpaid assistant to allow his return to Russia was a masterful political stroke.

By 1875 Markovnikov had left Odessa, where he had served as Professor of Chemistry from 1871-1873, and had become established in the Chair at Moscow University, where he was working diligently to upgrade the laboratory. Zaitsev, likewise, had settled into what was to become a productive, 40-year career at Kazan'. Insofar as I have been able to determine, the interaction between the two by this time was minimal, at best.

Markovnikov's international reputation had been established by his report of what we now call Markovnikov's Rule for addition, which appeared first in the *Annalen der Chemie und Pharmazie* in 1870 (4a). Zaitsev's paper, in which he set out what is now known as Zaitsev's Rule, appeared in 1875 (29). The paper, which was largely a literature review and contained results from his students Grabovskii and Vagner, appeared right after Markovnikov had begun publishing his series of three papers in the *Comptes Rendues* detailing his empirical rule for addition (4b). Zaitsev's was not the first report of regioselectivity in an elimination reaction, however. Some three years earlier, Popov had speculated on the regiochemistry of dehydration reactions in a letter to Butlerov, describing his oxidation work with chromic acid (30), and in a paper in 1873, where he speculated on the regiochemistry of dehydration during the oxidation of 3-methyl-2-butanol to acetone and acetic acid (31). In a paper presented at a conference in Kazan', Popov, speculating again on the regiochemistry of dehydration reactions during oxidation, suggested that this idea might be extended to dehydrohalogenation reactions (32). Zaitsev would certainly have been aware of Popov's papers but did not acknowledge his work in the 1875

paper; it is not clear why Popov's work was not cited or acknowledged.

What follows is, admittedly, speculative because we cannot know the extent to which the clash of personalities contributed to Zaitsev's decision to pursue this line of research, and, more importantly, to the timing of its publication. As implied above, Zaitsev's temperament is not illuminated by his actions nearly as much as is Markovnikov's. Nevertheless, it seems reasonable that there is enough circumstantial evidence to suggest that Zaitsev's Rule, at least, may ultimately be a result of a desire to get back at the one person who held him in contempt: Markovnikov. This, of course, leads to an ultimate irony, that these two rules of regiochemistry in organic reactions stand side by side in the sophomore organic chemistry curriculum, as neither of their protagonists would in life.

REFERENCES AND NOTES

* The names of the principal subjects of this paper will be transliterated from the Cyrillic as Zaitsev and Markovnikov throughout the body of this manuscript; in literature citations this spelling will be used in reference to articles in Russian. In the references to journal articles in German and French, their names will be spelled exactly as they appear in the journal (e.g. Saytzeff and Markownikoff). The same treatment has been applied to the journal articles of other Russian chemists (e.g. Butlerov).

1. There are several Russian-language biographies of Zaitsev: (a) A. N. Reformatskii, "Biografiya Aleksandra Mikhailovicha Zaitseva" ["Biography of Aleksandr Mikhailovich Zaitsev"], *Zh. Russ. Fiz.-Khim. Obshch.*, **1911**, *43*, 876; (b) A. S. Klyuchevich and G. B. Bykov, *Aleksandr Mikhailovich Zaitsev*, Science Publishing House, Moscow, 1980; (c) S. N. Reformatskii, "Pamyat' Professora A. M. Zaitseva [A Memorial of Professor A.M. Zaitsev]," *Univ. News*, Kiev, 1910, No. 11, Supplement 2 in *Dokl. Fiz.-Khim. Obshch.*, 1-7; (d) A. E. Arbuzov, *Kratkii Ocherk Razvitiya Organicheskoi Khimii v Rossii* [*A Brief Description of the Development of Organic Chemistry in Russia*], U.S.S.R. Acad. 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, 323-325; a list of his works is included on pp 325-332. Biographies in western European languages are less common: (f) "Alexander Micholajeff Saytzeff," *Ber. Dtsch. Chem. Ges.*, **1910**, *43*, 2784; (g) "Alexander Michajlowich Saytzeff," *Poggendorffs biographisch-literarisches Handwörterbuch zur Geschichte der exacten Wissenschaften*, Vol. III, 1176 (1898); Vol. IV, 1310 (1904); Vol. V, 1098 (1926); (h) D. E. Lewis, "Aleksandr Mikhailovich Zaitsev: Markovnikov's Conservative Contemporary," *Bull. Hist. Chem.*, **1995**, *17/18*, 21-30.
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20. 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]. This dissertation is cited in Ref. 2b, p 65.
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23. A reviewer has suggested an intriguing alternative explanation for Butlerov's actions in taking Zaitsev back into the mainstream: "My sense is that Butlerov did not have many students in the 1860s. The enrollment in the physics-mathematics faculty at Kazan was rather small, which limited the number of possible students."
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25. A. Saytzeff, Ueber eine neue Reihe organischer Schwefelverbindungen., D. Phil. Dissertation, Leipzig University, 1866.
26. A. M. Zaitsev, "O deistvi azotnoi kisloty na nekotorye organicheskie soedineniya dvuatomnoi ser' i o novom ryade organicheskikh sernistykh soedinenii, poluchennom pri etoi reaktsii [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]," M. Chem. Dissertation, Kazan' University, 1867. The abstract of this dissertation also appeared in *Student Writings of Kazan' University*, **1867**, *3*, 2. [Russ.]
27. A. M. Zaitsev, "Novyi sposob prevrashcheniya zhirnykh kislot v sootvetstvuyushchie in alkogoli. Normal'nyi butil'nyi alkogol' (propil-karbinol) i ego prevrashchenie 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. Dissertation, Kazan' University, 1870. The work was also published under the same title: *Zh. Russ. Khim. Obshch.*, **1870**, *2*, 292-310 [Russ.].

28. This letter can be found in "Pis'ma russkikh khimikov k A.M. Butlerovy" [Letters of Russian Chemists to A. M. Butlerov], *Sci. Heritage*, U.S.S.R. Acad. Sci. Publishers, Moscow, 1961, Vol. 4, 257. It is quoted in Ref. 2(b), p 22.
29. See Ref. 1(h).
30. 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 a footnote relating Popov's earlier work in the Russian language: "Ueber die Oxydation der Ketone mit einem Carbonyl, Kasan, 1869."
31. This paper is cited in Ref. 1(b), p 88.

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