



Industrial Organic Chemistry

Dec. 12th, 2017

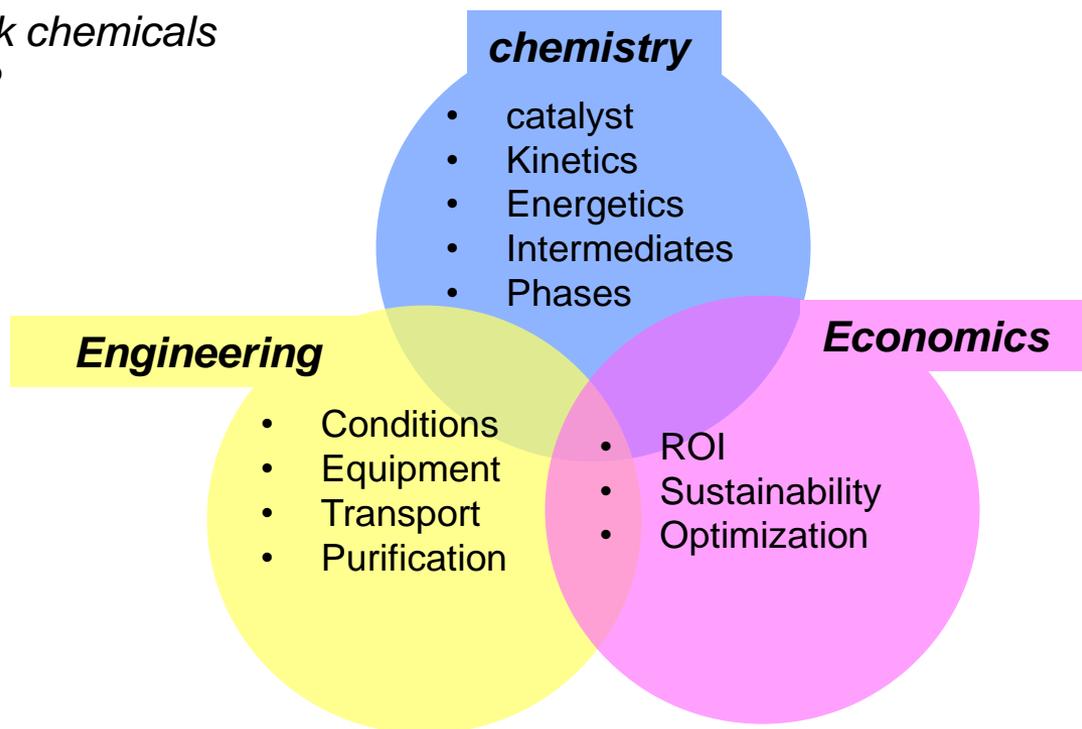
Malek Ibrahim

Group meeting



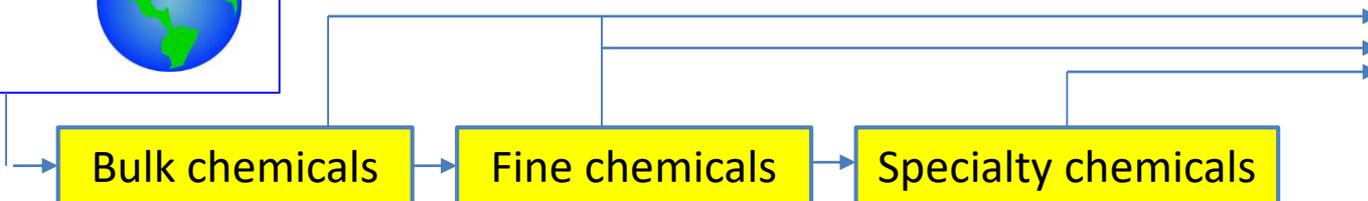
Outline

- *Overview of the organic chemicals industry*
- *Bulk Chemicals*
 - *Effect of raw materials on chemistry*
 - *Enabling technologies*
 - *Examples from industry*
- *Fine & Specialty chemicals*
 - *Comparison against bulk chemicals*
 - *Factors affecting GCMP*
 - *Future directions*



Overview

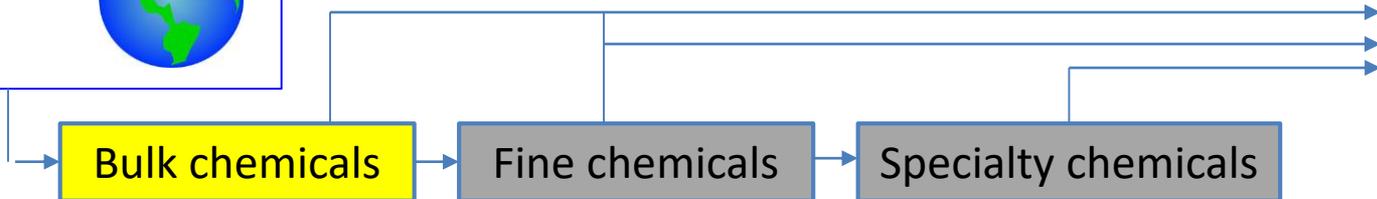
- > 1850 plants & animals, coal
- > 1920 acetylene (from coal)
- > 1950 oil
- > 1973 oil & gas



volume	> 10,000 t/y	< 10,000 t/y	< 1,000 t/y
# of products	100's	1000's	> 10,000's
price	5 \$ /kg	5-20 \$/kg	> 20 \$ kg
Value added	low	moderate	high
Key factor	cost	Function, cost	function

Examples of BC

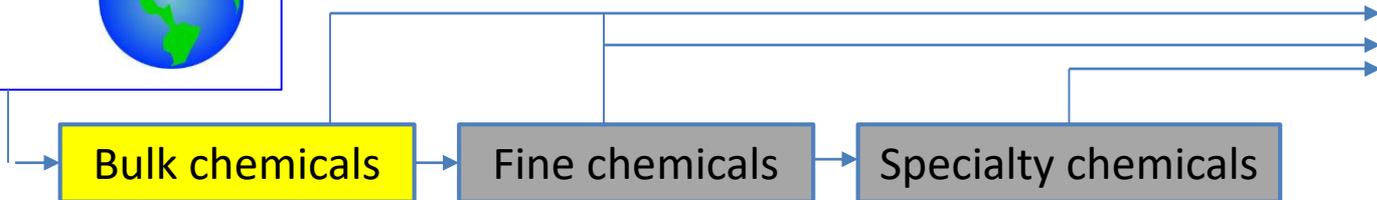
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- *Primary BC: Ethylene, propylene, butadiene, benzene, p-xylene, methanol*
- *Secondary BC: ethylene oxide, ethylene chloride, ethylbenzene, acrylonitrile, terephthalic acid, MTBE, cumene*
- *Tertiary BC: vinyl chloride, polyester, styrene*

Characteristics of BC industry

- > 1850 plants & animals, coal
- > 1920 acetylene (from coal)
- > 1950 oil
- > 1973 oil & gas



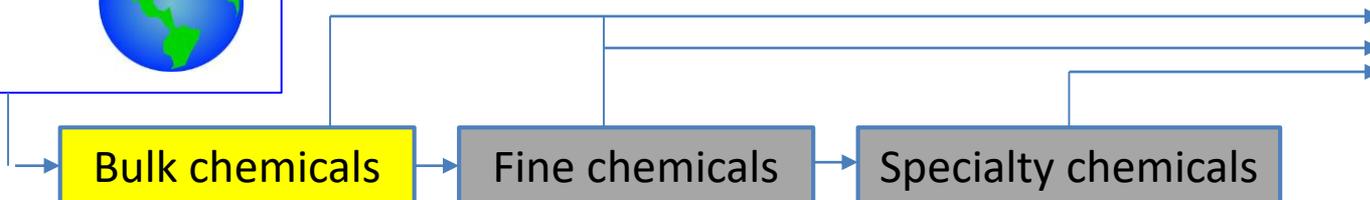
- *Large scale, dedicated production lines*
- *High temperature and pressure for high throughput*
- *Continuous flow chemistry and purification is common*
- *Highly engineered processes*
- *Heterogeneous catalysis (exceptions hydroformylation and p-xylene oxidation)*
- *Large investment, industrial clusters*
- *R&D trend is towards using alternative feedstocks and greener production (2-5 %)*

Big investments: BP, ExxonMobil, Shell, Chevron, SABIC, Sinopec

Process Licensors: Lurgi, Uhde, UOP, KBR, Lummus, Axens, Johnson Matthey

Why is this important for us?

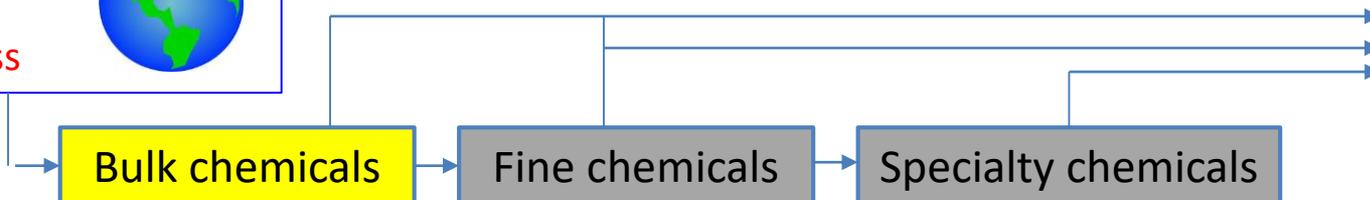
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- *Engineering solutions could be implemented in other sectors (flow chemistry, heterogeneous catalysis...)*
- *Well-studied reaction mechanisms could be intercepted/modified for more complex chemistries*
- *Awareness of the added value by each transformation avoid developing “de-evaluating” chemistries*
- *Help predict impurities in your feedstock and possible side reactions in your chemistry*

Opportunities for org. chemistry in renewables

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- > 1973 oil & gas
- CO₂ and biomass**



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- *Awareness of the value that each transformation adds avoid developing “de-evaluating” chemistries*
- *Help predict impurities in your feedstock and possible side reactions in your chemistry*
- *Awareness of what chemistries are needed to harness emerging feedstocks*

Opportunities for org. chemistry in renewables

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Bulk chemicals

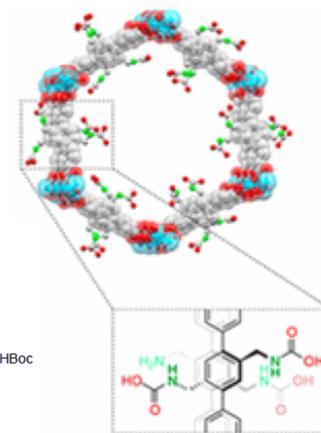
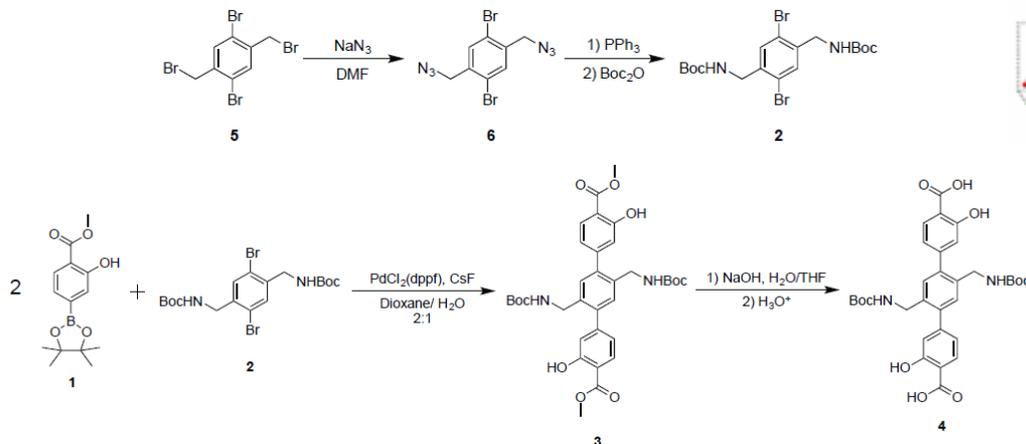
Fine chemicals

Specialty chemicals



Examples:

- CO₂ capture (MOF, hydroxylamines, ionic liquids...)
- CO₂ reactions (carboxylation, RWGS...)
- C-O bond cleavage reactions

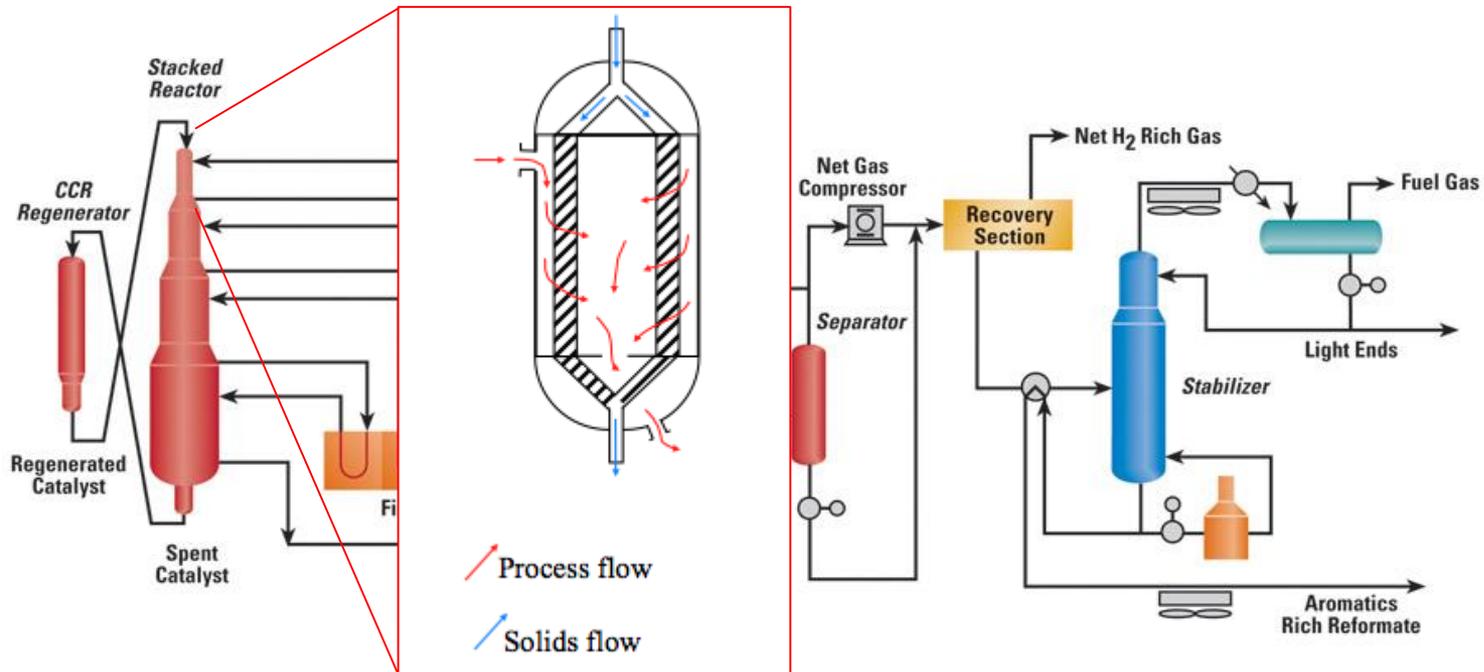
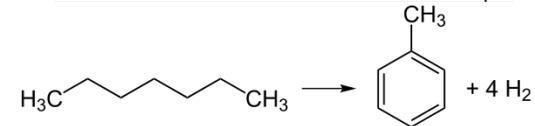
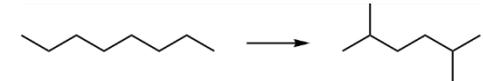
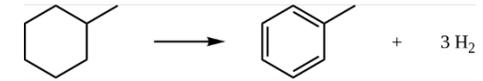


Naphtha reforming

Reactions: dehydrogenation, isomerization, dehydrogenative aromatization

Temperature: 450-550 C

Catalyst: Pt/Al₂O₃ (chlorinated)



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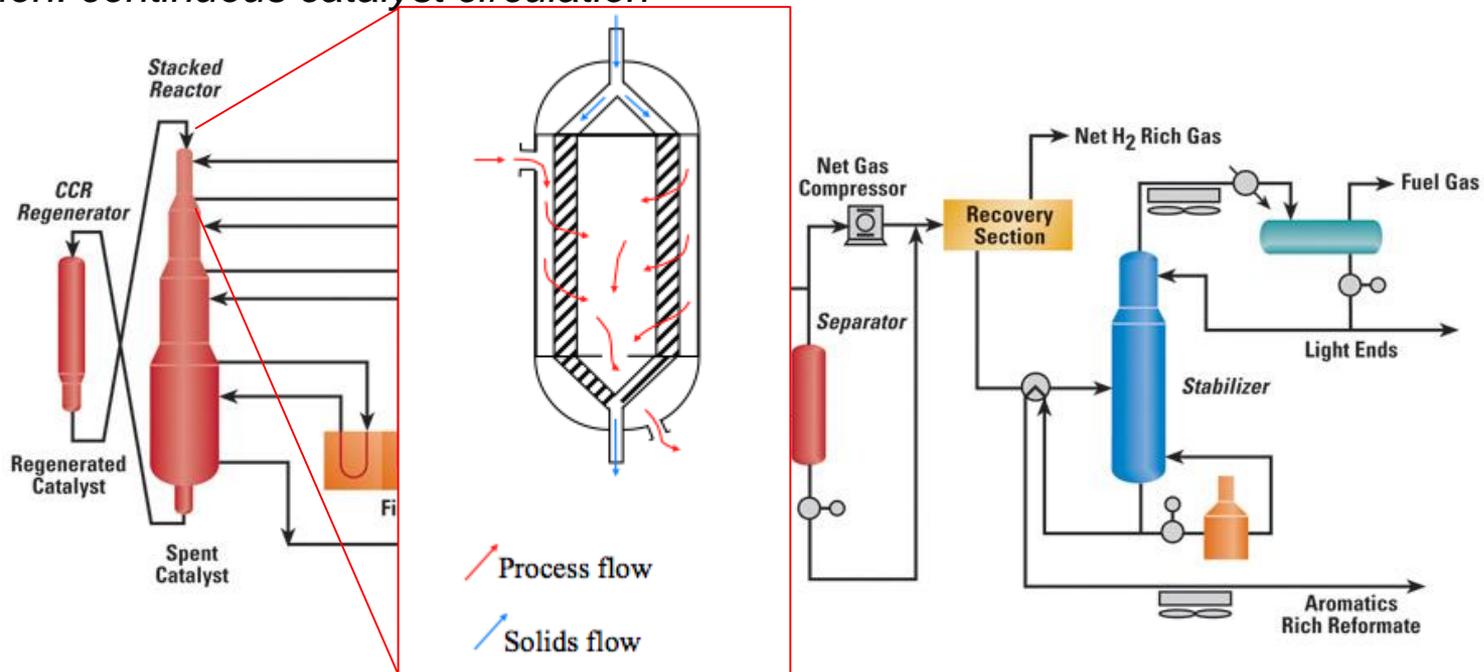
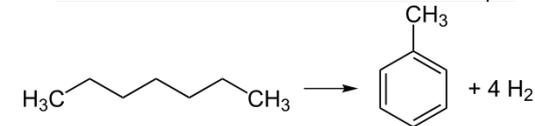
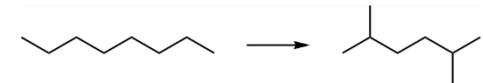
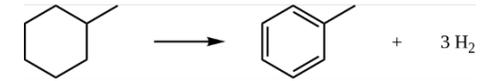
Temperature: 450-550 C

Catalyst: Pt/Al₂O₃ (chlorinated)

Challenges:

-catalyst deactivation by heavy hydrocarbon deposition (coking)

-solution: continuous catalyst circulation



Naphtha reforming

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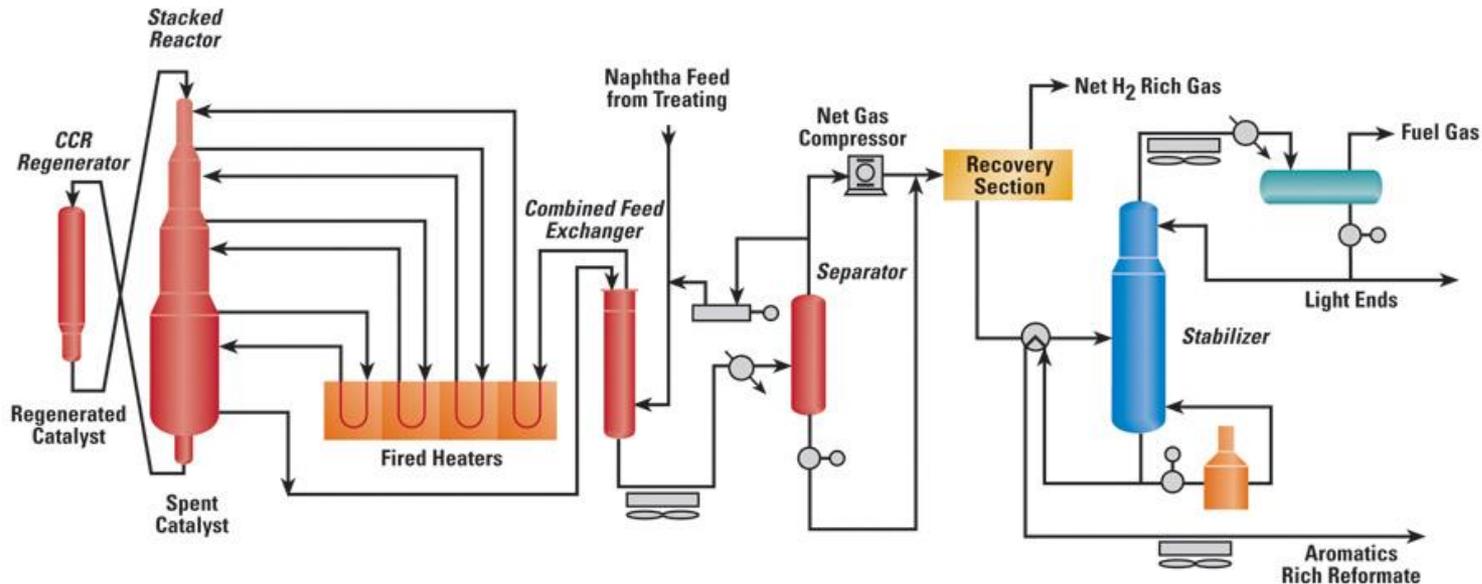
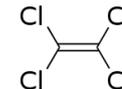
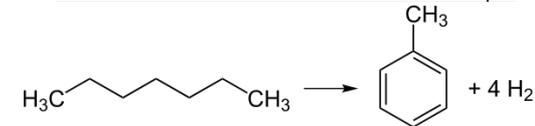
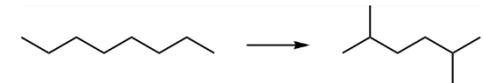
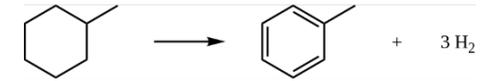
Temperature: 450-550 C

Catalyst: Pt/Al₂O₃ (chlorinated)

Challenges:

-catalyst deactivation by loss of chlorine

-solution: continuous addition of chlorine source (PERC)



Naphtha hydrotreating

Reactions: dehydrogenation, isomerization, dehydrogenative aromatization

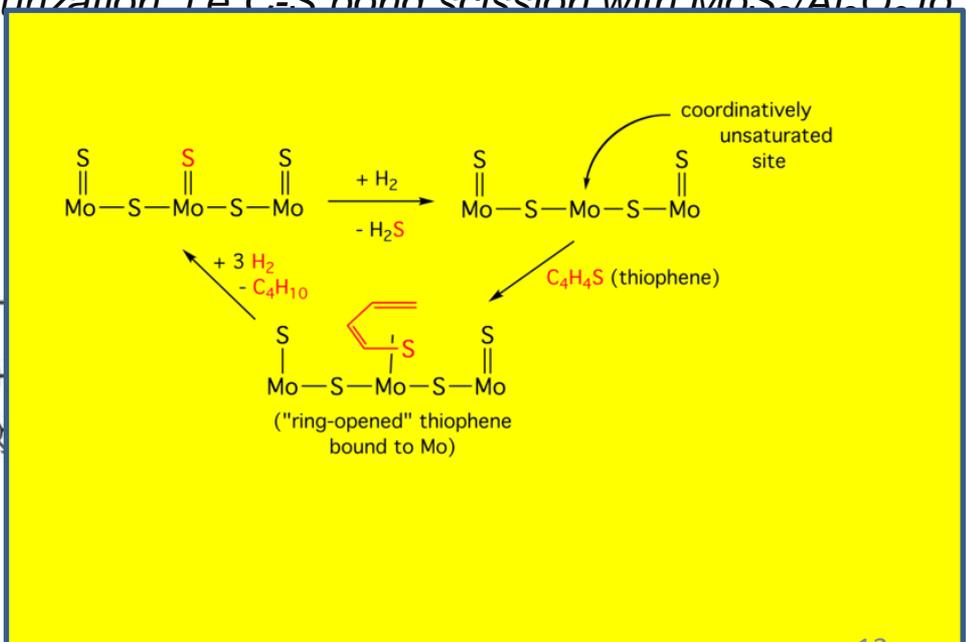
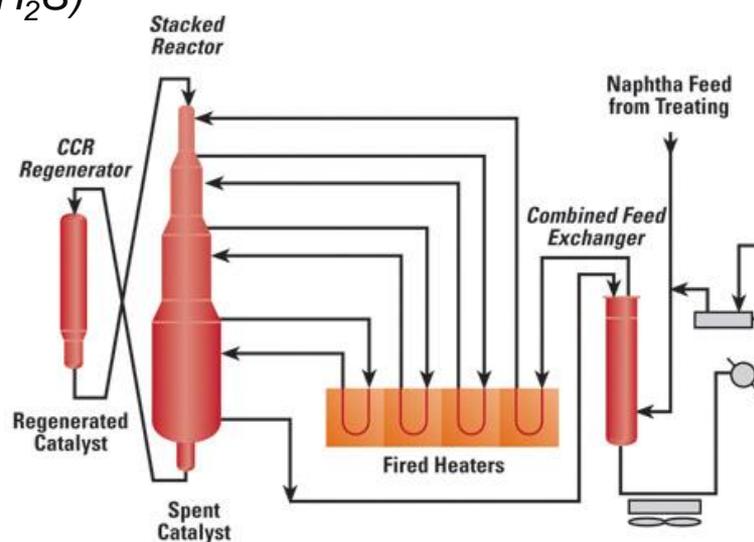
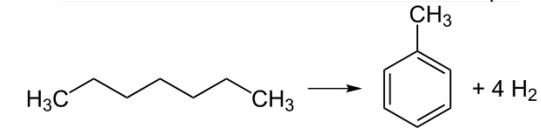
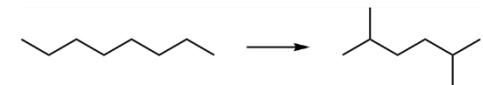
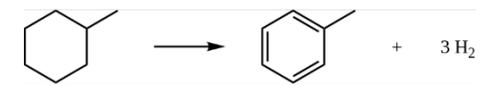
Temperature: 450-550 C

Catalyst: Pt/Al₂O₃ (chlorinated)

Challenges:

-catalyst deactivation by sulfur presence in the feed

-solution: naphtha pretreatment (hydro desulfurization i.e C-S bond scission with MoS₂/Al₂O₃ to form H₂S)



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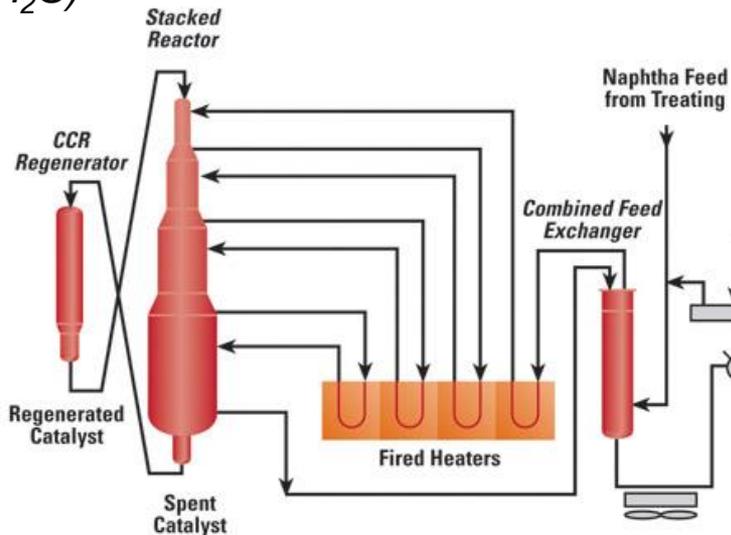
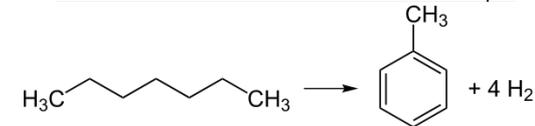
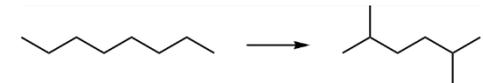
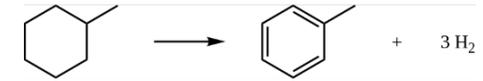


Diagram illustrating the mechanism of **In-situ catalyst sulfiding** on a molybdenum disulfide (MoS₂) catalyst surface.

The diagram shows the reaction of MoS₂ with H₂ to form a coordinatively unsaturated site (CUS) on the catalyst surface, releasing H₂S:

$$\text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo} + \text{H}_2 \rightarrow \text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo} + \text{H}_2\text{S}$$

The coordinatively unsaturated site (CUS) is shown as a Mo atom with a vacant coordination site. This site is then occupied by a thiophene molecule (C₄H₄S), forming a "ring-opened" thiophene bound to Mo:

$$\text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo} + \text{C}_4\text{H}_4\text{S} \rightarrow \text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo}(\text{C}_4\text{H}_4\text{S})$$

The diagram also shows the reaction of the CUS with H₂ to form a C₄H₁₀ molecule, which is a side reaction:

$$\text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo} + 3 \text{H}_2 \rightarrow \text{Mo}-\text{S}-\text{Mo}-\text{S}-\text{Mo} + \text{C}_4\text{H}_{10}$$

The diagram includes a photograph of a large industrial reactor tower and a chemical structure of a disulfide bridge (S-S).

Fluid catalytic cracking

Catalytic cracking: cleavage of C-C bonds in presence of solid acid catalysts (zeolite)

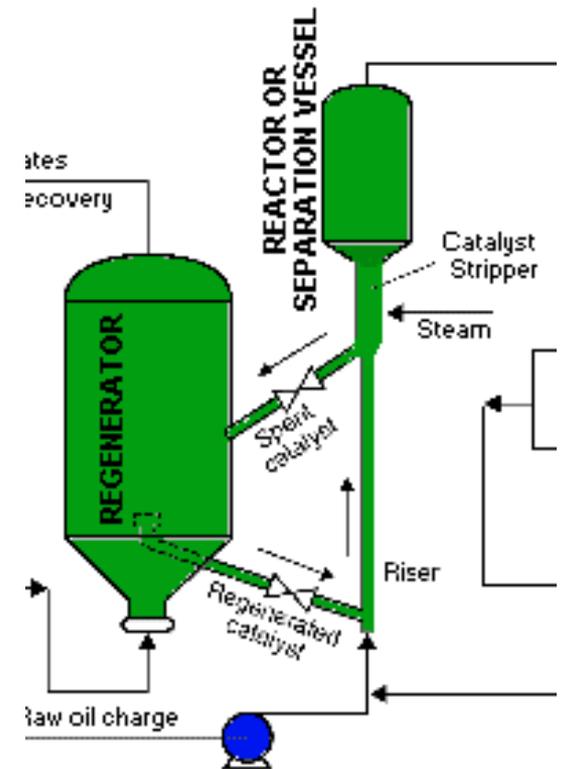
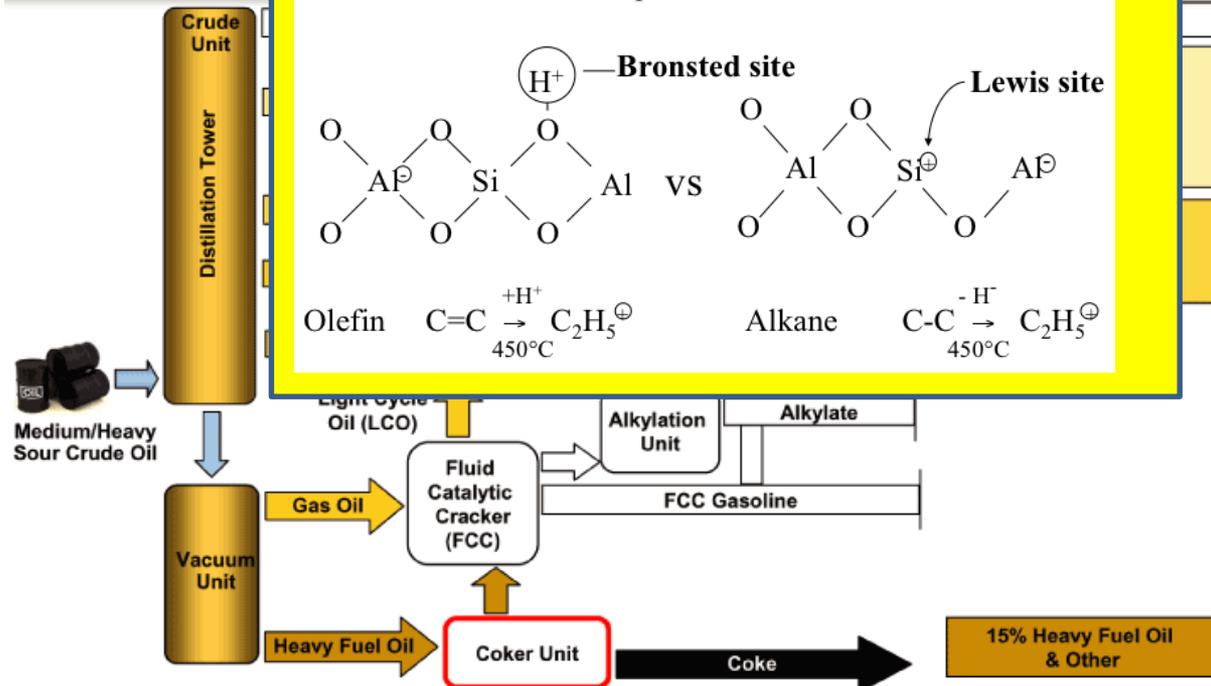
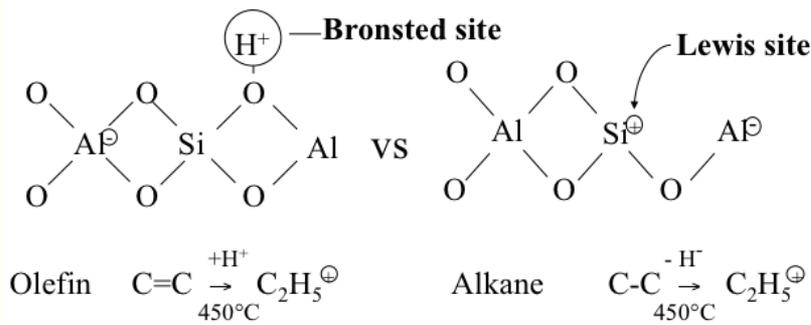
convert less usable longer chains to shorter more useful alkanes and alkenes

Reaction time is very short "milliseconds" ...fluid catalyst riser

Formation of Carbocations on Acid Sites of Catalysts

Bronsted acid sites – donate protons

Lewis acid sites – accept electrons



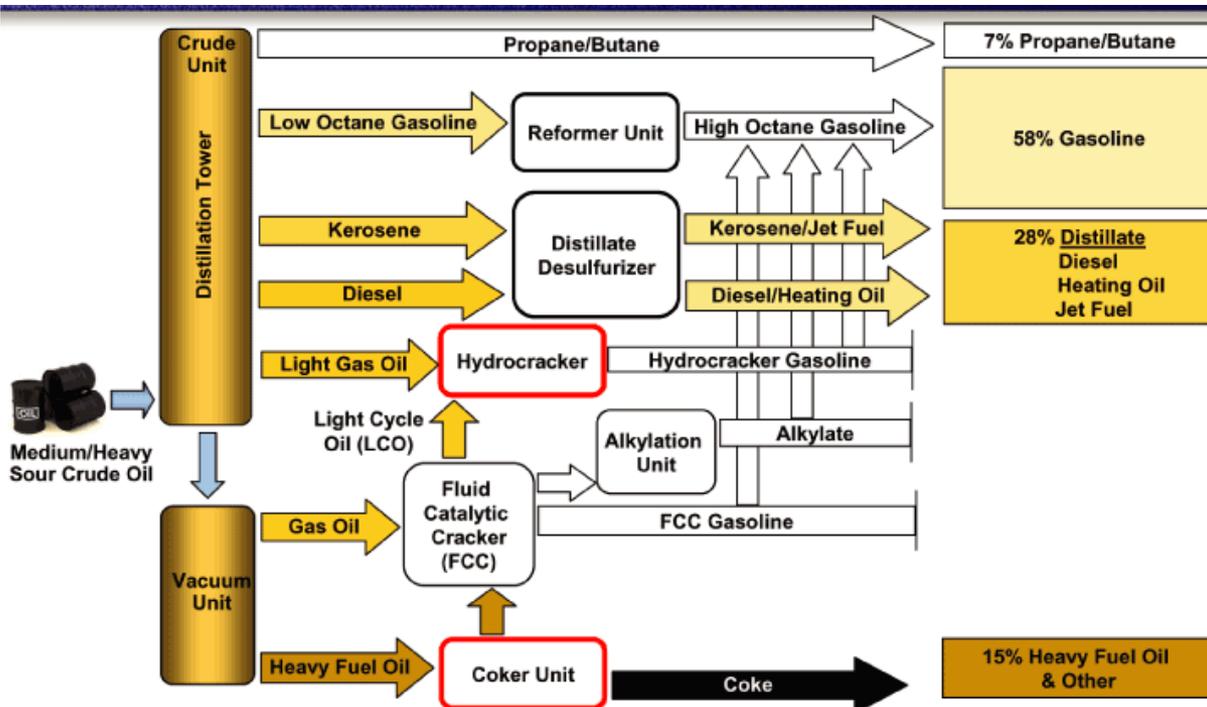
<http://www.apc-network.com>

- High complexity refineries typically run heavier and more sour crude oils and produce the highest yields of lighter/higher value products

Alkylation unit

Alkylation: formation of longer chain alkanes from volatile, shorter alkane/ene

- acid catalyzed by sulfuric or hydrofluoric acid in biphasic reaction
- efforts for finding solid-acid catalyst has been going on for decades, SbF_5 in acid washed silica, triflic acid on porous support...
- in 2015, first solid acid unit was commercialized by Albemarle "AlkyClean"



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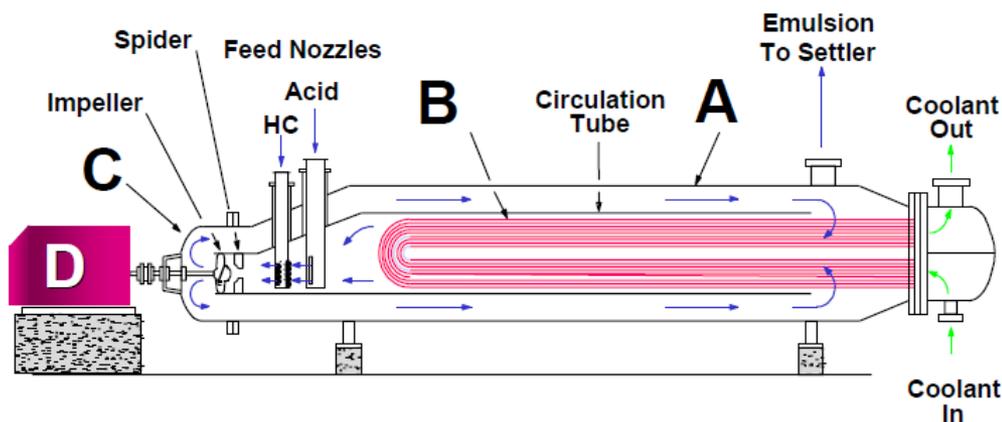
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STRATCO

Contactor™ Reactor

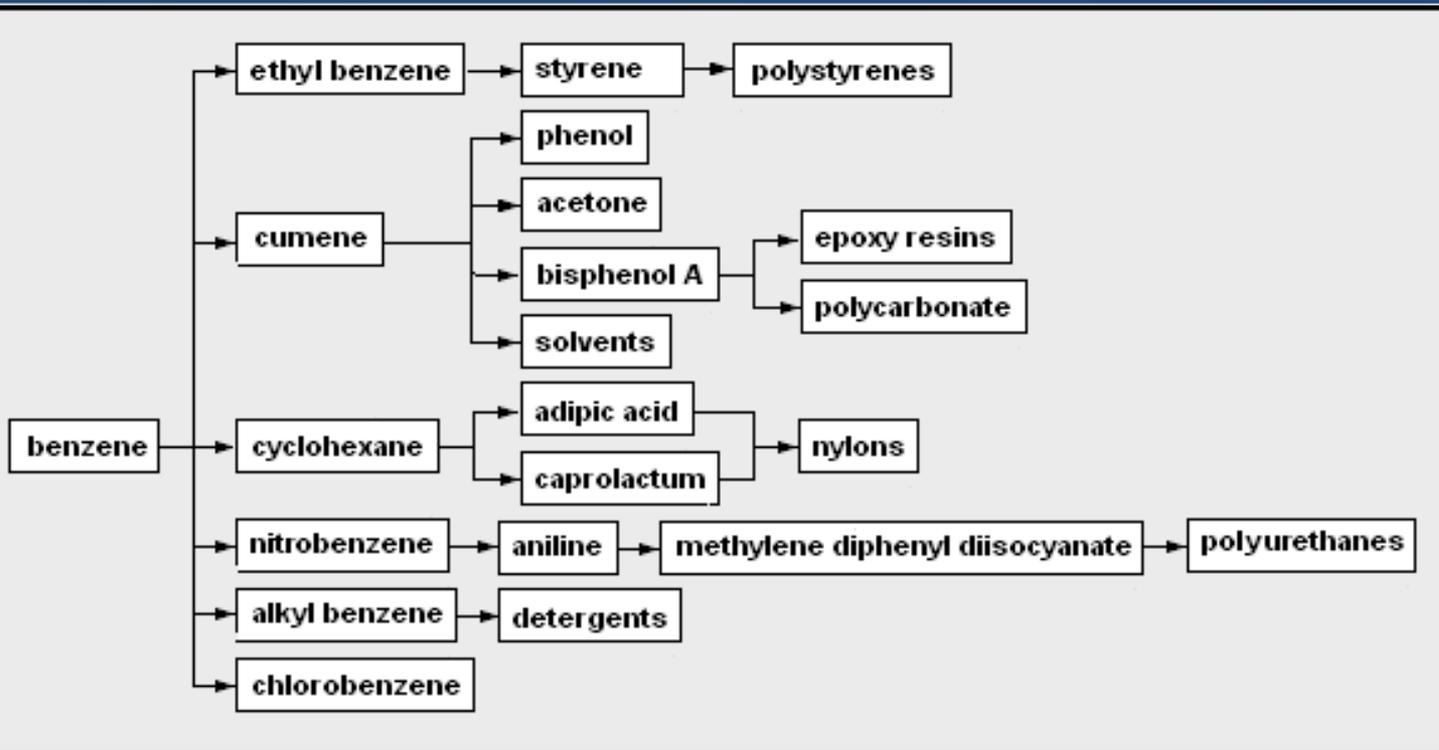


- A - Contactor Reactor Shell
- B - Tube Bundle Assembly
- C - Hydraulic Head Assembly
- D - Motor, Turbine/Driver

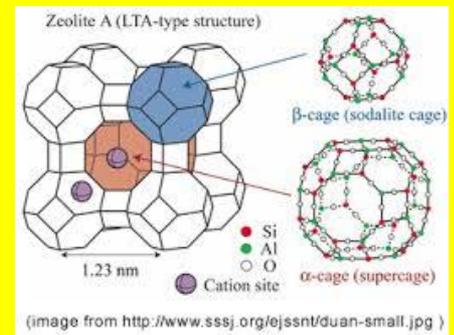
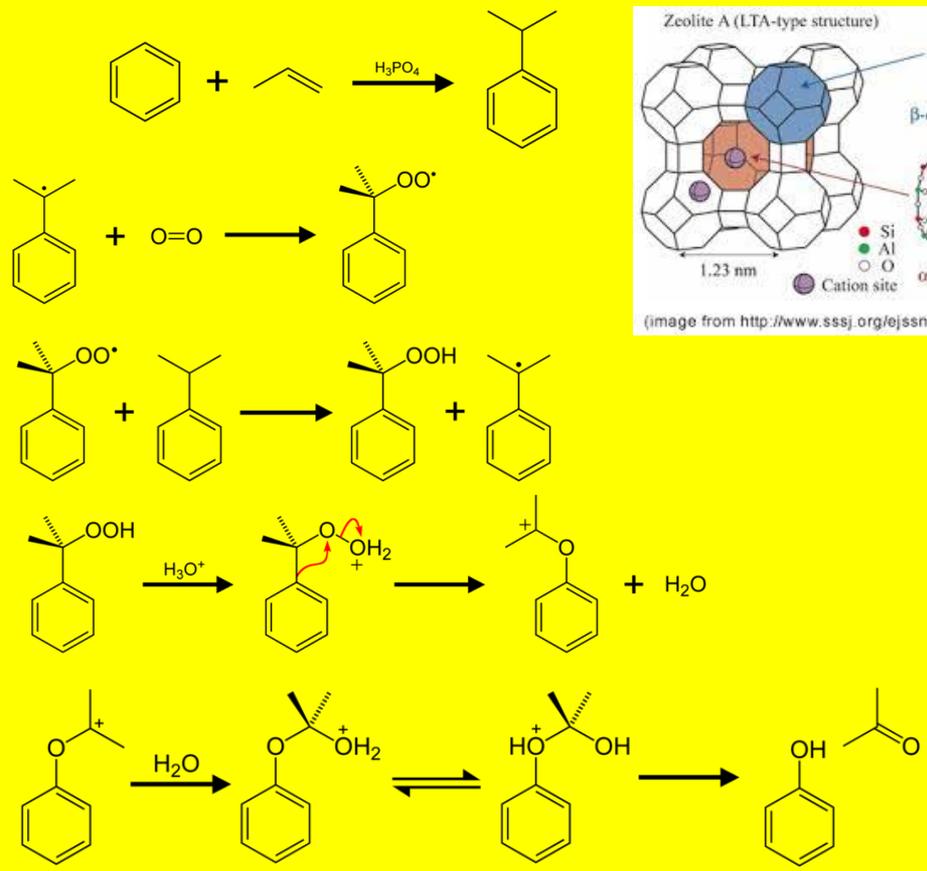
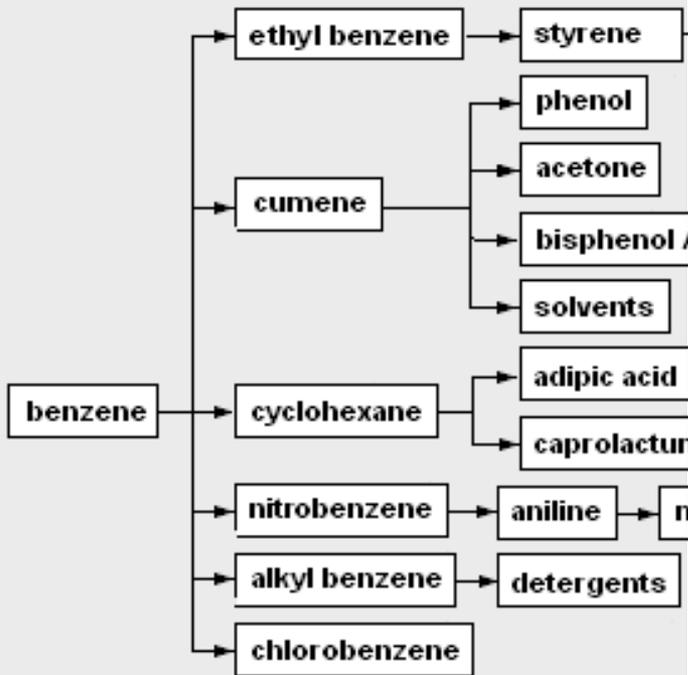


<http://www.dupont.com>

Benzene to chemicals

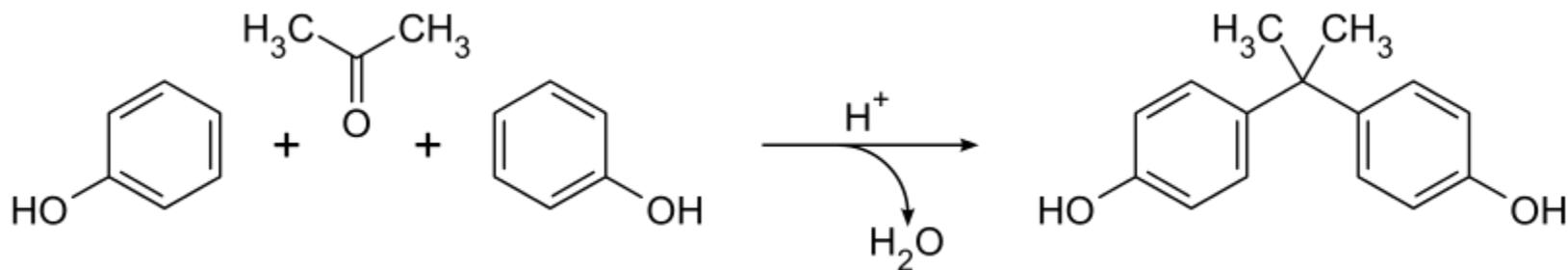
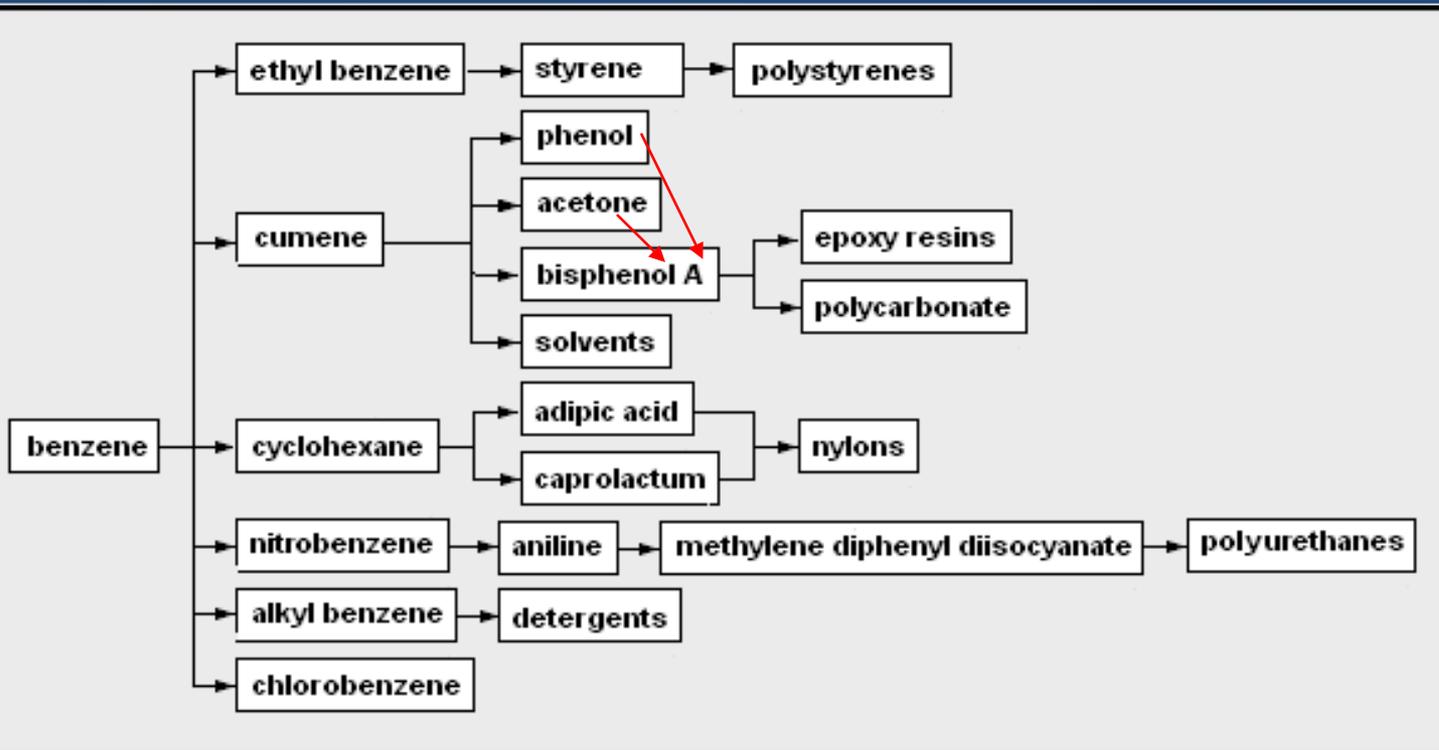


Benzene to phenol

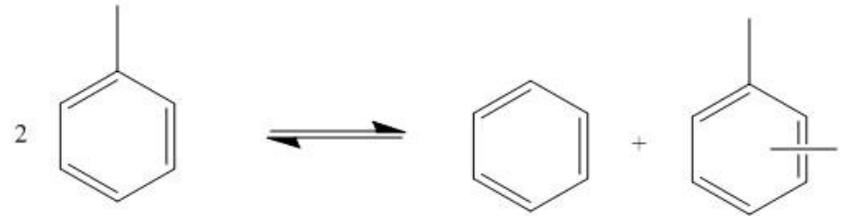
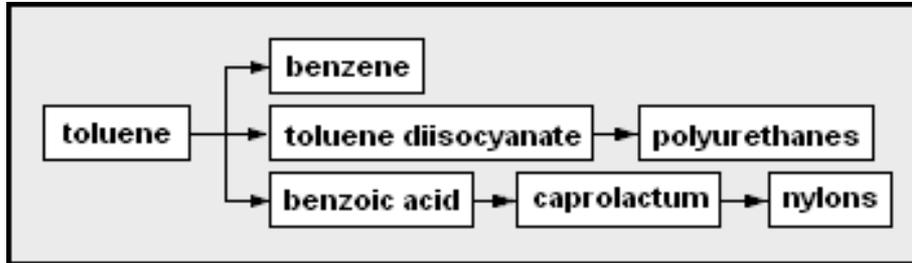


- Gas phase Friedel Craft: phosphoric acid has been replaced by zeolites
- Liquid phase oxidation with air in liquid phase to give phenol and acetone as a byproduct
- Decomposition of the peroxide in presence of acid

Benzene to chemicals



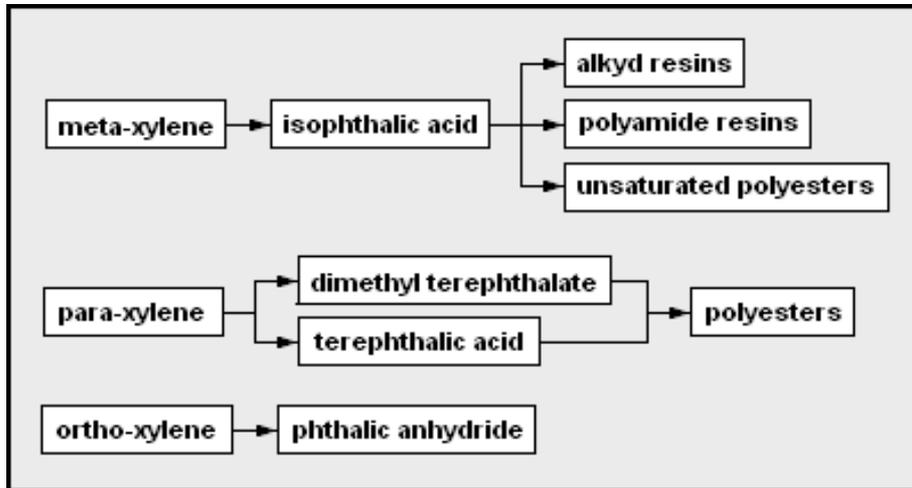
Aromatics to chemicals



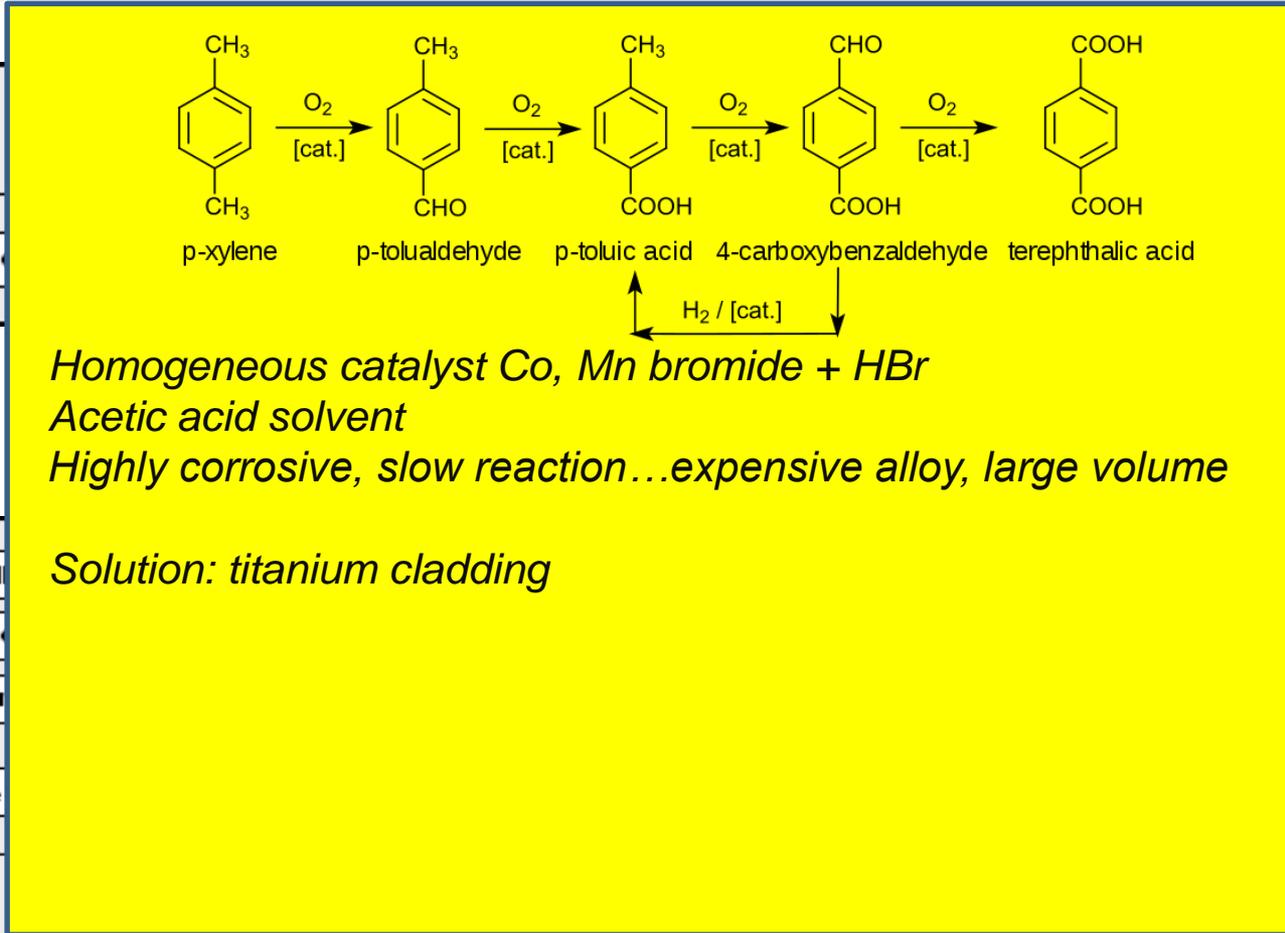
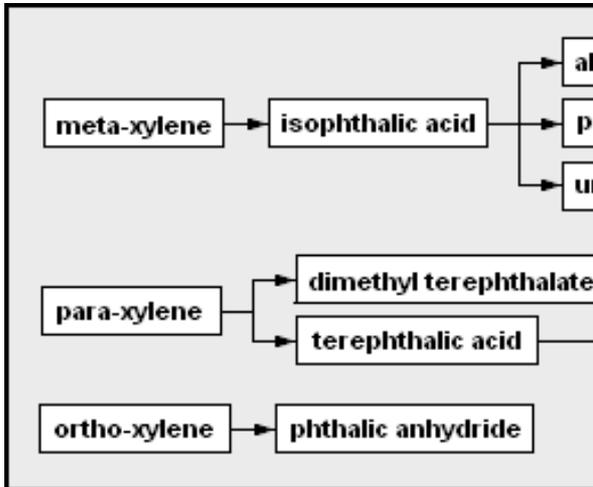
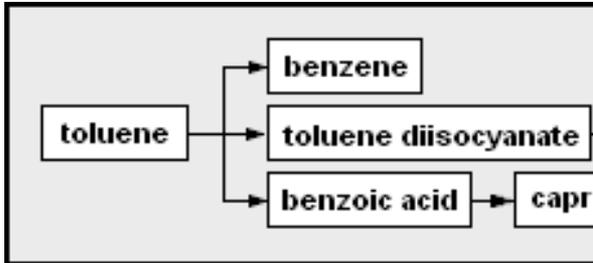
Less applications compared to benzene and xylenes

Trans-alkylation (disproportionation): gas phase conversion of toluene to benzene and xylenes

Zeolite catalysis

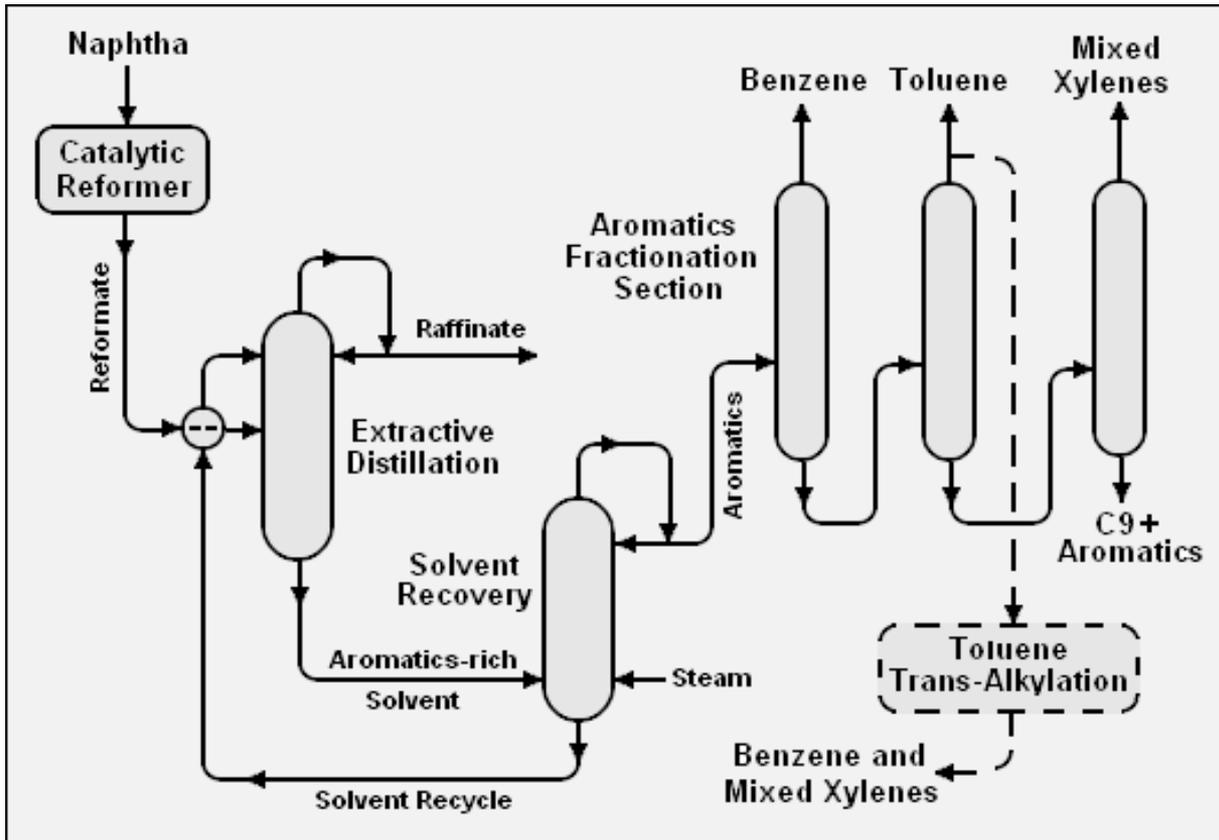


Aromatics to chemicals



Where do these aromatics come from?

Aromatics to chemicals

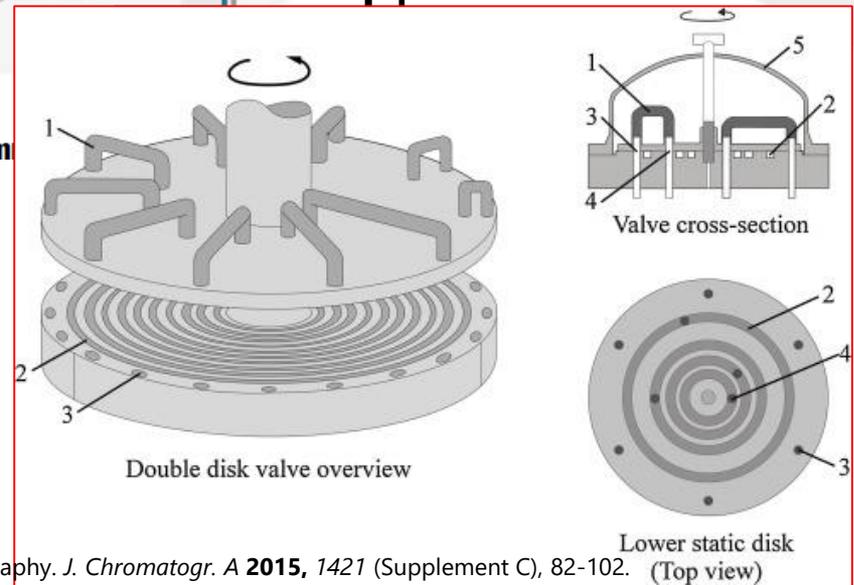
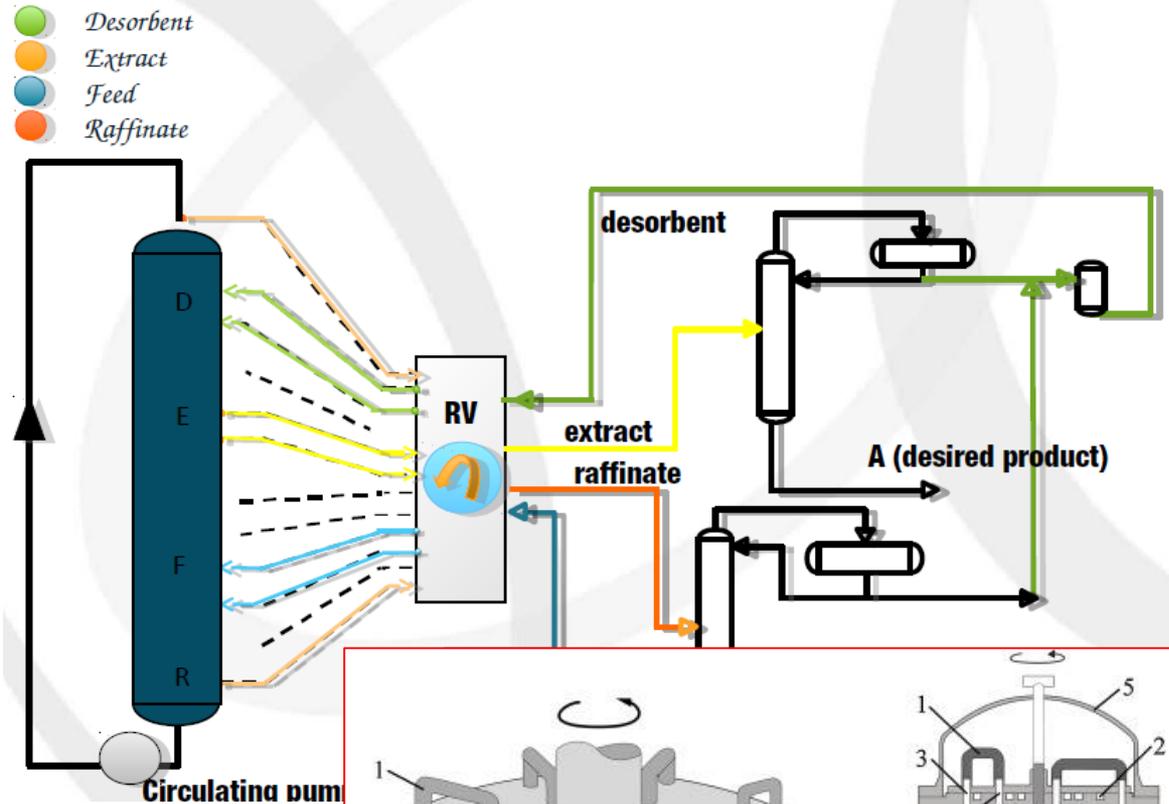
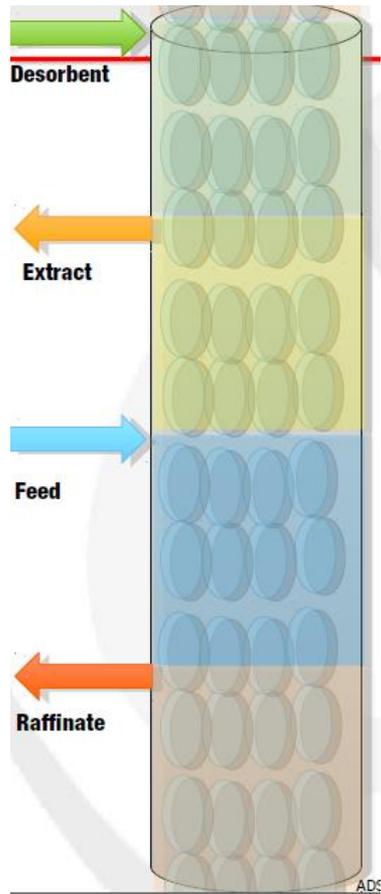


Xylenes separation

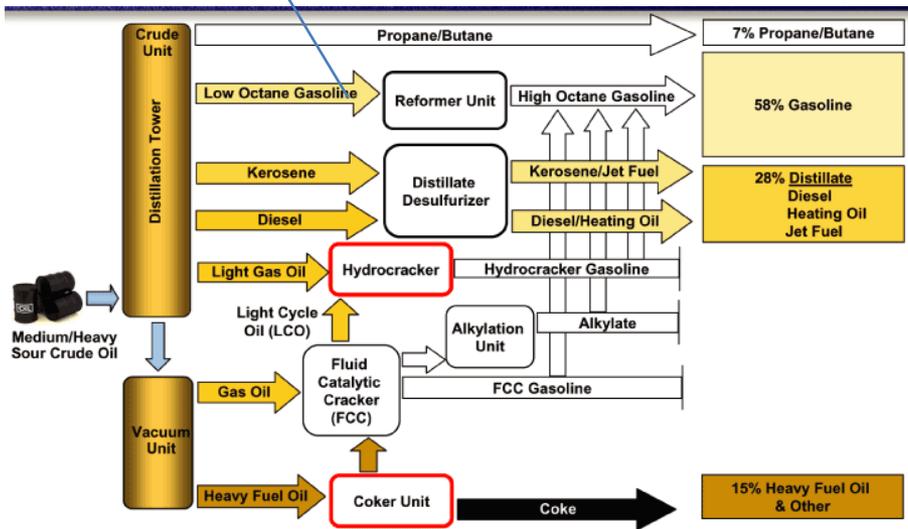
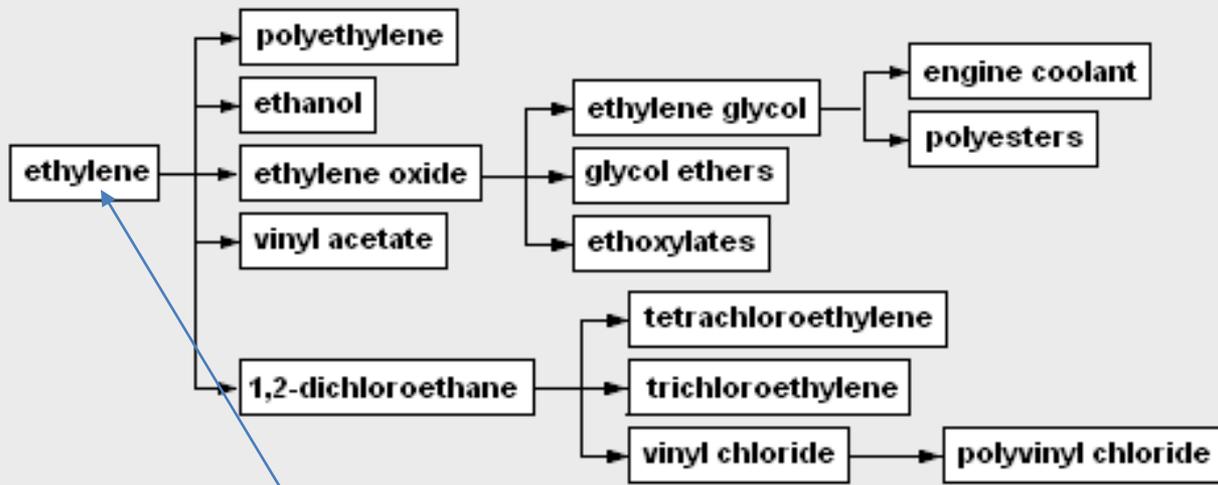
Simulated Moving Bed SMB, using zeolite

<https://www.youtube.com/watch?v=miUgGJO8ptc>

Xylenes separation by SMB



Oil to Olefins

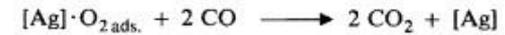
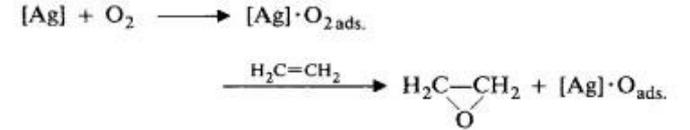
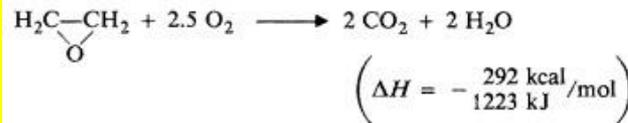
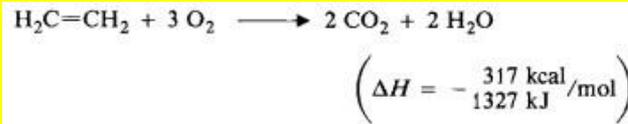
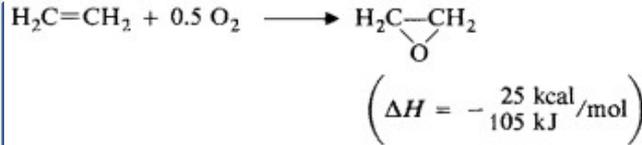
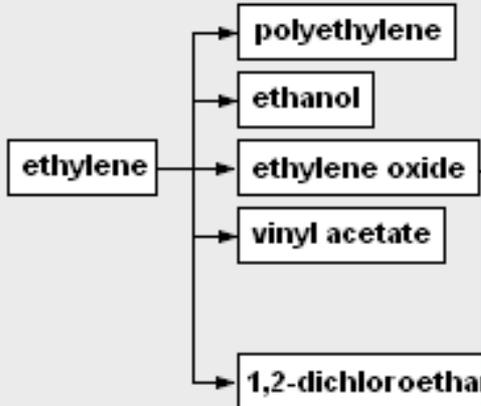


Naphtha again... "cracking" this time
 - high temperature fire heater reactors
 - besides Naphtha, LPG and ethane are often used too

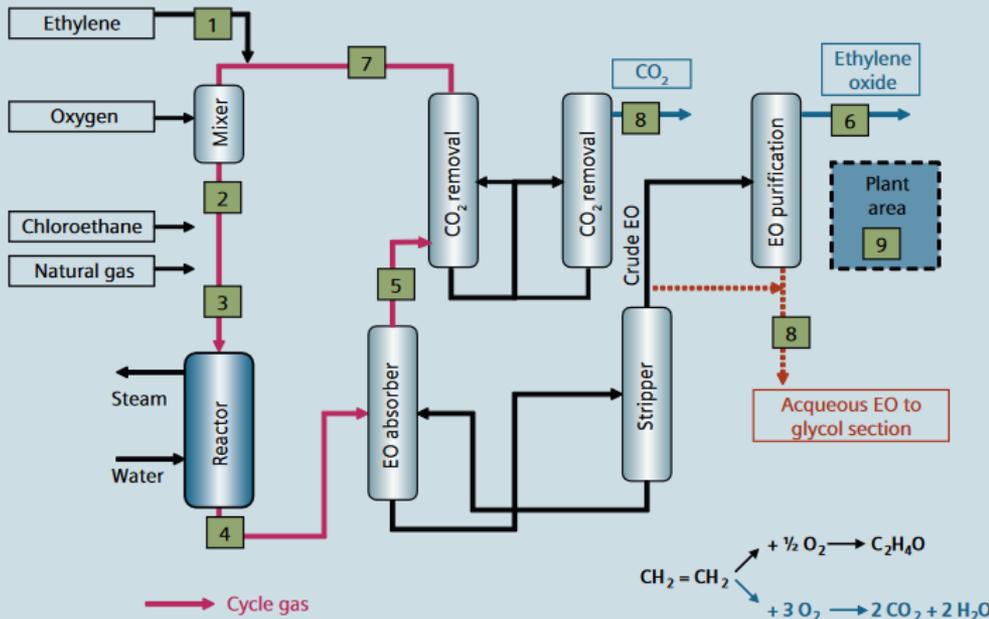


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Ethylene to ethylene oxide

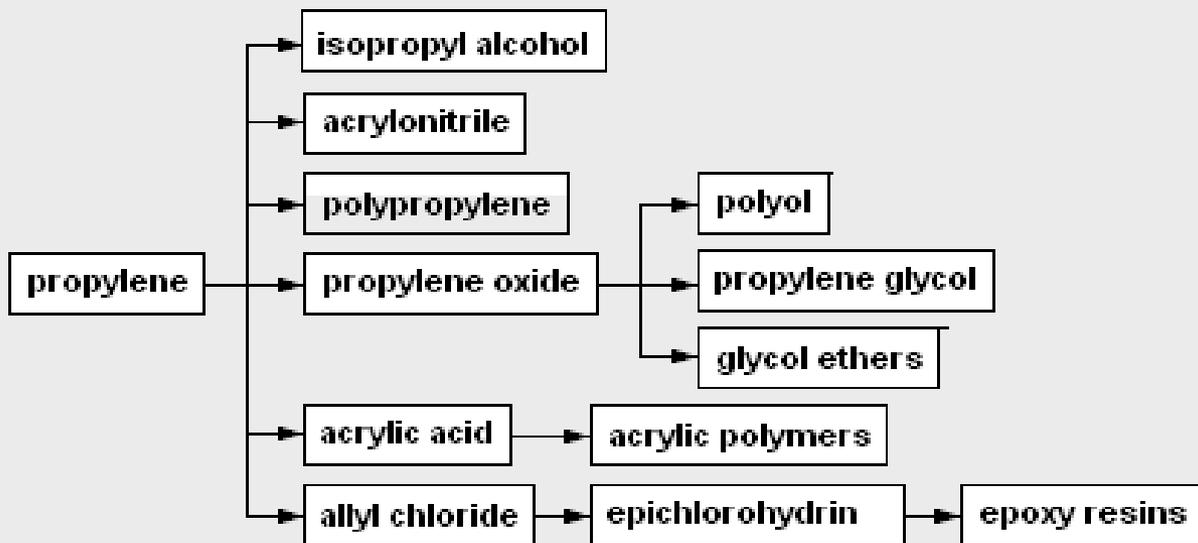


[Ag] = metal surface

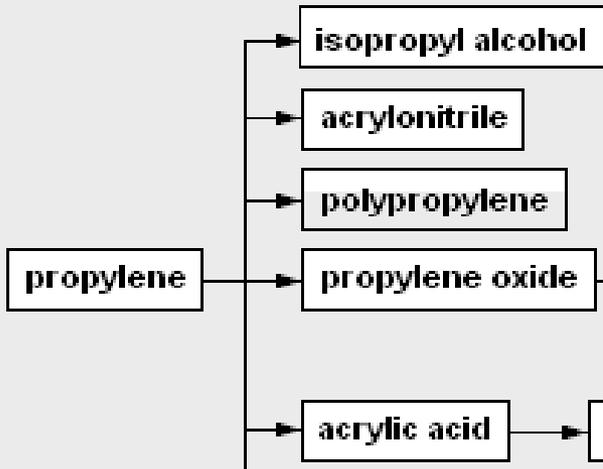


- Unique ability of silver to molecularly adsorb O₂
- Adsorbed atomic chlorine favors this ads. mode versus the dissociative mode
- Maximum achievable selectivity is 80%
- High silver loading (up to 15%) on alumina or other oxide supports

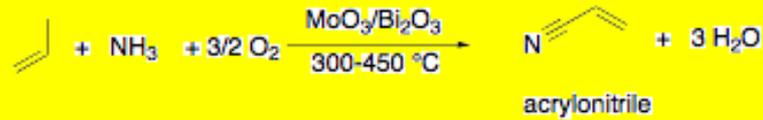
Benzene to chemicals



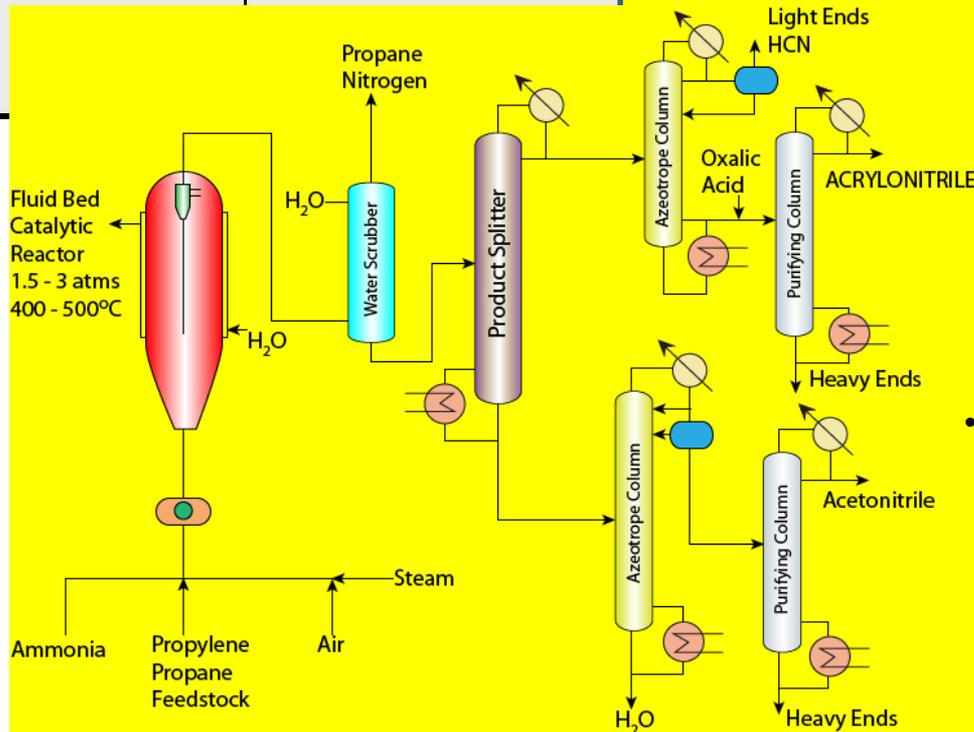
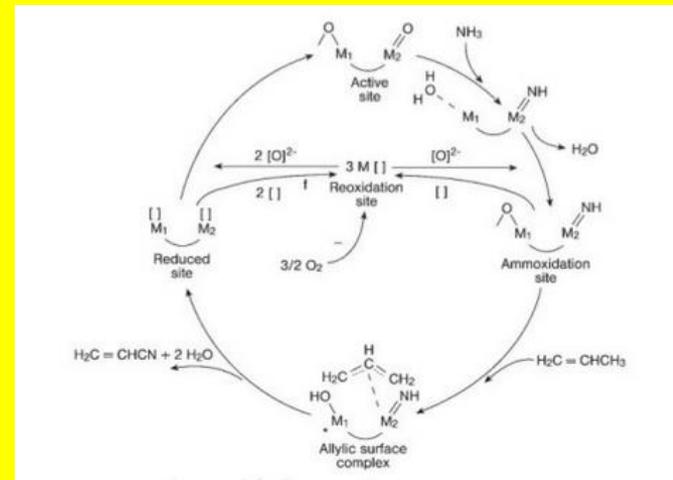
Benzene to chemicals



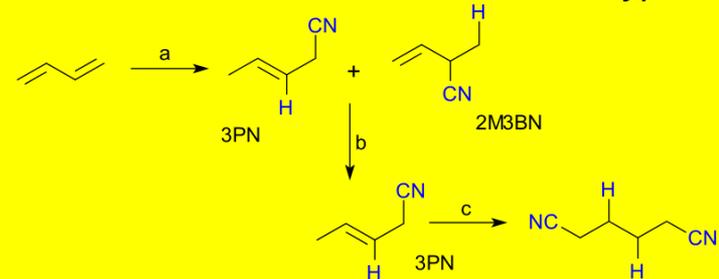
SOHIO Ammoxidation process:



Grasselli, R. K. *Catalysis Today* **2005**, 99, 23.



• *HCN and MeCN are the two main byproducts*



Opportunities for org. chemistry in renewables?

- > 1850 plants & animals, coal
- > 1920 acetylene (from coal)
- > 1950 oil
- > 1973 oil & gas
- CO₂ and biomass



Explosion at Oppau 1921

[http://www.reimerei.net/Oppauammoniak_\(FRB\).htm](http://www.reimerei.net/Oppauammoniak_(FRB).htm)



Walter Reppe (1892-1969)

Photo: www.euchems.org
PhD in Chemistry 1921

A number of accidents lead most countries to prohibit work with high P acetylene, BASF limit was 1.5 bar

Reppe's goal: use acetylene produced from CaC₂ as a primary building block

Reppe wants to go higher than 25 bar

Reppe focuses on developing equipment for safe operation to allow for studying the chemistry:

tube reactors instead of vessels

stainless steel (to avoid explosive salts formation with copper...)

delivery in a plurality of smaller parallel tubes

dilute with nitrogen



Opportunities for org. chemistry in renewables?

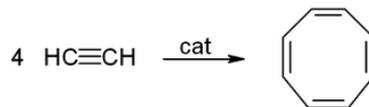
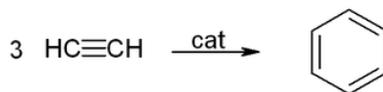
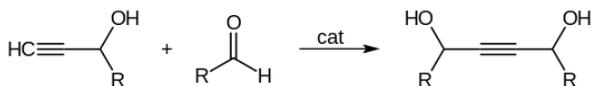
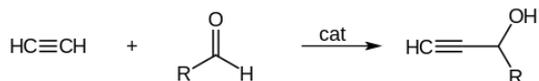
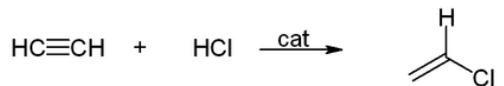
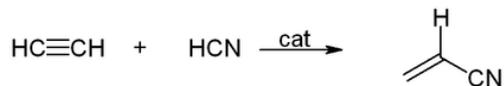
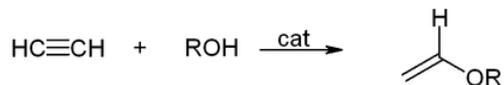
- > 1850 plants & animals, coal
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BASF butanediol unit today with the reactors built under Walter Reppe in 1943
Photo: www.basf.de



Reppe's efforts lead to a number of industrial processes

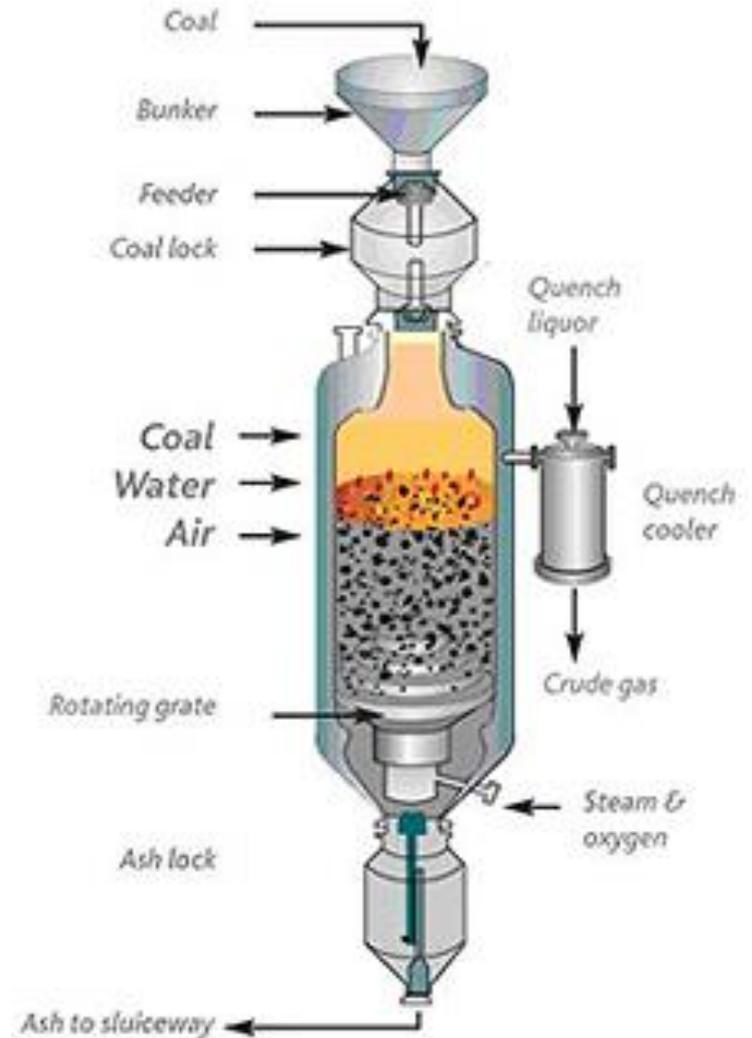
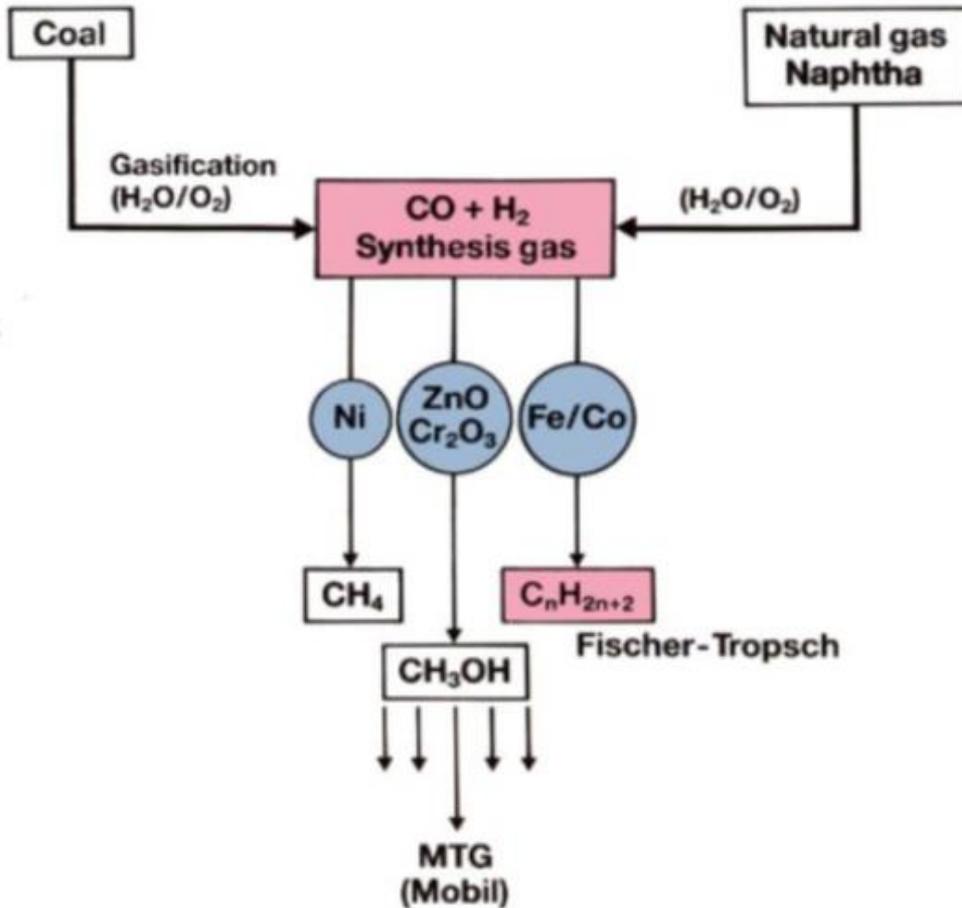


Walter Reppe (1892-1969)

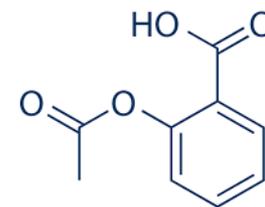
Photo: www.euchems.org
PhD in Chemistry 1921



Coal and NG to chemicals



How to make Aspirin in the era of petrochemicals?



Opportunities for org. chemistry in renewables?

- > 1850 plants & animals, coal
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- > 1973 oil & gas
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- *Small molecules: active ingredients in pharma and agro applications, pigments, flavors & fragrance, sealants & coatings, organometallics...*
- *Big molecules: peptides, proteins... mwt > 700*
- *Batch STR reactors, multipurpose production lines*
- *Homogeneous and bio catalysis*
- *In-house production or outsourced (CM)*
- *Besides petrochemicals, extraction from plants, animals and bioproduction is common*
- *R&D activities are designing the synthetic routes and to a lesser extent scale-up and optimization (5 to 10%)*

Opportunities for org. chemistry in renewables?

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Chemical(s) to serve a certain function: lubrication, adhesive, surfactant, cosmetics...

When in mixture called formulation.

Batch reactions

R&D efforts is to deliver better function rather than a certain chemical >10%

BASF, AkzoNobel, Lubrizol, Albemarle, Cabot

Process chemistry

Two arms of pharmaceutical industry:

1. medicinal chemistry (high throughput screen, SAR)
2. process chemistry (economic, safe, reproducible, scalable and green)

Routes serving these two arms can be different due to different goals

Need for GMP is driven by: regulations and the increasing production cost (20% in 10 years):

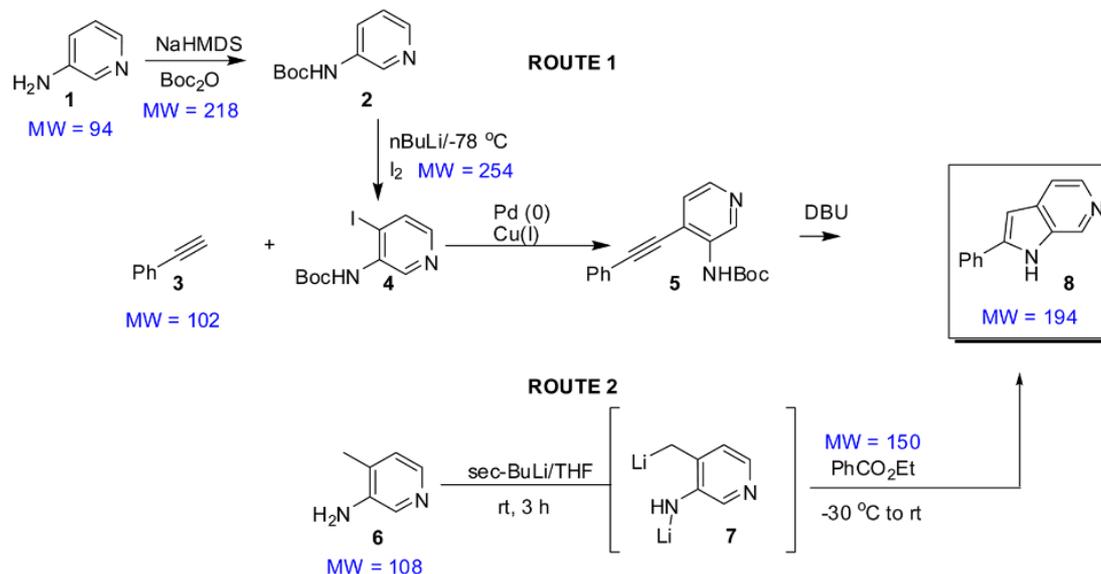
- Innovative engineering solutions: flow chemistry, biocatalysis, high pressure...
- Standardized measurable evaluation criteria for production routes:

1. Materials cost: reactants, solvent, catalyst, additives, eluents, extractants....are they sustainable?

Two synthetic pathways to 2-phenyl-6-azaindole (8)

2. Atom economy

$$AE = \frac{MW(\text{product}) \times 100\%}{\sum MW(\text{raw materials})}$$



Route 1: 24%

Route 2: 75%

Process chemistry

Standardized measurable evaluation criteria for production routes:

- 1. Materials cost: reactants, solvent, catalyst, additives, eluents, extractants....are they sustainable?*
- 2. Atom economy > 70%*
- 3. Yield, based on limiting reactant. convergent routes are more favored than sequential*

Besides loss of materials, the formed side products can be costly in terms of reactor cleaning and waste disposal ..e.g. genotoxic or explosive impurities

Linear Synthesis



Convergent Synthesis



4. Volume Time Output VTO

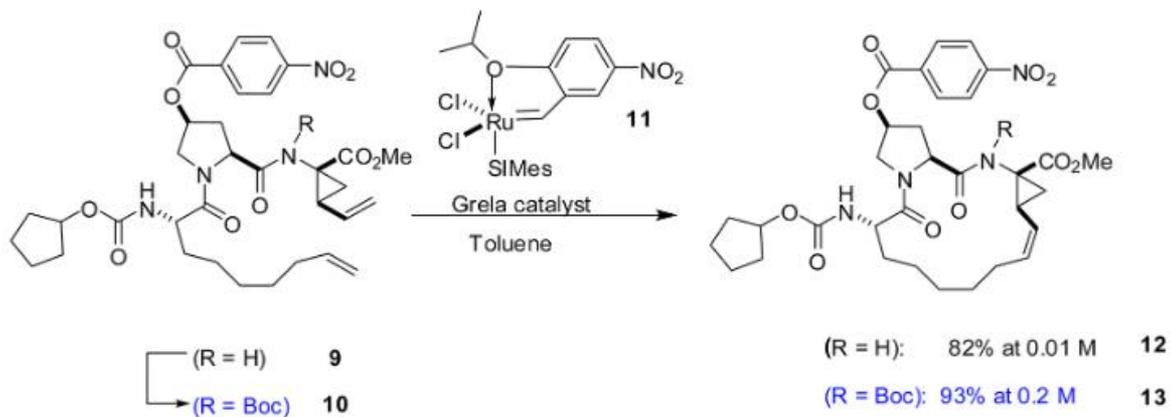
$$\text{VTO} = \frac{\text{nominal volume of all reactors}[\text{m}^3] \times \text{time per batch}[\text{h}]}{\text{output per step}[\text{kg}]}$$

Process chemistry

4. Volume Time Output VTO: <math>< 1 \text{ m}^3 \text{ h/kg}</math>

VTO =

$$\frac{\text{nominal volume of all reactors}[\text{m}^3] \times \text{time per batch}[\text{h}]}{\text{output per step}[\text{kg}]}$$



$\text{R} = \text{H}$, VTO = $8.2 \text{ m}^3 \text{ h/kg}$

$\text{R} = \text{Boc}$, VTO = $0.1 \text{ m}^3 \text{ h/kg}$

Reactor volume 100 m³
Op. cost 20 M USD/year
24h/day, 330 day/year
Capacity utilization 60%

Cost: 42 USD/m³. h

Process chemistry

5. *E-factor or PMI: 25-100*

$$E = \frac{\sum \text{mass of materials in [kg]} - \text{mass of product out [kg]}}{\text{mass of product out [kg]}}$$
$$= \frac{\text{mass of waste [kg]}}{\text{mass of product out [kg]}} \quad (5)$$

6. *Quality Service Level: how reproducible a reaction is from batch to batch: QSL: >98%*

7. *Process Excellence Index: how reproducible a process is in terms of yield and cycle time
PEI > 98*

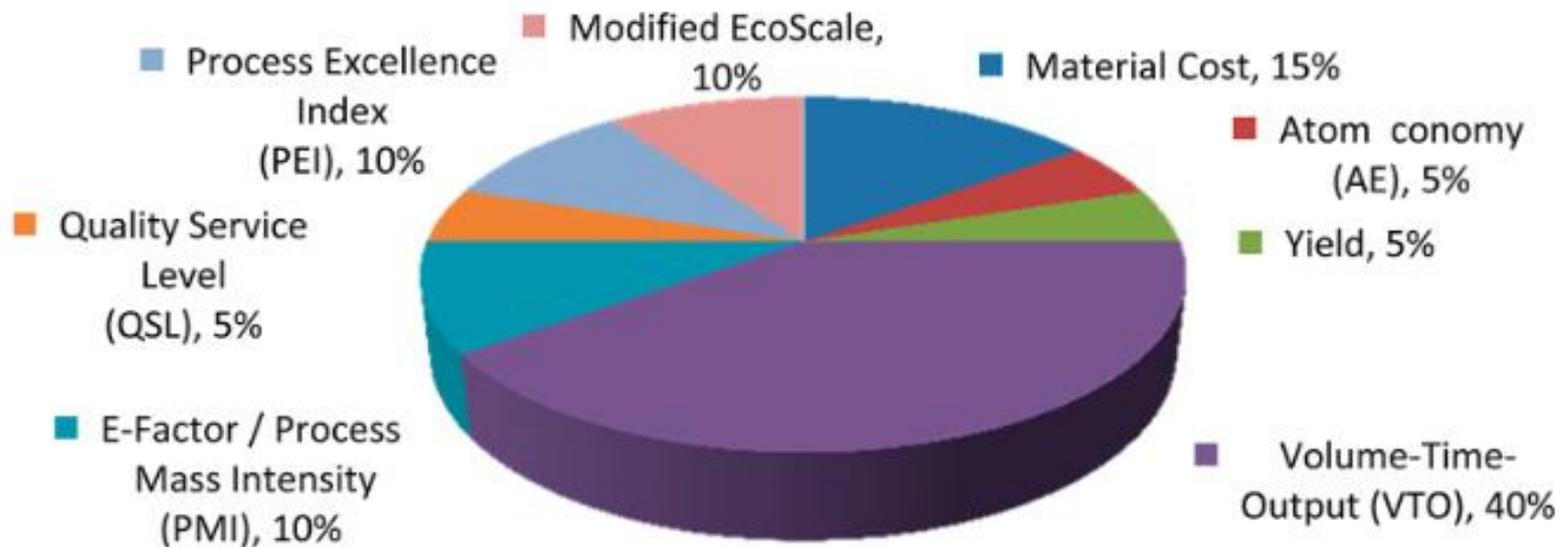
Process chemistry

8. Ecoscale

Table 2. Modified EcoScale template for step evaluation at Boehringer Ingelheim

Parameter		Question	Criterion	Points	RCM Route 1	RCM Route 2
1	Yield [%]	What is the yield?	> 95%	10	5	8
			80-95%	7		
			60-80%	3		
2	Quality [A or Wt%] of Product by GC, HPLC etc.	What is the quality?	> 98%	10	7	10
			95-98%	7		
			< 95%	3		
3	Workup & Purification	Filtration before final crystallization possible?	Yes	10	NA	NA
			No	0-9		
		Easy separation of suspension?	Yes	10	NA	NA
			No	0-9		
		Easy drying in tumble or paddle dryer possible?	Yes	10	NA	NA
			No	0-9		
4	Equipment	Multipurpose reactors suitable?	Yes	10	0	10
			No	0-9		
5	Reaction Time [h]	What is the reaction time?	< 3 h	10	3	10
			3-6 h	7		
			>10 h	3		
6	Reaction Temperature [°C]	What is the reaction temperature?	Room T	10	8	5
			< 90°C	8		
			90-150°C	5		
			> 150°C	3		
			< -10°C	3		
7	Raw Materials	Is chlorinated solvent used?	No	10	0	10
			Yes	0-9		
		Price for solvents < \$7/kg?	Yes	10	10	10
			No	0-9		
		All components are commodities?	Yes	10	10	10
			No	0-9		
8	EHS	Reaction highly exothermic?	No	10	10	10
			Yes	0-9		
		Hazardous or toxic material needed?	No	10	10	10
			Yes	0-9		
		Highly flammable or explosive material needed?	No	10	10	10
		TOTAL				

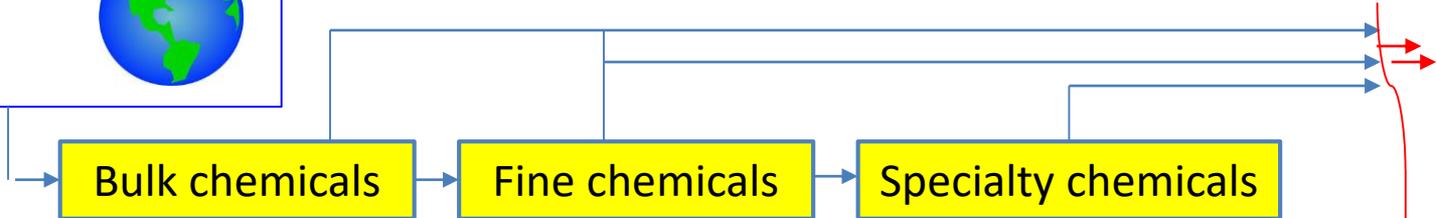
Process chemistry



Proposed weight of different factors by BI

Complete overview!

- > 1850 plants & animals, coal
- > 1920 acetylene (from coal)
- > 1950 oil
- > 1973 oil & gas



formulations, recipes...

Process chemistry

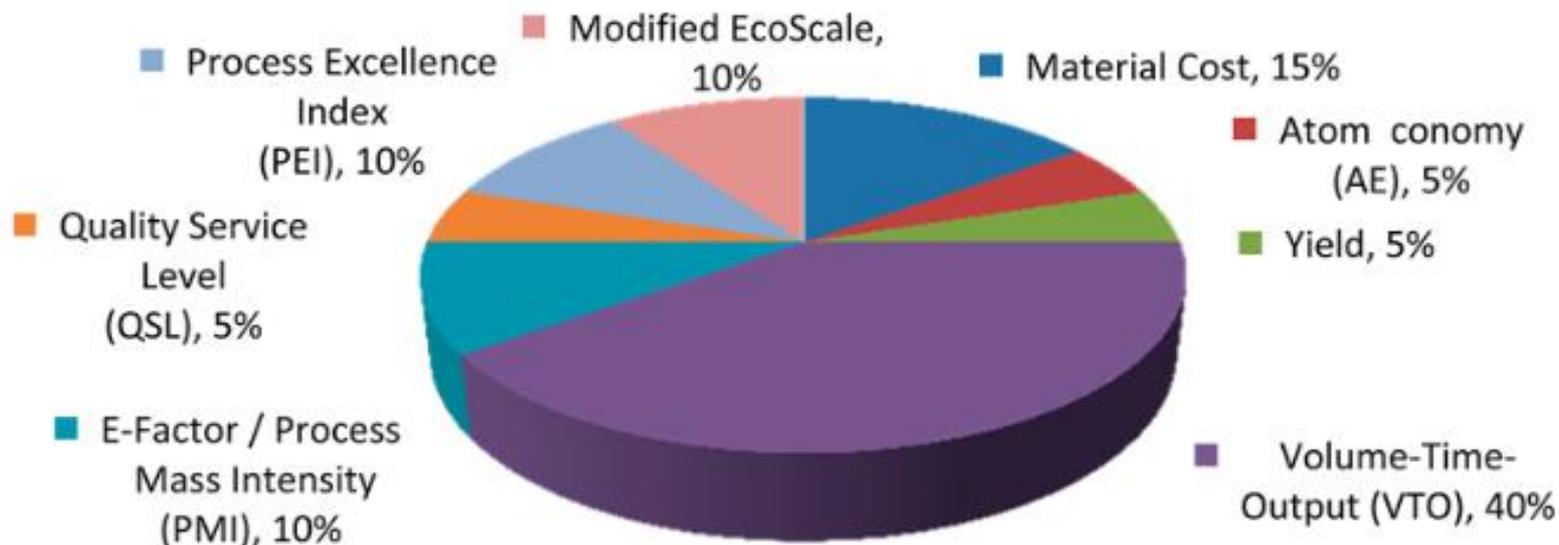
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- **Standardized measurable evaluation criteria for production routes:**



RESEARCH AND INDUSTRIAL ORGANIC CHEMISTRY¹

By Professor JAMES F. NORRIS
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

ical research adequately. An attempt was made by the division to bring about cooperative research in certain industries. The response by executives was not, at first, encouraging. The president of a large petroleum company told me it was not the business of the chemist to meddle in the affairs of the industry. His company had millions of dollars invested in plants. It was satisfied with the results. He did not want anybody to do anything to make these plants obsolete.

A high executive in another industry told me he did not believe it good business to spend money on research to develop new products or methods. He had found it better to let some one else bear the expense of such work, most of which proved of no value. If anything worth while came out of it he could afford to buy it. What a change has come about in seven years. The two industries to which I have just referred are now spending millions of dollars in research.

In recent years the methods and personnel of the industrial research laboratories have changed rapidly. The empirical approach to the solution of a problem has largely disappeared and has been replaced by coordinated investigation carried out with the use of the scientific methods and with a knowledge of the latest findings and instruments of fundamental science. The industrial laboratories keep informed as to the new knowledge resulting from research in the universities. Requests are received from such laboratories for reprints of papers which apparently are only of theoretical interest.

The change in the industrial laboratories has come about as the result of a change in personnel. I was consulted several years ago in regard to the appointment of a director of a proposed research laboratory for a chemical industry, which was conducted largely by rule-of-thumb methods. The directors insisted on the appointment of a well-informed organic chemist, preferably a university professor, who had no experience in the industry which he was expected to develop. In this case there was good judgment in the point of view.

Opportunities are rapidly decreasing for the advancement in his profession of the chemist whose scholastic experience is limited to a four years' course leading to the degree of bachelor of science. To get ahead he must put chemistry behind him and become a manager or executive. The men to-day who are developing the industry are some of the best of those

chemical equilibrium and ionization, catalysis, x-rays, and different types of energy with varying intensity factors—these and other important facts and generalizations have broadened the methods of research in organic chemistry, and have been applied in the solution of industrial problems.

For the research chemist who enters the industrial field a knowledge is important of the principles of chemical engineering which follow from the application of those laws of physics and physical chemistry which have to do with the physical relationships between molecules.

Those who direct the education of students of organic chemistry should see to it that the preparation for future work includes training in the principles of physical chemistry and their use. It was not so long ago that one of the leading universities of the country had no requirement in physical chemistry for men awarded the doctorate in organic chemistry. Happily, conditions are improving.

The growth of the use of research in the industries based on chemistry is indicated by the rapid increase in the number of men awarded the degree of doctor of philosophy in American universities. A compilation made by the National Research Council shows that much the larger number of these degrees is in the field of chemistry. Many of the young men awarded this degree have entered industrial research laboratories, where they are happily at work on problems of great interest, are supplied with every facility

Enabling Technologies

Laboratory Experiment

← Previous

Student-Fabricated Microfluidic Devices as Flow Reactors for Organic and Inorganic Synthesis

Z. Vivian Feng*, Kate R. Edelman, and Benjamin P. Swanson

Chemistry Department, Augsburg College, Minneapolis, Minnesota 55454, United States

J. Chem. Educ., 2015, 92 (4), pp 723–727

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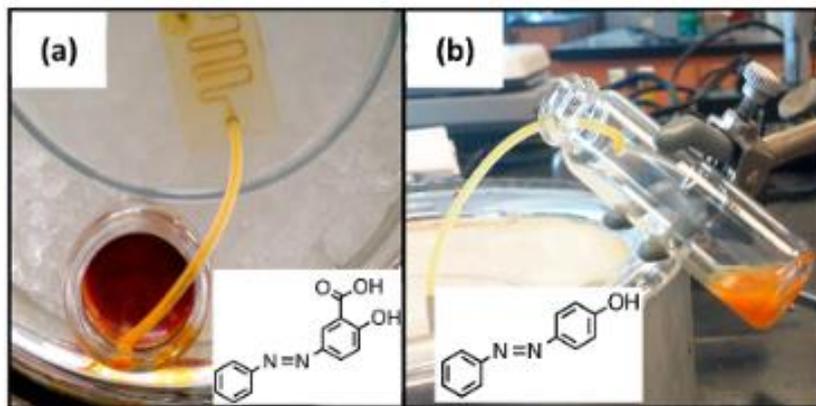


Figure 7. Synthesis of azo dyes: (a) 2-hydroxy-5-(2-phenyldiazenyl)benzoic acid, and (b) 4-(2-phenyldiazenyl)phenol in PDMS flow reactors.

Enabling Technologies

Review

← Previous

The Hitchhiker's Guide to Flow ChemistryII

[Matthew B. Plutschack](#)^{§†}, [Bartholomäus Pieber](#)^{§†}, [Kerry Gilmore](#)^{*†} , and [Peter H. Seeberger](#)^{*†‡} 

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Resources

bulk and commodity chemicals



Fine chemicals

