





Eco friendly fine chemical production with
significant economical benefits





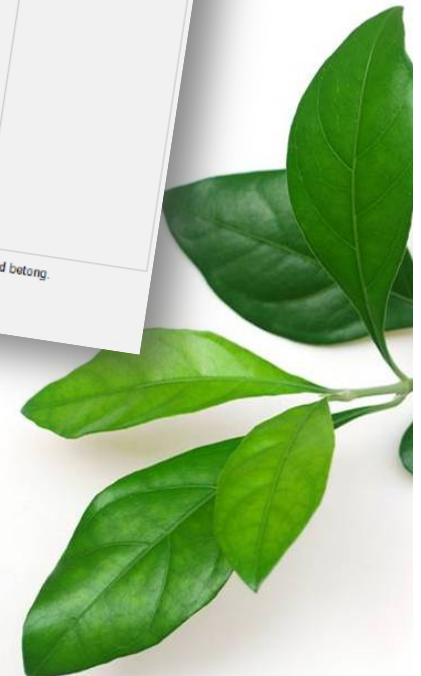
Methodology to shorten lead-times, use less energy and use less chemicals – with possibility to increase the yield.



Swedish inventors 2011



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



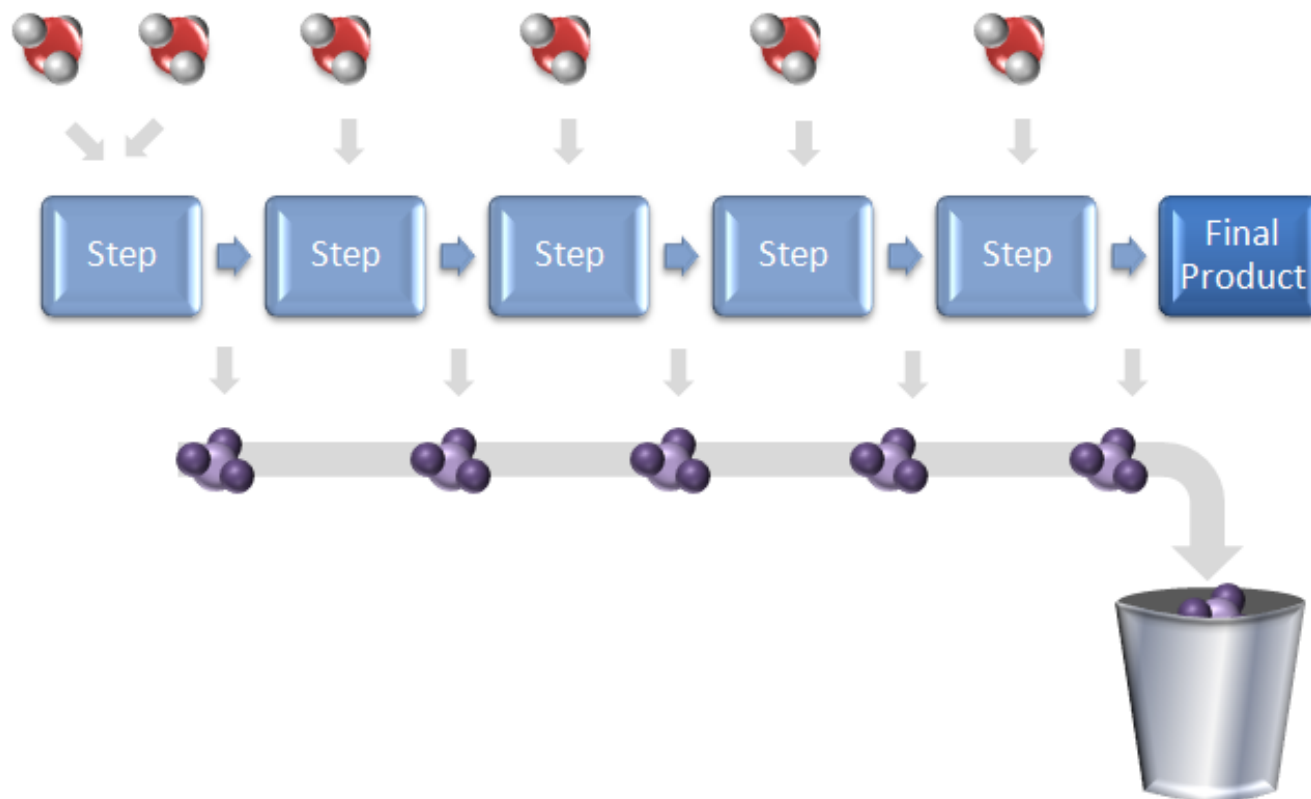
Phosphines in manufacturing today



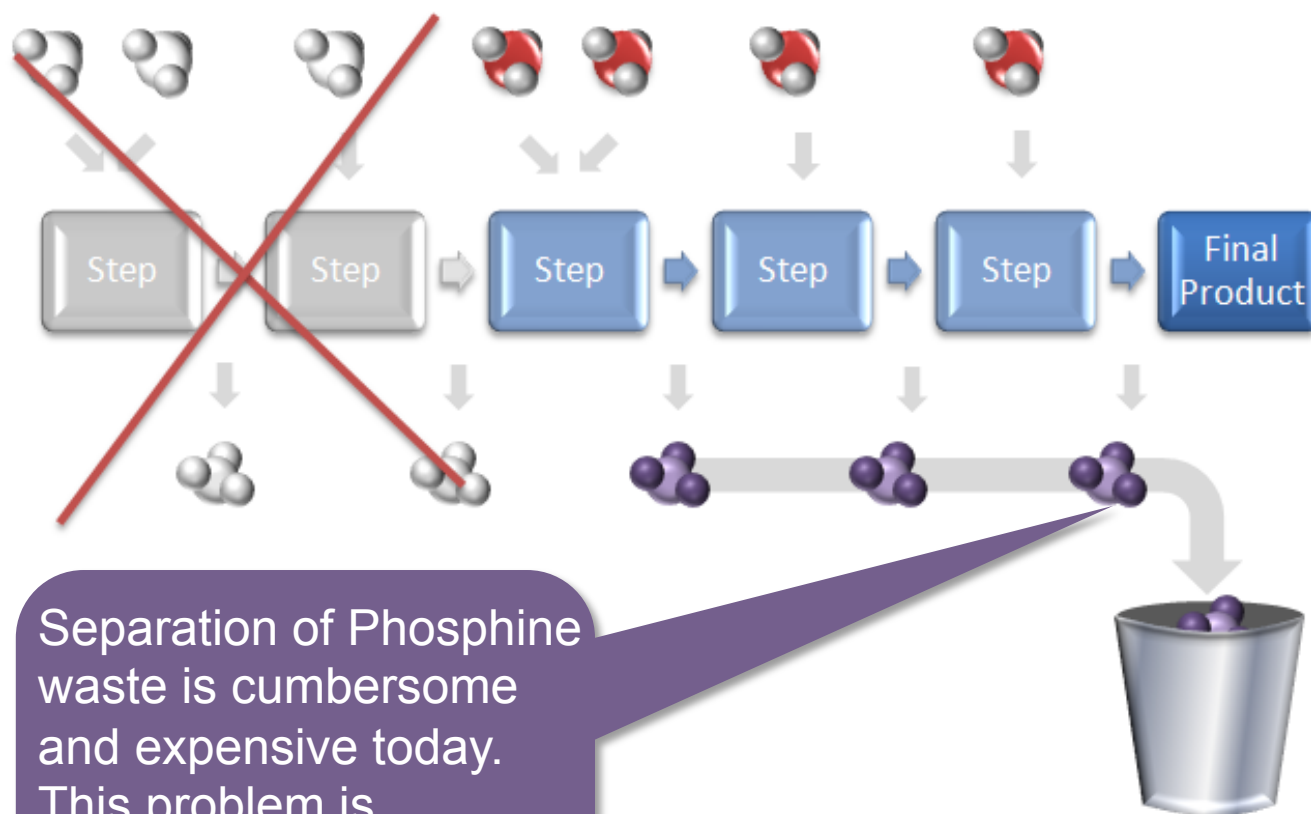
- Phosphines have unique properties
- Common in R&D
- Not as common in manufacturing, most often due to high costs, mostly associated with separation
- Waste management costs are high



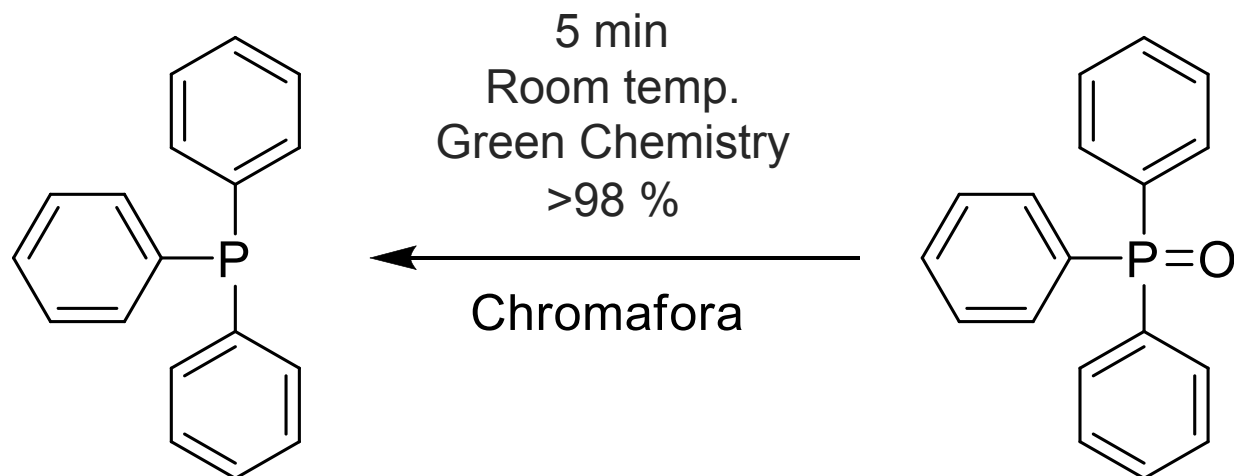
Non phosphine based chemistry



Phosphine based production



The Green Chromafora-process

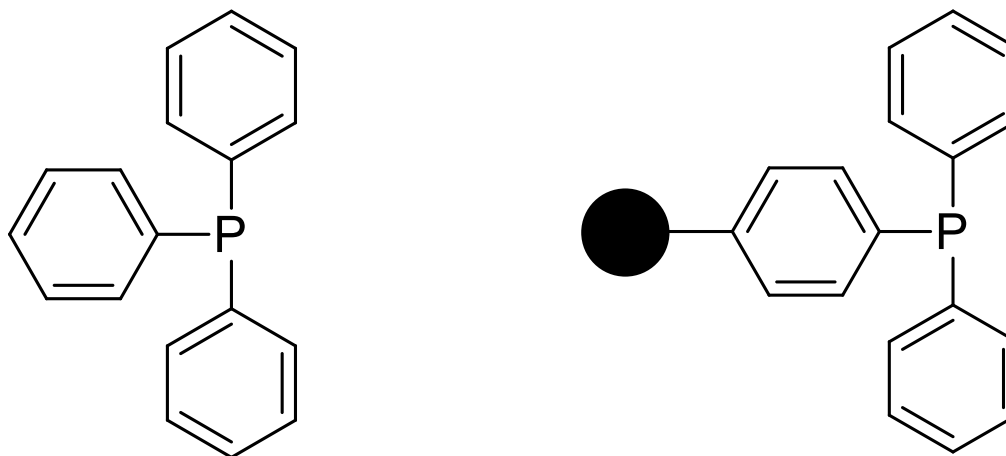


The process developed by Chromafora can be classified as green chemistry. This view is confirmed by the "excellent" score that it receives from the ecoscale¹, the process increases atom-economy² and reduces the "e-factor"³.

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

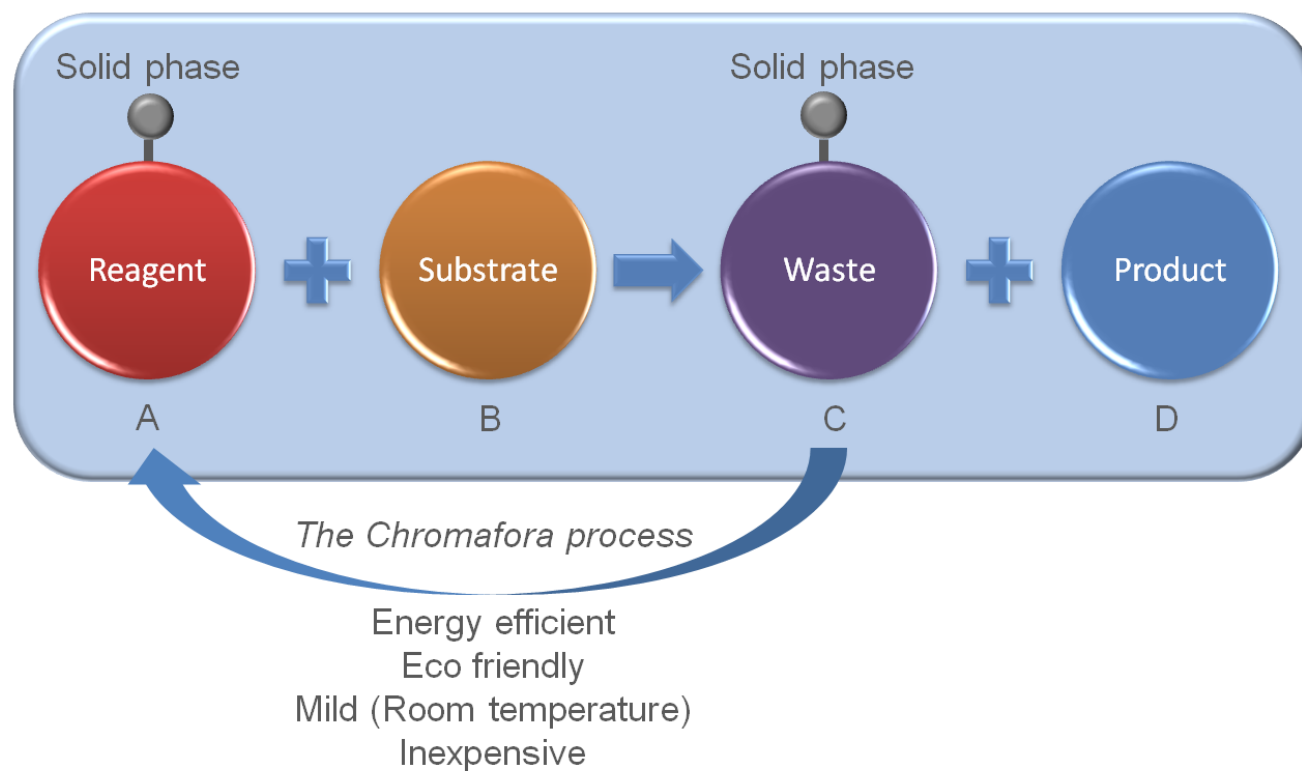


● = Polystyren, ROMP-gel, SILICA, PEG

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



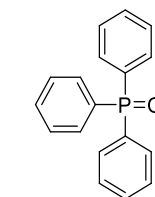
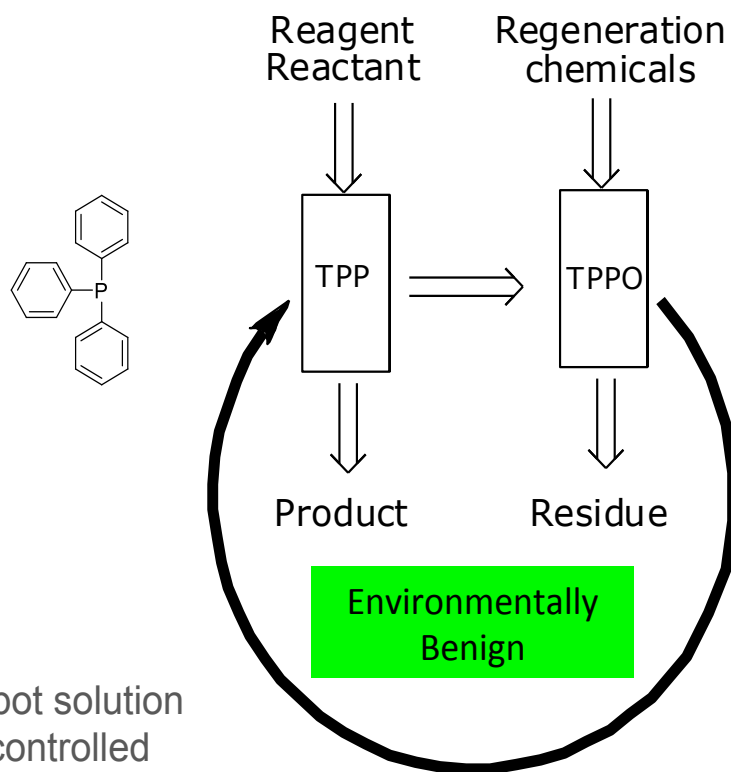
The Chromafora process



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



Waste produced



Chromafora's process

Reactants used



Waste produced



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

¹ Extracted from patents

² Based on SIAL catalog price

³ Beilstein

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



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



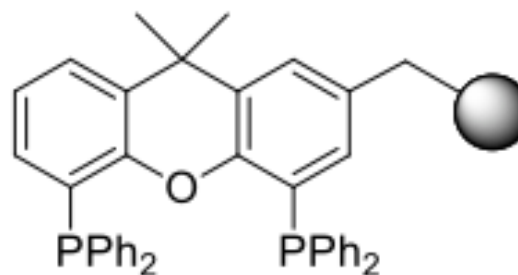
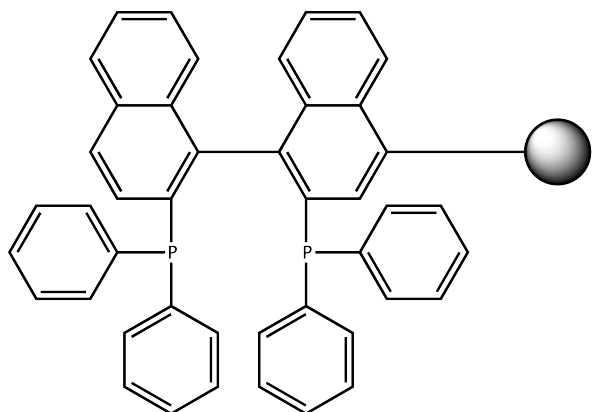
- A benefit is the simplified separation
- Possibly shorter lead time
- Possibly this leads to shorter R&D;
 - No separation methodology needs to be developed to separate the phosphine waste
 - No need to exchange the phosphine route
- We can reuse expensive phosphines, making them an inventory
- Decrease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



Ligand examples



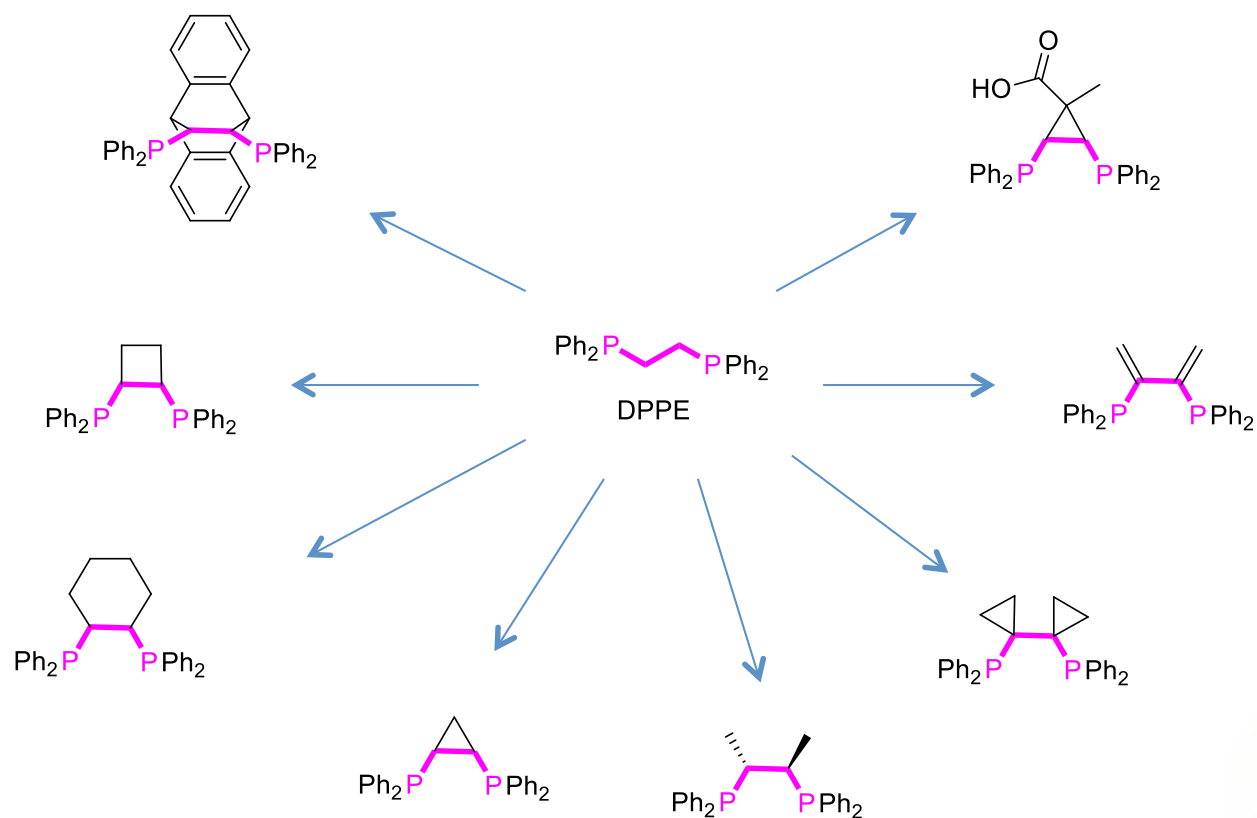
- Chromafora can attach BINAP and Xantphos to a solid particle
- Chromafora can recycle BINAP and Xantphos, thereby making them an inventory



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



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