From Trifluoroacetic acid to triflic derivatives : RHODIA's Fluorination tree

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Fluorination : a key technology for Rhodia

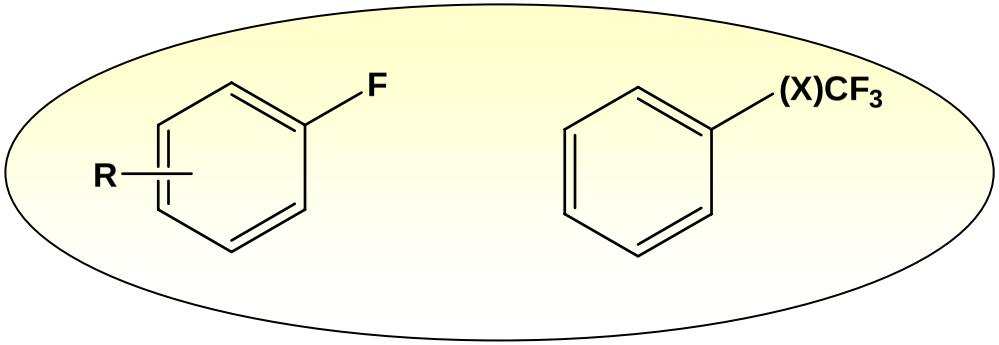
- For the past 20 years, fluorinated intermediates have known a great success in Life Science actives, as the introduction of one or several fluorine atoms can increase the active 's biological activity.

- As a result, fluorination is a technology in demand with 20% of Life Science actives containing one or several fluorine atoms (C&EN, **84**(23), 2006, pp15-23)

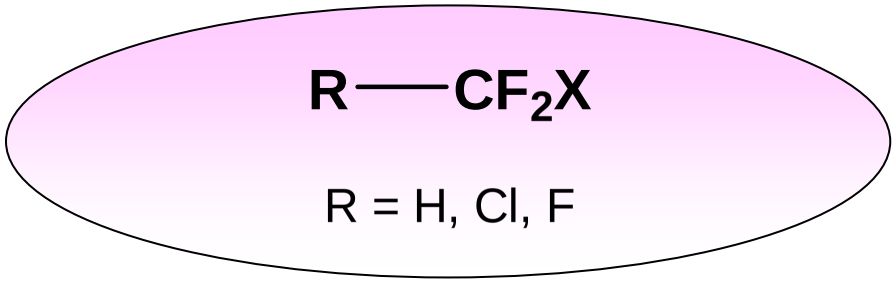
- Rhodia is recognised as a worldwide leader, with an extensive industrial experience and innovative chemistry in several fluorination technologies, to produce both fluoroaliphatic and fluoroaromatic compounds.

Rhodia's Fluorination Technologies

Fluorinated aromatic intermediates



Fluorinated aliphatic intermediates



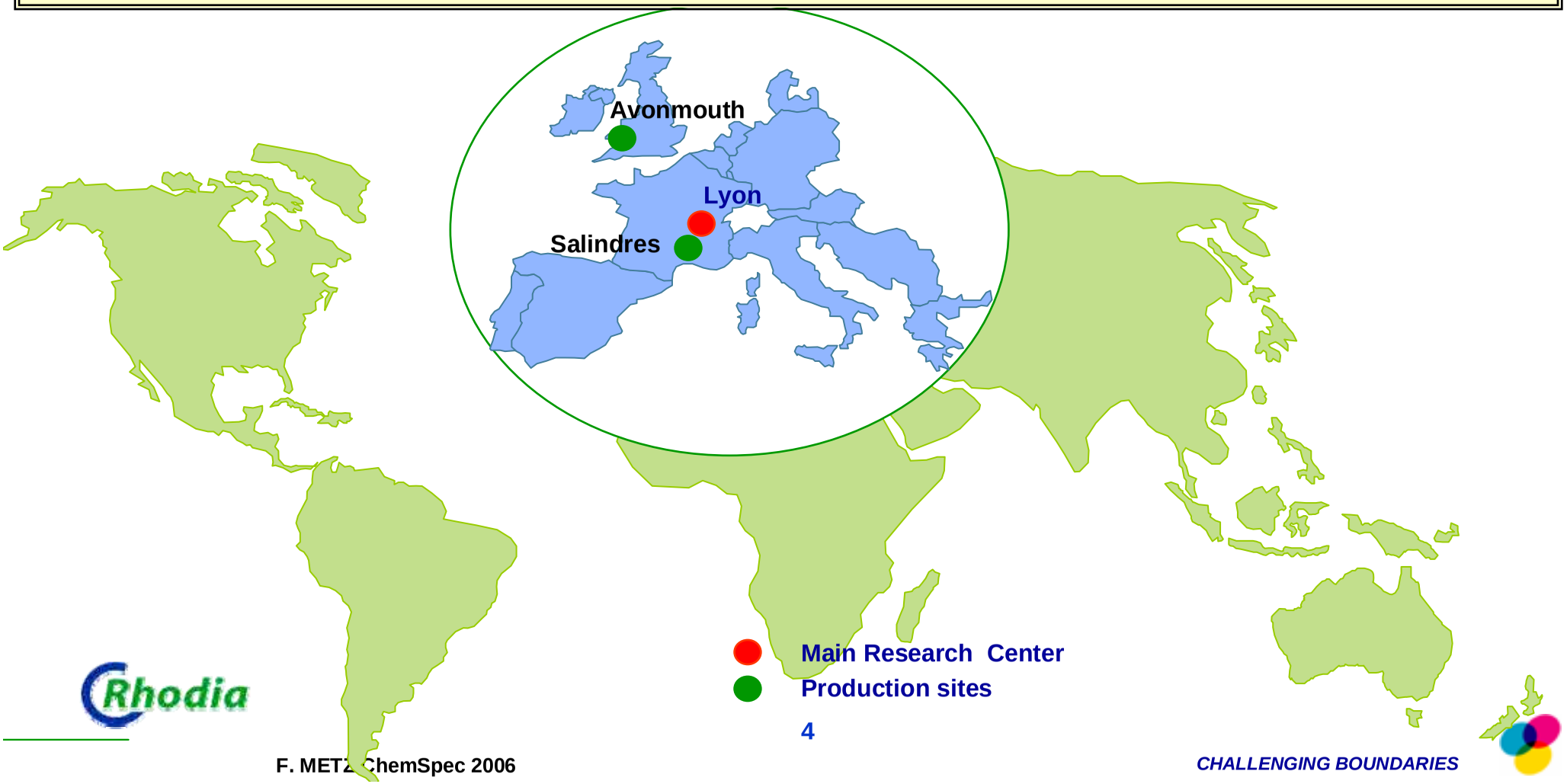
HALEX reaction | **HF liquid technology** | **HF gas technology** | **Direct trifluoromethylation**

Facilities

Fluorination sites location

- Industrial scale fluorination reactions are performed on dedicated and fully-integrated sites, designed for multi-products manufacturing.

- Research & Development teams are based in our central Research Center in Lyon.

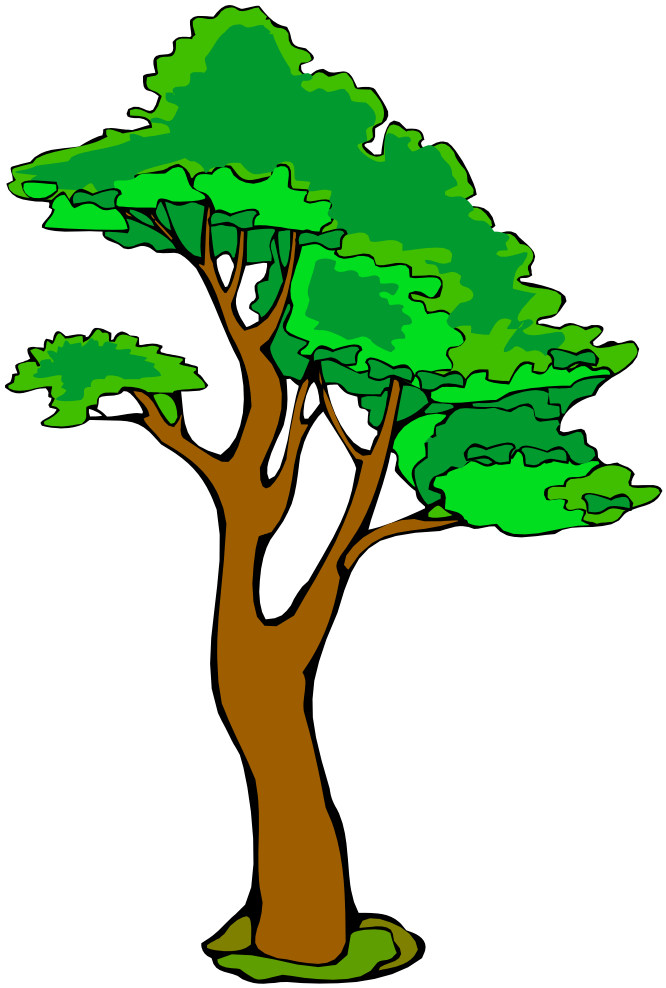


Fluoro-aliphatic intermediates tree

A solid and stable trunk :

$F_3C—CO_2H$

TFA



allowing a vigorous tree to grow

TFA : a three stages process

Unique CFC-free process

- **Photo-oxidation :**

$$CCl_2{=}\,CCl_2 + 1/2\ O_2 \xrightarrow{h\nu} CCl_3 - COCl$$

PER → TCAC

- **Fluorination :**

$$CCl_3\text{-}\,COCl + 4HF \longrightarrow CF_3\text{-}\,COF + 4HCl$$

TFAF

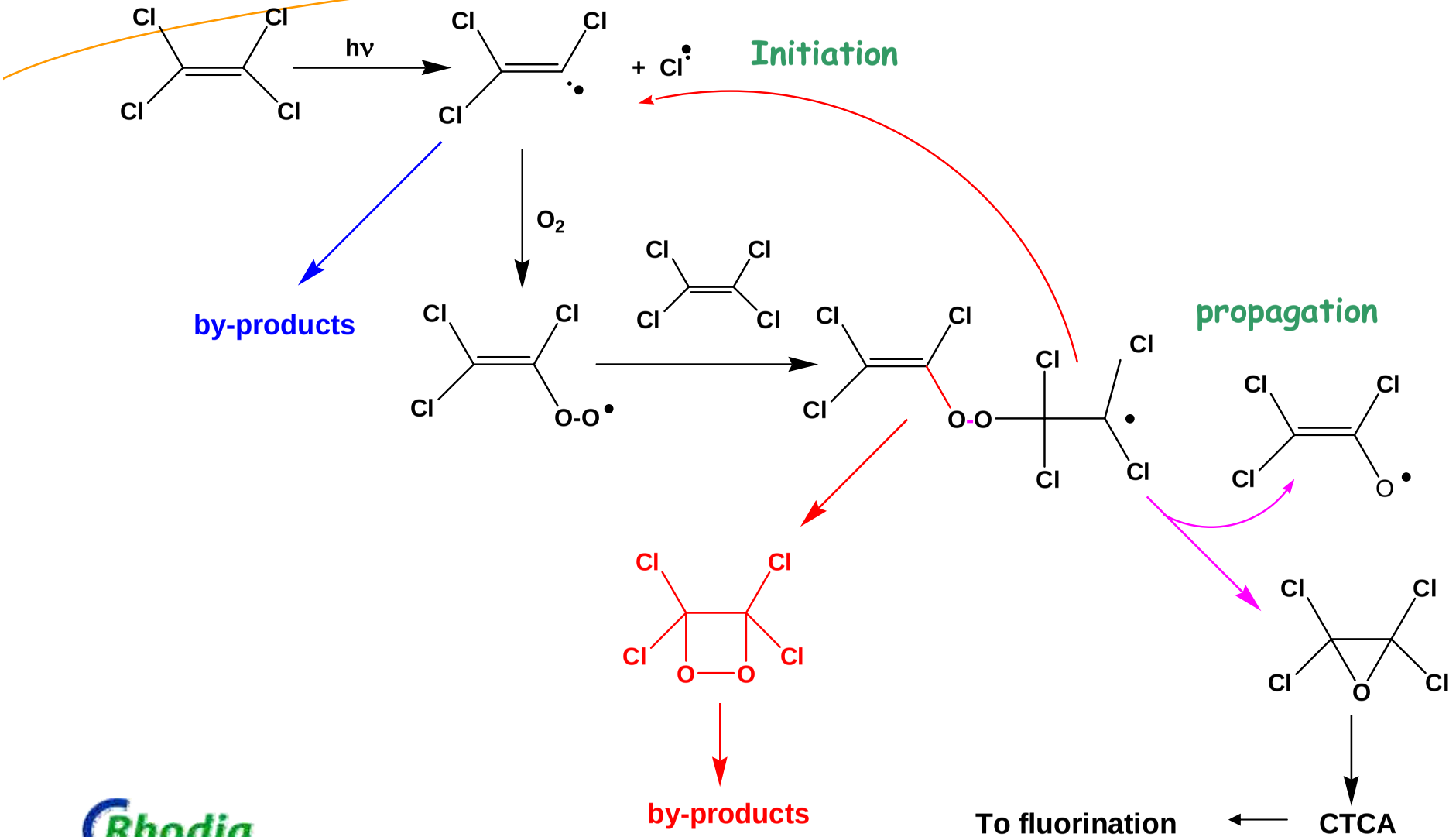
- **Hydrolysis :**

$$CF_3\text{-}\,COF + H_2O \longrightarrow CF_3\text{-}\,COOH + HF$$

TFA

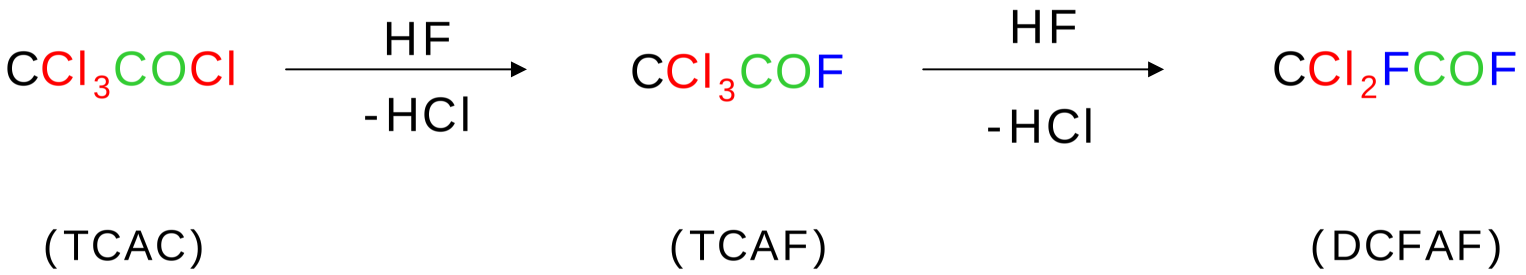
TFA : a three stages process process

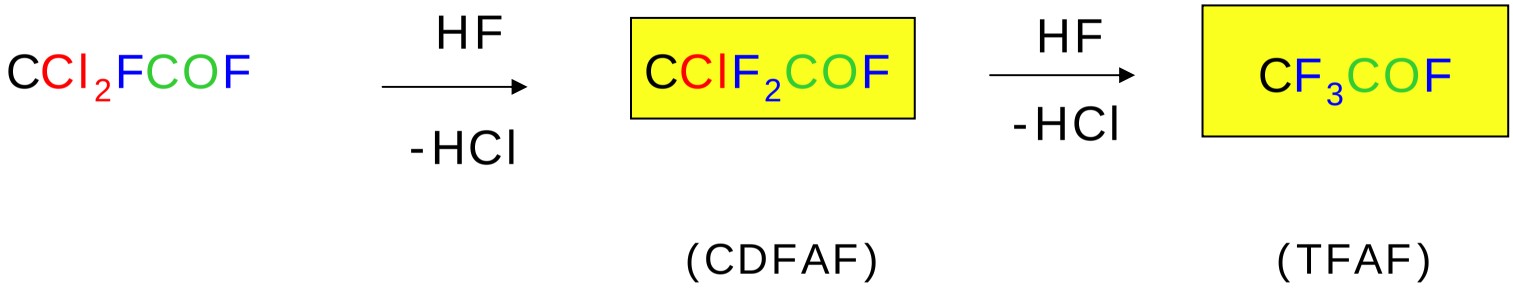
Photo-oxidation : Reaction mechanism (supposed)



TFA : a three stages process

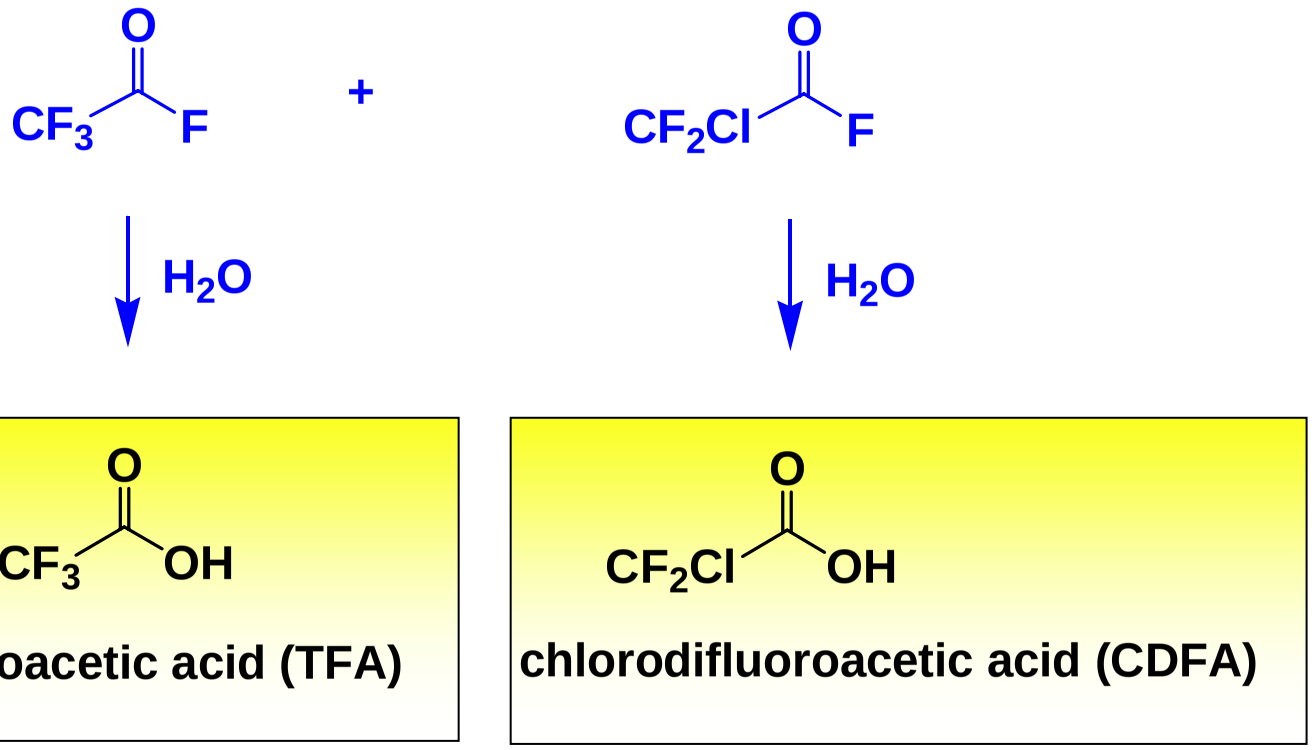
Fluorination : successive Cl-F exchanges





TFA : a three stages process

Hydrolysis : access to both TFA & CDFA



TFA and CDFA are key starting raw materials, which open the way to a extensive range of aliphatic fluorinated compounds.

TFA : specificities

Rhodia's advantages :

- Large capacity
- Unique and competitive process
- Environmentally friendly process : **CFC free**
- Experience in handling hazardous reagents
- Rhodia 's integration in other technologies

Cost competitive process

Sustainable technology

TFA : applications

Some examples :

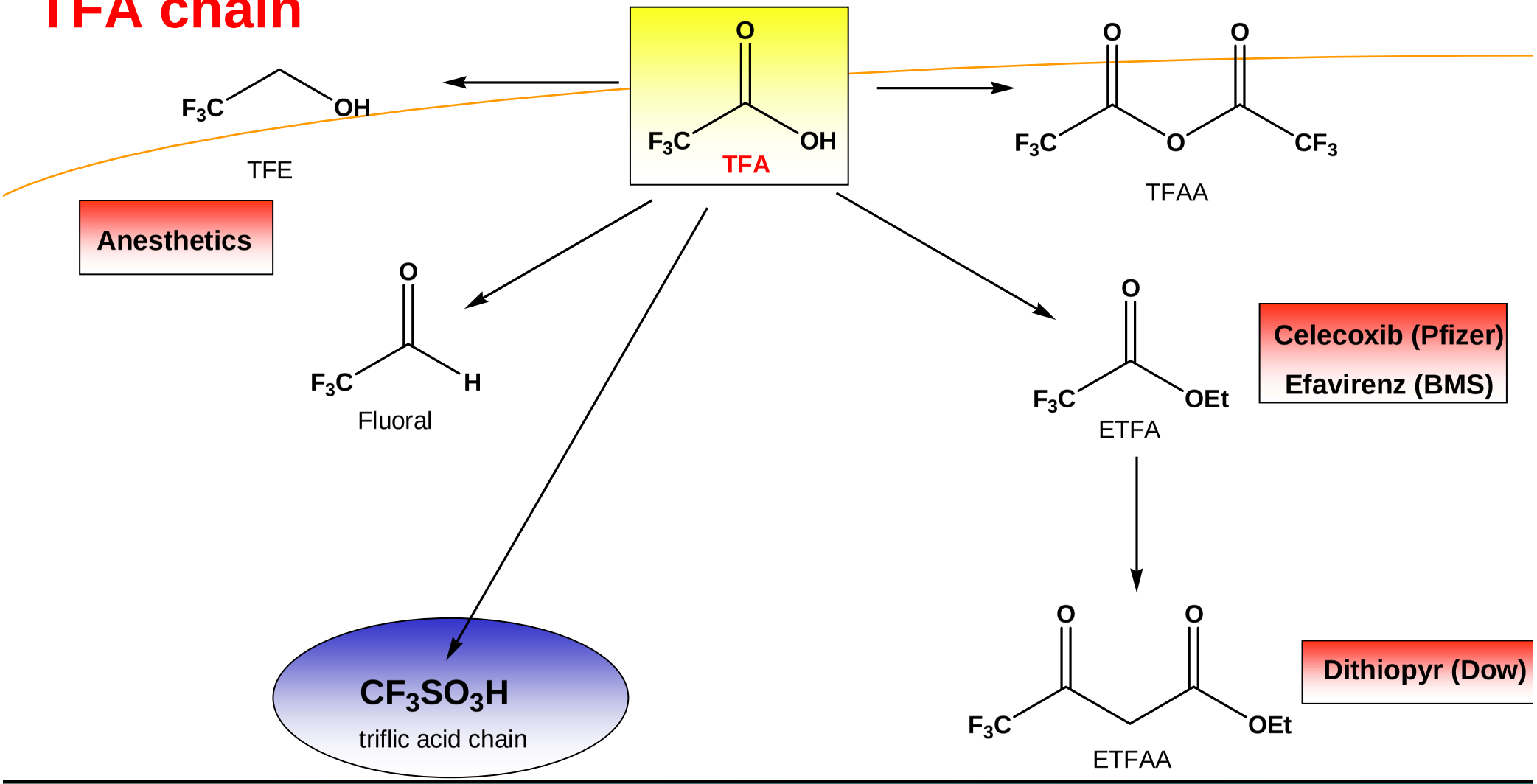
- **Protection and deprotection reactions**
  (of alcohols, amides, nucleosides, peptides, phenols, sugars, cleavage of dithioacetals….)

- **Catalyst and solvent**
  (Ring substitution, aromatic nitration, rearrangements, isomerization…)

- **Heterocyclization reactions**

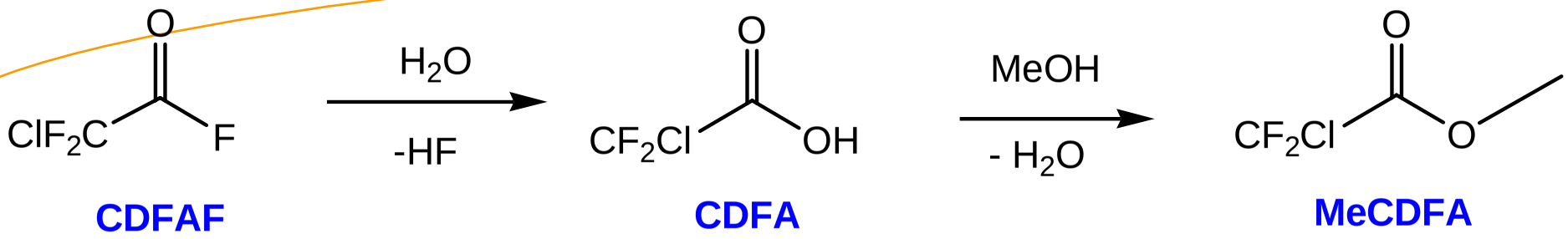
- **Reaction with halogenated compounds**

TFA chain

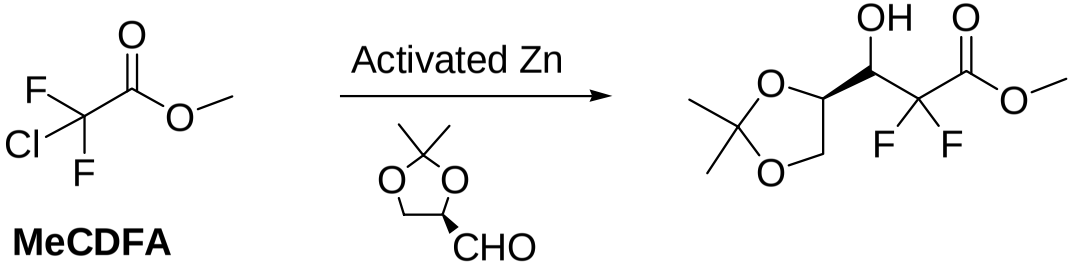


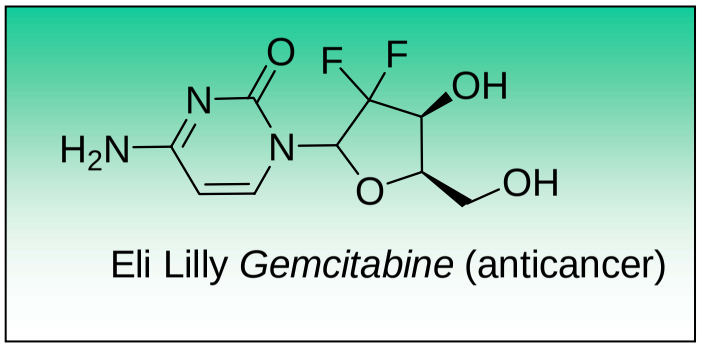
Starting from these building blocks and thanks to an extensive portfolio of technologies, Rhodia offers the widest range of TFA derivatives and advanced downstream intermediates .

CDFA chain



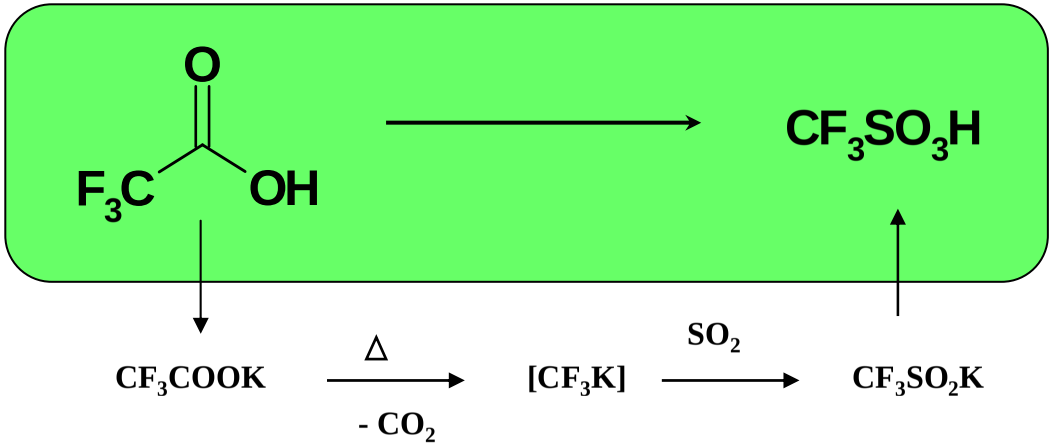
CDFAF **CDFA** **MeCDFA**





Triflic acid (TA) : a unique chemical pathway

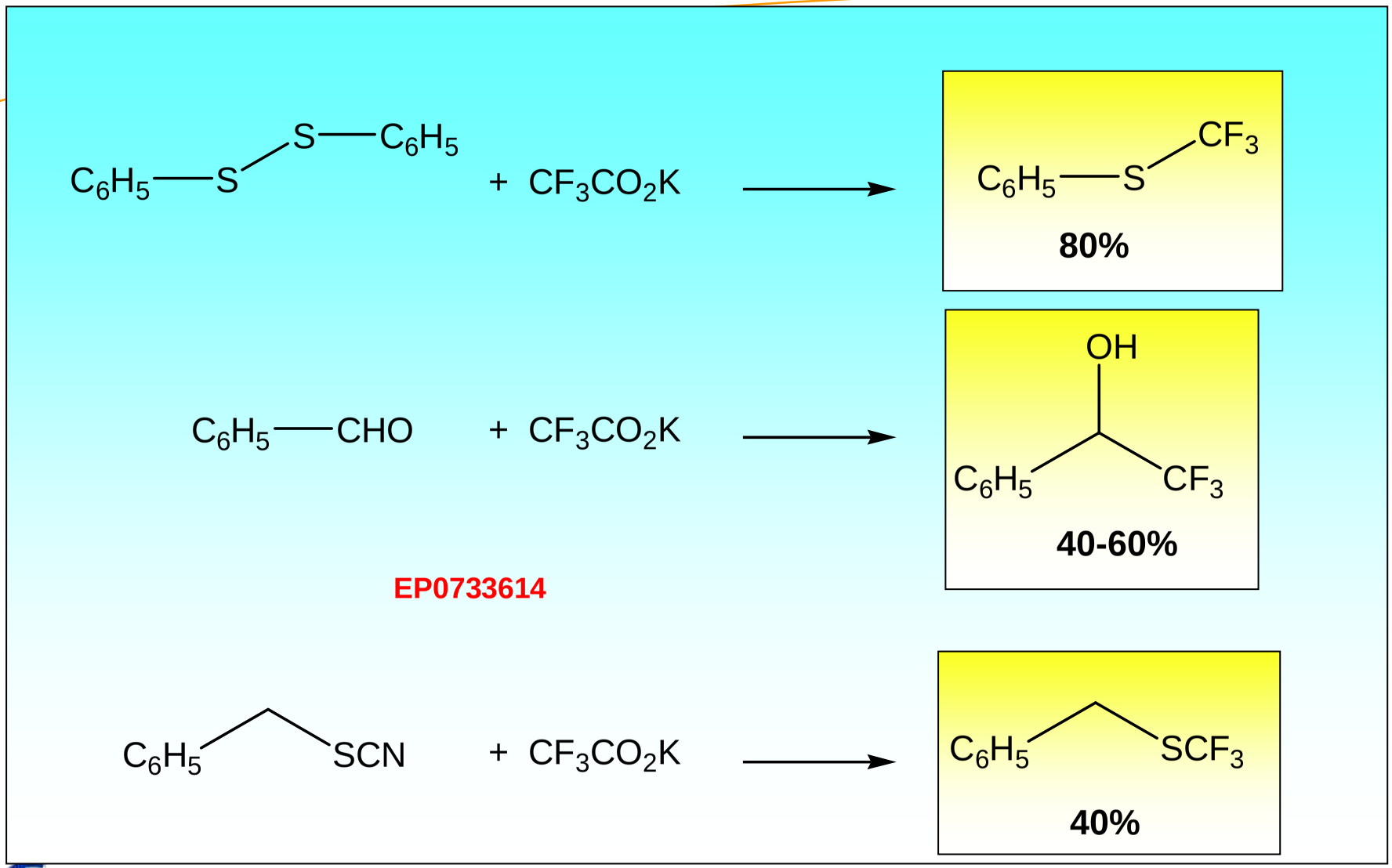
An innovative and clean process



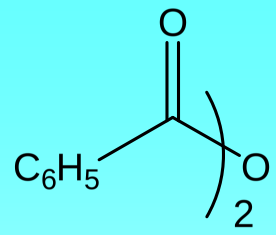
EP0735023

- Direct nucleophilic trifluoromethylation : a new process using CFC free innovative technology
- cation effect : K>Na>Li
- Influence of temperature and choice of solvent are key
- Process optimisation allows for reliable and competitive manufacturing conditions.

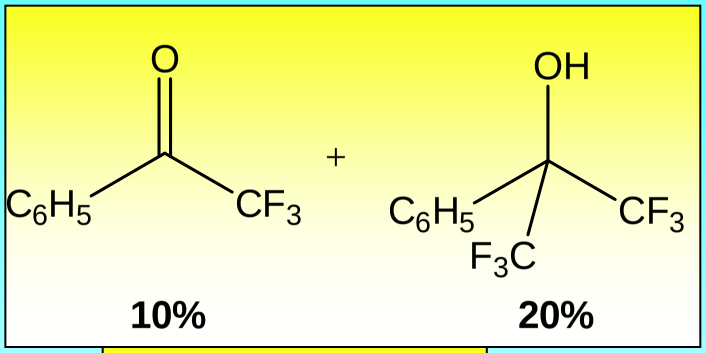
Anionic trifluoromethylation : scope &limitations

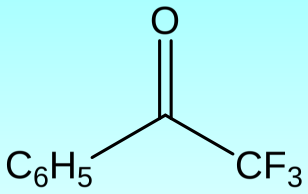


Anionic trifluoromethylation : scope & limitations

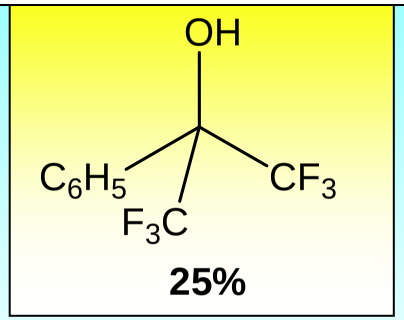


+ CF_3CO_2K →





+ CF_3CO_2K →



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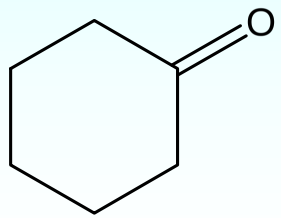
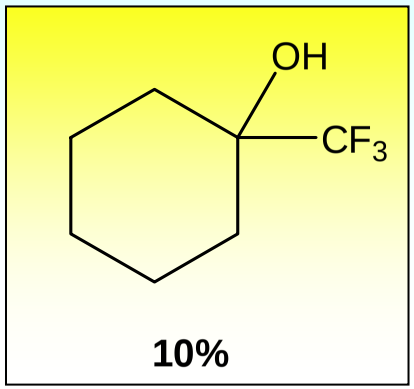


+ CF_3CO_2K →



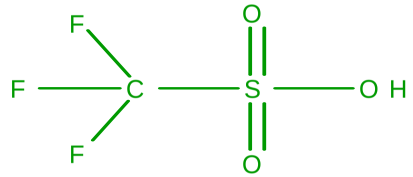
+ crotonisation

Acilys™ TA

Triflic Acid

CAS # 1493-13-6

MW	150 $g.mol^{-1}$
BP	162°C
Density	1.7 $kg.l^{-1}$
Inventories	All



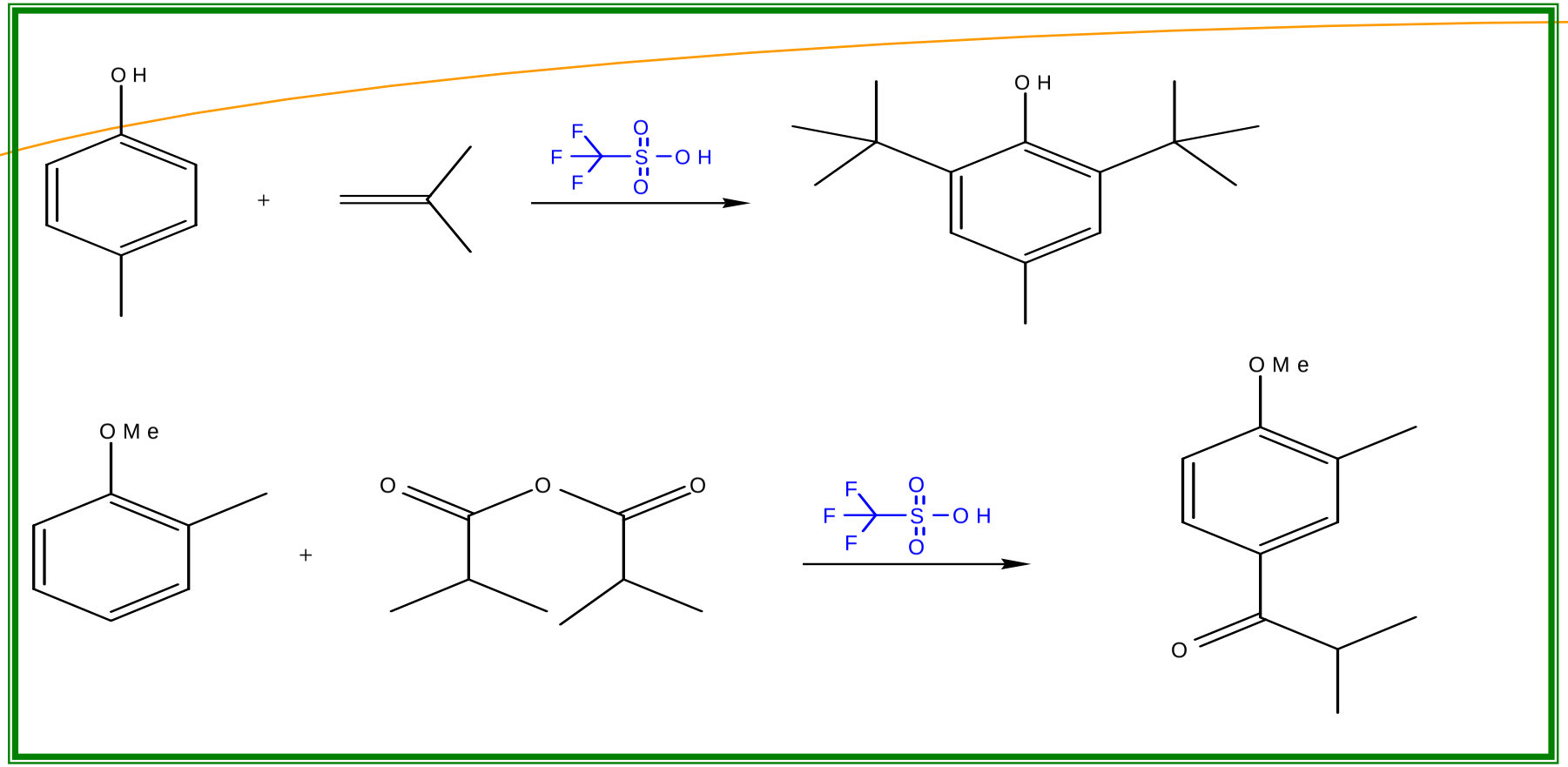
Trifluoromethanesulfonic acid, also known as **triflic acid**, is the **most acidic** of all the commercial chemicals available at the industrial scale.

Its unique chemical structure gives triflic acid an outstanding acid strength as well as chemical stability. It is **extremely resistant** towards thermal degradation, oxidation and reduction, and is also non-oxidizing.

*Triflic acid is widely used for specialty and fine chemical productions, for **acid catalyzed reactions** such as :*

- *Cationic polymerizations*
- *Aromatic alkylations*
- *Esterifications*
- *Acylations*

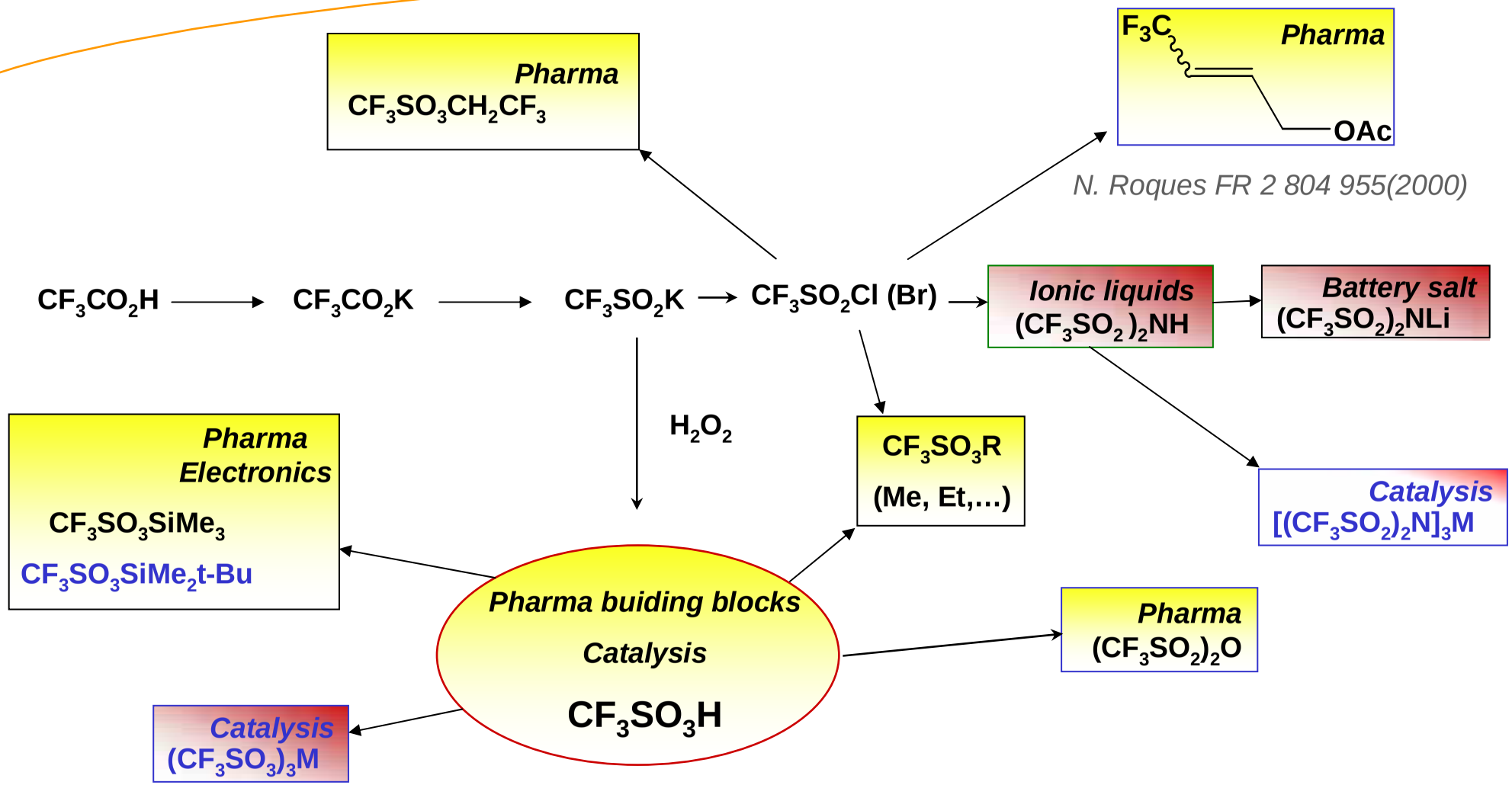
Examples of reactions using Acilys-TA



Rhodia commercializes triflic acid under the tradename **Acilys-TA**. It is readily available from few kilograms to multitons scale.

Moreover, **a large range of triflic acid derivatives** such as triflic anhydride, organic and silyl esters as well as metal triflates, are also available from Rhodia.

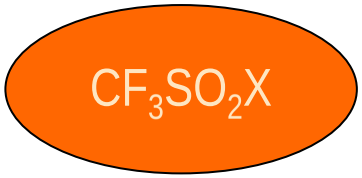
Triflic acid chain :
An extensive range of products for a wide range of applications

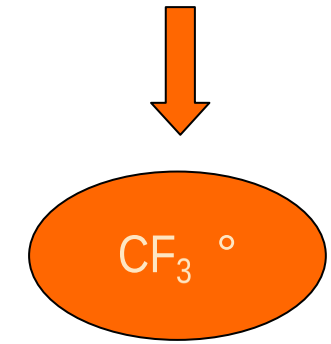


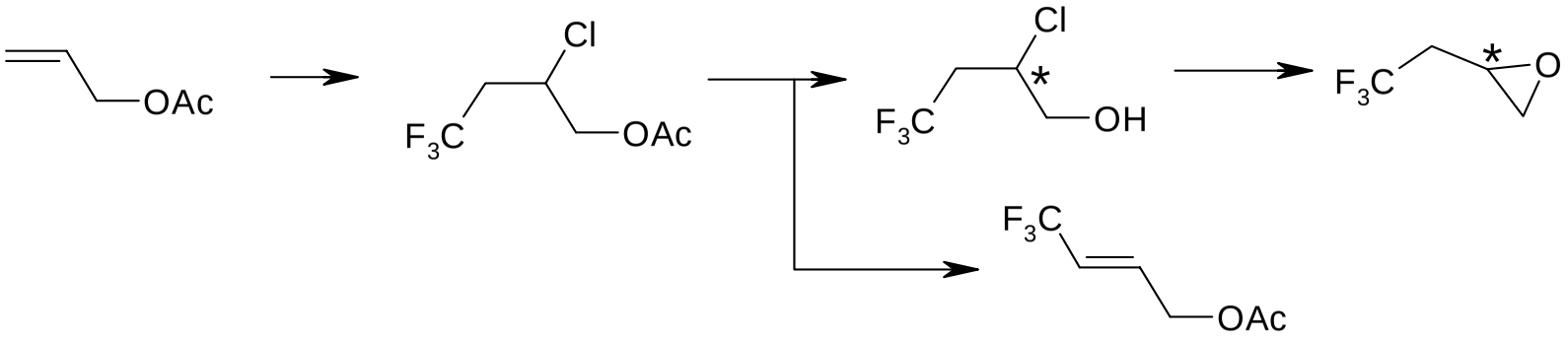
In blue : development products
M : rare earths e.g. Yb, La

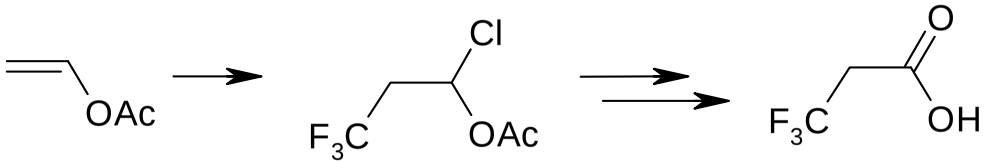
New technology: radical trifluoromethylation

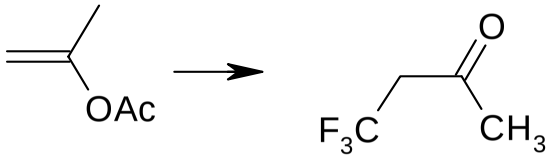
- A new range of building blocks









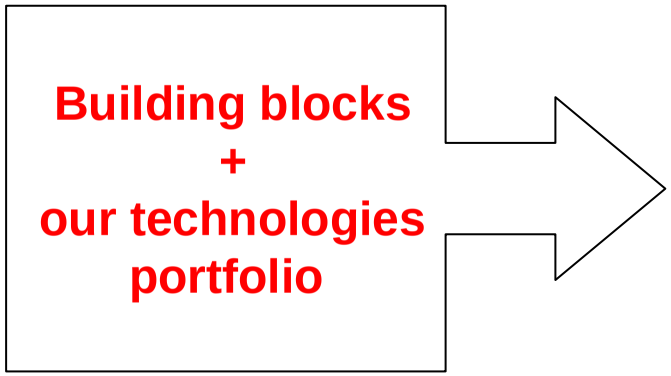


Lab scale ⇨ **Kilo Lab**

Rhodia Organics : a key player in fluorination

- Rhodia associates all these fluoroaliphatic building blocks with an extensive portfolio of technologies.

- We are your innovative partner in developing more advanced downstream intermediates.



Advanced fluorinated intermediates

- With you, let Rhodia's fluoroaliphatics tree grow and blossom !
- For more information, come and see us on Booth C11

Acknowledgments

This work is the result of a constant commitment of many teams :

- Synthesis chemistry,
- Analysis,
- Process development,
- Manufacturing,
- Marketing & Sales,
- Health & Safety,
- Regulatory
- …

THANKS TO EVERYBODY !!!