聲明

本檔案之內容僅供下載人自學或推廣化學教育之非營利目的使用。並請於使用時註明出處。
【如本頁取材自○○○○教授演講內容】。
工業界綠色永續合成實例
Cases of Green, Sustainable Synthesis in Industrial World

2010 綠色/永續合成化學講習會
December 3, 2010, 化學會年會，台灣大學

朝陽科技大學 周德璋
Green Chemistry

The design, development, and implementation of chemical products and processes to reduce or eliminate the use and generation of substances hazardous to human health and the environment.

[為縮減或淘汰對人類健康和環境具有危害性的物質的使用與產生，而進行化學產品和製造過程的設計、開發與執行。]

Anastas PT, Warner JC, editors.  
*Green Chemistry: theory and practice.*  

Anastas PT, Kirchhoff MM,  
*Origins, Current Status, and Future Challenges of Green Chemistry*  
The Twelve Principals of Green Chemistry

1. Prevent waste
2. Design safer chemicals and products
3. Design less hazardous chemical syntheses
4. Use renewable feedstocks
5. Use catalysts, not stoichiometric reagents
6. Avoid chemical derivatives
7. Maximize atom economy
8. Use safer solvents and reaction conditions
9. Increase energy efficiency
10. Design chemicals and products to degrade after use
11. Analyze in real time to prevent pollution
12. Minimize the potential for accidents

John C. Warner

Research chemist at Polaroid (1988)
Professor at the UMass, Boston (1996),
-- established first doctoral program in green chemistry
Professor at UMass, Lowell (2004)
-- founded Center for Green Chemistry

Chief technology officer and chairman of the board of Warner Babcock Institute for Green Chemistry (2007)

“Green chemistry is the mechanics of doing sustainable chemistry,”

Warner: “By focusing on green chemistry, it puts us in a different innovative space. It is a science that presents industries with an incredible opportunity for continuous growth and competitive advantage.”

Chemical & Engineering News, 88(40), October 04, 2010
Paul T. Anastas

Professor of chemistry for the environment at Yale University,
Director of Yale's Center for Green Chemistry & Green Engineering,
Widely regarded as one of the fathers of "green chemistry,“
The Environmental Protection Agency assistant administrator for the Office of R&D,

"Why did you become a chemist?"
Some are excited by the intellectual challenges of chemistry.
Others want to use chemistry and chemical engineering to solve problems and make the world a better place.

Anastas:
"The world needs both. Building a sustainable world is the most taxing intellectual exercise we have ever engaged in. It is also the most important for the future of the world."
Robert H. Grubbs, Richard R. Schrock, and France's Yves Chauvin won the 2005 Nobel Award for their development of the metathesis method in organic synthesis.

“This represents a great step forward for green chemistry, reducing potentially hazardous waste through smarter production. Metathesis is an example of how important basic science has been applied for the benefit of mankind, society, and the environment,……"
**Green Chemistry** is focused on the design, manufacture, and the use of chemicals and chemical processes that have little or no pollution potential or environmental risk.

**Sustainable Chemistry** not only includes the concepts of green chemistry, but also expands the definition to a larger system than just the reaction. Also considers the effect of processing, materials, energy, and economics.
綠色化學的終極目的是縮減或淘汰對人類健康和環境具有危害性的物質的使用與產生，因此任何化學產品及其相關活動—製造過程的設計、開發、與實行，當然包含化學合成，都要秉持此認知而思考。

Anastas and Warner:
"In virtually every aspect in society, it has long been acknowledged that preventing a problem is superior to trying to solve it once it has been created."

green chemistry
seeks to reduce and prevent pollution at its source.
What is the ideal synthesis

1. Convenient and practical -- Simple
2. High yield (100%!)
3. Short (1 step! // 1-pot!)
4. Mild conditions (room temperature or 37 °C)
5. Starting materials easy to obtain (natural or commercial)
6. Available controlled stimulus (mild reagents or catalysts)
7. Cheap and safe solvent (water!)
8. Easy isolation of products
9. Isolation of intermediates unnecessary (one-pot reaction)
10. Display novel chemistry or new applications

As Mother Nature Does!
Sitagliptin
The active ingredient in Januvia™ -- medication for type 2 diabetes.

Disodium iminodiacetate (DSIDA)
A key intermediate in the production of Roundup® herbicide

Ibuprofen
One of core non-steroidal anti-inflammatory medicines

Cytovene® [ganciclovir]
A prescription medication as “antivirals”.

Polyaspartate
Biodegradable Alternative to Polyacrylate
Case 1.

US Presidential Green Chemistry Challenge Awards:  
**Greener Synthetic Pathways Award** 2006

sitagliptin
What is Sitagliptin?

- the active ingredient in Januvia™.

- 具效力和選擇性的dipeptidyl peptidase type 4 (DPP-4)抑制劑，治療二型糖尿病（type 2 diabetes）的藥劑。
- 2006年10月成為第一個通過美國FDA核准的糖尿病藥。
- 抑制DPP-4對腸泌素激素的水解作用，進而提高glucagonlike peptide-1 (GLP-1)與glucose-dependent insulinotropic polypeptide (GIP)的濃度。

[Review: Drucker, Cell Metab., 2006, 3, 153]
first-generation synthesis of sitagliptin

(Old process)

1. (S)-BinapRuCl$_2$, 90 psi H$_2$, HBr, MeOH, 80 °C
2. NaOH, MeOH/H$_2$O

83% ee 94%

asymmetric hydrogenation
(Noyori)

BnONH$_2$·HCl
EDC, LiOH

peptide coupling

Mitsunobu reaction

81% 2 steps

ee 99%


**sitagliptin**

52% overall yield

crystallized from EtOH/H$_2$O

peptide coupling

deprotecting

1. H$_2$, Pd/C
2. H$_3$PO$_4$

78% from lactam

December 3, 2010
**Synthesis of 3-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine**

```
+NH₂NH₂ → NH₂NH₂ → TFAA → OCF₃
```

26% overall yield

**Triazolopiperazine**

**Peptide coupling**

```
F
F
F
F
+NH₂NH₂ → NH₂NH₂ → TFAA → OCF₃
```

1. HOBT, EDC, DIPEA
2. HCl, MeOH

78%

**second-generation synthesis of sitagliptin**

(New process – Green route)

One-pot, three-component reaction to key β-enamino amide intermediate

82% over 3 steps


December 3, 2010
Enantioselective hydrogenation of unprotected β-enamine amide

250 psig of H₂
NH₄Cl (0.15 mol %)
MeOH
[Rh(COD)Cl]₂ (0.15 mol %)
tBu JOSIPHOS (0.155 mol %)

98% yield
95% ee

recrystallized as the phosphoric acid salt

JOSIPHOS
ferrocenyl phosphine ligands

>99% conv (86% ee)
>90% conv (6% ee)
>99% conv (72% ee)
>99% conv (95% ee)


sitagliptin

December 3, 2010
The “greener” features

- Fewer steps (4 vs 8):
  - elimination Mitsunobu reaction
  - elimination one peptide coupling
  - No protection-deprotection of the amine nitrogen

- Increases yield (65% vs 52%)

- Waste reduction (>80%):
  - Eliminate 60 L of aqueous waste per kg of product
    (prevent formation of 150,000 metric tons of solid and aqueous process waste over the lifetime of Januvia)

- Unprecedented efficient hydrogenation of an unprotected enamine.
  - an excellent example of a scientific innovation resulting in benefits to the environment!
How is the Meldrum’s adduct formed?

Meldrum’s acid to act as an acyl anion equivalent

2-(2,4,5-trifluorophenyl)acetic acid

4-(2,4,5-trifluorophenyl)-3-oxobutanoic acid

sitagliptin
How is the β-ketoamide formed?
Biocatalytic Transamination

C K Savile et al. Science 2010;329:305-309

Biocatalytic Transamination

Pr = isopropyl

Presidential Green Chemistry Challenge Award Greener Reaction Conditions Award 2010

December 3, 2010
Case 2.

**Disodium iminodiacetate (DSIDA)**

US Presidential Green Chemistry Challenge Awards:  
*Greener Synthetic Pathways Award*  1996
What is Disodium iminodiacetate (DSIDA)?

Disodium iminodiacetate (DSIDA) is a key intermediate in the production of Monsanto’s Roundup® herbicide.

Roundup® agricultural herbicides are the flagship of Monsanto’s agricultural chemicals business.

Glyphosate: $N$-(phosphonomethyl)glycine in the form of its isopropylamine salt (41%)
**Strecker amino acid synthesis**

Traditionally, the Strecker process has been used to manufacture DSIDA. It requires formaldehyde, ammonia, hydrogen cyanide, and hydrochloric acid.
The Strecker process for synthesizing DSIDA

\[
\text{H}_2\text{C} = \text{O} + \text{NH}_3 + 2 \text{HNC} \rightarrow \text{H}_2\text{N} = \text{C} = \text{NH}_2
\]

- **hydrogen cyanide**: extremely toxic; requires special handling
- **exothermic reaction**: generating potentially unstable intermediates.
- **waste**: 1 kg for every 7 kg of product.
Green process for synthesizing DSIDA

**copper-catalyzed dehydrogenation of diethanolamine**

\[
\text{diethanolamine} \xrightarrow{2 \text{ NaOH}} \text{disodium iminodiacetate} + 4 \text{H}_2
\]

**Greener Synthetic Pathways Award**

1996

Disodium iminodiacetate

Disordered pathways
the dehydrogenation reaction is endothermic; avoid the use of cyanide and formaldehyde; fewer process steps, higher overall yield; no purification or waste cut is necessary; recover catalyst by filtration, ready for subsequent use in the manufacture of Roundup; This catalysis technology is applicable in the production of other amino acids and becomes a general method for conversion of primary alcohols to carboxylic acid salts.

1. Prevent Waste
2. Increase Atom Economy
3. Design Less Hazardous Chemical Syntheses
4. Design Safer Chemicals
9. Use Catalysts

Disodium iminodiacetate
Case 3.

**Ibuprofen**

US Presidential Green Chemistry Challenge Awards:

**Greener Synthetic Pathways Award** 1997
◆ What is ibuprofen?

(S)-2-(4-isobutylphenyl)propanoic acid, (S)-ibuprofen, is active form both *in vitro* and *in vivo*.

2-arylpropionyl-CoA epimerase (isomerase)

marketed as *racemic mixtures*.
One of core non-steroidal anti-inflammatory medicines (非類固醇消炎藥) in the World Health Organization's "Essential Drugs List", which is a list of minimum medical needs for a basic health care system ---- Over-the-Counter (不需處方可出售的) medicine. [others: aspirin, paracetamol (acetaminophen)]

Discovered by S. Adams, with J. Nicholson, A. R. M. Dunlop, J. B. Wilson & C. Burrows (Boots Company), and was patented in 1961. Dr. Adams initially tested the drug on a hangover (宿醉).
● It was launched in 1969 as a medication for the treatment of rheumatoid arthritis [風濕性關節炎] in the UK and in 1974 in the USA.

● The Boots Group was awarded *Queen's Award for Technical Achievement* for the development of ibuprofen in 1987.

● 具解熱、消炎和鎮痛的作用，可治療發燒、疼痛和發炎。

● 減輕關節炎(arthritis)，原發型痛經( primary dysmenorrhea)，發燒 (fever)，等症狀；作為止痛劑 (analgesic)；具抑制血小板凝集效應（antiplatelet effect）。

● Active ingredient in “Motrin”, “Advil”, Medipren”….，“炎熱消” (水液)， “普服芬” (錠劑), 宜痛炎錠,伊普®鎮痛, …. 

ibuprofen

December 3, 2010
◆ synthesis

- The industrial synthesis was developed and patented by Boots Company of England in 1961. --- brown synthesis

- A new greener industrial synthesis was developed and implemented by the BHC Company (now BASF Corporation) in 1991. --- green synthesis

- BHC won Presidential Green Chemistry Challenge Awards (USA) ---- Greener Synthetic Pathways Award in 1997.

BHC = Boots + Hoechst Celanese
Boots synthesis of ibuprofen
--- brown synthesis

developed and patented by Boots Company of England in the 1960s
<table>
<thead>
<tr>
<th>Reagent Used in ibuprofen</th>
<th>Unused in ibuprofen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formula</strong> Mw</td>
<td><strong>Formula</strong> Mw</td>
</tr>
<tr>
<td>( \text{C}<em>{10}\text{H}</em>{14} ) 134</td>
<td>( \text{C}<em>{10}\text{H}</em>{13} ) 133</td>
</tr>
<tr>
<td>( \text{C}<em>{4}\text{H}</em>{6}\text{O}_{3} ) 102</td>
<td>( \text{C}<em>{2}\text{H}</em>{3} ) 24</td>
</tr>
<tr>
<td>( \text{C}<em>{4}\text{H}</em>{7}\text{ClO}_{2} ) 122.5</td>
<td>( \text{CH} ) 13</td>
</tr>
<tr>
<td>( \text{C}<em>{2}\text{H}</em>{5}\text{ONa} ) 68</td>
<td>( \text{C}<em>{3}\text{H}</em>{6}\text{ClO}_{2} ) 109.5</td>
</tr>
<tr>
<td>( \text{H}_{3}\text{O} ) 19</td>
<td>( \text{H}_{3}\text{O} ) 19</td>
</tr>
<tr>
<td>( \text{NH}_{3}\text{O} ) 33</td>
<td>( \text{NH}_{3}\text{O} ) 33</td>
</tr>
<tr>
<td>( \text{H}<em>{4}\text{O}</em>{2} ) 36</td>
<td>( \text{HO}_{2} ) 33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>Ibuprofen</strong></td>
</tr>
<tr>
<td>( \text{C}<em>{20}\text{H}</em>{42}\text{NO}_{10}\text{ClNa} ) 514.5</td>
<td>( \text{C}<em>{13}\text{H}</em>{18}\text{O}_{2} ) 206</td>
</tr>
</tbody>
</table>

\[ \text{atom economy} = \frac{206}{514.5} \times 100 = 40\% \]

**Table 1. Atom economy in the Boots’ synthesis of ibuprofen**
Problems with Boots synthesis of ibuprofen

atom economy = 74.5%

Friedel-Crafts acetylation

aluminium trichloride, AlCl$_3$, is not a true catalyst. It is changed into a hydrated form, Al(OH)$_3$/H$_2$O, that has to be disposed of – usually in landfill sites.

atom economy = 71.6%

Darzens condensation

ibuprofen
hydrolysis $\text{H}^+/\text{H}_2\text{O}$

$\text{NH}_2\text{OH}$

atom economy = 92%

atom economy = 91%

$\text{NH}_3$

atom economy = 92.4%

$\text{CO}_2$ 
$\text{C}_2\text{H}_5\text{OH}$

$\text{H}_2\text{O}$

dehydration

$\text{H}_2\text{O}$

ibuprofen

December 3, 2010
6 steps!

If 90% yield for each step, then overall yield is 53%.

atom economy is 40%!

thus every 1 kg of ibuprofen produced is accompanied with more than 1.5 kg of waste.

UK market for ibuprofen is about 3,000,000 kg per year!

- about 4,500,000 kg of waste are produced.
- a typical tablet contains 200 mg of ibuprofen, then 15,000,000,000 (1.5 x 10^{10}) tablets are produced.

World population on November 2010 is estimated by the United States Census Bureau to be 6.884 billion (6,884,000,000).
BHC synthesis of ibuprofen
--- green synthesis

(USA) Presidential Green Chemistry Challenge Awards
Greener Synthetic Pathways Award in 1997

developed and implemented by
the BHC Company in 1991

ibuprofen
<table>
<thead>
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<th>Reagent</th>
<th>Used in ibuprofen</th>
<th>Unused in ibuprofen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Formula</td>
<td>Mw</td>
</tr>
<tr>
<td>1</td>
<td>C_{10}H_{14}</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>C_{4}H_{6}O_{3}</td>
<td>102</td>
</tr>
<tr>
<td>2</td>
<td>H_{2}</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>CO</td>
<td>28</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total</th>
<th>Ibuprofen</th>
<th>Waste products</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{15}H_{22}O_{4}</td>
<td>266</td>
<td>C_{13}H_{18}O_{2}</td>
</tr>
<tr>
<td></td>
<td>C_{2}H_{4}O_{2}</td>
<td>60</td>
</tr>
</tbody>
</table>

\[
atom\ economy = \frac{206}{266} \times 100 = 77.4\%\]

Table 2. Atom economy in the BHC synthesis of ibuprofen
Economic and Environmental Advantages of BHC Synthesis

- Greater overall yield (three steps vs. six steps)
- Greater atom economy (uses less feedstocks)
- Fewer auxiliary substances (products and solvents separation agents)
- **Less waste:** greater atom economy, catalytic vs. stoichiometric reagents, recovery of byproducts and reagents, recycling, and reuse, lower disposal costs.

*The BHC ibuprofen process is an innovative, efficient technology that has revolutionized bulk pharmaceutical manufacturing.*
Case 4.

The Cytovene® [ganciclovir]

US Presidential Green Chemistry Challenge Awards:
Greener Synthetic Pathways Award 2000
What is ganciclovir [“更昔洛韋”]?

Chemical Formula: C₉H₁₃N₅O₄
Exact Mass: 255.09675
Molecular Weight: 255.23062

IUPAC name:
2-amino-9-[(1,3-dihydroxypropan-2-yl)oxy]methyl]-6,9-dihydro-3H-purin-6-one

Ganciclovir is a prescription medication that belongs to the family of drugs known as “antivirals”.
[“更昔洛韋”是屬於抗病毒的處方藥劑]
Ganciclovir works by inhibiting cellular DNA polymerase that is associated with viral infections.

Ganciclovir is used to treat for cytomegalovirus (CMV) retinitis infections in immunocompromised patients, including patients with acquired immunodeficiency syndrome (AIDS) or patients undergoing chemotherapy.

[“更昔洛韋”是用於治療免疫損害患者中的巨細胞病毒 (CMV) 視網膜炎，包括獲得性免疫缺陷綜合征（愛滋病）或化療病人。]

Cytovene®, the registered trade name by the Roche Pharmaceuticals, contains ganciclovir sodium as the medicinal ingredient.
In 1974, scientists at Wellcome discovered the potent antiviral agent acyclovir (Zovirax®) for the treatment of various viral infections including herpes viruses HSV-1 and HSV-2.

In 1980, Dr. Kelvin Ogilvie and his research team at McGill University discovered Ganciclovir [CAN. J. CHEM. 1982, 60, 3005.], and developed by Verheyden and Martin at Syntex Research in 1980.

The first commercially viable process for the manufacture of ganciclovir was developed by Roche Colorado Corporation, formerly known as Syntex Chemicals, in the early 1990s.

The 1st generation process is known as Persilylation Process.
Persilylation Process --- Brown process

Propane-1,2,3-triol
Glycerin

Dimethoxymethane

Acetylation

Guanine

O-alkylation

N-alkylation

Cytovene (gancyclovir)

December 3, 2010
Cytovene (gancyclovir)
Problems with Persilylation Process

- A six-step process, in which 4-steps are protection-deprotection reactions.
- Involved 28 reagents and intermediates, and required the purification and isolation of 5 discrete intermediates.
- Involved at least 8 different kinds of solvents.
- Afforded specification grade ganciclovir in 54% yield.
- Involved a potentially hazardous palladium catalyzed hydrogenation step, which is needed to remove dibenzyl ether protecting group.
- Poor selectivity of key alkylation reaction, affording the desired N-7 isomer as minor product ($N-7:N-9 = 1:10$) and requiring costly and tedious chromatographic separation.
In 1993, the Boulder Technology Center of Roche Colorado Corporation completed the demonstration of a new and expedient process for the production of ganciclovir by (1) leveraging the **basic principles of molecular conservation** to minimize the creation and disposal of undesired wastes, and (2) formulating **efficient process engineering design** for streamlining process operation and the recycling of raw materials. The new (2\(^{nd}\) generation) process is called **The Guanine TriEster (GTE) Process**.

This technology was awarded the Presidential Green Chemistry Challenge Award [Greener Synthetic Pathways Award] in the U.S. in 2000.
The Guanine TriEster (GTE) Process
--- Green process

Guanine

HMDS, TfOH
(EtCO)₂O, DMAP
MeOH, PhCH₃

Isolated by selective crystallization

propionic acid
propane-1,2,3-triol
glycerin

Ganciclovir

Cytovene (gancyclovir)

December 3, 2010
The “greener” features of the GTE process

- Fewer process steps:
  - The process demonstrates the potential for a “one step” process for the production of ganciclovir.

- Waste quantity reduction/elimination:
  - Reduced the number of chemical reagents and intermediates from 28 to 11.
  - Eliminated 2 hazardous solid waste streams (SiO$_2$-AlO$_2$ & Pd(OH)$_2$).
  - Eliminated 11 different byproducts from the liquid waste streams.
  - Efficiently recycled and reused 4 of the 5 raw materials not incorporated into the final product.

Involved virtually no protection-deprotection steps, and thus eliminated a potentially hazardous palladium catalyzed hydrogenation step.

The process thus reduced air emissions by $\sim 66\%$ and liquid/solid waste generation by $\sim 89\%$.

- **Yield improved:**
  The process provides more than a 25% increase in overall yield and a 100% increase in production throughput.

- **Greener:**
  The process achieves applying the principles of
  1. Prevent Waste
  2. Increase Atom Economy
  3. Design Less Hazardous Chemical Syntheses
The process designed and used a 4-carbon triester coupling reagent, which generated innocuous byproduct (EtCOOH) via simple hydrolysis.

The process demonstrated the novel design of the direct silylation of guanine, that gives rise to a highly regioselective alkylation and thus less unwanted alkylated byproduct.

For a review of synthetic approaches to N-9 substituted guanines.
- V. V. N. K. V. Prasada Raju, et. al. *ARKIVOC* 2009 (xii) 296-301.

For the study describing a possible approach to selective alkylation of guanines.
References

Case 5.

Polyaspartate

Biodegradable Alternative to Polyacrylate

US Presidential Green Chemistry Challenge Awards:
Award in the small business category 1996
Aspartic acid

2-Aminobutanedioic acid

Polyaspartic acid

Acrylic acid

propenoic acid

Polyacrylic acid

poly(succinimide)
What are polyaspartate and polyacrylate in common?
Polyanion, Hydrophilic, Water soluble
Polyelectrolytes

- Polymers whose repeating units bear an electrolyte group, dissociating in aqueous solution (water) to generate positive or negative charge.
- Also called macroions or polyions or polysalts.
- Can be polyanions or polycations.
- Generally water soluble polymers if their structure is linear.
- The polymer will be highly expanded in aqueous solution.
- Can be modified to function as antiscalant (抗垢劑) and dispersant (分散劑).

Examples
- Polypeptides (proteins), DNA,
- Poly(sodium styrene sulfonate, PSS),
- Polyacrylic acid (PAA).

Polyaspartate

December 3, 2010
Polyacrylate (PAC)

**Synthesis**

Polyacrylate

\[
\text{COOH} \quad \text{H} \quad \text{H} \\
\downarrow \quad \text{free radical polymerization} \\
\text{H} \quad \text{H} \quad \text{H} \\
\text{NaOH} \\
\text{H} \quad \text{H} \quad \text{H} \\
\downarrow \\
\text{COO}^{-} \quad \text{Na}^{+} \\
\text{n} \\
\text{Polyacrylate} \\
\text{Na} \quad \text{H} \\
\text{COOH} \\
\text{n} \\
\text{Polyacrylic Acid} \\
\text{H} \quad \text{H} \\
\text{H} \\
\text{Na} \quad \text{H} \\
\text{COOH} \\
\text{n}
\]

PAC can function as both an antiscalant (抗垢劑) and a dispersant (分散劑).
PAC and the Environment

- PAC is nontoxic and environmentally benign, **but it is not biodegradable.**
- Because it is widely used for many applications, it poses an environmental problem from a landfill perspective.
- When PAC is used as an antiscalant or a dispersant, it becomes part of wastewater.
- PAC is nonvolatile and not biodegradable, so the only way to remove it from the water is to precipitate it as an insoluble sludge.
- The sludge must then be landfilled.
- Feedstocks are made from fossil fuels.
Polyaspartate

- Polyaspartate has similar properties to the polyacrylates and so it can be used as a dispersant, or an antiscalant, or a superabsorber.
- Polyaspartate is **nontoxic, biodegradable** (可生物分解的), and environmentally safe.
- Biodegradation results in decomposition of TPA to environmentally benign products such as carbon dioxide and water.
- The **Donlar Corporation** developed an economic way to produce “thermal polyaspartate (TPA)” in high yield (~97%), that eliminates use of organic solvents, cuts waste, and uses less energy.
- Polyaspartate is a biopolymer synthesized from L-aspartic acid, a natural amino acid.
Synthesis of thermal polyaspartate (TPA)

L-aspartic acid

heat (180 °C)

poly(succinimide)

NaOH

60 °C

sodium poly(aspartate)

30% α-linkage
70% β-linkage

Polyaspartate

December 3, 2010
Green Chemistry in ACTION

- In April 1997, Donlar opened the world's largest manufacturing facility for biodegradable polyaspartates, in Peru, Illinois, with a production capacity of more than 30 million pounds a year.
- The opening of this facility resulted in commercial availability of TPA.
- TPA is marketed and sold as a corrosion and scale inhibitor, a dispersing agent, a waste water additive, a superabsorber, and also as an agricultural polymer.
- As an agricultural polymer, TPA is used to enhance fertilizer uptake by plants. Less fertilizer is added to the soil and the environmental impact from fertilizer run-off is reduced.
British Petroleum Exploration and others have achieved success with a TPA additive that helps to sustain the flow of crude from oil wells in North Sea offshore oil fields.

**TPA is a green alternative to Polyacrylate and other currently used water soluble polymers!**

**References**

感謝您的聆聽，請指教