

the delocalization of electron density over numerous conjugated things.

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0. “Stand firm in your refusal to remain conscious during algebra. In real life, I assure you, there is no such thing as algebra.” – *Fran Lebowitz*

Michaelis-Menton kinetics is useful in mechanistic analyses of catalytic and enzymatic systems. A typical catalytic equation is shown:



Derive a Michaelis-Menton equation by using the Steady State Approximation and the estimation that the total concentration of catalyst is equal to the concentration of bound and unbound enzyme (your answer should include the terms k_1 , k_2 , and k_{-1}).

Biologists and biochemists tend to use a different form of Michaelis-Menton, as shown:

$$V = V_{max} \left(\frac{[S]}{[S] + K_m} \right)$$

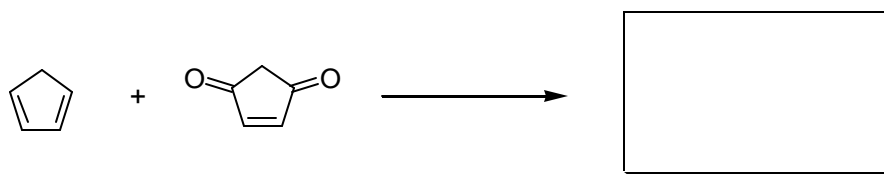
Which terms in your MM equation correspond to V , V_{max} , and K_m ?

Interesting interpretations of the Michaelis-Menton equation: V is the rate of product formation and K_m is the substrate concentration at which $V = V_{max}$, and can be used to measure the dissociation of ES (a.k.a. K_d). On the other hand, V_{max} is the maximum rate when the enzyme is saturated with substrate. The equation $V_{max} = k_{cat} * [E_{tot}]$ can be useful when the amount of enzyme is not precisely known.

1. "It is logically impossible to demonstrate that something does not exist, as the scholastic philosophers know well." – *Luis Salvatella et. al.*

Secondary orbital interactions have traditionally been used to explain the *endo* selectivity of a Diels-Alder reaction, however, recently there has been some controversy over the existence of these interactions. Salvatella, especially, has been adamant about the non-existence of these interactions in the cycloadditions and uses other factors (e.g. solvent effects, sterics, hydrogen-bonding, and electrostatic forces) to explain the *endo* selectivity.

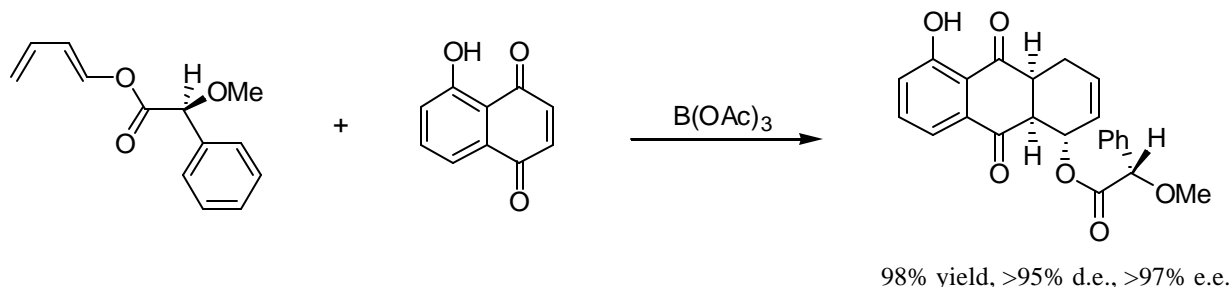
a. The following reaction proceeds with high *endo* selectivity. Construct a Woodward-Hoffmann correlation diagram for this cycloaddition and predict the product. Use a secondary orbital interaction argument to explain the selectivity.



b. Other than secondary orbital interactions, what explanations could one invoke to explain the *endo* selectivity?

2. "The [product], isolated in 98% yield, showed a single set of absorptions in the 270-MHz NMR spectrum suggestive of complete asymmetric induction." – *Barry M. Trost et. al.*

Based on a p-stacking model, Trost had reported an asymmetric Diels-Alder reaction through the use of a chiral auxiliary.



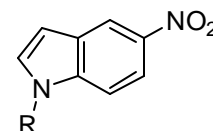
Trost and Houk later collaborated to further investigate the question of p-stacking in the selectivity of this reaction. Their calculations predicted that conformer of the diene having a p-stacking arrangement lies at least 6.8 kcal/mol higher in energy than the lowest energy conformer, in which the dienyl carbons, the carbonyl group, and the C_a-O bond are approximately co-planar. They thus concluded that the stereoselectivity could be understood in terms of ground state conformational preferences, without invoking the use of p-stacking. Draw a transition state of this reaction.

3. “In the transmission of human culture, people always attempt to replicate, to pass on to the next generation the skills and values of the parents, but the attempt always fails because cultural transmission is geared to learning, not DNA.” – *Gregory Bateson*

a. Below is a list of calculated Hydrogen Bond strengths for base pairs in a variety of conditions. Explain the trend. What do hydrogen bonds do for the structure of DNA?

Solvent:			ΔH (kcal/mol)
Gas Phase	G+C	\rightleftharpoons	G:C -21.0
Gas Phase	A+T	\rightleftharpoons	A:T -14.5
CHCl ₃	A+U	\rightleftharpoons	A:U -6.2
DMSO	G+C	\rightleftharpoons	G:C -5.8
Water	A+T	\rightleftharpoons	A:T negligible
Water	G+C	\rightleftharpoons	G:C negligible

b. 5-nitroindolyl-2'-deoxyriboside triphosphate (dNITP) has been used as a DNA base analogue to investigate the factors required for DNA replication and other processes. In investigating DNA replication with bacteriophage T4 DNA polymerase, Berdis discovered that the insertion rate of dNITP opposite abasic sites was significantly faster than a similar insertion of dATP (or any other natural base, for that matter).



dNTP	Surface area (? ²)	K _{obs} (10 x K _d concentration) (s ⁻¹)
dATP	255.7	0.13 ± 0.01
5-NITP	278.7	>0.3
dGTP	264.7	0.011 ± 0.002
N ² -Me-dGTP	283.2	0.011 ± 0.002
dCTP	235.8	0.0043 ± 0.0004

Polymerase catalyzed incorporation of nucleoside triphosphate opposite an abasic site.

Furthermore, it was found that there was a high efficiency for insertion of dNITP opposite A or T, but a poor efficiency for insertion opposite C or G. What's going on between the polymerase and this base analogue to afford such funky results?

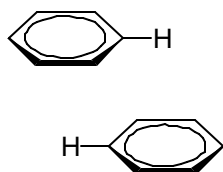
4. "This work was supported by the Petroleum Research Fund." – Marcey L. Waters

p-stacking can help determine tertiary and quaternary structure in protein folding. Take a look at the following study on p-stacking and answer the following questions.

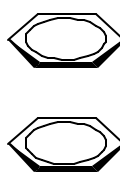
a. There are three main geometries of aromatic interactions, as illustrated below. Between two benzenes, edge-face and offset-stacked interactions are generally favorable; however, face-to-face stacked is not. On the other hand, face-to-face stacked between benzene and hexafluorobenzene is more favorable than edge-face or offset stacked benzene/benzene interactions. Explain.



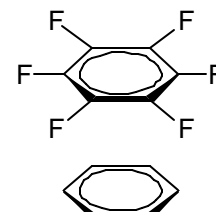
edge-face:
favorable



offset-stacked:
favorable



face-to-face stacked:
unfavorable

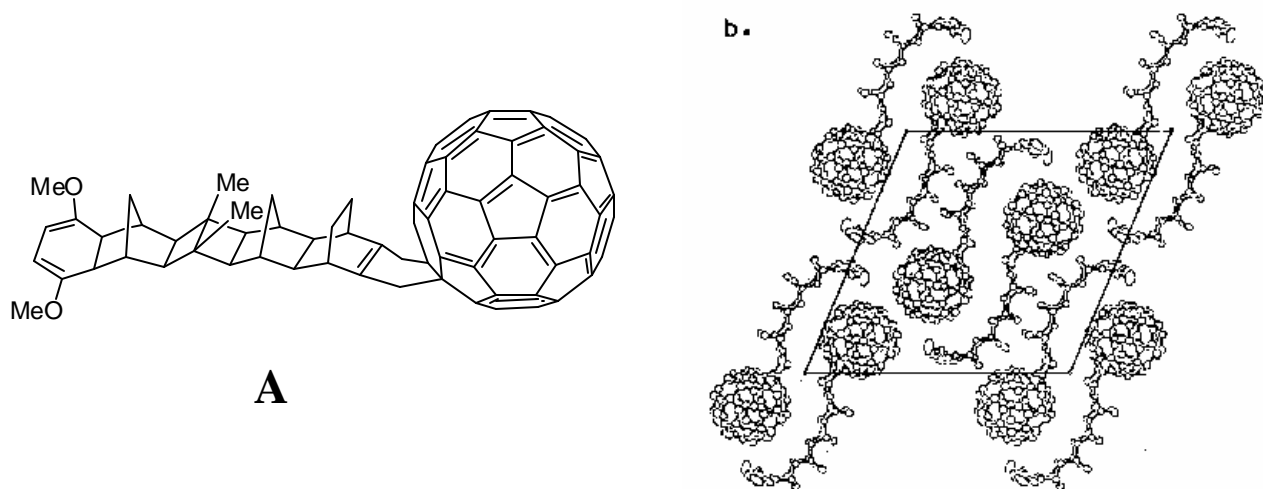


face-to-face stacked:
favorable

b. The incorporation of phenylalanine-phenylalanine (F-F) interactions, as well as pentafluorophenylalanine-phenylalanine (F- f_5 F) interactions, can stabilize α -helices of proteins, however the strength of the F-F interaction is largely dependent on the sterics resulting from the other side chains on the peptide. Interestingly, F-F and F- f_5 F interaction energies are the same at internal positions; however, at the C-terminus, the F- f_5 F interaction energy is greater than F-F interaction. Explain this result.

5. "Everything you've learned in school as "obvious" becomes less and less obvious as you begin to study the universe. For example, there are no solids in the universe. There's not even a suggestion of a solid. There are no absolute continuums. There are no surfaces. There are no straight lines." – *R. Buckminster Fuller*

In their investigations into Buckminsterfullerenes (a.k.a. C_{60} or Bucky Balls), Paddon-Row and Rubin synthesized "ball-and-chain" systems that appended rigid tethers onto Bucky balls. After the synthesis of **A**, they obtained a crystal structure in which the molecules are in extended form, with the adducts are paired up (figure **b**). This form of packing is interesting as calculations predict the folded structure to be more stable than the extended structure. If calculations are believable, then the best explanation for the extended forms in a crystal packing structure can be attributed to a combination of crystal-packing forces, intermolecular electrostatic interactions, and π -stacking interactions between the C_{60} and dimethoxybenzene groups.



Follow their synthesis of **A**:

