The Nobel Prize in Chemistry 1964
"for her determinations by X-ray techniques of the structures of important biochemical substances"

She belonged to many international peace organizations and, owing to Cold War restrictions, was not permitted to obtain a U.S. visa until 1990.
Photodimerization of \textit{trans}-Cinnamic acids

\begin{center}
\textbf{Topochemical principle: Reactions in the solid state take place with minimum atomic movements.}
\end{center}

$\alpha$-trans-Cinnamic acid
Leads to centrosymmetric dimer

$\beta$-trans-Cinnamic acid
Leads to mirror symmetric dimer
Packing arrangement of methyl-meta-bromocinnamate.

Note that the two reactive double bonds are not parallel to one another.

**Topochemical principle:** Reactions in the solid state take place with minimum atomic movements.

*Crystal Engineering*

The next decade will surely see more use of crystallographic information in the field of large-amplitude molecular motions in the solid state

J. D. Dunitz, V. Schomaker and K. N. Trueblood (1988)
Difference Fourier maps of (E)-stilbene

Pedal motion of stilbenes

Harada and Ogawa, JACS, 126, 3539 (2004).
Photodimerization of criss-cross alkenes

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Time of h\text{\textsubscript{\textgamma}} (hrs)</th>
<th>% conv.</th>
<th>\beta-truxinate</th>
<th>cis</th>
<th>\delta-dimer</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
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<td>3</td>
<td>trace</td>
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<td>30</td>
<td>4</td>
<td>1</td>
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<td>45</td>
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<td>2</td>
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<tr>
<td>32</td>
<td>57</td>
<td>49</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>
$d_1 = 3.9 \text{ Å}$ and $d_2 = 4.1 \text{ Å}$
Large motions are tolerated in the crystal

- **C=C** exists in criss-crossed arrangement.

- **Pedal-like conformational change** by one of the cinnamic acid molecules is required for $\beta$-dimer formation.
Cis-Trans Photoisomerization in Crystals

<table>
<thead>
<tr>
<th>Temp °C</th>
<th>Duration</th>
<th>%Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT</td>
<td>12</td>
<td>100</td>
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<tr>
<td>50°C</td>
<td>6</td>
<td>100</td>
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<tr>
<td>RT</td>
<td>12</td>
<td>15</td>
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<tr>
<td>50°C</td>
<td>18</td>
<td>60</td>
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<tr>
<td>RT</td>
<td>45</td>
<td>80</td>
</tr>
<tr>
<td>50°C</td>
<td>21</td>
<td>100</td>
</tr>
</tbody>
</table>

T. Arai
Photoisomerization of cis-8-fluoranthenyl styrene

Large distance between the reactive double bonds 6.77 Å precludes cyclobutane intermediate.
Photoisomerization of *cis*-8-fluoranthenyl styrene

Absence of short contacts near reaction site favors rotation.

- $C\cdots C > 3.4 \text{ Å}$
- $C\cdots H > 2.8 \text{ Å}$
- $H\cdots H > 2.4 \text{ Å}$

Empty channel along $c$ axis
Pre-organization with a guest: Non reactive molecule made to react

In solution isomerization
In crystals no reaction

MacGillivray et al., JACS, 2000, 122, 7817.
Overview of templated dimerization of olefins in solid-state

For ex:

$M = \text{metal}$
Thiourea as a possible template (Cambridge Structural Database)

CSD refcode: AMILIR

CSD refcode: AMILOX

4.46 Å

3.87 Å
An overview of photochemistry of stilbazoles in thiourea co-crystals

$\text{X = H, F, Cl, Br, Me and OMe}$

$\text{X = H, F, Cl, Br, Me, OMe and CN}$

$\text{X = H, F, Cl, Br, Me, OMe and CN}$

$\text{X = H}$

$\text{X = F}$

$\text{X = Cl}$

$\text{X = Br}$

$\text{X = CH}_3$

$\text{X = OCH}_3$

$\text{X = CN}$

$^1\text{H NMR (CDCl}_3\text{) of cyclobutane protons in dimer products}$
Anomalous orientation of 4-cyanostilbazole in thiourea co-crystals
5.04 Å 4.94 Å
4.49 Å 4.62 Å
5.04 Å 4.94 Å

Does Not Dimerize

4.47 Å 4.79 Å
4.79 Å

Does Not Dimerize

CH₂CH₃

N
C
H₂
C
H₃

N

Py
Acknowledgements
Controlling Products in Photocycloaddition Reactions

Poor alignment
Multiple products

Highly aligned
Single product

de Mayo et al.,
JCS. Chem. Comm., 1980, 994
Water Soluble Hosts as Confined Media

Cyclodextrins
Tabushi

Cucurbiturils
Kim

Pd Nano Cage
Fujita

Calixarenes
Shinkai

SDS / CTAC

NaCh / NaDCh

Dendrimers

Octa acid
Supramolecular Containers

Reaction cavity

Boundary

Guest

Free Space
2 \times \pi - \pi interaction

Syn head-head

Anti head-tail
trans-Cinnamic acids photo inactive in solid state ($\gamma$-form)

$\text{Ar} = \text{R-Ph}$

<table>
<thead>
<tr>
<th>Ar</th>
<th>Solid state</th>
<th>% of dimer in CB[8]</th>
<th>% of cis isomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>R=4-CH$_3$</td>
<td>--</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>R=3-CH$_3$</td>
<td>--</td>
<td>83</td>
<td>17</td>
</tr>
<tr>
<td>R=3-CH$_3$</td>
<td>--</td>
<td>72</td>
<td>28</td>
</tr>
</tbody>
</table>

syn H-H dimer
trans-Cinnamic acids that yield anti H-T dimer upon irradiation in solid state (α-form)

<table>
<thead>
<tr>
<th>Ar</th>
<th>Solid state % of anti H-T dimer</th>
<th>% of Syn H-H dimer in CB[8]</th>
<th>% of cis isomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>R=H</td>
<td>100</td>
<td>54</td>
<td>46</td>
</tr>
<tr>
<td>R=4-OH</td>
<td>100</td>
<td>38</td>
<td>62</td>
</tr>
<tr>
<td>R=4-NH₃⁺</td>
<td>100</td>
<td>88</td>
<td>12</td>
</tr>
</tbody>
</table>
### Substrate % of Syn H-H dimer in nanocage % of cis isomer

<table>
<thead>
<tr>
<th>Substrate</th>
<th>% Syn H-H dimer</th>
<th>% cis isomer</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Substrate Structure" /></td>
<td>63</td>
<td>37</td>
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<tr>
<td><img src="image2" alt="Substrate Structure" /></td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td><img src="image3" alt="Substrate Structure" /></td>
<td>42</td>
<td>58</td>
</tr>
<tr>
<td><img src="image4" alt="Substrate Structure" /></td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>

The reaction proceeds as follows:

- **Substrate** + **Pd(dppf)Cl2** → **Product**

where:

- **Ar = R-Ph**
- **hv** indicates light irradiation
- **syn H-H dimer** refers to the specific isomer formed.
1) Top-^1^H NMR of O-methoxy cinnamate in D$_2$O
2) Bottom-^1^H NMR of encapsulated O-methoxy cinnamate in Pd-Nanocage (0.5 eq.)
$R_1 = R_2 = R_3$ = H

Water: 60%

Pd-nanocage: >90%

$R_1$ = Me, $R_2 = R_3$ = H

Water: 15%

Pd-nanocage: >90%

$R_2$ = OMe, $R_1 = R_3$ = H

Water: >90%

Pd-nanocage: >90%

$R_3$ = OMe

Water: Not soluble

Pd-nanocage: >90%
Charge repulsion

Cation-π interaction

Syn H-H

Anti H-T
### Cation-π interaction

Minimized ionic repulsion

<table>
<thead>
<tr>
<th>Guest</th>
<th>Medium</th>
<th>anti H-T</th>
<th>syn H-T</th>
<th>cis</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Guest" /></td>
<td><img src="image2.png" alt="Medium" /></td>
<td><img src="image3.png" alt="anti H-T" /></td>
<td><img src="image4.png" alt="syn H-T" /></td>
<td><img src="image5.png" alt="cis" /></td>
</tr>
<tr>
<td>Water</td>
<td>03</td>
<td>02</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>CB[8]</td>
<td>90</td>
<td>05</td>
<td>05</td>
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</tr>
<tr>
<td><img src="image6.png" alt="Guest" /></td>
<td><img src="image7.png" alt="Medium" /></td>
<td><img src="image8.png" alt="anti H-T" /></td>
<td><img src="image9.png" alt="syn H-T" /></td>
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<tr>
<td>Water</td>
<td>02</td>
<td>02</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>CB[8]</td>
<td>82</td>
<td>00</td>
<td>18</td>
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</tr>
</tbody>
</table>
Photochemistry of Stilbazoles

Counter anion Cl-

<table>
<thead>
<tr>
<th>Medium</th>
<th>anti H-T</th>
<th>syn H-T</th>
<th>cis</th>
</tr>
</thead>
<tbody>
<tr>
<td>dil. HCl</td>
<td>13</td>
<td>16</td>
<td>71</td>
</tr>
<tr>
<td>PHBSA</td>
<td>24</td>
<td>14</td>
<td>62</td>
</tr>
<tr>
<td>CA[6]SO₃H</td>
<td>76</td>
<td>5</td>
<td>19</td>
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<tr>
<td>CA[8]SO₃H</td>
<td>86</td>
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<td>12</td>
</tr>
<tr>
<td>CB[8]</td>
<td>90</td>
<td>--</td>
<td>10</td>
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</tbody>
</table>

Cation-π interaction

CA[8]  CB[8]
Can additional weak interactions (eg. Cl--Cl) alter the olefin pre-orientation?

Counter anion Cl−
<table>
<thead>
<tr>
<th>Guest</th>
<th>Medium</th>
<th>Cis+ Cyclized</th>
<th>Head-tail</th>
<th>Head-head</th>
</tr>
</thead>
<tbody>
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<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
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<td><img src="image7" alt="Image" /></td>
<td><img src="image8" alt="Image" /></td>
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<tr>
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<td><img src="image12" alt="Image" /></td>
<td><img src="image13" alt="Image" /></td>
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<td><img src="image16" alt="Image" /></td>
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<td><img src="image18" alt="Image" /></td>
<td><img src="image19" alt="Image" /></td>
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<td><img src="image28" alt="Image" /></td>
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Acknowledgements