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]。
永續化學合成(4)
可再生性資源在合成上的利用

劉廣定
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(December 3, 2010)
The use of chemicals and solvents from renewable resources

永續化學十二原則 (Anastas and Warner, 1998)
7. A raw material or feedstock should be renewable rather than depleting, whenever technically and economically practicable.

永續工程十二原則 (Anastas and Zimmerman, 2003)
7. Material and energy inputs should be renewable rather than depleting.

永續十律 Ten commandments of sustainability (Manahan, 2005)
7. Material demand must be drastically reduced; materials must come from renewable resources, be recyclable and, if discarded to the environment, be degradable.
Renewable resources and reagents

• Chemicals from renewable feedstock
• CO$_2$, water, carbohydrates and products
• Terpene (essential oils) and lignin
• Fatty acids from fats and oils
• Glycerol as starting materials and solvents
• Organic carbonate and other green substitutes
• etc.
二氧化碳

無毒(但能令人窒息)
不自燃也不助燃
有廉價之高純度商品
液態或超臨界態\textbf{[Liq CO}_2\textbf{ (50-60 bar, rt); SCF CO}_2\textbf{ (>74 bar, >31℃)]}
易除去或回收再用
故可用為溶剤及反應試劑

\textit{Green Chemistry Using Liquid and Supercritical Carbon Dioxide} (DeSimone and Tumas, Ed., Oxford, \textbf{2003})
\textit{Green Reaction Media in Organic Synthesis} (Mikami, Ed., Chapter 4, Blackhill, \textbf{2005})
\textit{Alternative Solvents for Green Chemistry} (Kerton, Chapter 4, RSC, \textbf{2009})
Phase diagram and critical points

![Phase Diagram]

Temperature $T_c$ (°C) | Pressure $P_c$ (bar)
--- | ---
Ammonia | 132.4 | 113.2
Carbon dioxide | 31.1 | 73.8
Ethane | 32.2 | 48.7
Ethene | 9.2 | 50.4
Fluoroform | 25.9 | 48.2
Propane | 96.7 | 42.5
Water | 374.2 | 220.5
Surfactants for SCF-CO₂

(a) \[\text{Organophilic} \quad \text{CO}_2\text{-philic}\]

(b) \[\text{CO}_2\text{-philic} \quad \text{metalophilic}\]

(c) \[\text{CO}_2\text{-philic} \quad \text{metalophilic}\]

Non-fluorinated (ether-carbonate) copolymer by Beckman and coworkers at U. of Pittsburgh. **PGCC Award of 2002**

Chemical reactions in supercritical carbon dioxide
Examples

Hydrogenation in Biphasic IL-scCO₂ system

\[
\text{CO}_2 \text{H} + \text{H}_2 \xrightarrow{\text{(i) Ru(O}_2\text{CMe)}_2(\text{tolBINAP})} \xrightarrow{\text{[Bmim]}\text{PF}_6 / \text{H}_2\text{O}} \xrightarrow{\text{(ii) SFE, 35 °C, 175 bar, 1 ml min}^{-1}} \text{CO}_2 \text{H}
\]

conversion >95%

ee 85-91%

Biocatalytic esterification

(Kerton, pp. 81-82)

Suzuki coupling

90°C, 20MPa, 24h
61-99% yield

(Green Chem. 2010, 12, 1758-1766)
Courtesy of Professor C. M. Wai, U. Idaho.
Hydrogenation of nitrile in scCO$_2$: a tunable approach to amine selectivity

Chatterjee, et al. Green Chem. 2010, 12, 87-93

By tuning the CO$_2$ pressure changes the product selectivity (more than 90%) from benzylamine to dibenzylamine, with 90+% conversion.
CO₂ Transformations

Incertion of CO₂ into M-H, M-C and M-O bonds
(Darensbourg *Inorg. Chem.* 2010, 49, 10765-10780)

Direct carboxylation with CO$_2$

Greenhouse gas makes good


Angew. Chem. **2010**, **49**, 8674-8677
Aerobic oxidative carboxylation of olefins with metalloporphyrin catalysts


Amidine-mediated delivery of CO$_2$ from gas phase to reaction system for highly efficient synthesis of cyclic carbonates from epoxides

Production of **Dimethyl carbonate (DMC)** from ethylene oxide and CO₂ as a more effective way for the **reuse of CO₂**

*(Clean Technologies and Environmental Policy 2009, 11(4), 459-472)*

Cyclic carbonates from epoxides and CO₂

*(Review: Green Chem. 2010, 12, 1514-1539)*

Cat. 1: MgO, CaO

Cat. 2: zeolites exchanged with alkali or alkali earth metal ions
Transesterification of Cyclic Carbonates to Dimethyl Carbonate Using Solid Oxide Catalyst at Ambient Conditions: Environmentally Benign Synthesis

*(ChemSusChem 2010, 3, 575-578)*

**Continuous synthesis at ambient conditions:**
Dimethyl carbonate (DMC) is an important methylating and carbonylating agent. Transesterification of cyclic carbonates using methanol for the synthesis of DMC is environmentally benign. CaO–ZnO catalysts, prepared by a wet impregnation method, are effective catalysts for the transesterification of ethylene carbonate using methanol in batch and in continuous reactors. Yields of ca. 84 % DMC can be achieved at ambient conditions
Dimethyl Carbonate as a Green Reagent

Low toxicity, no mutagenic or irritating effect.

Biodegradable (> 90% in 28 days)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point (°C)</td>
<td>4.6</td>
</tr>
<tr>
<td>Boiling point (°C)</td>
<td>90.3</td>
</tr>
<tr>
<td>Density (d₂⁰)</td>
<td>1.07</td>
</tr>
<tr>
<td>Viscosity (μ²⁰, cps)</td>
<td>0.625</td>
</tr>
<tr>
<td>Flashing point (°C, O.C.)</td>
<td>21.7</td>
</tr>
<tr>
<td>Dielectric constant (ε²⁵)</td>
<td>3.087</td>
</tr>
<tr>
<td>Dipol moment (μ, D)</td>
<td>0.91</td>
</tr>
<tr>
<td>ΔH vap (kcal/kg)</td>
<td>88.2</td>
</tr>
<tr>
<td>Solubility H₂O (g/100g)</td>
<td>13.9</td>
</tr>
<tr>
<td>Azeotropical mixtures</td>
<td>With water, alcohols, hydrocarbons</td>
</tr>
</tbody>
</table>

Useful methylation and alkoxy carbonylation agents

\[
\begin{align*}
\leq 90 \text{ C} & \quad \text{PhOH} + \text{CH}_3\text{OCOOCH}_3 & \quad \text{Cat. base} & \quad \text{PhOCH}_3 + \text{CO}_2 + \text{CH}_3\text{OH} \\
\geq 160 \text{ C} & \quad \text{ROH} + \text{CH}_3\text{OCOOCH}_3 & \quad \text{Cat. base} & \quad \text{ROCOOCH}_3 + \text{CH}_3\text{OH}
\end{align*}
\]

(Tundo and Selva, in *Methods and Reagents for Green Chemistry*, pp. 77-102)
Methylation of 2-naphthol using dimethyl carbonate under continuous-flow gas-phase conditions

Continuous Acid-Catalyzed Methylation in Supercritical CO₂: Comparison of Methanol, Dimethyl Ether and Dimethyl Carbonate as Methylating Agents

Optimised MW-assisted synthesis of methylcarbonate salts: a convenient methodology to prepare intermediates for ionic liquids

Holbrey, et al., Green Chem. 2010, 12, 407-410
Organic carbonates as solvents

(Chem. Rev. 2010, 110, 4554-4581)

Table 1. Transport and Thermodynamic Properties

<table>
<thead>
<tr>
<th>organic carbonate</th>
<th>bp [K]</th>
<th>$d$ (293 K) [g/cm$^3$]</th>
<th>viscosity (298 K) [cP]</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMC</td>
<td>$363^b$</td>
<td>$1.07^b$</td>
<td>$0.590^b$</td>
</tr>
<tr>
<td>DEC</td>
<td>$399^b$</td>
<td>$0.98^b$</td>
<td>$0.753^c$</td>
</tr>
<tr>
<td>BC</td>
<td>$521^d$</td>
<td>$1.34^{a,d}$</td>
<td>$2.56^{a,d}$</td>
</tr>
<tr>
<td>PC</td>
<td>$515^d$</td>
<td>$1.20^d$</td>
<td>$2.50^d$</td>
</tr>
<tr>
<td>BC</td>
<td>$524^d$</td>
<td>$1.14^d$</td>
<td>$3.14^c$</td>
</tr>
</tbody>
</table>

Acetone 0.320 cP
Water 0.891 cP
1-butanol 2.99 cP

The palladium-catalysed direct 2-, 4- or 5-arylation of a wide range of heteroaromatics with aryl halides proceed in moderate to good yields using the eco-friendly solvents carbonates.

Green Chem. 2010, 12, 2053-2063
Polarities and basicity of some solvents

Chem. Rev. 2010, 110, 4564
Organic reactions in aqueous media

Reference books and review articles:

• Adams, et al., *Chemistry in Alternative Reaction Media*, 2004, Wiley
• Li and Chan, *Comprehensive Organic Reactions in Aqueous Media*, 2nd Ed, 2007, Wiley
• Dallinger and Kappe, *Chem. Rev.* 2007, 107, 2563-91 (*MW assisted*)
• Minakata and Komatsu, *Chem. Rev.* 2009, 109, 711-724 (*on silica*)
• Chanda and Fokin, *Chem. Rev.* 2009, 109, 725-748 (*on water*)
# Dielectric and ionization constants

<table>
<thead>
<tr>
<th></th>
<th>Ambient</th>
<th>Near-critical</th>
<th>Supercritical</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Temperature, °C</strong></td>
<td>25</td>
<td>275</td>
<td>400</td>
</tr>
<tr>
<td><strong>Pressure, bar</strong></td>
<td>1</td>
<td>60</td>
<td>230</td>
</tr>
<tr>
<td><strong>Density, g per cc</strong></td>
<td>1</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Dielectric constant</strong></td>
<td>80</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td><strong>Relative ionization constant</strong></td>
<td>1</td>
<td>1,000</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

\[ a \text{ Kw/Kw}(25^\circ \text{C}) \]
Reactions in near-critical water (NCW)

No acid or base catalyst is required. Also for other hydrolysis, hydration, elimination, rearrangement, etc.
Some microwave assisted reactions at NCW

Fischer indole synthesis

\[
\text{苯胺} + \text{乙酸乙酯} \xrightarrow{\text{H}_2\text{O}} \text{苯并咪唑} \\
\text{MW, 270 °C, 49 bar, 30 min}
\]
isolated yield 64%
(column chromatography, \(\text{CH}_2\text{Cl}_2\))

Diels-Alder reaction

\[
\text{1,3-二烯} + \text{氰丙烯} \xrightarrow{\text{H}_2\text{O}} \text{六元环}
\]
\text{MW, 295 °C, 77 bar, 20 min}
conversion 100%
isolated yield 65%
(extraction, \(\text{Et}_2\text{O}\)
(column chromatography, \(\text{CH}_2\text{Cl}_2\))

(Kerton, p. 88)
This short review focuses on the potential use of water as a reaction solvent, highlighting advantages and the range of reactions that can be carried out in water.

Hydrophobic Effects

Figure 5.5  The hydrophobic effect. Aggregation of hydrocarbon molecules in water reduces the number of molecules with restricted motion.

Scheme 5.1  Indium mediated imine coupling

(Adams, p.101)
**Diels-Alder Reaction**

Enhanced Selectivity and Reactivity

![Diels-Alder Reaction Diagram](image)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Kinetics $10^5 k$ (M$^{-1}$s$^{-1}$)</th>
<th>Selectivity Endo/Exo Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>isoctane</td>
<td>5.94$^a$</td>
<td></td>
</tr>
<tr>
<td>methanol</td>
<td>75.5$^a$</td>
<td>8.5$^c$</td>
</tr>
<tr>
<td>formamide</td>
<td>318$^b$</td>
<td>8.9$^b$</td>
</tr>
<tr>
<td>ethylene glycol</td>
<td>480$^b$</td>
<td>10.4$^b$</td>
</tr>
<tr>
<td>water</td>
<td>4400$^a$</td>
<td>25$^d$</td>
</tr>
<tr>
<td>water (LiCl 4.86 M)</td>
<td>10800$^a$</td>
<td>28$^d$</td>
</tr>
<tr>
<td>water ((NH$_2$)$_3$CCl 4.86 M)</td>
<td>4300$^a$</td>
<td>22$^d$</td>
</tr>
<tr>
<td>$\beta$-cyclodextrin (10 mM)</td>
<td>10900$^a$</td>
<td></td>
</tr>
<tr>
<td>$\alpha$-cyclodextrin (10 mM)</td>
<td>2610$^a$</td>
<td></td>
</tr>
</tbody>
</table>
Suzuki–Miyaura Cross-Coupling Reactions in Aqueous Media: Green and Sustainable Syntheses of Biaryls

Suzuki–Miyaura reactions are among the most widely used protocols for the formation of carbon–carbon bonds. These reactions are generally catalyzed by soluble palladium complexes with various ligands. However, the use of toxic organic solvents remains a scientific challenge and an aspect of economical and ecological relevance. **This review** will summarize various recently developed significant methods by which the Suzuki–Miyaura coupling was conducted in aqueous media, and analyzes if they are “real green” protocols.

Grignard-type Reactions

**Allyl indium (1)**

Indium has low first ionization potential (5.70 eV), and is not sensitive to water or base. The regioselectivity is governed by the bulkiness of the substituent on the C=C.
Grignard-type Reactions

Similarly, in the tin-mediated allylation reaction, allyltin intermediates are generated (13). Both allyltin(II) bromide (2) and diallyltin(IV) dibromide (3) are formed, and can be observed by NMR in the aqueous media (Scheme 3).

High chemoselectivity
Organic Reactions on Silica in Water

Heterogenization of homogeneous catalytic reaction allows for the facile recovery and recycling of catalysts. Two basic approaches have been developed.

1. Immobilization of catalysts on silica supports in a water-only phase.

2. To employ a biphasic system:
   - Water – organic solvent
   - Water – ionic liquid
   - Fluorous reverse-phase silica and water

Silica without modification is also generally used.
Mesoporous Silica-supported catalyst and Suzuki Coupling

1) $\text{Br}^-\text{KOH}$
2) EtBr, KOH
3) $\text{H}_2\text{PtCl}_6$, HSi(OEt)$_3$
4) SBA-15

$\text{HO-} \xrightarrow{\text{Pd(PPh}_3)_4} \text{HO-} $ SBA-Si-PEG-Pd(PPh$_3$)$_4$

$\text{HO-} \text{I} + \text{PhB(OH)}_2 \xrightarrow{\text{SBA-Si-PEG-Pd(PPh}_3)_4, (0.001 \text{ mol\%}) \xrightarrow{\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}} \xrightarrow{\text{H}_2\text{O, 50 °C, 24 h}} \text{HO-} \text{Ph}$

98%
Straightforward radical organic chemistry in neat conditions and on water

Shapiro et al., *Green Chem.*, 2010, 12, 582 - 584

Radicals generated during aldehyde oxidation to carboxylic acids can be efficiently trapped under environmentally friendly conditions, either in neat conditions or “on water.”
Switchable Water: Aqueous Solutions of Switchable Ionic Strength

Mercer and Jessop, *ChemSusChem* 2010, 3, 467-470
The method has been shown to be successful for a wide range of electron-deficient and electron-neutral aryl substrates, which results in their direct precipitation from the reaction mixture in >70% yields. The aqueous process can be readily scaled up and has significant environmental benefits.

A Scalable Zinc Activation Procedure Using DIBAL-H in a Reformatsky Reaction

Chemicals from renewable feedstocks

Monographs:


Review articles:

• Chem. Rev. 2007, 107, 2411-2502 (general)
• Chem. Soc. Rev. 2007, 36, 1788-1802 (polymers)
• Green Chem. 2008, 10, 13-30 (glycerol)
• Chem. Soc. Rev. 2008, 37, 527-549 (glycerol, commodity chemicals)
• Green Chem. 2009, 11, 13-26 (succinic acid)
• ChemSusChem 2009, 2, 1072-1095 (myrcene)
• Green Chem. 2010, 12, 539-554 (biorefinery carbohydrates)
• Chem. Rev. 2010, 110, 3552-3599 (lignin)
• Green Chem. 2010, 12, 1127-1138 (glycerol as solvents)
• ChemSusChem. 2010, 3, 1227-1235 (lignin)
Renewable resources: Carbohydrates (sugar, starch, cellulose, etc.), 75%
Lignin, 20%
Fats and oils, proteins, terpenes, etc., 5%

An idealized bio-refinery

BIOMASS FEEDSTOCKS

Pretreatment: Starch, Cellulose, Hemicellulose

(Bio)Processing: Sugars, Syngas

Building blocks: Sugars derived biochemicals, Biofuels, Aromatics

Derived chemicals: General chemical intermediates, monomers, solvents, etc.

Product uses: Industrial, transportation, textiles, food packaging, consumer goods
**Carbohydrates**

- Hemicellulose (containing xylose, arabinose, glucose, etc.)
- Sucrose (glucose and fructose)

- **β-1,4’-glycosidic linkage**

- **α-1,4’-glycosidic linkage**

**Starch**

**Sorbitol, Xylitol** \( C_5H_{12}O_5, \text{HOCH}_2(\text{CHOH})_3\text{CH}_2\text{OH} \) isomers

\[ \text{Sorbitol, Xylitol} \quad C_5H_{12}O_5, \quad \text{HOCH}_2(\text{CHOH})_3\text{CH}_2\text{OH} \quad \text{isomers} \]

\[ \text{醣類発酵産生乙醇: e.g.} \quad \text{C}_6\text{H}_{12}\text{O}_6 \rightarrow 2 \text{C}_2\text{H}_5\text{OH(ethanol)} + 2\text{CO}_2 \]

\[ \text{Sorbitol, Xylitol} \quad C_5H_{12}O_5, \quad \text{HOCH}_2(\text{CHOH})_3\text{CH}_2\text{OH} \quad \text{isomers} \]
Glucose to other chemicals

Glucose $\rightarrow$ Catechol $\rightarrow$ hydroquinone

$H_3PO_4$ (shikimic acid) $\rightarrow$ quinic acid $\rightarrow$ Catechol $\rightarrow$ hydroquinone

Darths and Frost (MSU), PGCC Award, 1998
More from fermentation of glucose

KOH (1.5 eq)/alumina, MW
(Green. Chem. 2010, 12, 502-506)
Important chemicals from lactic acid

(Ethyl lactate as a solvent)

Acrylic Acid
Acetaldehyde
2,3-pentanedione

Lactic Acid

Oxidation
Pyruvic acid

Hydrogenation
1,2-propanediol

Esterification
Ethyl lactate

Polyactic acid (PLA)
Succinic acid as C-4 building block

Green Chem. 2009, 11, 13-26
Top chemical opportunities from carbohydrates

**DOE(USA, 2004)**
- Succinic, fumaric and malic acids
- 2,5-Furandicarboxylic acid (FDCA)
- 3-Hydroxypropionic acid
- Aspartic acid
- Glucaric acid
- Glutamic acid
- Itaconic acid
- Levulinic acid
- 3-Hydroxybutyrolactone
- Glycerol
- Sorbitol
- Xylitol

**Bozell and Peterson (suggested 2010)**
- Ethanol
- Furans (Furfural, HMF, FDCA)
- Glucerol and derivtives
- Biohydrocarbons (including isoprenes)
- Lactic acid
- Succinic acid
- Hydroxypropionic acid/aldehyde
- Levulinic acid
- Sorbitol
- Xylitol

*Green Chem. 2010, 12, 539-554*
Inexpensive terpenes to useful chemicals

**Limonene**
- a by-product of the juice industry (ca 50000 tpa)
- a good solvent to replace xylene in medical application
- to give p-cymene by hydrogenation and dehydrogenation

**p-cymene**
- a solvent
- an important intermediate chemical in the fragrance industry
- an intermediate (to terephthalic acid)
- a p-cresol intermediate
- a raw material for synthesis of non-nitrated musks

\[
\text{D-limonene} \xrightarrow{\text{H}_2 + 0.5\% \text{ Pd/SiO}_2, +2\text{H}_2} \text{p-methane} \xrightarrow{\text{heat}} \text{p-cymene}
\]

1,8-Cineole (eucalyptus oil) Pd/gamma-alumina at 250°C → p-cymene + H₂

*(Green Chem. 2010, 12, 70-76)*
Solvent-free dehydrogenation of γ-terpinene in a ball mill: investigation of reaction parameters

(Stolle, Ondruschka, et al. Green Chem. 2010, 12, 1288-1294)

Variation of chemical (oxidant, oxidant-to-substrate ratio) and technical parameters (rotation frequency, number of milling balls, diameter of milling balls)

KMnO₄ or NaIO₄
Alumina, 800 rpm
Size of balls has no difference (d: 2, 10, 15 mm)

Up to 99% yield (selectivity > 99%) within 5 min!
Myrcene as a Natural Base Chemical in Sustainable Chemistry

Takasago (-)-Menthol process

ChemSusChem 2009, 2, 2072-2095

(Catalysis for Renewables, 2007, p. 107)
Beta-Pinene to nopinone


A solvent-free method for the synthesis of nopinone from the renewable monoterpene β-pinene in a ball mill is evaluated. The envisioned synthesis pathway uses non-hazardous reagents and is performed under ambient, non-inert reaction conditions. The influence of both technical and chemical reaction parameters on conversion, selectivity, and yield is assessed.

Fats and oils (Triglycerides)

Soybean oil is a statistical mixture of glycerol esters of palmitic acid (10%), stearic acid (3%), oleic acid (23%), linoleic acid (55%), and linolenic acid (9%).

and glycerol (glycerin) \( \text{CH}_2(\text{OH})\text{CH(OH)CH}_2\text{OH} \)
Bio-refinery of vegetable oils

- Polyols for polyurethanes
- Vegetable oil

  Transesterification

  - Glycerine
  - Biodiesel

  Many applications

  - Fatty acid ester

  Metathesis

  - Ethenolysis

  1-Decene

  Metathesis catalyst

  - 1-Decene

  +

  - Methyl 9-decenoate

Solvents, etc.

- α,ω-Unsaturated esters (9-Decenoate methyl ester)
- α-Olefin (1-decene)

  - Thermosets (Epoxy)
  - Thermoplastic (Nylons)
  - Surfactants, lubricants

  + Polyelefins
  + Surfactants
  + Lubricants
The use of fatty acids and glycerol

- The acidic function (COOH) can be modified.
- The alkene function (C=C) can be modified.
- Glycerol is a sustainable solvent ([Green Chem. 2010, 12, 1127-1138](#))
- Glycerol (glycerin) is a potentially versatile feedstock. ([C&EN, pp. 16-17, June 16, 2009](#))
### Solvents from renewable resources

2-MeTHF  | Ethyl lactate  | γ-Valerolactone  
---|---|---

#### Alcohols and polyols

- Glycerol carbonate
- (and other organic Carbontes)

#### Fatty acid ester (Biodiesel component)

---

**Industrial uses of esteric green solvents**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Industrial use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerol carbonate</td>
<td>Non-reactive diluent in epoxy or polyurethane systems</td>
</tr>
</tbody>
</table>
| Ethyl lactate                 | **Degreaser**  
|                                | Photo-resist carrier solvent                                                  |
|                                | Clean-up solvent in microelectronics and semiconductor manufacture           |
| 2-Ethylhexyl lactate          | **Degreaser**  
|                                | Agrochemical formulations                                                    |
| Fatty acid esters (and related compounds) | Biodegradable carrier oil for green inks  
|                                | Coalescent for decorative paint systems                                       |
|                                | Agrochemical/pesticide formulations                                           |
唯永續化學能使化學永續

歡迎討論

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