# Hot Topics in Contemporary Crystallography

Šibenik, Croatia, May 10-15, 2014

## The whole is more than the sum of its parts

Alternatively:
"The whole is greater than the sum of its parts"
attributed to Aristotle

το σύνολο είναι μεγαλύτερο από το άθροισμα των μερών του
to sýnolo eínai megalýtero apó to áthroisma tο̲n merό̲n tou

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# Introduction

- Goal #1 of the workshop:

  ***Promotion of excellence and innovation in crystallography***

- List of speakers addresses two aspects of this goal:

  1) ***technical***: how to do the best possible experiment with state of the art instrumentation and software

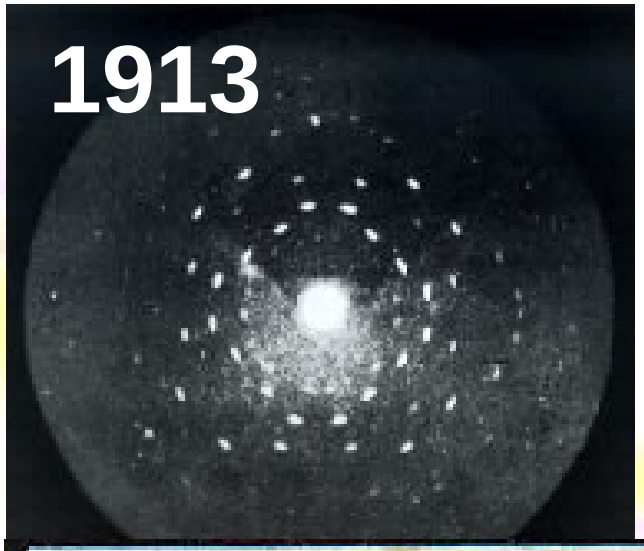
  2) ***biological, chemical and physical questions*** that can be addressed with state of the art techniques.

- By the way:

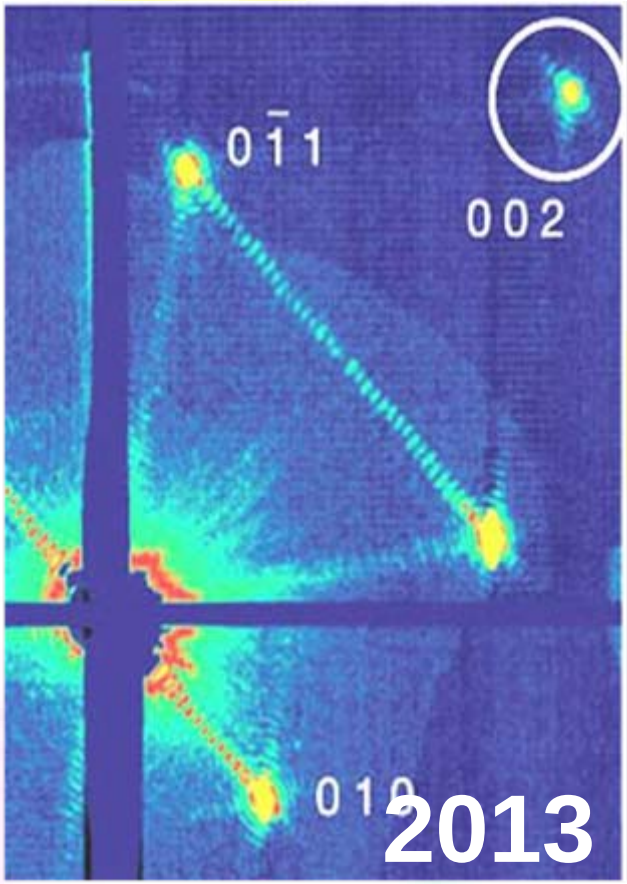
  crystallography = crystal structure determination?

2

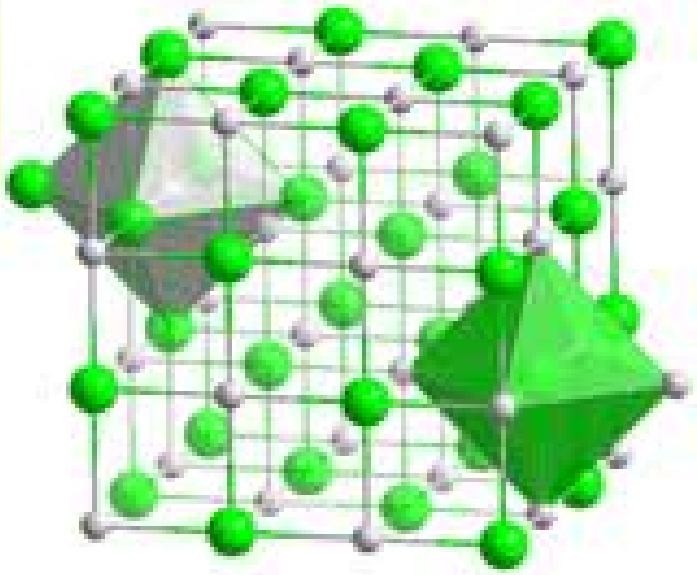
# 100 Years of X-Ray Crystallography

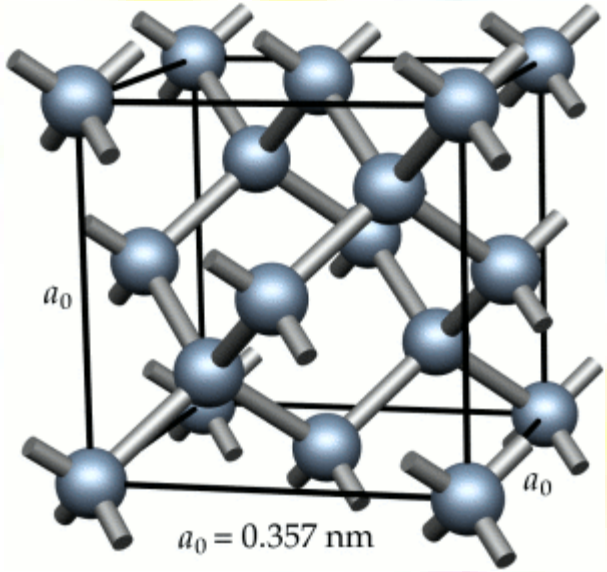






# First contributions to chemistry by father and son Bragg, 1913






Rock salt does NOT consists of NaCl molecules, but of octahedrally coordinated Na and Cl ions

In diamond carbon atoms are surrounded by four other carbon atoms in a tetrahedral arrangement, d(C-C) = 1.52 Å

# Some more History

Some Nobel prizes in the 21st century

- 2003: Peter Agre: "for the discovery of water channels"
  Roderick MacKinnon: "for structural and mechanistic studies of ion channels"
- 2006: Roger D. Kornberg "for his studies of the molecular basis of eukaryotic transcription"
- 2007: Gerhard Ertl "for his studies of chemical processes on solid surfaces"
- 2009: Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath“ for studies of the structure and function of the ribosome"
- 2011: Dan Shechtman "for the discovery of quasicrystals"
- 2012: Robert J. Lefkowitz and Brian K. Kobilka
  “for studies of G-protein coupled receptors"

# Conclusion

- The scientific community has awarded prizes to work that included crystallographic studies, but – more importantly – answered relevant questions from the molecular sciences. Exception: Quasicrystals.

- The following lectures: contributions of crystallography to physical chemistry. Exception: Disorder and diffuse scattering

- Lectures by Prof. Stalke discuss electron densities in crystals in relation to chemical bonding

- Lecture 1 on ’Structure-structure and structure-energy correlations’ addresses the paradox of obtaining dynamic information from static structures.

- Lecture 2 on ’Atomic Displacement Parameters (ADP), crystal dynamics, thermodynamics and disorder’ discusses a potpourri of things, e.g. the structure of benzene, specific heat and pitfalls in interpreting ADPs.

- Lecture 3 ’Beyond Bragg diffraction, disorder and diffuse scattering’ looks at the vast spaces between the Bragg reflections.

# What I do and do not plan to do

- There will be ample time for each lecture, 1.5 hrs
- and no formal hands-on exercises
- Instead let me tell you some case studies illustrating my past endeavors for excellence and innovation, some successful, others not
- However, let‘s try not to have this as a monolog of formal lectures, but  more as conversations among all of us

# What I hope for

- If there are concepts popping up that you are not very familiar with, …
- **Interrupt and ASK! ASK! ASK!**
- Hopefully these conversations will provide you with stimulation and help for building and shaping your own carriers.

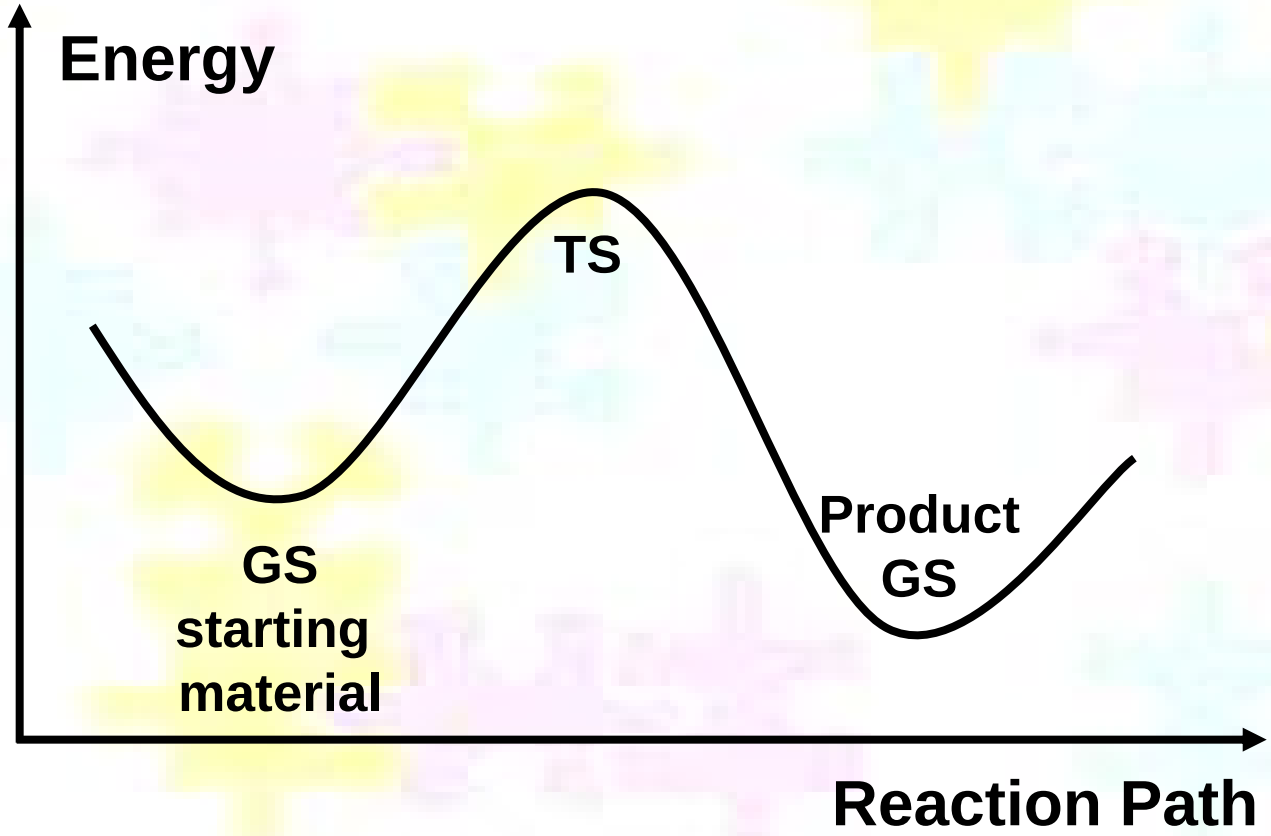
# Dynamic information from static structures?

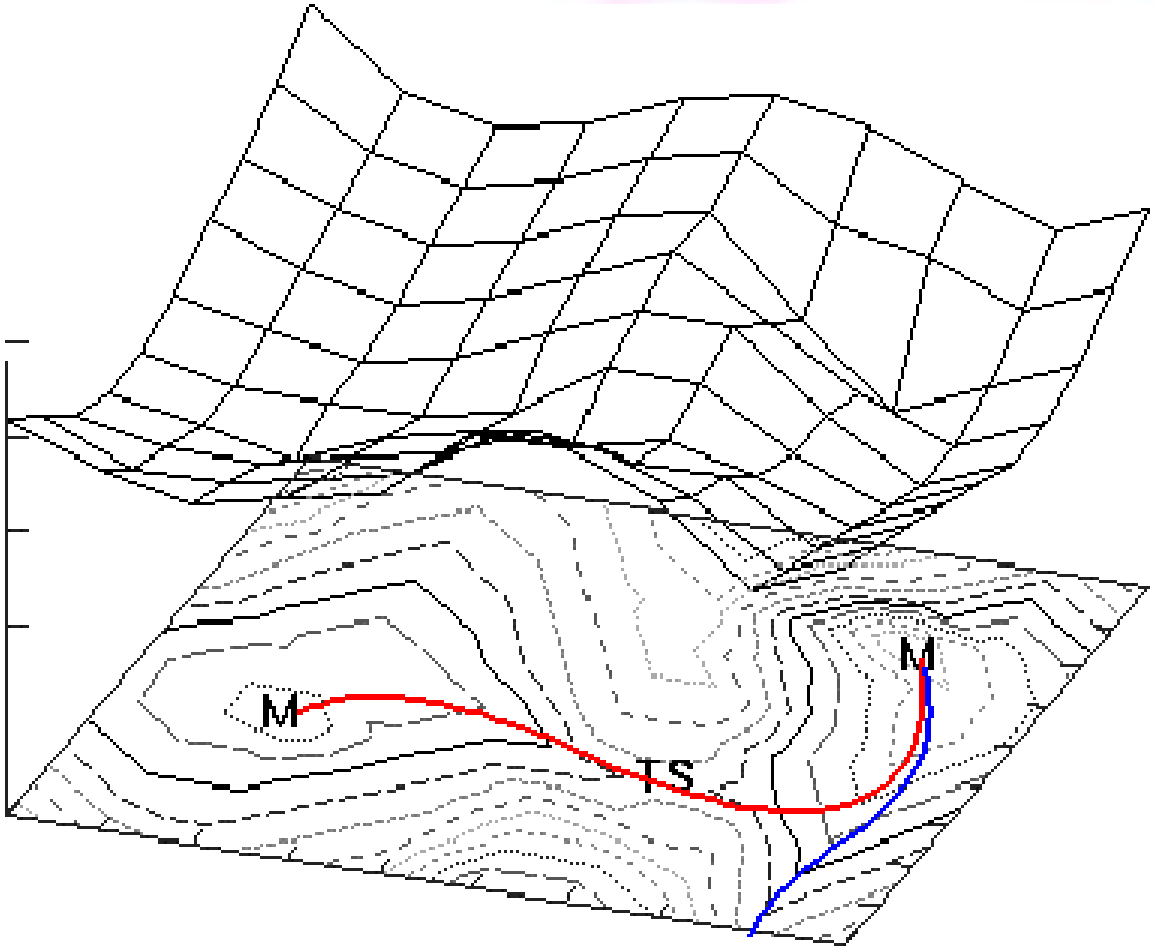
or

**Structure-Structure Correlations**
and
**Structure-Energy Correlations**

H.B. Bürgi, Faraday Discuss., **122** (2002) 41–63 'What we can learn about fast chemical processes from slow diffraction experiments'

# Textbook representation of a chemical reaction

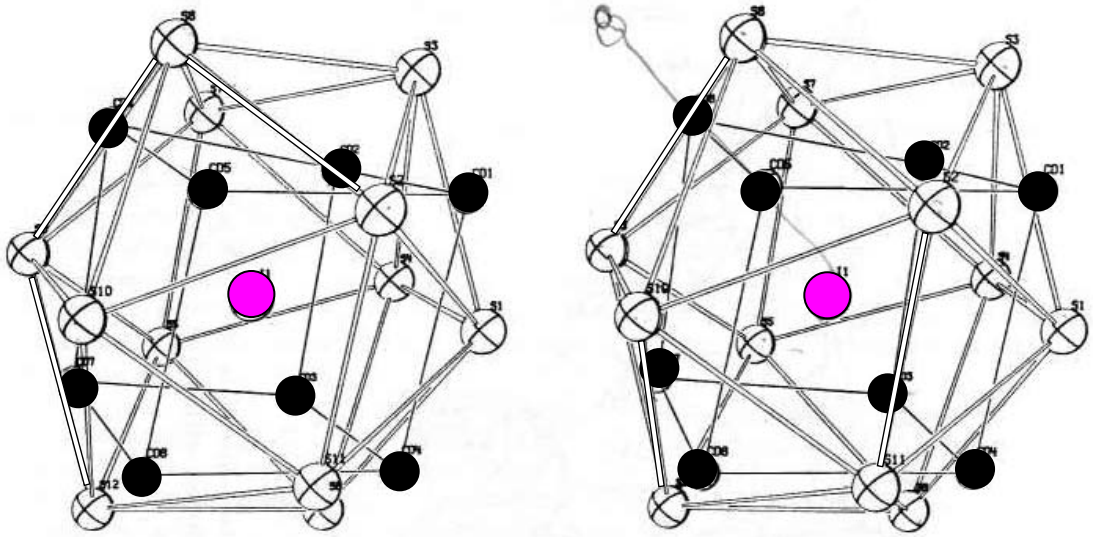





# More realistically …

# Question: how can one determine reaction path from crystal structures?

## My answer: do a few service structures



(CD2 L3 I) 4 (CD2 L3 I) 4

Fig. 1. *Stereoscopic drawing of the polynuclear species* $(ICd_8L_{12})^{3+} \cdot 5\,I^- \cdot H_2O$

275. Stereochemistry of Polynuclear Cadmium(II)thioglycolates: Crystal Structure of $[ICd_8(SCH_2CH_2OH)_{12}]^{3+} \cdot 3\,I^- \cdot H_2O$

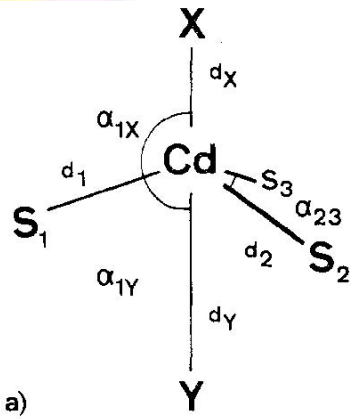
Hans Beat Bürgi, Hermann Gehrer, Peter Strickler and Fritz Karl Winkler

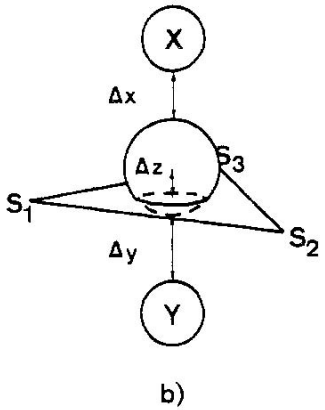
HELVETICA CHIMICA ACTA
Vol. 59, Fasc. 7, p. 2558–2565 (1976)

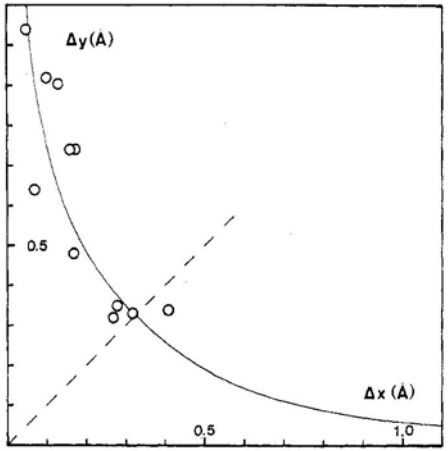
# Chemical Reaction Coordinates from Crystal Structure Data. I

H. B. BURGI

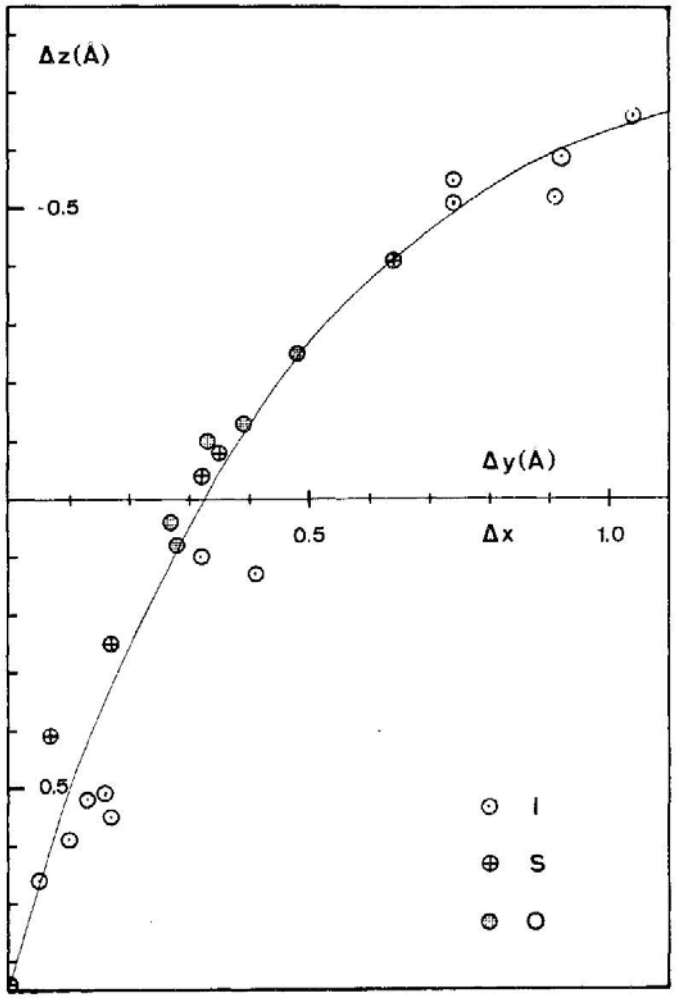
*Inorganic Chemistry, Vol. 12, No. 10, 1973* 2321

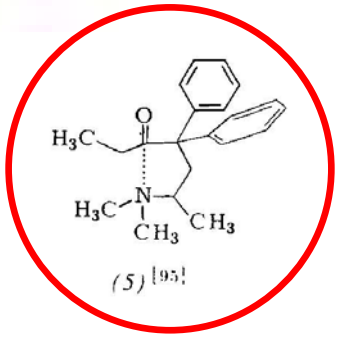



- X, Y = I, S, O
- $\Delta x = d_X - r_{Cd} - r_X$
- $\Delta y = d_Y - r_{Cd} - r_Y$



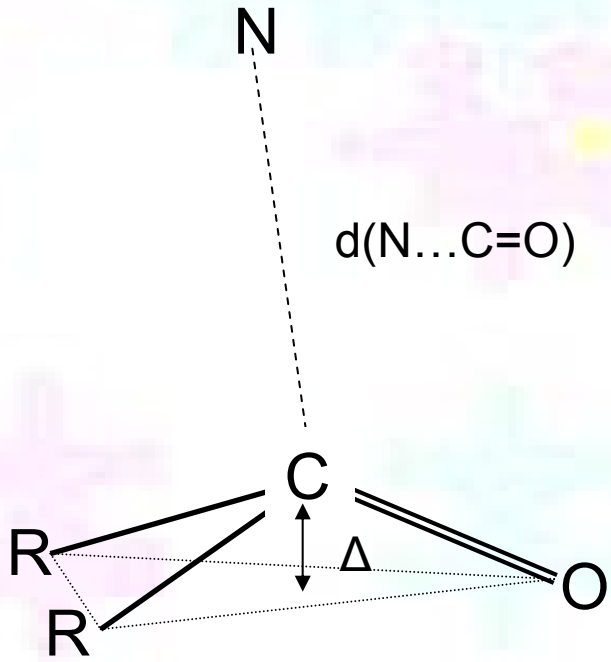



Prof. Eli Shefter

# Methadone

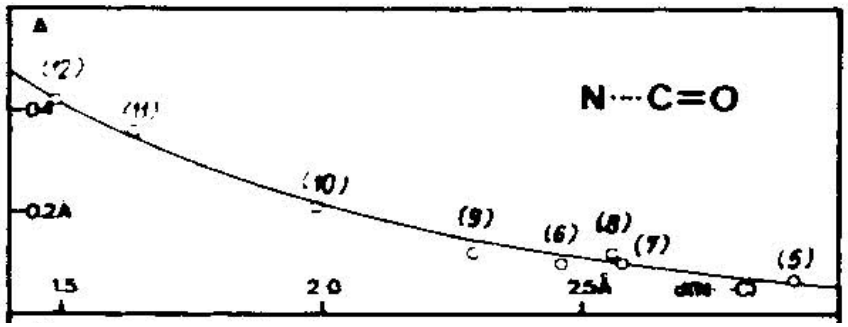
d(N…C=O) = 2.91 Å

Δ = 0.064 Å

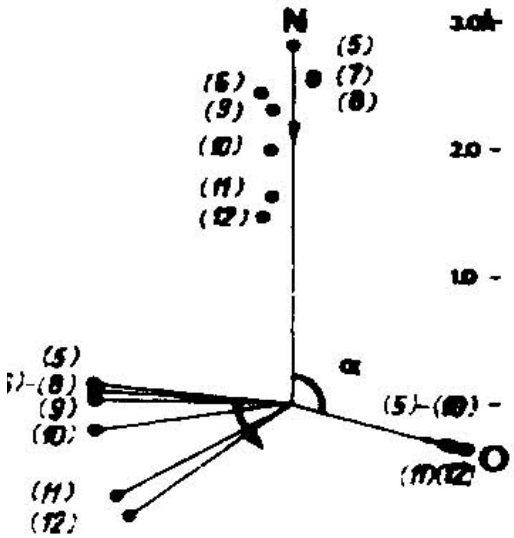


# Geometrical Reaction Coordinates. II+III Nucleophilic Addition to a Carbonyl Group

Δ

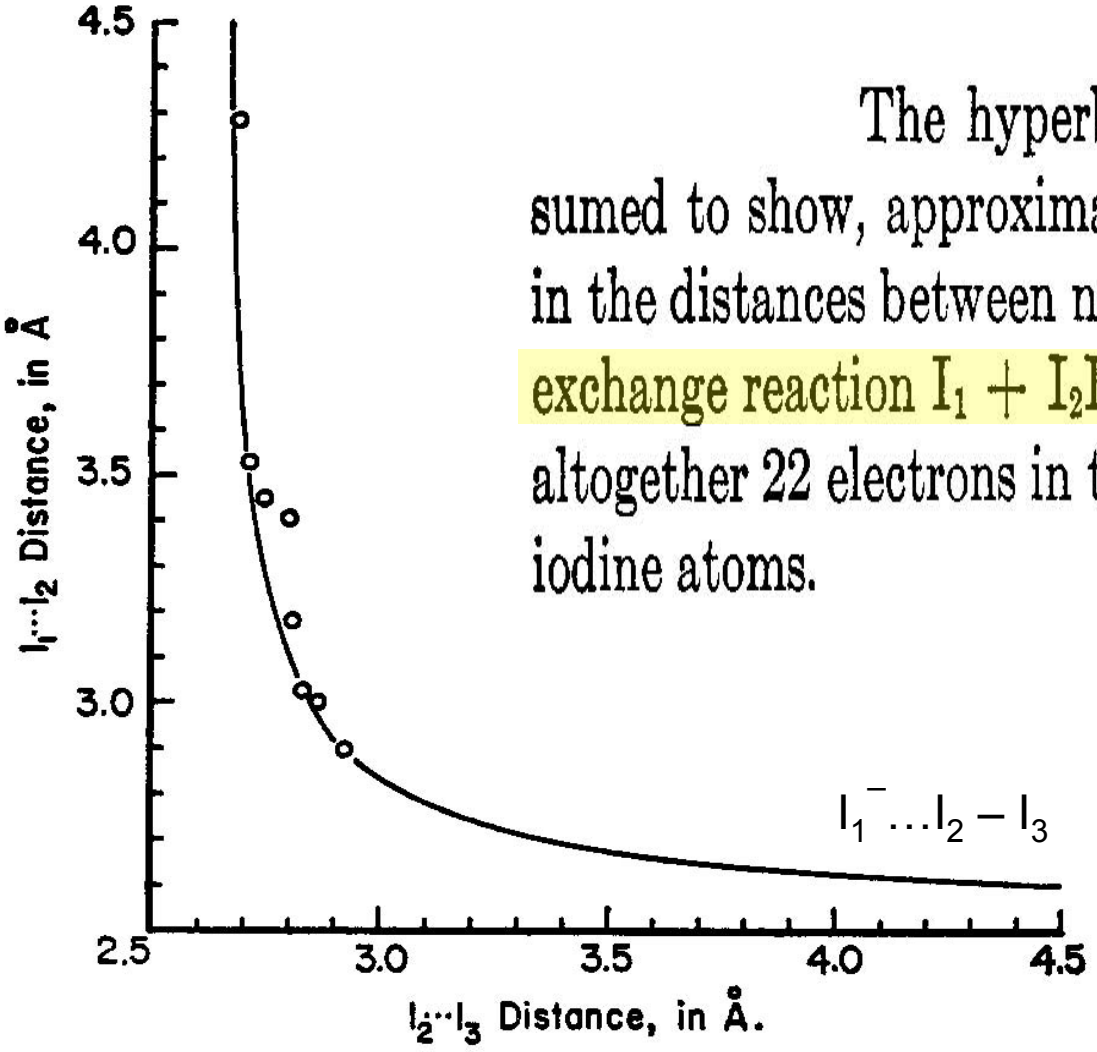



d(N…C=O)




H.B. Bürgi, J.D. Dunitz, Eli Shefter, JACS **95** (1973) 5065

# Putting Things into Context

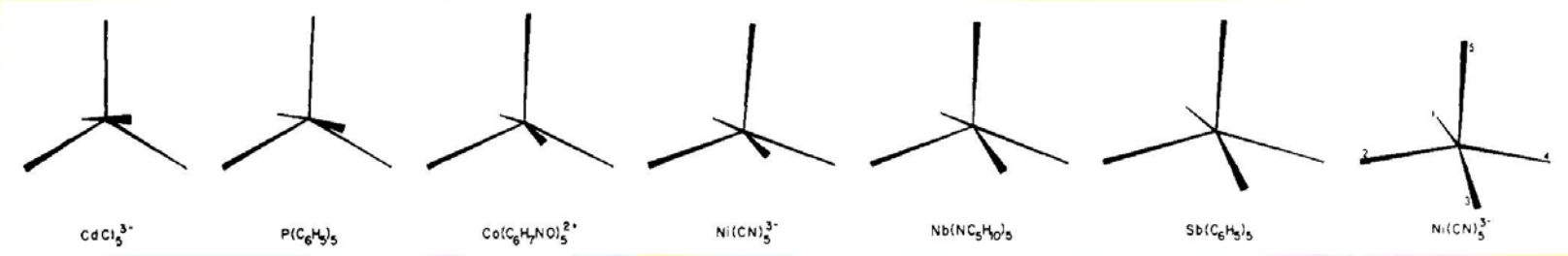



The hyperbolic-like curve may be presumed to show, approximately, the changes that occur in the distances between nearest neighbors in the linear exchange reaction $I_1 + I_2I_3 = I_1I_2 + I_3$ when there are altogether 22 electrons in the valence shells of the three iodine atoms.

H.A. Bent, Structural Chemistry of Donor-Acceptor interactions, Chem. Rev. **68** (1968) 587-648 (534 references)

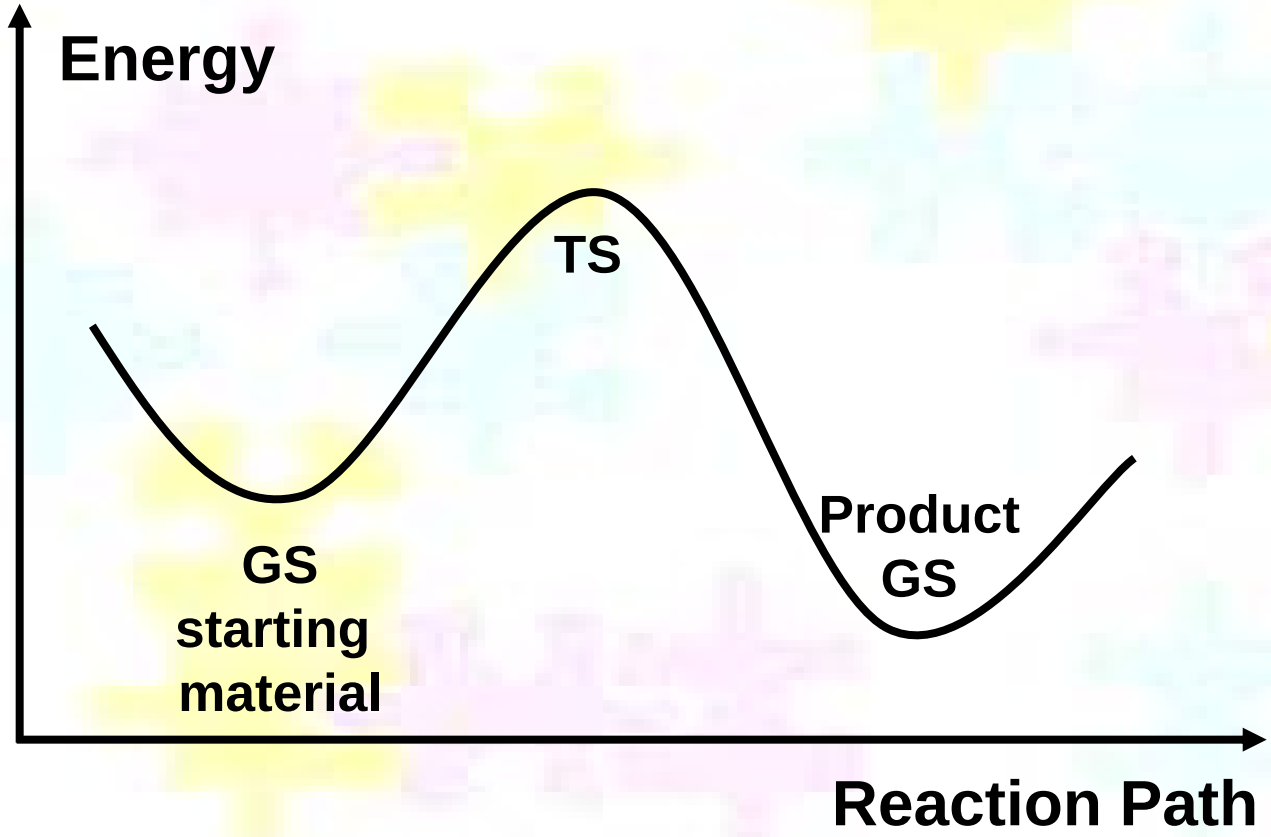
# … More Context

The Berry pathway

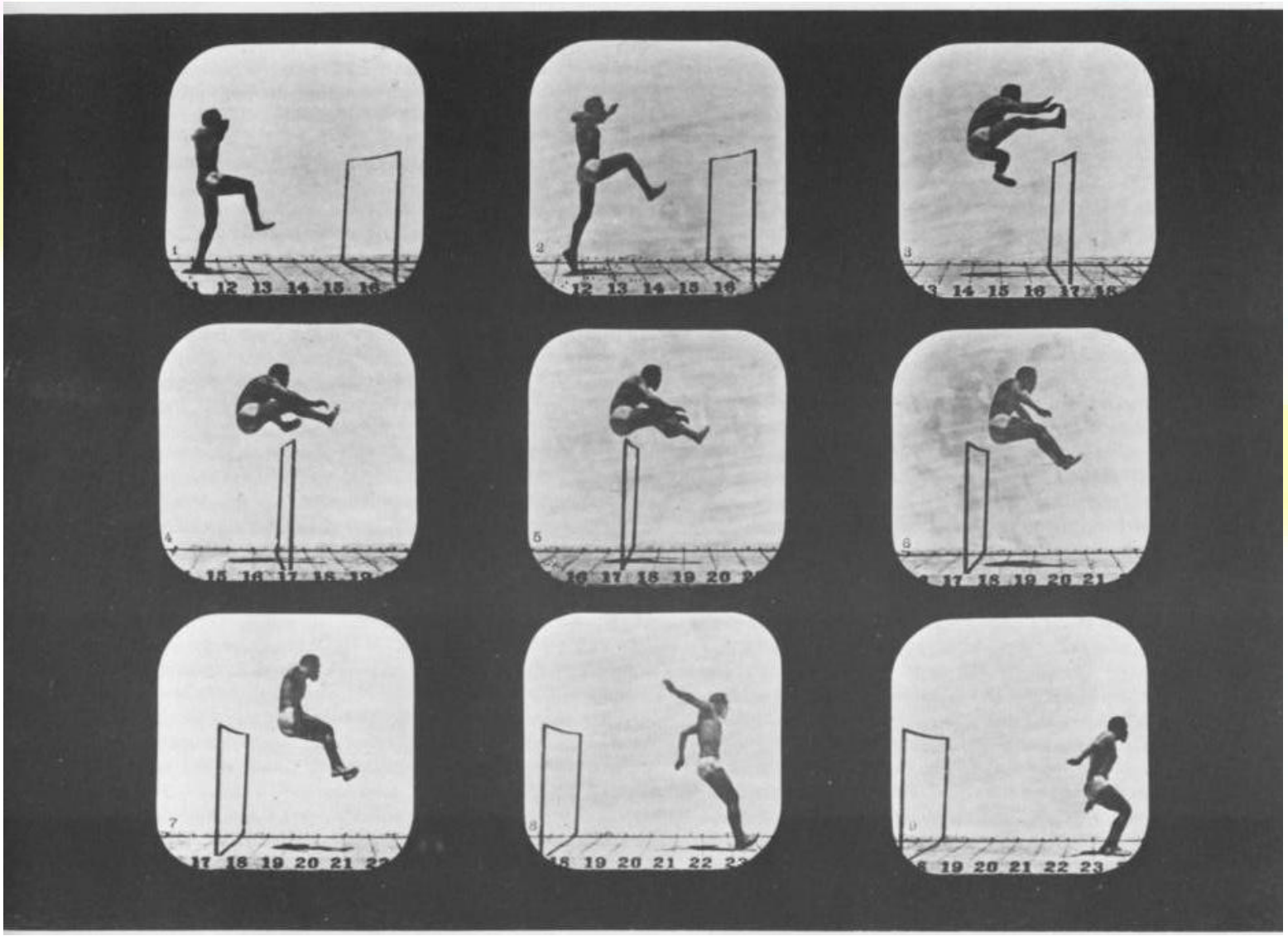


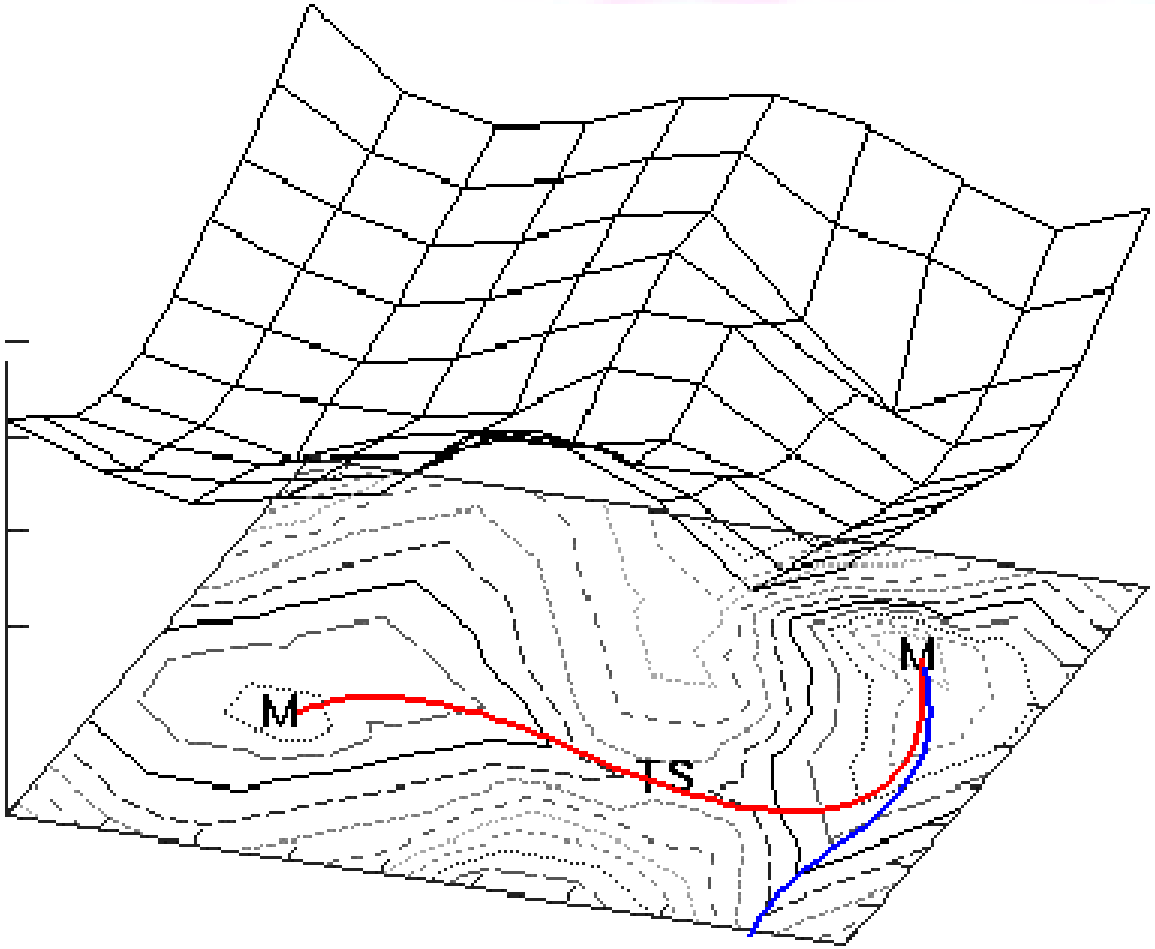

E.L. Muetterties and L.J. Guggenberger, JACS 96 (1974) 1748

# Structure Correlation shed some light on the somewhat diffuse notion of ‘The Reaction Pathway‘



# Muybridge (~1885)



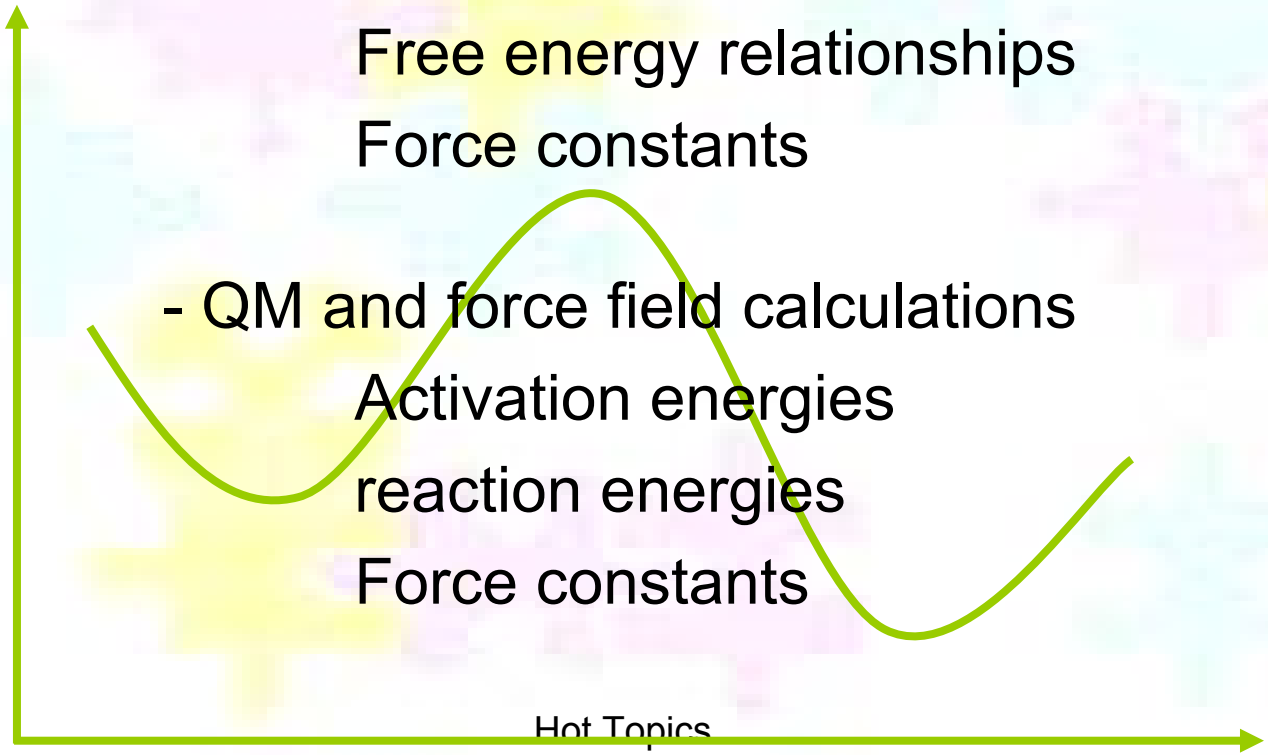



# What about Energy?

# Where to take energies from?

- Calorimetry, Kinetics, Spectroscopy
  - Reaction energies
  - Activation energies
  - Free energy relationships
  - Force constants

- QM and force field calculations
  - Activation energies
  - reaction energies
  - Force constants



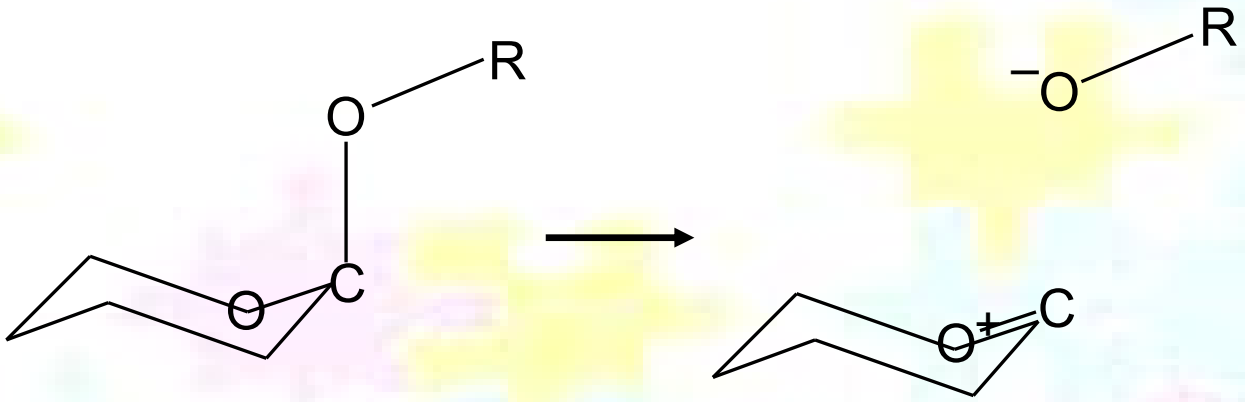
# Structure-Energy Correlations

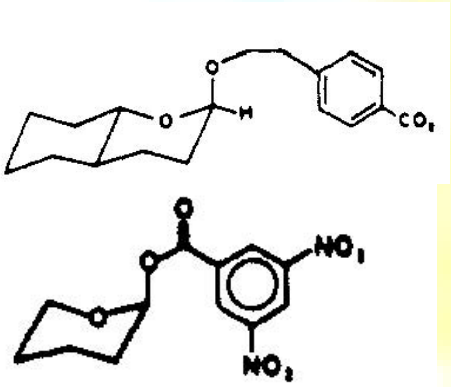
- *Observation 1*: different members of a given class of compounds tend to undergo the same chemical reaction, i.e. tend to follow similar reaction path.

- *Observation 2*: substituent effects on chemical reaction rates may amount to many orders of magnitude similar to those observed in enzymatic catalysis.

- *Observation 3*: steric and electronic substituent effects on reactant structure tend to be relatively small.

# Acetal hydrolysis



| $d(C\text{-}O_{ring})$ | $d(C\text{-}O_{axial})$ | $E^{‡}$ |
|---|---|---|
| 1.422 Å | 1.409 Å | 39 kcal/mol |
| 1.379 Å | 1.476 Å | 18 kcal/mol |

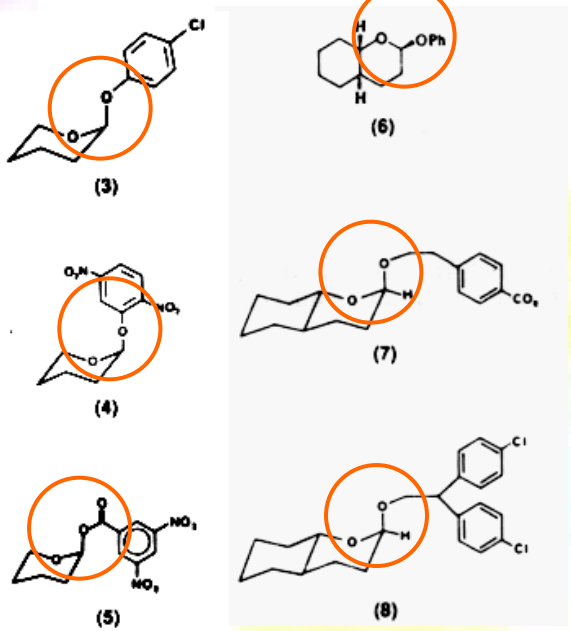
# Some Questions ….

- *Question 1*: are there simple relationships between the characteristics of related reactions of similar substrates?

- *Question 2*: if so, what is their origin and what can be deduced from such relationships about energy surfaces?

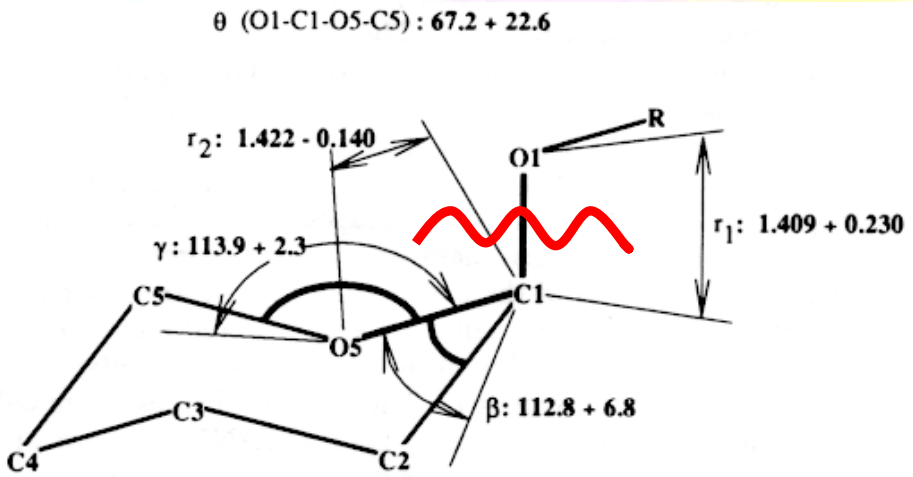
- *Question 3*: what can be learned about catalysis?

# Acetal hydrolysis: structure correlation




Principal component analysis shows

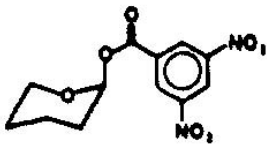
correlated changes of structural parameters

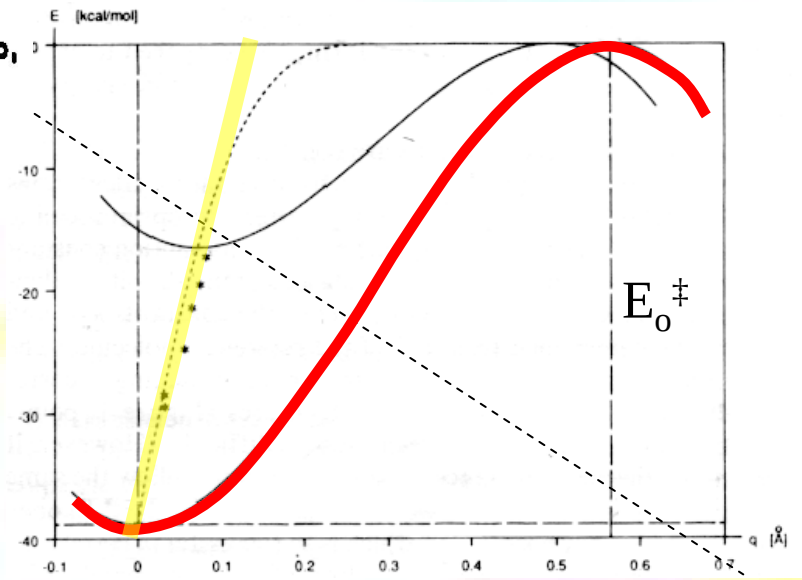


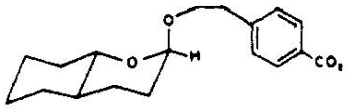

P.G. Jones, A.J. Kirby, *JACS* **106** (1984) 6207

H.B. Bürgi, K.C. Dubler-Steudle, *JACS* **110** (1988) 7291

# Acetal hydrolysis: energy surface





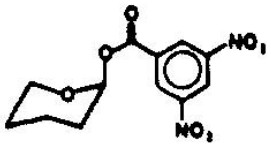
$\Delta E^{\ddagger}/\Delta q$ (Exp):
300 kcal/(mol Å)

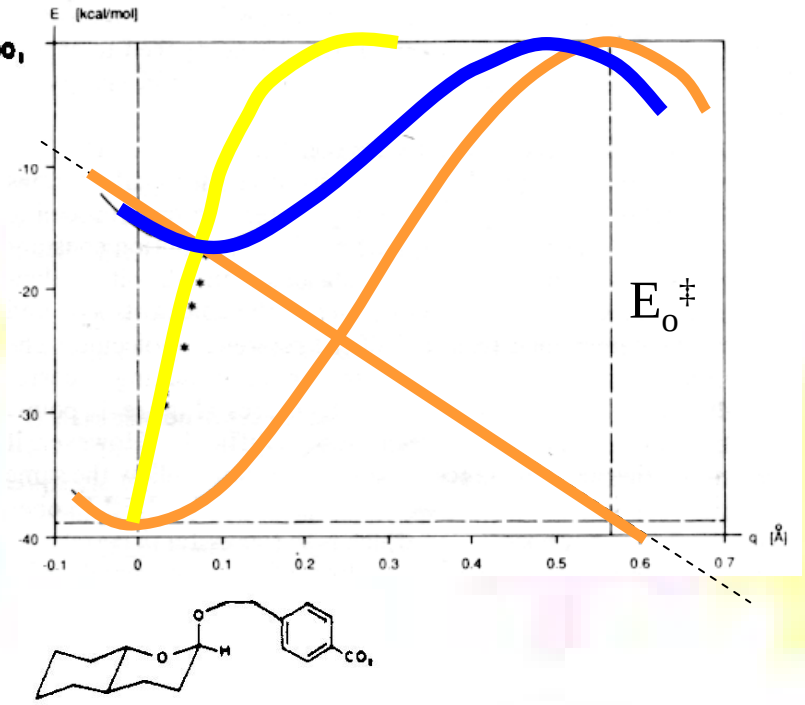
$E = k_2*q^2/2 - k_3*q^3$

$dE/dq = 0 = k_2*q - 3k_3*q^2$
$\rightarrow q = 0,\ q^{\ddagger} = k_2/3k_3$
$\rightarrow E_o^{\ddagger} = k_2^3/k_3^2$


P.G. Jones, A.J. Kirby, *JACS* **106** (1984) 6207
H.B. Bürgi, K.C. Dubler-Steudle, *JACS* **110** (1988) 7291

# Acetal hydrolysis: structure-energy correlation

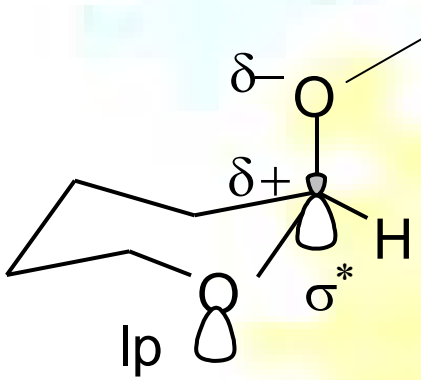





$$E = k_2 q^2/2 - k_3 q^3 - k_1 q$$

$$\Delta E^{\ddagger}/\Delta q = -(6\, E_o^{\ddagger} * k_2)^{1/2}$$





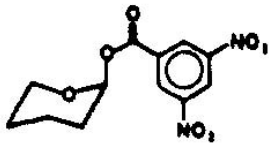

Calc: 320 kcal (mol Å)$^{-1}$

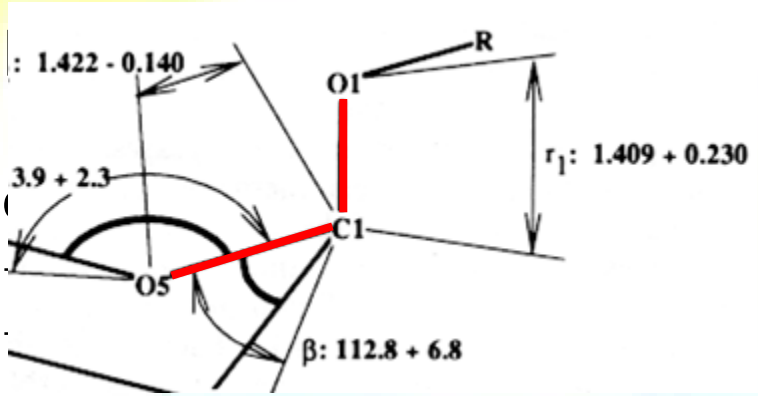
Exp: 300 kcal (mol Å)$^{-1}$

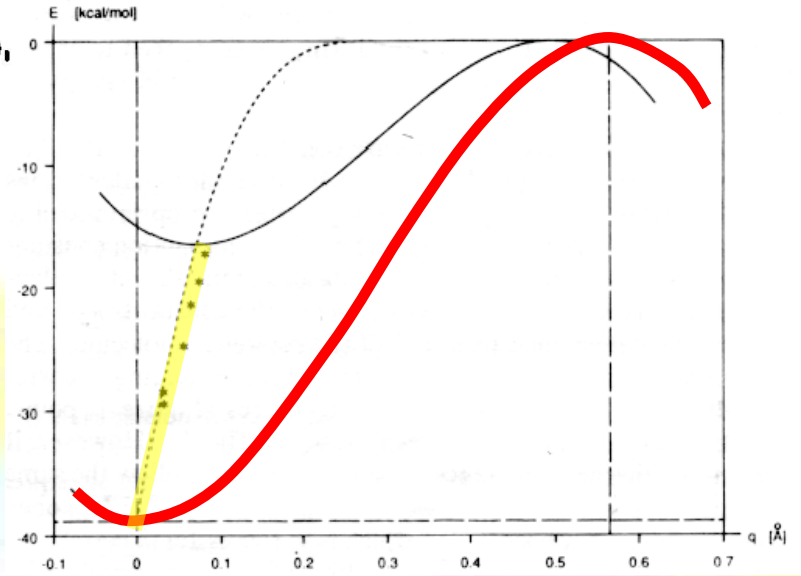
H.B. Bürgi, K.C. Dubler-Steudle, *JACS* **110** (1988) 7291

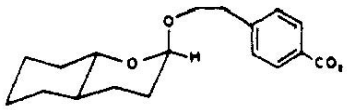
P.G. Jones, A.J. Kirby, *JACS* **106** (1984) 6207

# Acetal hydrolysis: transition state structure





$q^{\ddagger} = (6\ E_o{}^{\ddagger} / k_2)^{1/2}$

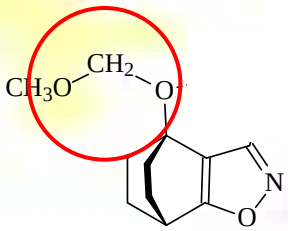
$q^{\ddagger}$

| Δ(C1-O5) | Δ(C1-O1) |
|---|---|
| -0.15 Å | 0.55 Å |
| → 1.26 Å | 1.97 Å |

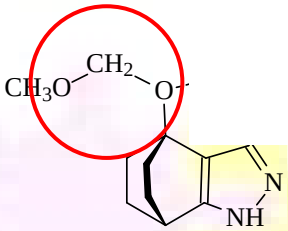
*Ab initio:*

| | | |
|---|---|---|
| $OC(OH)_2.H_2O$ | -0.07 | 0.17 |
| $CH_2C(OH)_2.H_2O$ | -0.11 | 0.34 |
| $H_2C(OH)_2.H_2O$ | -0.16 | 0.38 |

# Acetal hydrolysis: model of enzymatic catalysis

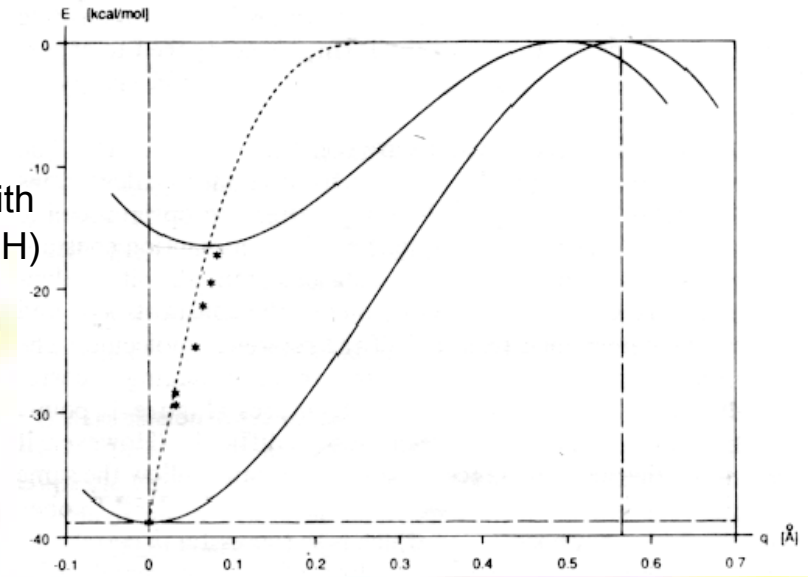



**1**




**2**

**2** (with COOH)




**2** (no COOH)

Structural data from **1**:

| | No COOH | with COOH |
|---|---|---|
| $CH_3O–CH_2$ | 1.398 | 1.383 Å |
| $CH_2–OR_3$ | 1.408 | 1.424 Å |

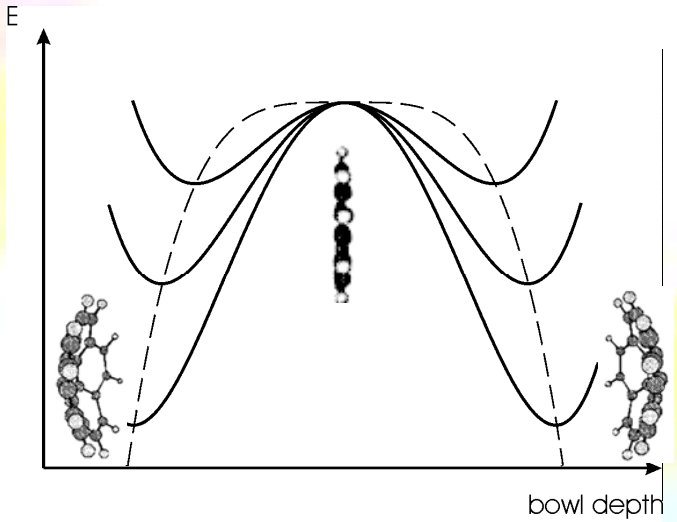
Relative rates of hydrolysis from **2**

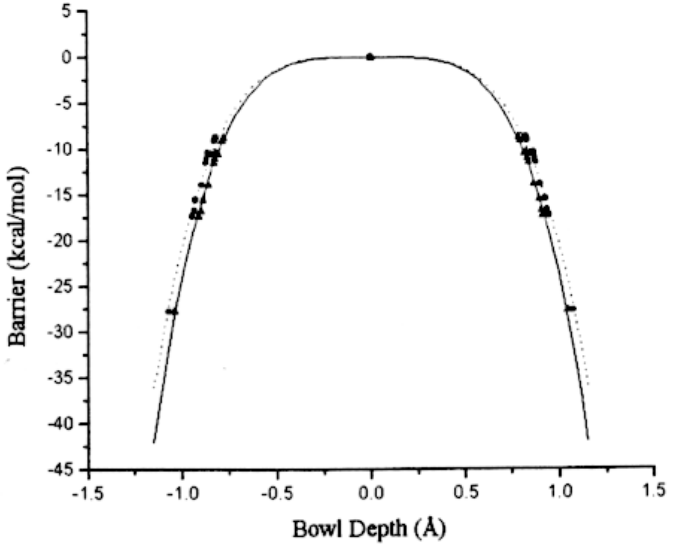
1 $10^{10}$

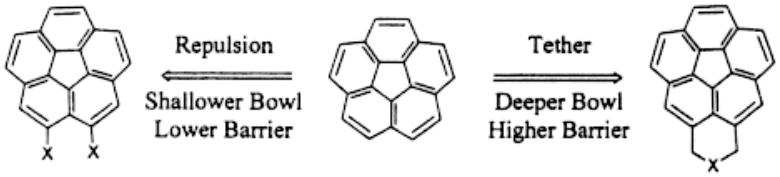
A.D. Bond, A.J. Kirby, E. Rodriguez, *Chem. Commun* (2001) 2266

E. Hartwell, D.R.W. Hodgson, A.J. Kirby, *JACS* **122** (2000) 9326

# Bowl depth and inversion barrier in corannulenes



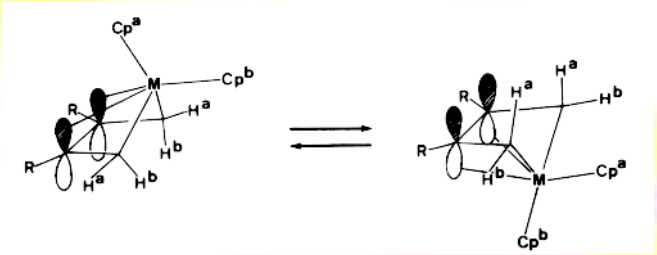

small a large a

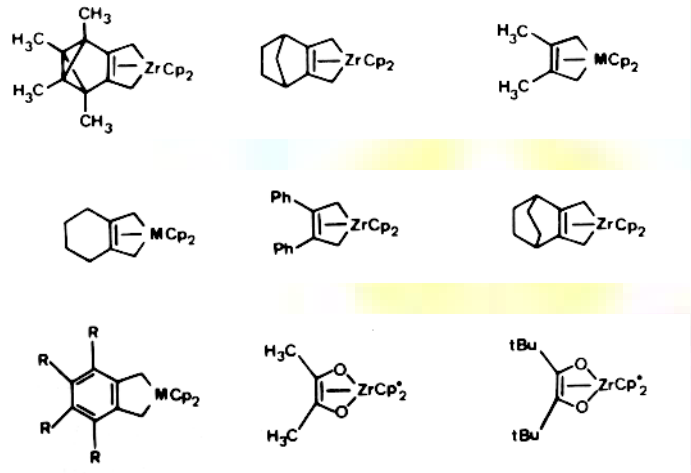
$$E = x^4 - a * x^2$$

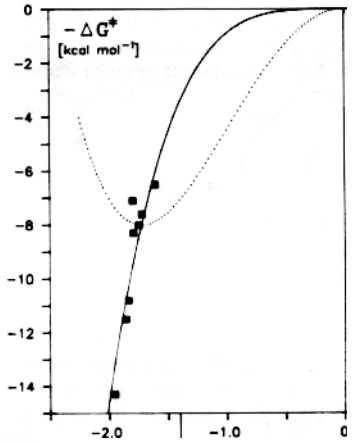
$$x_{eq} = \pm (a / 2)^{1/2}$$

$$\Delta E^{\ddagger} = - x_{eq}^4$$

# Metallacyclopentene ring inversion in (s-cis-$\eta^4$-butadiene)metallocene complexes




$$E = b^*s^4 - a^*s^2$$

$$s_{eq} = \pm (a / 2b)^{1/2}$$

$$\Delta E^{\ddagger} = b^*s_{eq}^4$$

M = Zr, Hf  cp* = pentamethyl-cp



H.B. Bürgi, K.C. Dubler-Steudle, *JACS* **110** (1988) 4953

# …. Some answers

- Energy surfaces and reaction pathways of related compounds undergoing the same type of reaction are intimately related (through simple energy perturbations).

- As a consequence the quantities characterizing related reactions, such as activation energies and transition state structures, also show definable relationships.

- Unlike Marcus relationships, this approach explicitly accounts for the interdependence of structure and energy.

# Summary

## Structure-Structure Relationships
## Structure-Energy Relationships

- Along a rection path many different structural parameters tend to change in a highly correlated fashion.
- Small structural differences in ground state structures may be associated with large differences in reaction rates.
- To obtain these conclusions series of related structures had to be analyzed and combined with non-crystallographic information on chemical reactivity

**Thank you!**