From Structural Theory to Stereochemistry: The Critical Role of the Kazan Chemists

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Historical Development and Use of the Concept of Structure

Evolution of Theories in Organic Chemistry

- J. Berzelius, Afhandlingar i fysik, kem och mineralogi, 1815.

The Rise of Structure

- 1858-1874: Structural Theory (Kekulé, Couper, Butlerov, Kolbe)
- 1874: Stereochemistry (van't Hoff, Le Bel)
- 1896-1933: Reaction stereochemistry (Walden, Hughes, Ingold)
- 1950: Conformational analysis (Barton, Hassell)
- 1960s: Guest-host chemistry (Charles J. Pedersen, Donald J. Cram, Jean-Marie Lehn, Fritz Vögtle)
- 1990s: complex self-assembly; supramolecular chemistry
The Initial Form of Structural Theory: 1858
Kekulé and Couper

Structural Theory of Organic Chemistry

May, 1858 – Kekulé

Friedrich August Kekulé (1829-1896)

14 June 1858 – Couper

Archibald Scott Couper (1831-1892)
A.-S. Couper. Comptes rends 1858, 46, 1157-1160.

Aleksandr Mikhailovich Butlerov (1828-1886)

- Kandidat Kazan 1849 (entomology)
- M. Khim. Kazan’ 1851 (under Klaus)
- Dr. Khim. Moscow, 1854 (under Klaus)

- study abroad (komandirovka) in western Europe 1857-1858, 1867-1868
  - met Erlenmeyer and Kekulé
  - spent six months with Wurtz in Paris
  - not supposed to be a research trip

- Kazan’ University
  - Professor of Chemical Technology 1861-1868
  - Rector twice

- University of St. Petersburg
  - Professor of Chemistry 1869-1880
Structural Theory, 1859

Butlerov’s initial response to Couper’s theory

Butlerov in western Europe 1857-1858:
Why did he align himself with Kekulé instead of Couper?

- Met twice with Kekulé in Heidelberg
- Spent 6 months in Wurtz’s laboratory
  - Elected to the Société Chimique de Paris, December 1857
  - Couper was elected in January, 1858
- Presented a paper (now lost) to the new Société Chimique on 17 February, 1858
  - This paper contained ideas similar to Kekulé, Wurtz and Kolbe

Why was Structural Theory not accepted immediately?

- Adherents of the theory of electronic dualism were not yet ready to accept the theory
  - Even Couper later tried to develop an electronic theory
- Chemists were very reluctant to abandon Type Theory completely
  - Kekulé’s version of the theory still retained some aspects of type theory
- Chemists (Butlerov among them) objected to Couper’s theory on the basis that it went too far
Structural Theory, 1861

- Versammlung deutscher Naturforscher und Ärzte in Speyer vom 17. bis 24. September 1861
  - [Meeting of German naturalists and physicians in Speyer from 17 to 24 September 1861]
- Butlerov presented a paper at this meeting

Speyer 1861

- Butlerov’s ideas had matured since his komandirovka in western Europe
- Butlerov withdrew his criticism of Couper’s theory and his support of Kekulé’s theory
- Butlerov had a fresh view that became an important contribution in its own right
  - Butlerov discerned the latent power in the new theory for predicting the existence of previously unknown (or only theoretical) compounds
Chemical Structure, not Physical Structure


1864: The Problem…

- Three different views of same evidence
- Little real difference between them
- Required someone to be the “template”

1864: The Solution?...

• Butlerov’s 1864 paper in the Bulletin de la Société Chimique de France attempted to reconcile and clarify the views of Kolbe and Kekulé on different types of isomers by using his version of Structural Theory as the foundation.

Butlerov, 1864: Reconciling diverse points of view

Using Structural Theory

- Butlerov
  - used structural theory to predict the existence of new compounds
    - Alcohols:
      $$\text{H}_3\text{C} \quad \text{O} \quad \text{H}$$
      $$\text{H}_3\text{C} \quad \text{C} \quad \text{H}_2 \quad \text{O} \quad \text{H}$$
      $$\text{H}_3\text{C} \quad \text{C} \quad \text{H}_2 \quad \text{O} \quad \text{H}$$
      $$\text{C} \quad \text{H}_3$$

- confirmed those predictions by the syntheses of the predicted compounds

Butlerov: Predicting existence of different classes of alcohols

Butlerov: Predicting existence of different classes of alcohols

Butlerov: Vvedenie, 1864

• The first textbook based entirely on structural theory
• Pre-dates Kekulé’s Lehrbuch by a year
• Translated into German, 1867-1868

Butlerov Synthesis: Alcohols


Butlerov’s apparatus

• Apparatus is charged with carbon dioxide

  – A: opening; closed with a three-hole stopper
  – B: glass tip drawn out to a small diameter
  – C: dimethyleine
  – D: narrow neck to be sealed after charging is complete
  – E, F: after sealing, the tube is stored so this line is horizontal during the reaction (3 days)
  – R: Liebig condenser (réfrigérant Liebig); the acetyl chloride is added by distillation into the reaction mixture through the distal end of the condenser
  – h: tube for introduction of the dimethylzinc
  – t: connecting tube to condenser

Butlerov’s apparatus diagram
Markovnikov: Exploring the limits of Structural Theory

- Markovnikov’s M. Khim. dissertation was a brilliant exposition of the state of knowledge about isomers.

The Next Advance: The Link Between Structure, Properties, and Reactivity

Dedication

To much respected Aleksandr Mikhailovich Butlerov
from a grateful student.

Vladimir Vasil’evich Markovnikov (Markownikoff) (1838-1904)

- kandidat Kazan’ 1860 (economic science)
- M. Khim. Kazan’ 1865
- Dr. Khim. Kazan’ 1869
- study abroad in western Europe 1865-1867
  - studied with Kolbe at Leipzig
  - studied with Erlenmeyer in Heidelberg
- Kazan’ University
  - docent 1867
  - Extraordinary Professor of Chemistry 1868
  - Professor of Chemistry 1869-1871
- Odessa (Novorossiisk) University
  - Professor of Chemistry 1871-1873
- Moscow University
  - Professor of Chemistry 1873-1893
Markovnikov: Effects of structure on physical properties


Markovnikov’s Rule


Markovnikov or Markovnikov?

“Writing his family name using — Markovnikov — was almost universal in official documents and journal articles in the 1860s, although it also occurs much later (emphasis added). Markovnikov himself explained that Butlerov kept writing the first syllable of his name using ə, and that he was imitated by others. According to the original version by A. Klyuchevich and G. V. Bykov, ‘on admission to the university, he was named just Markovnikov on the passport. He later corrected it to ‘Markovnikov,’ <but> Butlerov did not always remember about this.” (A. S. Klyuchevich, G. V. Bykov, Aleksandr Mikhailovich Zaitzev (1841-1910), Kazan University Press: Kazan, 1980, p. 18).


Expanding Structural Theory from Compounds to Reactions
1864: Butlerov hints that it may become possible to elucidate a physical structure for a molecule

M. A. Boudierov
"Sur les explications différentes de quelques cas d’isomérie," Bulletin de la Société Chimique de Paris, Nouvelle Série, 1864, 1, 100-128

J. H. van’t Hoff

1874: Stereochemistry and Modern Structural Formulas

Jacobus Henricus van't Hoff
(1852-1911)
J. A. Le Bel


And the Critical Role of the Kazan Chemists…?

• The use of Structural Theory to predict the existence of new isomers of hydrocarbons and alcohols (Butlerov)
• The confirmation of the predictions of Structural Theory by synthesis of predicted compounds
  • Synthesis of alcohols with organozinc nucleophiles (Butlerov; then Zaitsev, Vagner, Reformatskii)
• The first explicit proposal of double bonds in the structures of alkenes (Butlerov), and the observation of a type of tautomerism in alkenes (Butlerov)
• The extension of Structural Theory from static (structural–Butlerov) predictions to dynamic (reactivity–Markovnikov) predictions
  • Markovnikov’s Rule for addition of unsymmetrical reagents to unsymmetrical alkenes

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