# Discrete Taylor Series as a Simple Way to Predict Properties of Chemical Substances like Benzenes and Cubanes

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November 5, 2009

# Introduction to the Practical Problem

- Many substances are obtained from a template molecule by replacing its H atoms with *ligands*.
- Examples of templates: benzene $C_6H_6$ and cubane $C_8H_8$.

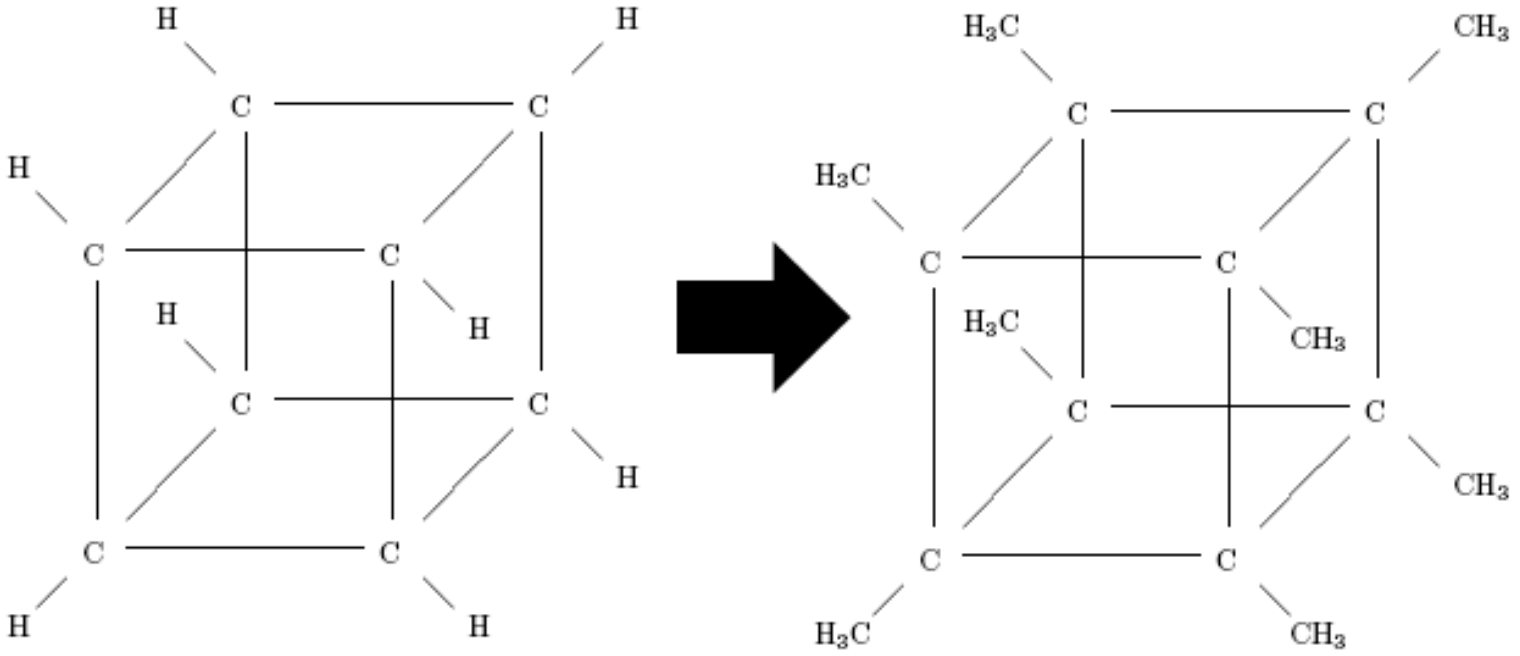



Figure: Example of a cubane derivative

# Introduction to the Practical Problem (cont-d)

- For each template, there are many possible substances.
- It is desirable to predict properties of these substances based on results of measuring a few of them.
- Such predictions are very important, since, e.g. cubanes, while kinetically stable, are highly explosive.
- As a result, at present, they are actively used as high-density, high-energy fuels and explosives.
- Researchers are investigating the potential of using cubanes in medicine and nanotechnology.

# How This Problem Is Solved Now and What We Propose

- It is desirable to predict properties of these substances based on results of measuring a few of them.
- Current approach proposed by D. J. Klein et al. in their 2007 Journal of Mathematical Chemistry.
- They used the ideas of the famous MIT mathematician Gian-Carlo Rota on partially ordered sets.
- Klein et al. showed that accurate predictions can be obtained by using these ideas.
- In this talk, we show that similar predictions can be made by using much simpler Taylor series techniques.

# Step-by-step Transitions as a Way to Predict Properties of Derivative Compounds

- Natural idea of synthesis: add ligands one by one
- Problem: use the properties of mono- and di-substituted substances to predict the properties of others

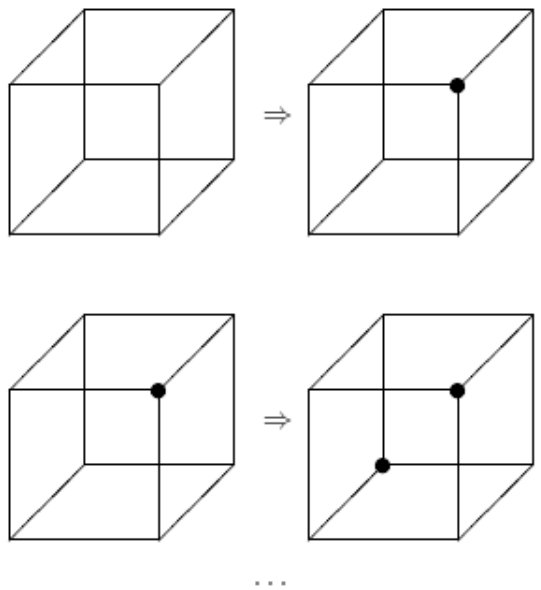


Figure: Step-by-step synthesis

# Another Practically Important Example: Benzene-Based Molecules

- Most organic molecules contain derivatives of benzene $C_6H_6$
- Adding ligands to benzene is one of the main ways to synthesize new organic molecules

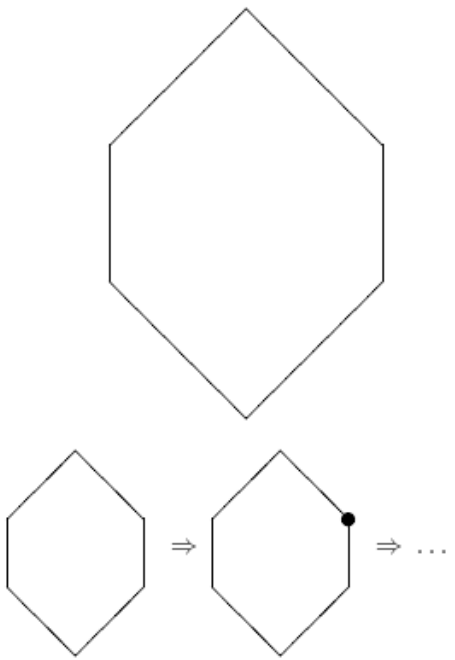



Figure: Benzene step-by-step substitution

# The Importance of Symmetry

- Molecules such as benzene or cubane have the additional property of symmetry
- Rotation does not change the chemical properties of a molecule
- This helps us reduce the number of tested substances

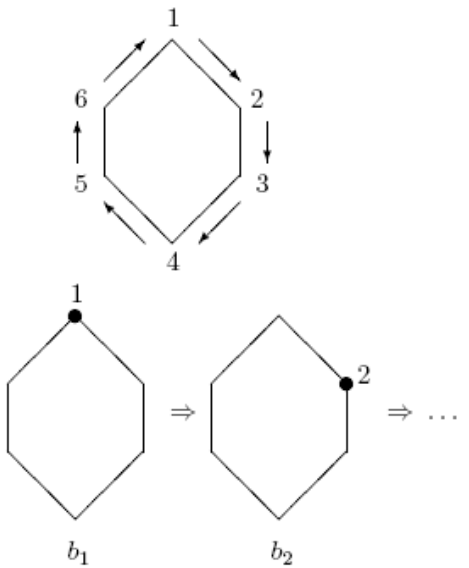



Figure: Benzene – rotation by 60°

# Extrapolation Example: Toxicity

- We perform measurements for several substances.
- We want to predict the values for all other substances.

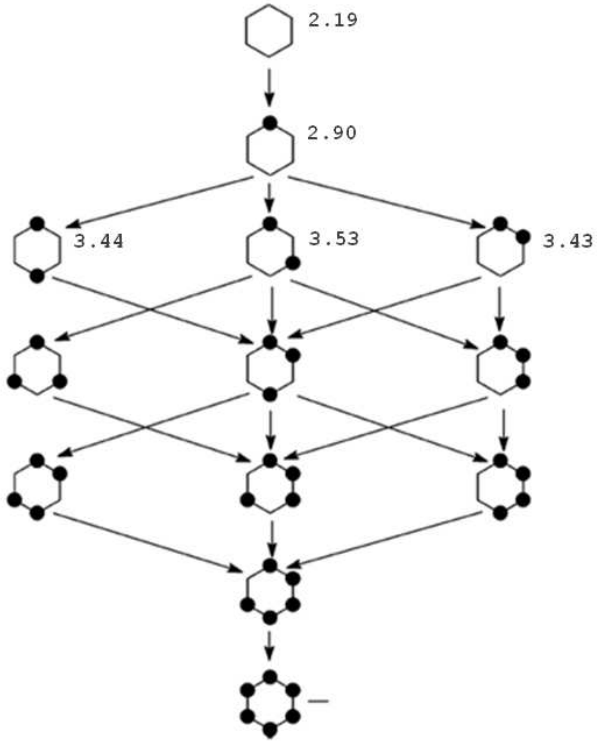



Figure: Extrapolation Example

# Heuristic Extrapolation Algorithms Based on Posets

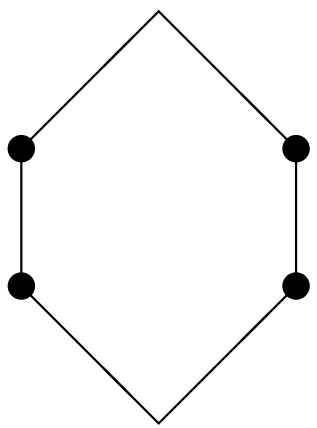
- In many practical situations, there is a natural partial order $x \le y$
- Example: $x \le y$ if a chemical substance $y$ can be obtained from a substance $x$ by a reaction of certain type
- Prediction on partially ordered sets (posets) according to Gian-Carlo Rota (MIT):
  - in general, we have $v(a) = \sum_{b:b \le a} V(b)$ for some $V(b)$
  - in practice, some values $V(b)$ are negligible, so we set $V(b) = 0$ for these $b$
- Resulting heuristic algorithm for estimating $v(a)$ from $v(a_1), \ldots, v(a_n)$:
  - use Least Squares method to find values $V(b)$ from the equations $v(a_i) \approx \sum_{b:b \le a_i} V(b)$, $1 \le i \le n$
  - use $\sum_{b:b \le a} V(b)$ as a predicted value of $v(a)$

# Poset-Based Extrapolation in Organic Chemistry

- General idea: $v(a) = \sum_{b:\, b \le a} V(b)$
- Natural relation $a \le b$: $b$ is obtained by $a$ by substituting some Hs by ligands
- Empirical fact (D. J. Klein et al.): $V(b) \approx 0$ for 3- and more-substituted molecules $b$
- Result: estimate $v(a)$ as $\sum_{b:\, b \le a} V(b)$, where $b$ goes over 0-, 1-, and 2-substituted molecules.
- For the original molecule $b$, we have $v(b) = V(b)$
- For a monosubstituted molecule $b_1$, we have $v(b_1) = V(b) + V(b_1)$, so $V(b_1) = v(b_1) - V(b)$
- For a disubstituted molecule $b_{12}$, $v(b_{12}) = V(b) + V(b_1) + V(b_2) + V(b_{12})$, so $V(b_{12}) = v(b_{12}) - V(b) - V(b_1) - V(b_2)$

# The Use of Symmetry

- Natural symmetries simplify the problem
- Example: all monosubstituted molecules are equivalent: $V(b_1) = V(b_2) = \ldots$
- Conclusion: $v(b_{12}) = V(b) + V(b_1) + V(b_2) + V(b_{12})$ becomes $v(b_{12}) = V(b) + 2V(b_1) + V(b_{12})$
- General case: $v(a) = \sum_{b:\, b \leq a} n(b) \cdot V(b)$. Example:



$$v(a) = V(b_0) + 4V(b_1) + 2V(b_{12}) + 2V(b_{13}) + 2V(b_{14}).$$

# Extrapolation Example: Toxicity

- Perform measurements for $v(a_1), \ldots, v(a_m)$.

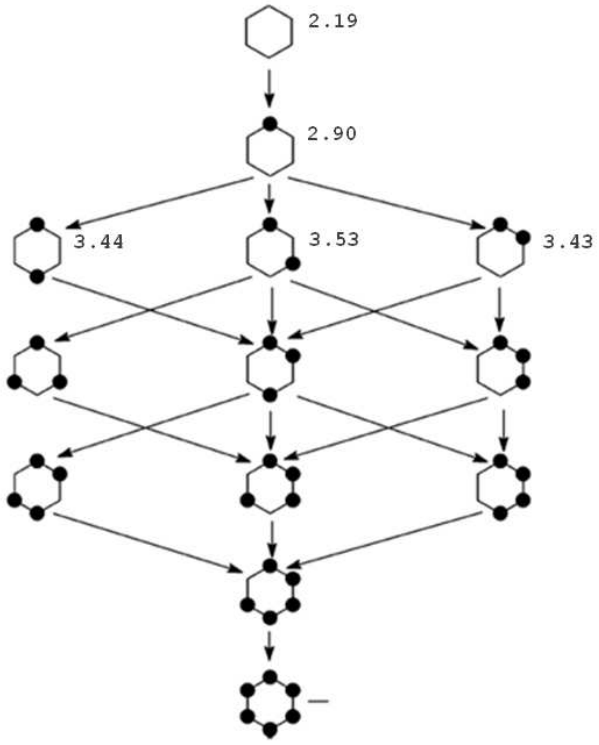



Figure: Extrapolation Example

# Extrapolation Example (cont-d)

- Use least squares to find values $V(b)$

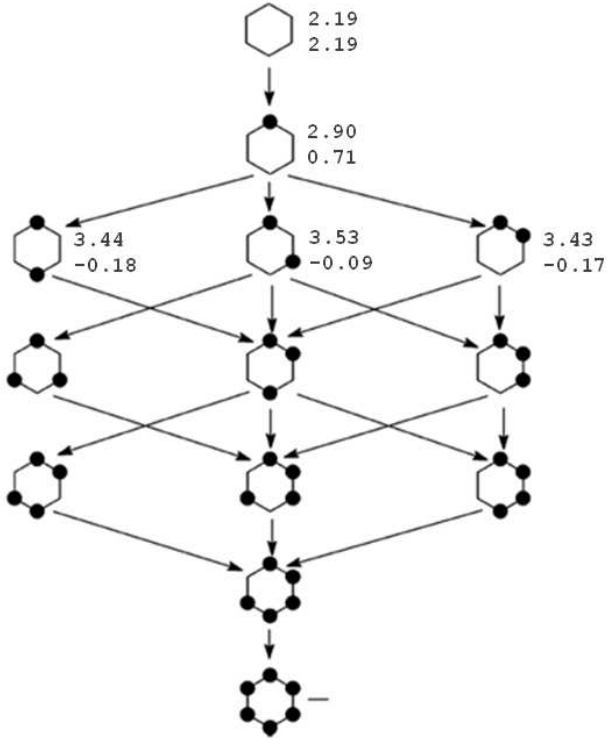



Figure: Extrapolation Example (cont-d)

# Extrapolation Example (cont-d)

- Extrapolate using the formula $v(a) = \sum_{b:b \leq a} V(b)$

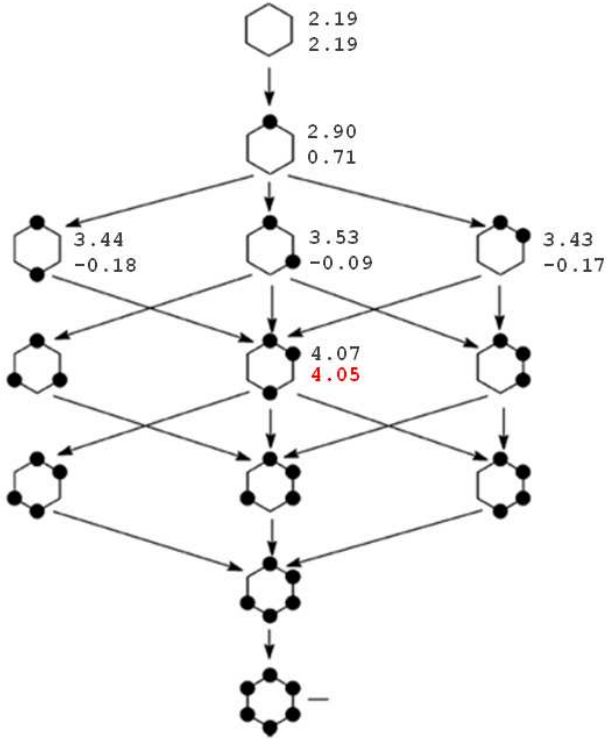



Figure: Poset Extrapolation

# Poset-Based Extrapolation is Empirically Successful

- Reminder: we extrapolate by using a heuristic formula

$$v(a) = \sum_{b:\, b \le a} n(b) \cdot V(b).$$

- Reminder: $n(b)$ is the number of $b$-type substances from which $a$ can be obtained by substitution.
- The resulting formulas lead to very good quality predictions of different quantities:
  - energy
  - boiling point
  - vapor pressure at a certain temperature
  - etc.

# Limitations of the Poset Approach and Our Work

- Poset-related approaches have relatively few empirically successful applications
- As a result, researchers may not have high confidence in these results
- To increase confidence, it is desirable to justify this heuristic approach
- We justify poset approach by using a technique with a much longer history of successful applications: Taylor series
- Specifically, we show that poset-based approach is equivalent to the approach based on Taylor series

# Taylor Series: A Standard Tool for Solving (Continuous) Problems in Science and Engineering

- In physical and engineering applications, most parameters $x_1, \ldots, x_n$ (coordinates, velocity, etc.) are *continuous*
- The dependence $y = f(x_1, \ldots, x_n)$ is also usually continuous and smooth (differentiable)
- Smooth functions can be usually expanded into Taylor series around some point $\widetilde{x} = (\widetilde{x}_1, \ldots, \widetilde{x}_n)$:

$$f(x_1, \ldots, x_n) = f(\widetilde{x}_1, \ldots, \widetilde{x}_n) + \sum_{i=1}^{n} \frac{\partial f}{\partial x_i} \cdot \Delta x_i +$$

$$\frac{1}{2} \cdot \sum_{i=1}^{n} \sum_{i'=1}^{n} \frac{\partial^2 f}{\partial x_i \partial x_{i'}} \cdot \Delta x_i \cdot \Delta x_{i'} + \ldots,$$

where $\Delta x_i \stackrel{\text{def}}{=} x_i - \widetilde{x}_i$

# Taylor Series (cont-d)

- In practice, we can ignore higher-order terms
- Example: if linear approximation is not accurate enough, we can use quadratic approximation
- If we do not know the exact expression for $f(x_1, \ldots, x_n)$, we do not know the values of its derivatives $\dfrac{\partial f}{\partial x_i}$ and $\dfrac{\partial^2 f}{\partial x_i \partial x_j}$
- All we know is that we approximate a general function by a general linear or quadratic formula

$$f(x_1, \ldots, x_n) \approx c_0 + \sum_{i=1}^{n} c_i \cdot \Delta x_i + \sum_{i=1}^{n} \sum_{j=1}^{n} c_{ii'} \cdot \Delta x_i \cdot \Delta x_{i'}$$

- The values of the coefficients $c_0$, $c_i$, and (if needed) $c_{ii'}$ can then be determined experimentally

# From Continuous to Discrete Taylor Series

- For each possible ligand location $i$, let $x_{i1}, \ldots, x_{ij}, \ldots, x_{iN}$ be parameters characterizing this location.
- Examples:
  - the density at a certain point,
  - the distance to a certain atom,
  - the angle between this atom and the given direction,
  - the angle describing the direction of the spin, etc.
- We are interested in the situations in which, at each location, there is either a ligand, or there is no ligand.
- For each location $i$ and for each parameter $x_{ij}$:
  - let $x_{ij}^-$ denote the value of the $j$-th parameter in the situation with no ligand at the location $i$, and
  - let $x_{ij}^+$ denote the value of the $j$-th parameter in the situation with a ligand at the location $i$.
- Default: when there is no ligand, i.e., $x_{ij} = x_{ij}^-$

# From Continuous to Discrete Taylor Series (cont-d)

- General case: $y = f(x_{11}, \ldots, x_{1N}, \ldots, x_{n1}, \ldots, x_{nN})$, so

$$y = y_0 + \sum_{i=1}^{n}\sum_{j=1}^{N} y_{ij} \cdot \Delta x_{ij} + \sum_{i=1}^{n}\sum_{j=1}^{N}\sum_{i'=1}^{n}\sum_{j'=1}^{N} y_{ij,i'j'} \cdot \Delta x_{ij} \cdot \Delta x_{i'j'},$$

  where $\Delta x_{ij} \stackrel{\text{def}}{=} x_{ij} - x_{ij}^{-}$
- Let $\varepsilon_i$ describe the presence of the ligand at the location $i$:
  - when there is no ligand, $\varepsilon_i = 0$, and
  - when there is a ligand, $\varepsilon_i = 1$.
- Reminder: $x_{ij} = x_{ij}^{-}$ if no ligand, $x_{ij} = x_{ij}^{+}$ if ligand
- General formula: $\Delta x_{ij} = \varepsilon_i \cdot \Delta_{ij}$, where $\Delta_{ij} \stackrel{\text{def}}{=} x_{ij}^{+} - x_{ij}^{-}$
- Substituting $\Delta x_{ij} = \varepsilon_i \cdot \Delta_{ij}$ into the formula for $y$:

$$y = a_0 + \sum_{i=1}^{n} a_i \cdot \varepsilon_i + \sum_{i=1}^{n}\sum_{i'=1}^{n} a_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}, \text{ where } a_i = \sum_{j=1}^{N} y_{ij} \cdot \Delta_{ij}$$

# Discrete Taylor Expansions can be Further Simplified

- First, for each $\varepsilon_i \in \{0, 1\}$, we have $\varepsilon_i^2 = \varepsilon_i$
- Thus, the term $a_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}$ corresponding to $i = i'$ is equal to $a_{ii} \cdot \varepsilon_i$, hence

$$y = c_0 + \sum_{i=1}^{n} c_i \cdot \varepsilon_i + \sum_{i \neq i'} c_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'},$$

  where $c_0 = a_0$, $c_{ii'} = a_{ii'}$, and $c_i = a_i + a_{ii}$
- Second, we combine terms proportional to $\varepsilon_i \cdot \varepsilon_{i'}$ and to $\varepsilon_{i'} \cdot \varepsilon_i$
- As a result, we obtain the following simplified expression

$$y = v_0 + \sum_{i=1}^{n} v_i \cdot \varepsilon_i + \sum_{i < i'} v_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'},$$

  where $v_0 = c_0$ and $v_{ii'} = c_{ii'} + c_{i'i}$

# Example

$$y = a_0 + \sum_{i=1}^{n} a_i \cdot \varepsilon_i + \sum_{i<i'} a_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}$$


$$y = a_0$$


$$y = a_0 + a_1$$


$$y = a_0 + (a_1 + a_2) + a_{12}$$


$$y = a_0 + (a_1 + a_2 + a_4) + (a_{12} + a_{24} + a_{14})$$

# Comparing Poset and Discrete Taylor Series Approaches

- Reminder: $\varepsilon_i = 0$ means no ligand, $\varepsilon_i = 1$ means ligand
- Taylor series: $y = v_0 + \sum_{i=1}^{n} v_i \cdot \varepsilon_i + \sum_{i<i'} v_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}$
- Poset approach: $v(a) = \sum_{b:\, b \le a} V(b)$
- Here, $b \le a$ means that $a$ can be obtained from $b$ by adding ligands
- So, if $b = (\varepsilon'_1, \ldots, \varepsilon'_n)$ and $a = (\varepsilon_1, \ldots, \varepsilon_n)$, then $b \le a$ means that for every $i$, we have $\varepsilon'_i \le \varepsilon_i$
- Resulting formula:

$$y = V(a_0) + \sum_{i:\, \varepsilon_i = 1} V(a_i) + \sum_{i<i':\, \varepsilon_i = \varepsilon_{i'} = 1} V(a_{i,i'})$$

# Proof that The Discrete Taylor Series are Indeed Equivalent to the Poset Formula

- Taylor series: $y = v_0 + \sum_{i=1}^{n} v_i \cdot \varepsilon_i + \sum_{i<i'} v_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}$
- Poset: $y = V(a_0) + \sum_{i:\, \varepsilon_i = 1} V(a_i) + \sum_{i<i':\, \varepsilon_i = \varepsilon_{i'} = 1} V(a_{i,i'})$
- Proof that these formulas coincide:

$$\sum_{i:\, \varepsilon_i = 1} V(a_i) = \sum_{i:\, \varepsilon_i = 1} V(a_i) \cdot \varepsilon_i = \sum_{i=1}^{n} V(a_i) \cdot \varepsilon_i$$

$$\sum_{i<i':\, \varepsilon_i = \varepsilon_{i'} = 1} V(a_{i,i'}) = \sum_{i<i':\, \varepsilon_i = \varepsilon_{i'} = 1} V(a_{i,i'}) \cdot \varepsilon_i \cdot \varepsilon_j$$

$$\sum_{i<i':\, \varepsilon_i = \varepsilon_{i'} = 1} V(a_{i,i'}) = \sum_{i<i'} V(a_{i,i'}) \cdot \varepsilon_i \cdot \varepsilon_j$$

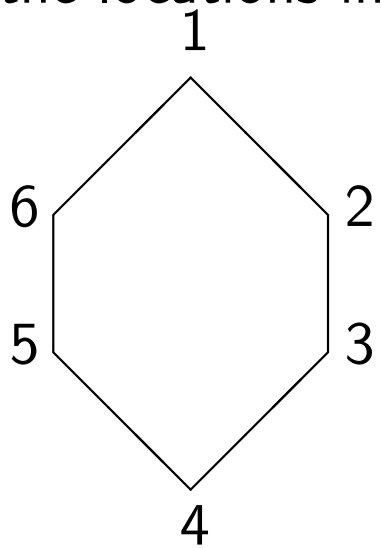
- So, we can take $v_0 = V(a_0)$, $v_i = V(a_i)$, $v_{ii'} = V(a_{i,i'})$

# Important Observation: The Presence of Symmetry Does Not Change the Equivalence

- Reminder: symmetry means that some of the coefficients $v_i$ and $v_{ii'}$ coincide.
- Example: for benzenes and cubanes, symmetry means
  - that $v_1 = v_2 = \ldots = v_i = \ldots$, and
  - that the value $v_{ii'}$ depends only on the distance $d(i, i')$ between the locations $i$ and $i'$
- Notations: $V \stackrel{\text{def}}{=} v_i$, $V_d$ denotes $v_{ii'}$ when $d(i, i') = d$

# Symmetry: Example

- Let us number the locations in a sequential order:



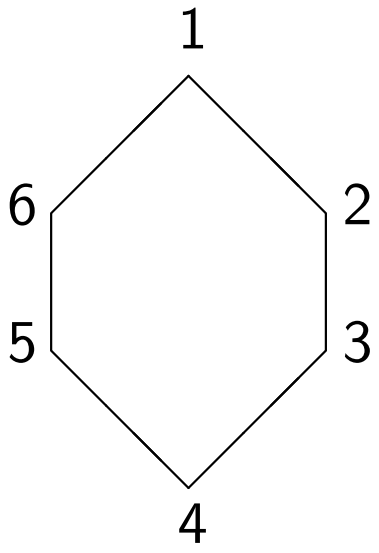

- In these notations, the general quadratic formula takes the form $y = v_0 + V \cdot \left(\sum_{i=1}^{n} \varepsilon_i\right) +$

$$V_1 \cdot (\varepsilon_1 \cdot \varepsilon_2 + \varepsilon_2 \cdot \varepsilon_3 + \varepsilon_3 \cdot \varepsilon_4 + \varepsilon_4 \cdot \varepsilon_5 + \varepsilon_5 \cdot \varepsilon_6 + \varepsilon_6 \cdot \varepsilon_1) +$$

$$V_2 \cdot (\varepsilon_1 \cdot \varepsilon_3 + \varepsilon_2 \cdot \varepsilon_4 + \varepsilon_3 \cdot \varepsilon_5 + \varepsilon_4 \cdot \varepsilon_6 + \varepsilon_5 \cdot \varepsilon_1 + \varepsilon_6 \cdot \varepsilon_2) +$$

$$V_3 \cdot (\varepsilon_1 \cdot \varepsilon_4 + \varepsilon_2 \cdot \varepsilon_5 + \varepsilon_3 \cdot \varepsilon_6)$$

# Symmetry: Example (cont-d)




In other words, we have $y = v_0 + V \cdot N + \sum_{d=1}^{3} V_d \cdot N_d$, where

- $N$ is the total number of ligands, and
- $N_d$ is the total number of pairs $(i, i')$ of ligands with $d(i, i') = d$

# Main Advantage of the Taylor Representation

- Taylor series is a more familiar technique for a wide range of scientists
- Taylor series have a much larger number of successful applications than the poset-related methods;
- Therefore, scientists are more confident in Taylor series techniques.

# Additional Advantage: Taylor Series can Clarify the Equivalence of Different Arrangements

- Consider, in the poset formulation, instead of the original order $b \le a$, the *dual* order $b \le' a$ which is defined as $a \le b$
- $a \le b$ means: we can obtain $b$ from $a$ by *adding* ligands
- The dual order $b \le' a$ means: we can obtain $b$ from $a$ by *removing* ligands
- In the original order $\le$, the minimal element is the original substance $a_0$
- 2nd order poset approximation means: use values $V(b)$ corresponding to substances with 0, 1, and 2 ligands
- In the dual order $\le'$, the minimal element is the substance with the ligands in all the places
- 2nd order poset approximation means: We use values $V(b)$ corresponding to substances with 0, 1, and 2 missing ligands

# Additional Advantage of the Taylor Representation (cont-d)

- Will this new order lead to a different approximation?
  - difficult to immediately answer this question
  - the two orders are different, it may look like the resulting approximations are different too.
- Reformulate this question in terms of the discrete Taylor series
  - $\varepsilon'_i = 0$ (no change) if there is a ligand at the $i$-th location
  - $\varepsilon'_i = 1$ (change) if there is no ligand at the $i$-th location
  - hence $\varepsilon'_i = 1 - \varepsilon_i$ and $\varepsilon_i = 1 - \varepsilon'_i$
  - so, expressions quadratic in $\varepsilon_i$ are also quadratic in $\varepsilon'_i$ and vice versa
  - conclusion: the resulting approximation is exactly the same for the new order

# Additional Advantage: A Detailed Description

- Reminder: $y = v_0 + \sum_{i=1}^{n} v_i \cdot \varepsilon_i + \sum_{i<i'} v_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'}$
- We substitute $\varepsilon_i = 1 - \varepsilon'_i$ into this formula
- We get general quadratic formula

$$y = v_0 + \sum_{i=1}^{n} v_i \cdot (1 - \varepsilon'_i) + \sum_{i<i'} v_{ii'} \cdot (1 - \varepsilon_i) \cdot (1 - \varepsilon_{i'})$$

- Opening parentheses, we conclude that

$$y = v'_0 + \sum_{i=1}^{n} v'_i \cdot \varepsilon'_i + \sum_{i<i'} v'_{ii'} \cdot \varepsilon'_i \cdot \varepsilon'_{i'}, \text{ where}$$

$$v'_0 = v_0 + \sum_{i=1}^{n} v_i + \sum_{i<i'} v_{ii'}, \quad v'_i = -v_i - \sum_{i' : i<i'} v_{ii'} - \sum_{i' : i'<i} v_{i'i},$$

and $v'_{ii'} = v_{ii'}$

# Additional Advantage: A Detailed Description (cont-d)

- Similarly, we can start with

$$y = v_0' + \sum_{i=1}^{n} v_i' \cdot \varepsilon_i' + \sum_{i<i'} v_{ii'}' \cdot \varepsilon_i' \cdot \varepsilon_{i'}'$$

- We substitute $\varepsilon_i' = 1 - \varepsilon_i$
- We get

$$y = v_0 + \sum_{i=1}^{n} v_i \cdot \varepsilon_i + \sum_{i<i'} v_{ii'} \cdot \varepsilon_i \cdot \varepsilon_{i'},$$

where

$$v_0 = v_0' + \sum_{i=1}^{n} v_i' + \sum_{i<i'} v_{ii'}', \quad v_i = -v_i' - \sum_{i' : i<i'} v_{ii'}' - \sum_{i' : i'<i} v_{i'i}',$$

and $v_{ii'} = v_{ii'}'$.

# Example

- Reminder: for benzene, $y = v_0 + V \cdot N + \sum_{d=1}^{3} V_d \cdot N_d$, where
  - $N$ is the total number of ligands, and
  - $N_d$ is the total number of pairs $(i, i')$ of ligands with $d(i, i') = d$
- Here,

$$v_0' = v_0 + 6V + 6V_1 + 6V_2 + 3V_3$$
$$V' = -V - 2V_1 - 2V_2 - V_3$$
$$V_1' = V_1, \quad V_2' = V_2, \quad V_3' = V_3$$

- Correspondingly,

$$v_0 = v_0' + 6V' + 6V_1' + 6V_2' + 3V_3'$$
$$V = -V' - 2V_1' - 2V_2' - V_3'$$
$$V_1 = V_1', \quad V_2 = V_2', \quad V_3 = V_3'$$

# Conclusion

- Case study: predicting properties of new chemical substances
- Several chemical substances can be obtained by adding ligands to a "template" molecule like benzene $C_6H_6$ or cubane $C_8H_8$
- There is a large number of such substances, and it is difficult to synthesize all of them
- It is desirable to synthesize only a few of them and to extrapolate
- Such an extrapolation has been obtained by using Rota's ideas related to partially ordered sets
- We show that the same extrapolation follows from a more familiar mathematical technique: Taylor series
- This makes the chemical prediction results more reliable

# Acknowledgments


- We wish to extend our gratitude to Dr. Larry Ellzey for his encouragment
- Thanks to Dr. Guillermo Restrepo for his collaboration in the Chemistry case study