

Was Markovnikov's Rule an Inspired Guess?

Peter Hughes

Westminster School, 17 Dean's Yard, London SW1P 3PB, United Kingdom; *deph15@hotmail.com

When Vladimir Vasil'evich Markovnikov died over 100 years ago on February 11, 1904, he was remembered for the work that he had done on petroleum products and alicyclic compounds. The well-known rule that bears his name was considered of only secondary importance and was not mentioned in his obituary in *Berichte* (1). Michael (2) had made an effort to get Markovnikov's early work on structure to be recognized, but it was not recognized until much later, after Kharasch (3) had clarified the conditions under which the rule applied. This ignorance of the rule has been attributed to Markovnikov's nationalism and his failure to publish in languages other than Russian (4). However, this assertion is not borne out by the facts. During the relevant period when Markovnikov was particularly interested in structure (1865–1875) he published 20 articles in German and French (5, 6), some of which were translations of earlier Russian articles (7, 8). Thus while it may be true that initially he wrote in Russian, his work soon became available to the wider chemical community.

The article in which Markovnikov first states his rule was written in German (9). In it he says "wenn ein unsymmetrisch constituirter Kohlenwasserstoff sich mit einer Haloïdwasserstoffsäure verbindet, so addirt sich das Haloïd an das weniger hydrogenisirte Kohlenstoffatom, d.h. zu dem Kohlenstoff, welcher sich mehr unter dem Einflusse anderer Kohlenstoffe befindet." This may be translated as "when an unsymmetrical alkene combines with a hydrohalic acid, the halogen adds on to the carbon atom containing the fewer hydrogen atoms, that is the carbon that is more under the influence of other carbons."¹ Later he considers the addition of HX to alkenes that already contain a halogen atom, such as vinyl bromide (bromoethene, $\text{CH}_2=\text{CHBr}$), and *gechlortes Propylen* (2-chloropropene $\text{CH}_3\text{CHCl}=\text{CH}_2$) and notes "sich das Haloïd immer zu dem Kohlenstoffatom addiren werde, welches schon mit einem Haloïd verbunden ist"; that is, the halogen adds on to the carbon atom that already has a halogen attached to it.

Why then was this rule ignored for so long? The first point is that the rule is included in a four-page addendum to a much longer 26-page article on isomeric butyric acids (ref 9, pp 255–259). It has been pointed out that the whole article is diffuse and rambling and would certainly not be accepted by a journal at the present time (10). There would have been no incentive for anyone to read the article right through to the end particularly as one of its main themes, namely that the hydrogen atoms on the carbon atom adjacent to the carboxyl group in the butyric acids were the most easily brominated, had already been expounded in an earlier article (11). In this earlier article Markovnikov also quotes Butlerov's work on the chlorination of alkanes; Butlerov showed that the hydrogen atom joined to a carbon atom attached to three alkyl groups was the most easily substituted. It is likely that this is what Markovnikov had in mind when

he talks about "zu dem Kohlenstoff, welcher sich mehr unter dem Einflusse anderer Kohlenstoffe befindet." As a tertiary (or secondary) carbon atom readily attracts a halogen to it during substitution of an alkane, it would not be surprising that it did the same during addition of HX to an alkene. The rule is then a natural extension of the rules he formulated about substitution in alkanes and carboxylic acids (11).

Secondly, in 1870 his generalizations about reactivity would have been viewed with suspicion. The well-documented Butlerov–Kekulé controversy over the priority of using structural formulas (12) in organic chemistry split chemists along Eastern–Western European lines and as Markovnikov supported his mentor Butlerov, his work was inevitably treated with suspicion in France and Germany. We may also note that between 1870 and 1875 Markovnikov changed his representation of organic structures from a radical formulation to one using Crum Brown's chemical bonds (Figure 1). In 1870 formulas were considered a convenient way to show chemical change; they were not meant to show how the atoms were arranged in space. This contrasted with Markovnikov's emphasis on the reactivity of atoms in different structural positions, a view that must imply that atoms are physically next to one another to produce the necessary reciprocal influence. This idea was too advanced for the chemical establishment of 1870; it was only when the stereochemistry of van't Hoff and Le Bel had become accepted after 1875, and more particularly the electronic theory of organic chemistry pioneered by Robinson and Ingold had become formulated 60 years later, that the idea of reciprocal influence became fundamental to organic chemistry.

However, arguably, the main reason why his rule was ignored for so long was that Markovnikov provided little experimental evidence for it. In 1870, it was difficult to make alkenes combine with hydrogen halides under controlled conditions and almost impossible unequivocally to identify the principal reaction product. The principal physical methods of analysis, for nonchiral compounds, were boiling point and density determination and these assumed that one had a sample of the pure substance to act as a standard.

As an alternative, structure might be determined by chemical means. An example of this is the work of Butlerov

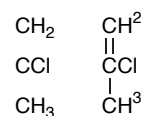


Figure 1. An example of the way in which Markovnikov wrote chemical formulas in 1870 (left) (9) and 1875 (right) (13). The radical formulation (left) showed what groups were present in the molecule but was not meant to indicate their physical juxtaposition.

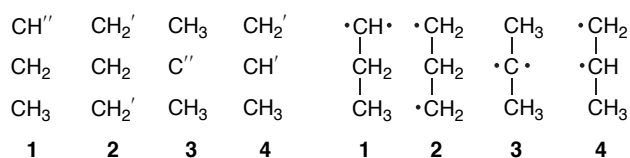


Figure 2. Butlerov's structures for propylene (left) and the equivalent modern formulas using unpaired electrons (right). Nowadays, structure 2 would be written as cyclopropane and structure 4 as propene.

on the structure of propylene. Butlerov considered four possible structures (Figure 2) (14). It was known that the addition of chlorine to propylene gave a dichloride that lost HCl when heated with alcoholic KOH. As it had a relatively low boiling point Butlerov thought the product was probably 2-chloropropene, eliminating structures 1 and 2. Hydrolysis of the dichloride yielded a glycol and not acetone, eliminating structure 3, leaving structure 4.

Butlerov's doubt over the structure of the chloropropene was only resolved a year later in 1868 by Oppenheim (15); the removal of this doubt also enabled Markovnikov to use addition reactions to 2-chloropropene as an example to illustrate his rule.

The Reactions Used by Markovnikov

In his 1870 article Markovnikov used a number of addition reactions to illustrate his two rules. It is not clear which of these were reactions he had carried out himself, which had been investigated by other people, and which were predictions. He states "Ich kann hier nicht ausführlich in die Betrachtung der verschiedenen Thatsachen eingehen, welche uns erlauben, ein solches Gesetz aufzustellen", which we can translate as "I cannot here enter into a detailed examination of the various facts that permit us to establish such a law." He almost apologizes that the experimental evidence is so slight. We will consider each reaction in turn.

Addition of HI to Propylene (Propene), Isobutylene (Methylpropene), and Butylene (1-Butene)

M. V. de Luynes (16) stated that when butylene was passed through saturated hydroiodic acid, the gas was absorbed and a liquid with a boiling point of 118 °C was obtained, corresponding to that of 2-iodobutane (modern value 117 °C). His formulas for the butylenes were incorrect as he (following Wurtz) used 6 for the atomic weight of carbon, with the result that the butylenes were thought to contain eight and not four carbon atoms. It may be that Markovnikov carried out similar reactions with propene and isobutylene but he does not record that in his article.

Addition of HCl to 3-Methyl-1-butene and HI to 2-Pentene²

The HCl is almost certainly a misprint. Markovnikov previously recorded this reaction as the addition of HI and it is unlikely that success had been achieved with the much less reactive HCl. His most likely source of this information is M. Simpson (17).

Addition of HBr and HI to Acetylene (Ethyne)

Markovnikov stated that M. E. Reboul treated acetylene with HBr to give first vinyl bromide and then 1,1-dibromethane. M. Berthelot (18) said that Reboul did get acetylene to react with concentrated hydrobromic acid at 100 °C (presumably in a sealed tube) to give vinyl bromide but made no reference to the second stage. Berthelot himself claimed that concentrated hydroiodic acid slowly absorbed acetylene at room temperature to give 1,1-diiodoethane, boiling point 182 °C (modern value 179 °C). Thus Markovnikov was correct in stating that the halogens both became attached to the same carbon atom, even though the reaction was actually with the HI and not HBr.

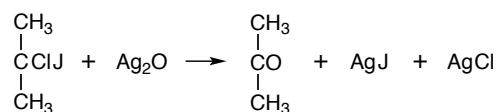
Addition of HI to Vinyl Bromide

M. Pfaundler (19) heated vinyl bromide with concentrated hydroiodic acid in a sealed tube at 100 °C for several days and obtained C₂H₄BrI with a boiling point of 147 °C (modern value 142–143 °C). Markovnikov stated that Reboul had made vinyl bromide react with HBr although no such claim was made in the cited reference. It may be that Markovnikov confused the addition of HBr to vinyl bromide with the work of Pfaundler with HI; as the latter reaction was so slow it is extremely unlikely that anyone at that time had succeeded in making HBr add to vinyl bromide.

When treated with moist silver oxide C₂H₄BrI gave ethanal showing that the bromine and the iodine were on the same carbon atom.

The Addition of HI to Gechlortes Propylen (2-Chloropropene)

Oppenheim (15) showed that *Jodwasserstoffsäure* (hydroiodic acid) and *gechlortes Propylen* reacted together when placed in a sealed flask and kept in a water bath (temperature not recorded) for a long time. He showed that the product was 2-chloro-2-iodopropane, CH₃CClI(CH₃), by treating it with silver oxide to give propanone:



(The use of J instead of the modern I is derived from the German word for iodine, *Jod*.)

The Addition of HOCl to Propylene and Isobutylene

When propylene and isobutylene were treated with chlorine water, Markovnikov stated that CH₂ClCHOHCH₃ and CH₂OHCCl(CH₃)CH₃ were formed. It is unlikely that he was able to identify which isomer had been produced. We now know that the addition of HOCl to alkenes often gives a mixture of products and it was, therefore, sensible of Markovnikov not to include this addition reaction in his rule.

Conclusions from These Reactions

This section about the rule in the 1870 article is poorly organized and shows all the signs of having been added to the main article as an afterthought. Markovnikov gave in-

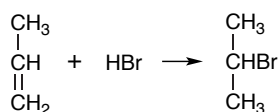


Figure 3. The addition of hydrogen bromide to propene.

correct or incomplete references to the articles of de Luynes and Reoul and for two reactions he quoted the incorrect hydrogen halide. The article would certainly not have been accepted 50 years later when it would have been refereed; even by the end of the 19th century editors were beginning to exercise more control over their publications and few would have accepted glaring errors such as those quoted here.

The Markovnikov rule only became established as a result of the careful work started by Maas in 1924 (20). Maas dissolved anhydrous hydrogen halides and alkenes in hexane and found that the addition reactions took place rapidly at room temperature. Under these conditions, the direction of addition was always as predicted by Markovnikov. This was the first time that HBr was convincingly added to propene to give exclusively 2-bromopropane (Figure 3). It was this work of Maas that made it possible for Kharasch to explain anti-Markovnikov addition as a free radical mechanism. The story of this and subsequent development is well known (21) and as a result Markovnikov has become, after Mendeleev, the most quoted Russian chemist at the present time.

The addition of hydrogen bromide or hydrogen chloride to propene are often quoted as paradigm reactions for Markovnikov addition (21–23), even though Markovnikov never carried them out (though he did claim that hydrogen iodide gave 2-iodopropane). Heating propene with concentrated HBr in a sealed tube gives a mixture of products depending on the conditions. Only under anhydrous conditions does the uncatalyzed reaction take place at room temperature to give exclusively 2-bromopropane (20). Presumably the use of a phase-transfer catalyst would speed up the reaction, but even under these conditions it takes two hours of heating to make 1-hexene react with concentrated HBr to give 2-bromohexane (24). It would take even longer to react with hydrogen chloride. Thus it is extremely unlikely that Markovnikov ever carried out these reactions that are so often attributed to him.

Does Markovnikov deserve such fame? The answer is undoubtedly yes. It is easy to point out the limitations of his 1870 article, but his idea was an inspired extension of the excellent work that he had been doing, in extremely difficult circumstances, for the previous five years. Kerber (25) points out that as there are so many exceptions to his rule it would be better not to teach it as a “rule” at all, but to concentrate instead on the subtle electronic effects that underpin its mechanism. These exceptions, however, which required years of painstaking work to explain, in no way belittle Markovnikov’s work. To make an inspired guess, that only becomes recognized and explained 60 years later, is a notable

scientific achievement. We should continue to mention his rule if only to keep his name alive.

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Notes

1. In current organic textbooks the rule is stated in terms of the addition of the hydrogen; for example, “in the addition of HX to an alkene, the hydrogen atom adds to the carbon atom of the double bond that already has the greater number of hydrogen atoms” (Solomons, T. W. G.; Fryhle, C. B. *Organic Chemistry*, 7th ed.; John Wiley & Sons: New York, 2000; p 325.)

2. Markovnikov referred to 3-methyl-1-butene and 2-pentene as β -Amylen and α -Amylen, respectively, in his 1870 article.

Literature Cited

1. Decker, H. *Ber.* **1905**, *38*, 4249–4262.
2. Michael, A. J. *Prakt. Chem.* **1899**, *60*, 286–289.
3. Kharasch, M. S.; Mayo, F. R. *J. Am. Chem. Soc.* **1933**, *55*, 2468–2496.
4. Leicester, H. M. *J. Chem. Educ.* **1941**, *18*, 53–57.
5. The Royal Society of London; *Catalogue of Scientific Papers, 1861–1873*; John Murray: London, 1879; pp 232–233.
6. The Royal Society of London; *Catalogue of Scientific Papers, 1874–1883*; Cambridge University Press: Cambridge, 1894; p 724.
7. Platé, A. F.; Bykov, G. V.; Markovnikov, V. V. *Izbrannye Trudy; Izo-vo Akademi nauk SSSR*, Moscow, 1955; pp 125–134.
8. Markovnikov, V. V. *Zeitschrift für Chemie* **1865**, *1*, 280–287.
9. Markovnikov, V. V. *Ann.* **1870**, *153*, 228–259.
10. Cooksey, C. J.; Dronsfield, A. T. *Educ. Chem.* **2004**, *41*, 47–50.
11. Markovnikov, V. V. *Ann.* **1868**, *146*, 339–352.
12. Rocke, A. J. *Brit. J. Hist. Sci.* **1981**, *46*, 27–57.
13. Markovnikov, V. V. *Compt. Rend.* **1875**, *81*, 668–671.
14. Butlerov, A. *Ann.* **1867**, *145*, 271–283.
15. Oppenheim, A. *Ann.* **1868**, *Supplement 6*, 353–364.
16. de Luynes, M. V. *Compt. Rend.* **1864**, *58*, 1089–1092.
17. Simpson, M. *Ann.* **1862**, *65*, 366–370.
18. Berthelot, M. *Compt. Rend.* **1864**, *58*, 977–978.
19. Pfaundler, M. *Bull. Soc. Chem.* **1865**, *3*, 242–249.
20. Maas, O.; Wright, C. H. *J. Am. Chem. Soc.* **1924**, *46*, 2664–2673.
21. Isenberg, N.; Grdinic, M. *J. Chem. Educ.* **1969**, *46*, 601–604.
22. Wade, L. G. *Organic Chemistry*, 2nd ed.; Prentice-Hall: London, 1991; p 317.
23. Fessenden, R. J.; Fessenden, J. S. *Organic Chemistry*, 5th ed.; Brooks/Cole: Monterey, CA, 1993; pp 423–424.
24. Roberts, R. M.; Gilbert, J. C.; Martin, S. D. F. *Experimental Organic Chemistry*; Saunders: New York, 1994; pp 340–341.
25. Kerber, R. C. *Foundation of Chemistry* **2002**, *4*, 61–72.