



# Eco friendly fine chemical production with significant economical benefits





Methodology to shorten lead-times, use less energy and use less chemicals – with possibility to increase the yield.

### Swedish inventors 2011





**NyTeknik** Skapapris till miljövänlig medicin En metod att framställa läkemedel genom att återanvända material i stället för att skapa nytt avfall belönas med året Skapapris. Gaston Lavón och Martin Kullberg kan titulora sig Sveriges uppfinnare 2011. I samband med ovenges uppmarere zo m. i semoanu meo unugningen av Tekniska mässan i Älvsjö utanför inngningen av Tekniska massan i Ansju utamor Stockholm fick de diplom och en check på 300000 uryns motivering är att metoden sänker oosyvas rivorenny as ass meroven admer miljökostnaden och förbättrar arbetsmiljön. Man återanvänder material i stället för att producera are anvender macenar i stanes no are producera avfall. Genom att återvinna fastfasbundna reagene ervan, Oktrom dit dietriffind idetidebuttende foegene kan man nu använda processer som tidigare vant för Skapastiftelsen har även premierat två andra bidrag. Skapastitiesen nar även premierat tva antina diciragi. Pehr Dahl från Örebro får 100000 kronor för en app i mobilelefonen som gör det möjligt för nödstallda att Johan Persson från Norrbottens lan får aven han uomar reneoun mar invisuoseno ian iai oren mar. 100000 kronor för en metod att öka hållfasthetan i armerad betong.

A method to produce pharmaceuticals and other chemicals by reuse of material instead of today's methods that generates lots of waste, is rewarded with the SKAPA price.



# Different possibilities



- The simplified use of Phosphines in Fine chemical manufacturing
  - Advantage compared to when phosphines are used
  - Advantage compared to when phosphines are not used



### Phosphines in manufacturing today

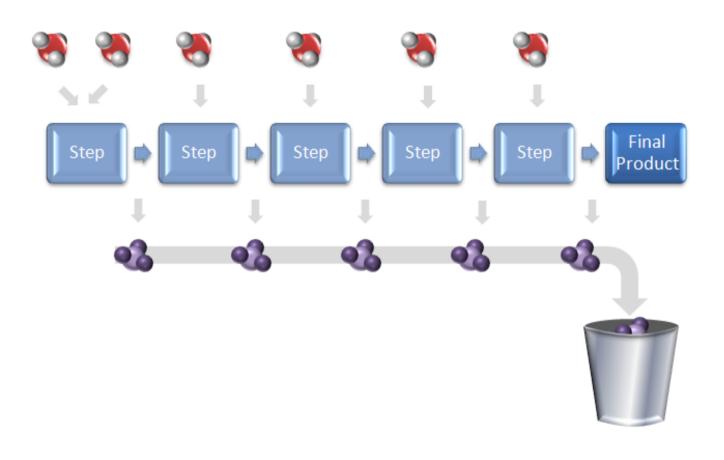


- Phosphines have unique properties
- Common in R&D
- Not as common in manufacturing, most often due to high costs, mostly associated with separation
- Waste management costs are high



# Non phosphine based chemistry

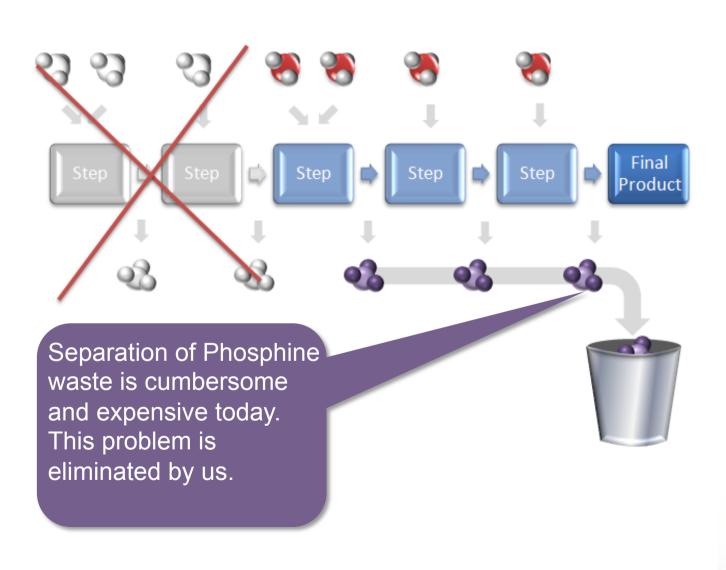






# Phosphine based production







### The Green Chromafora-process



The process developed by Chromafora can be classified as green chemistry. This view is confirmed by the "excellent" score that it receives from the ecoscale<sup>1</sup>, the process increases atom-economy<sup>2</sup> and reduces the "e-factor"<sup>3</sup>.

- 1. Aken, KV; Strekowski, L; Patiny, L. Beilstein Journal of Organic Chemistry 2006, 2, No. 3
- 2. Trost, BM Science 1991, 254, 1471
- 3. Sheldon, RA; CHEMTECH 1994, 38-47

# HOW we do it-Chromafora phosphine solution



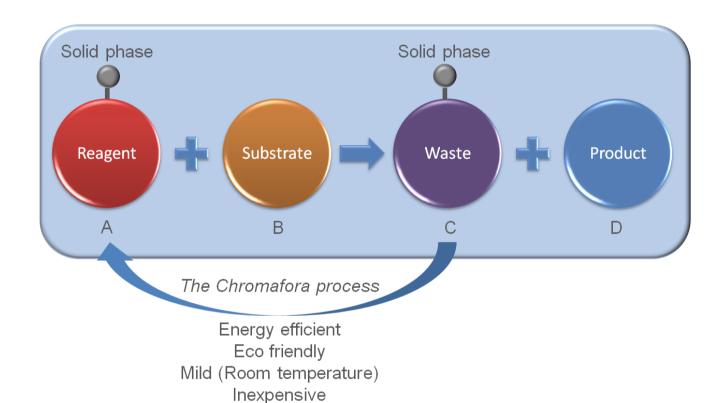
Polystyren, ROMP-gel, SILICA, PEG

As the only company in the world we are able to reuse solid supported phosphines cost efficiently



# The Chromafora process



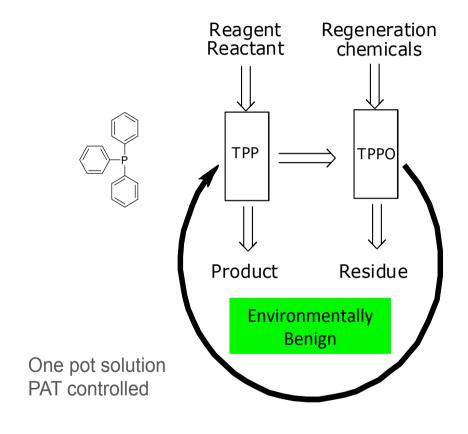


Chromafora's process (Solid phase) with significant cost-savings



# **Proposed solution**







One pot solution:

Step 1:

do reaction, filter off crude.

Step 2:

Reactivate Phosphine

again:

System ready for Step 1.



### How much less?



#### **Classical Chemistry**

Reactants used

#### **Chromafora's process**

Reactants used













Waste produced







### Stochiometric reaction



- A benefit is the simplified separation
- Possibly shorter lead time
- Possibly this leads to shorter R&D;
  - No separation methodology needs to be developed to separate the phosphine waste
  - No need to exchange the phosphine route
- Less waste is generated, at least 21%, compared to using TPP in ordinary way
- Phosphines become an inventory
- Increased AE

### Other possible benefits



- Minimizing the formation of by-products
- Drive the reaction towards the sought enantiomer
- After filtration intermediate is ready for next step
  - No other separation technique needs to be used to separate phosphine-oxide,
- Reaction can possibly be ran at a higher temperature
- Possibly less solvents can be used in reaction as well as in separation

### Case Study Comparison, API



	Synthesis		
	Chromafora	Today <sup>1</sup>	Difference
Reaction steps	6	8	- 25 %
Overall yield	31%	18%	+ 72 %
Chromatographic purification	1	2	- 50 %
Cost per kilo <sup>2</sup>	880 kUSD	1 500 kUSD	- 41 %
Waste	53	100	- 47 %
Ecoscale penalty <sup>3</sup>	-61	-110.5	- 45 %

Cost reduction due to shorter lead time & less chromatographic purification not included



<sup>&</sup>lt;sup>1</sup> Extracted from patents

<sup>&</sup>lt;sup>2</sup> Based on SIAL catalog price

<sup>&</sup>lt;sup>3</sup> Beilstein

# Versatility of phosphines



- Phosphines (such as TPP) is excellent for several reactions types, such as
  - Wittig
  - Staudinger
  - Appel
  - Mitsunobu
  - Ligand and catalyst chemistry



### Catalytic reactions



- A benefit is the simplified separation
- Possibly shorter lead time
- Possibly this leads to shorter R&D;
  - No separation methodology needs to be developed to separate the phosphine waste
  - No need to exchange the phosphine route
- We can reuse expensive phosphines, making them an inventory
- Decrease metal contamination in product

### Ligand examples



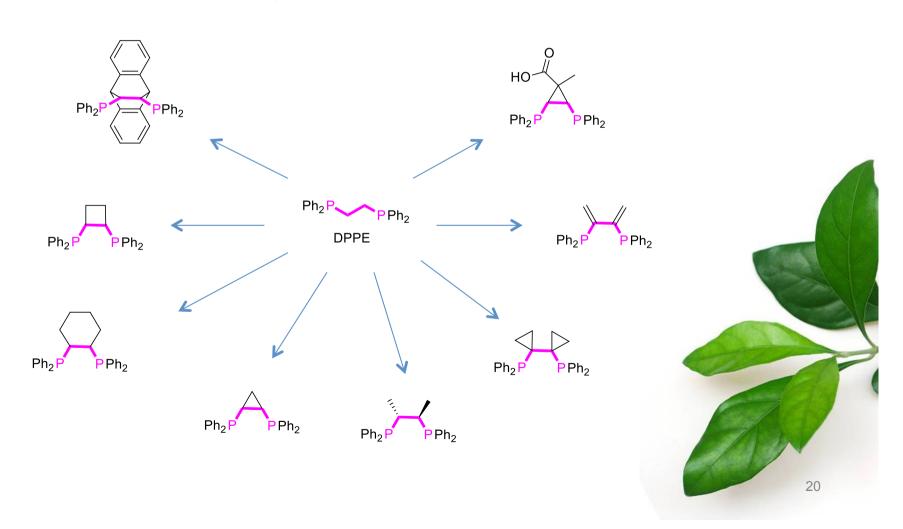
- Chromafora can attach BINAP and Xantphos to a solid particle
- Chromafora can recycle BINAP and Xantphos, thereby making them an inventory



### Different bidentates



We have used DPPE as a model substrate for more complicated bidentate ligands which are all made from their oxide counterparts.



### Chromafora Offer



- CHROMAFORA SUPPORTS CUSTOMER IN ROUTE ANALYSIS AND PROCESS DEVELOPMENT
- CHROMAFORA CAN PROVIDE SPECIALTY CHEMICALS
- CHROMAFORA CAN SUPPORT CUSTOMER WITH RECYCLING OF SOLID-PHASE PHOSPHINES
- CHROMAFORA PROVIDES A TECH-LICENSE



### Contact



WWW.CHROMAFORA.COM info@chromafora.com

Henrik Rundgren, CEO
henrik@chromafora.com
Mobile: +46-733 643959
CHROMAFORA AB
Banvaktsvägen 22
171 48 Solna
Sweden

