Molecular Design and Synthesis

> Links to Session 1: Light/Matter

> History of Making Things

> Structure and Reactivity 101

> Design Process/Matter Lifecycle

> Polymeric Metal Complexes

> Design Process/Matter Lifecycle

- Target molecule
- Synthetic strategy
- Chemicals
- Laboratory notebook
- Reaction setup
- Isolation
- Purification
- Then where?

> Design Process/Matter Lifecycle

- Target molecule
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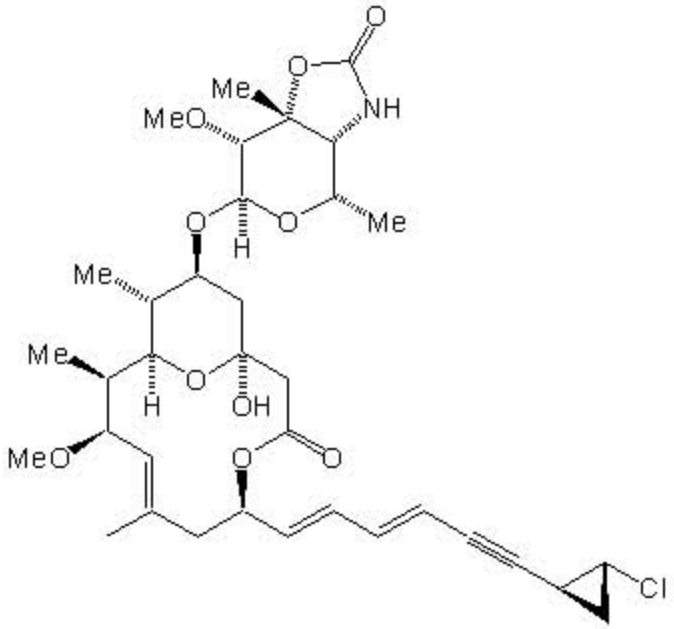
- Then where?

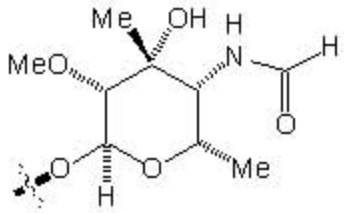
Traditional Synthesis

Combinatorial Synthesis

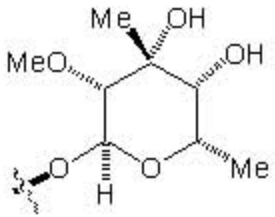
•Target molecule



Callipeltoside A



Callipeltoside B



Callipeltoside C

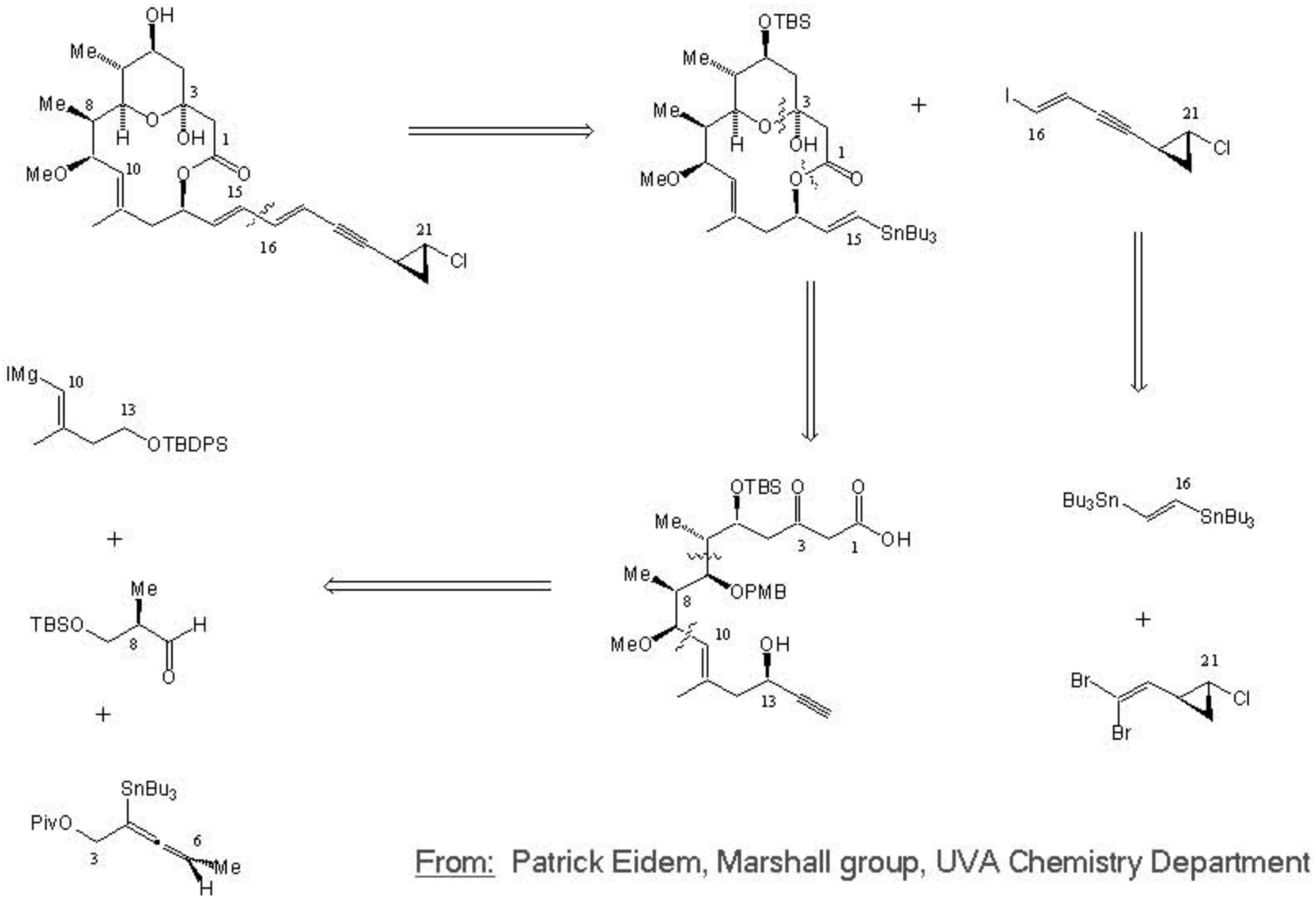
Isolation: From marine sponges, Minale et al, University of Naples.
2.5 kg of sponge furnished 3.5 mg of the natural product.

Activity: Callipeltoside A inhibit in vitro proliferation of cancer cells; HIV infected cell protection.

Previous Total Synthesis: Paterson, Evans, and Trost. **Fragment Synthesis:** Hoye, Olivo

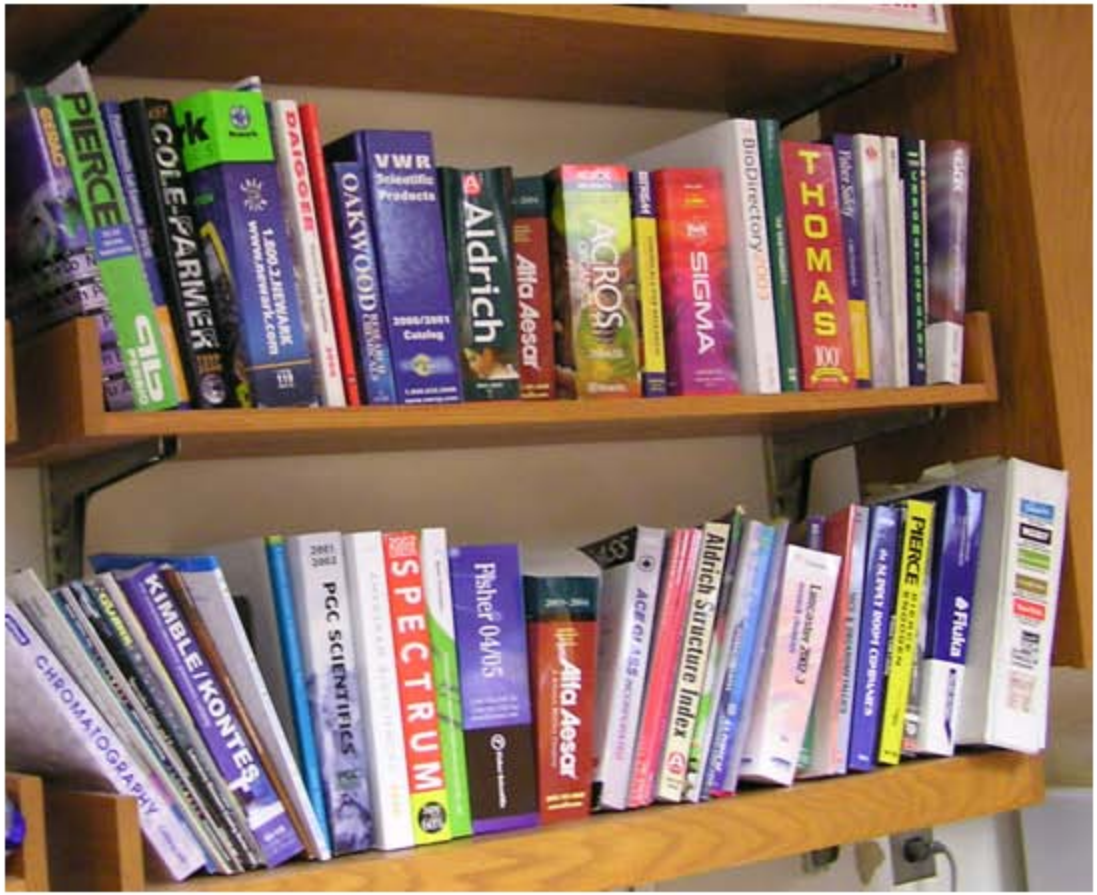
From: Patrick Eidem, Marshall group, UVA Chemistry Department

•Strategy: Retrosynthetic analysis

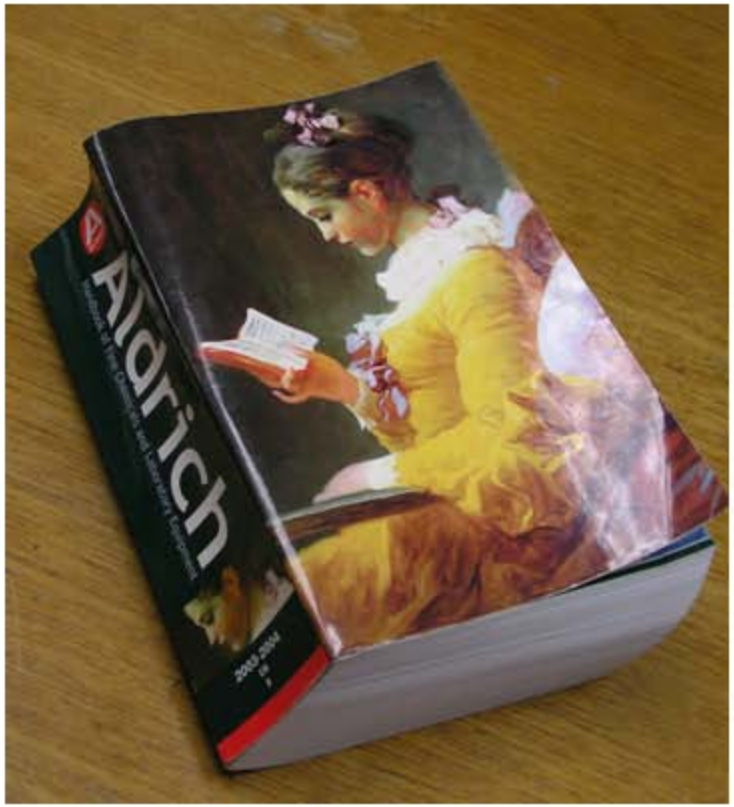


From: Patrick Eidem, Marshall group, UVA Chemistry Department

• Chemicals: Selection



•Chemicals: Selection



Tetrabromobisphenol A, see 33,039-6, 4,4'-Isopropylidenebis(2,6-dibromophenol)
page 1102

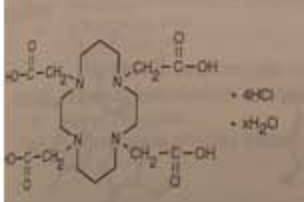
41,122-1 ★ **2,2',6,6'-Tetrabromobisphenol A diallyl ether,** 99% [*25327-89-3*] 250g 34.50
$(CH_3)_2C[C_6H_2(Br)_2OCH_2CH=CH_2]_2$ FW 624.03 mp 118-120° 1kg 97.80

43,747-6 ★ **2,2',6,6'-Tetrabromobisphenol A ethoxylate (1 EO/phenol) diacrylate** 100g 26.00
[*66710-97-2*] $[H_2C=CHCO_2(CH_2CH_2O)_nC_6H_2(Br)_2$-4-$]_2C(CH_3)_2$ mp 136-138° 500g 86.50
IRRITANT
Average M_n ca. 740. Contains 300-500 ppm monomethyl ether hydroquinone

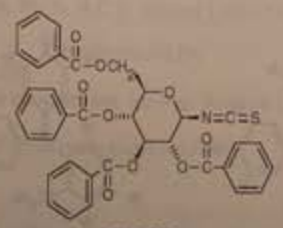
T480-3 **Tetrabromocatechol,** 96% [*488-47-1*] (tetrabromopyrocatechol) C_6Br_4-1,2-$(OH)_2$ 5g 20.70
FW 425.72 mp 189-193° *Beil.* **6**,786 *FT-NMR* **1**(2),298C *FT-IR* **1**(1),1103C 25g 68.60
Safety **2**,3232B *R&S* **1**(1),1295A *RTECS#* UX2430000 *IRRITANT*

27,706-8 ★ **3,4,5,6-Tetrabromo-*o*-cresol,** 98% [*576-55-6*] $CH_3C_6Br_4OH$ FW 423.75 ..... 100g 34.30
mp 209-212° *Beil.* **6**,362 *Merck Index* **13**,9260 *FT-NMR* **1**(2),293C *Safety* **2**,3232C 500g 111.40
R&S **1**(1),1291B *RTECS#* GP3135000 *IRRITANT*

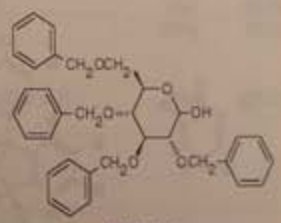
3',3'',5',5''-Tetrabromo-*m*-cresolsulfonephthalein, see Bromocresol Green



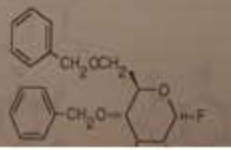
40,040-8

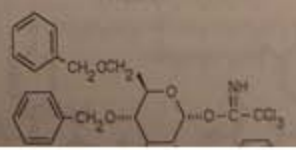


33,562-2

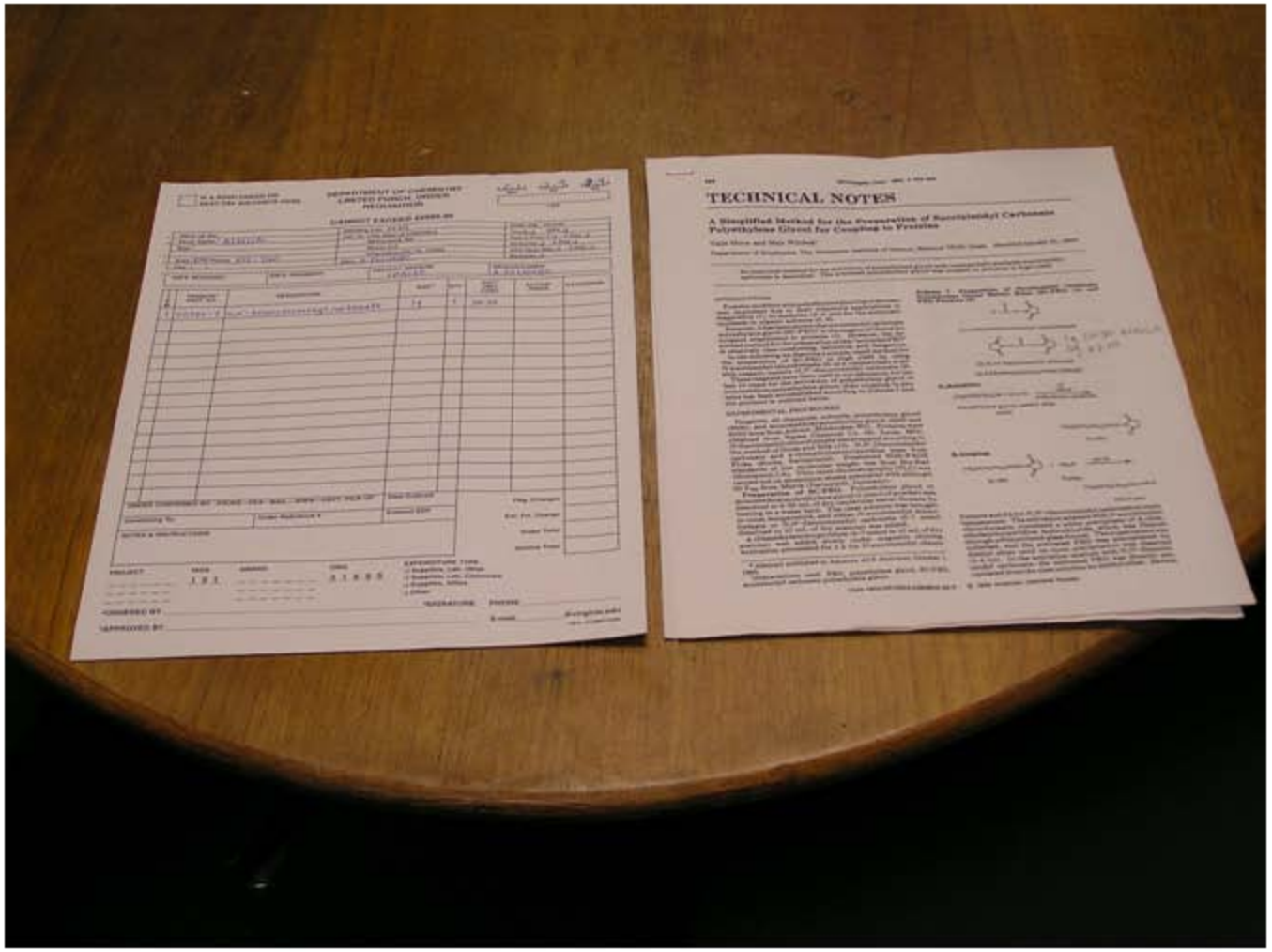


44,741-2





• Chemicals: Ordering

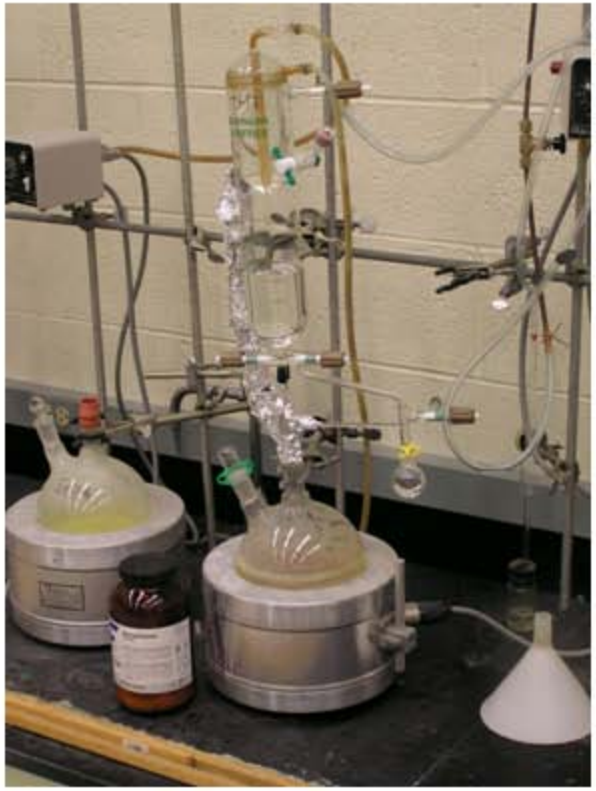


• Chemicals: Organics

• Chemicals: Inorganics

• Chemicals: Solvents

solvent cabinet



solvent stills

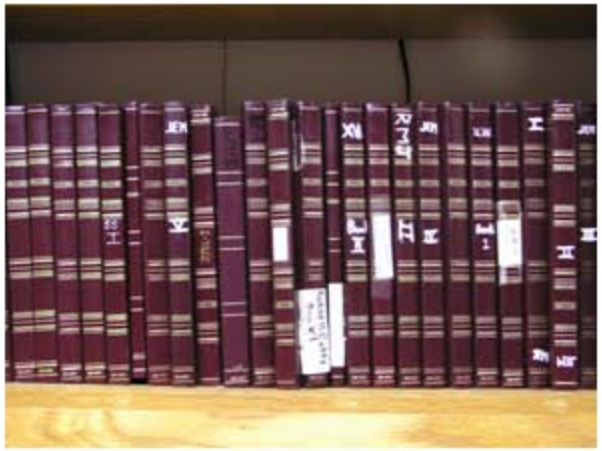
solvent columns

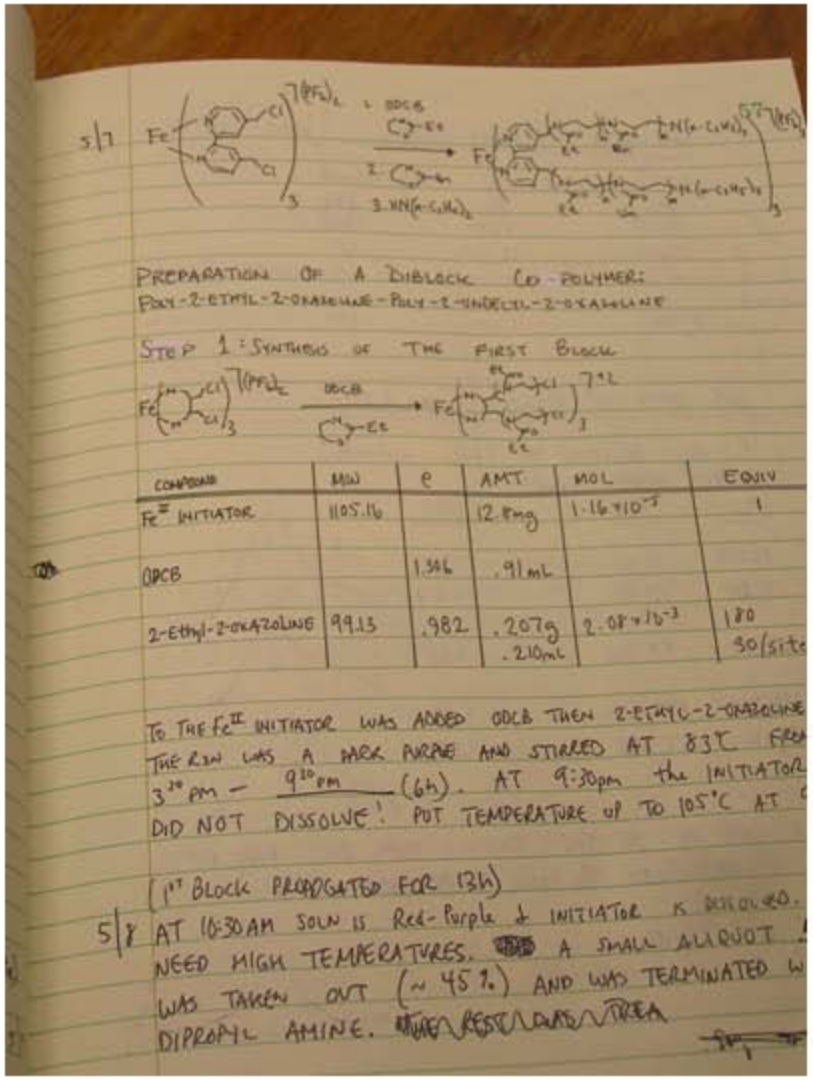
- Workspace: Bench

- workspace: Fume hood

- Workspace: Glovebox

• Laboratory notebook





5/7

PREPARATION OF A DIBLOCK CO-POLYMER:
POLY-2-ETHYL-2-OXAZOLINE - POLY-2-UNDECYL-2-OXAZOLINE

STEP 1: SYNTHESIS OF THE FIRST BLOCK

COMPOUND	MW	ρ	AMT	MOL	EQUIV
Fe^{II} INITIATOR	1105.16		12.8mg	1.16×10^{-5}	1
ODCB		1.316	.91mL		
2-Ethyl-2-oxazoline	99.13	.982	.207g .210mL	2.08×10^{-3}	180 30/site

TO THE Fe^{II} INITIATOR WAS ADDED ODCB THEN 2-ETHYL-2-OXAZOLINE. THE RXN WAS A DARK PURPLE AND STIRRED AT 83°C FROM 3:20 PM – 9:30 PM (6h). AT 9:30pm the INITIATOR DID NOT DISSOLVE! POT TEMPERATURE UP TO 105°C AT

(1ST BLOCK PROPOGATED FOR 13h)

5/8 AT 10:30 AM SOLN IS Red-Purple & INITIATOR IS DISSOLVED. NEED HIGH TEMPERATURES. A SMALL ALIQUOT WAS TAKEN OUT (~ 45%) AND WAS TERMINATED W DIPROPYL AMINE.

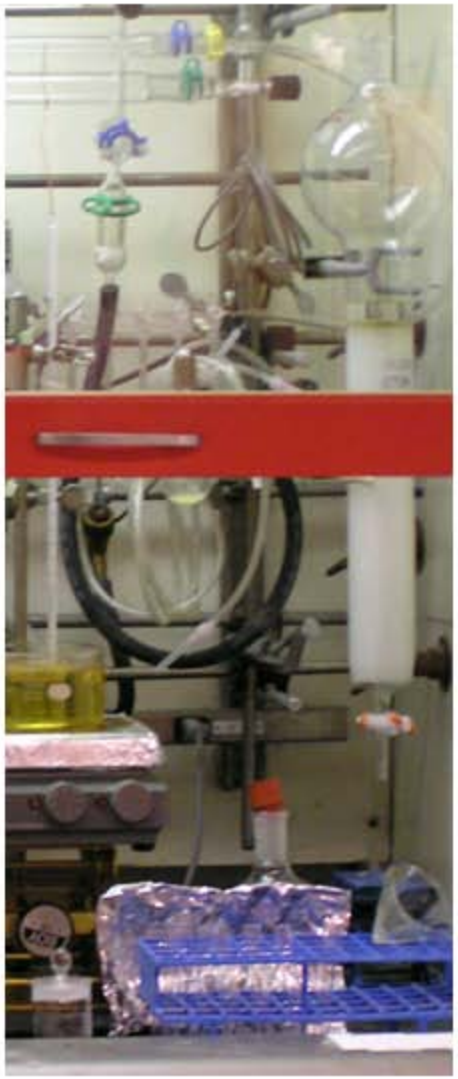
- Reaction setup

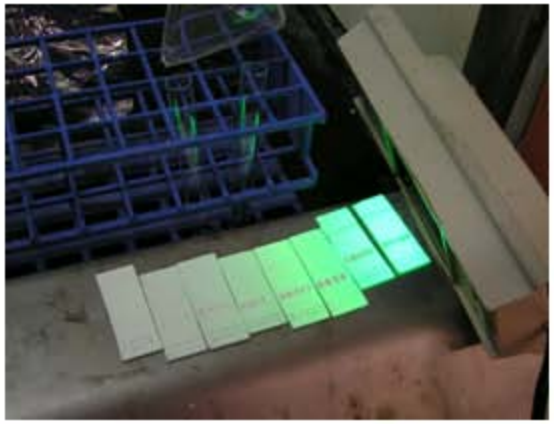
•Isolation

Separatory funnel

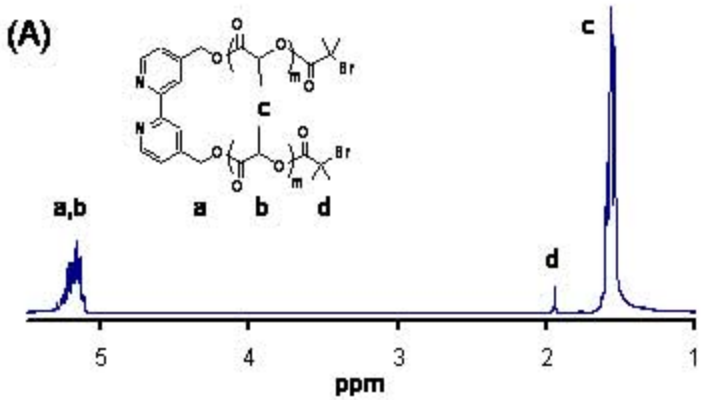
Rotary evaporator

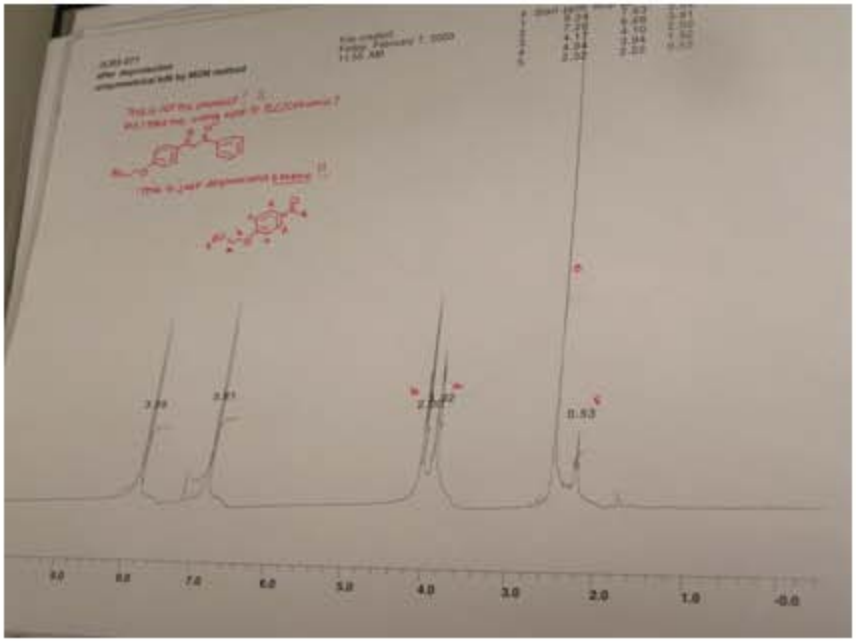
• Purification



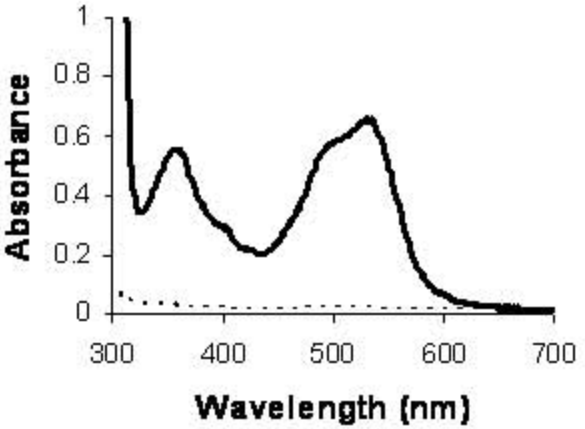


• Characterization: ^{1}H NMR spectroscopy





•Characterization: UV/Vis spectroscopy

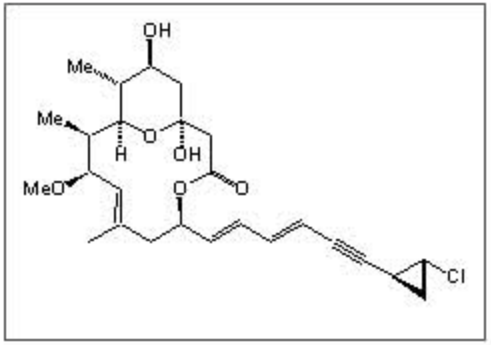


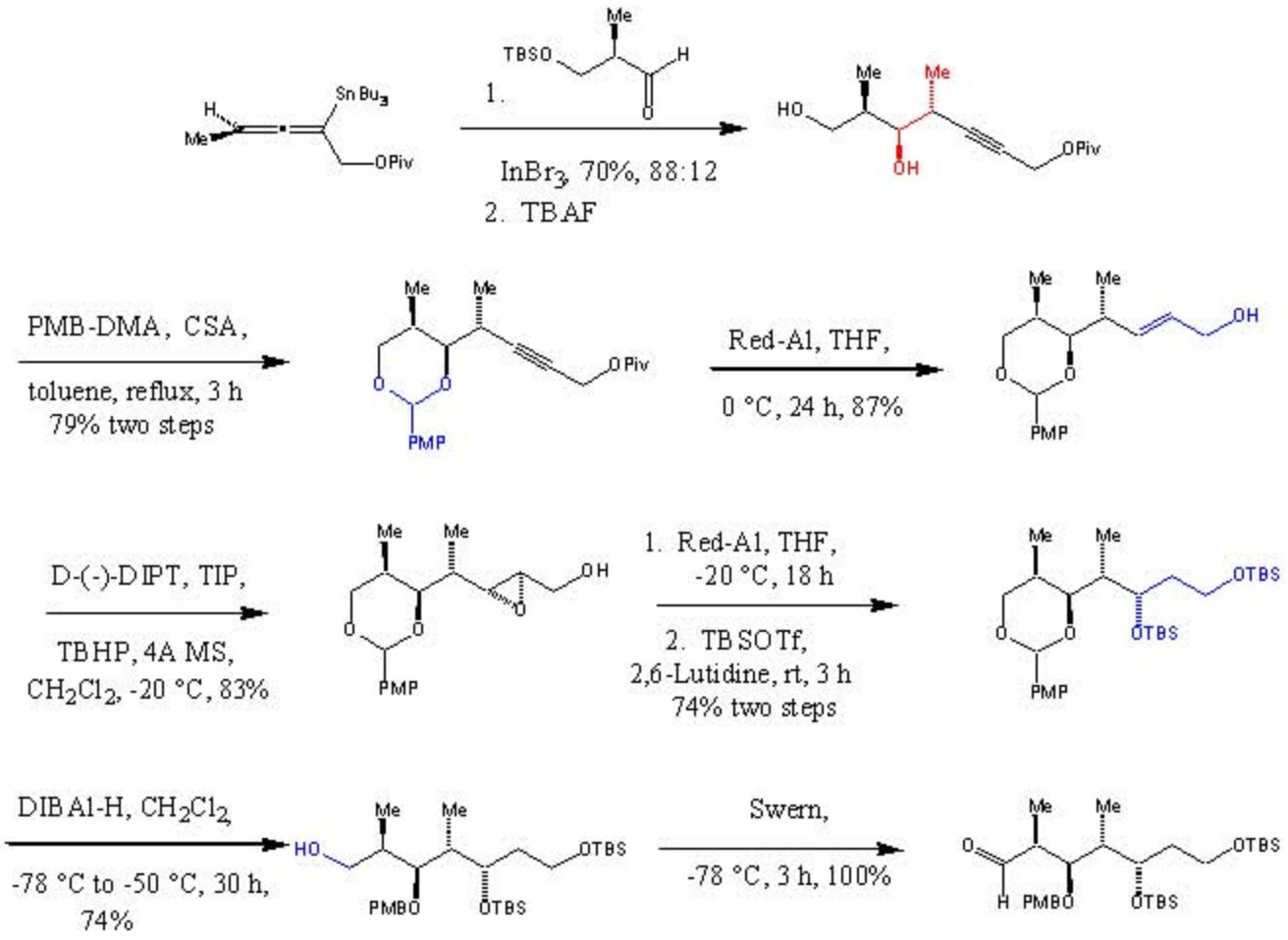
Iron Tris(bpy) PLA

•Characterization: thermal methods

thermal analysis: decomposition, melting/glass transition temperature
(also: elemental analysis)

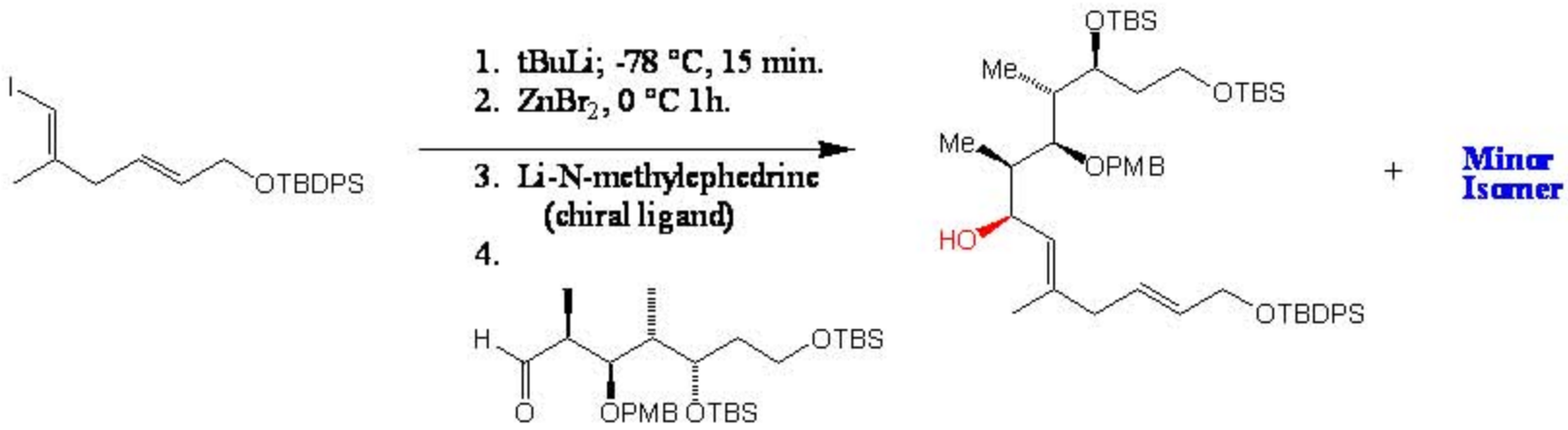
• Synthetic Scheme: C_3–C_9 Fragment





From: Patrick Eidem, Marshall group, UVA Chemistry Department

•Reaction optimization: selectivity



Metal	P	Ligand	Yield	R : S
Li	TBDPS	None	63	1 : 1
MgBr	TBDPS	None	63	3 : 1
ZnBr	TBDPS	None	68	4 : 1
ZnBr	TBDPS	(1R, 2S) NME	73	13 : 1

From: Patrick Eidem, Marshall group, UVA Chemistry Department

-Then where? In the literature

*Graphic from American Chemical Society Website

-Then where? on the shelf

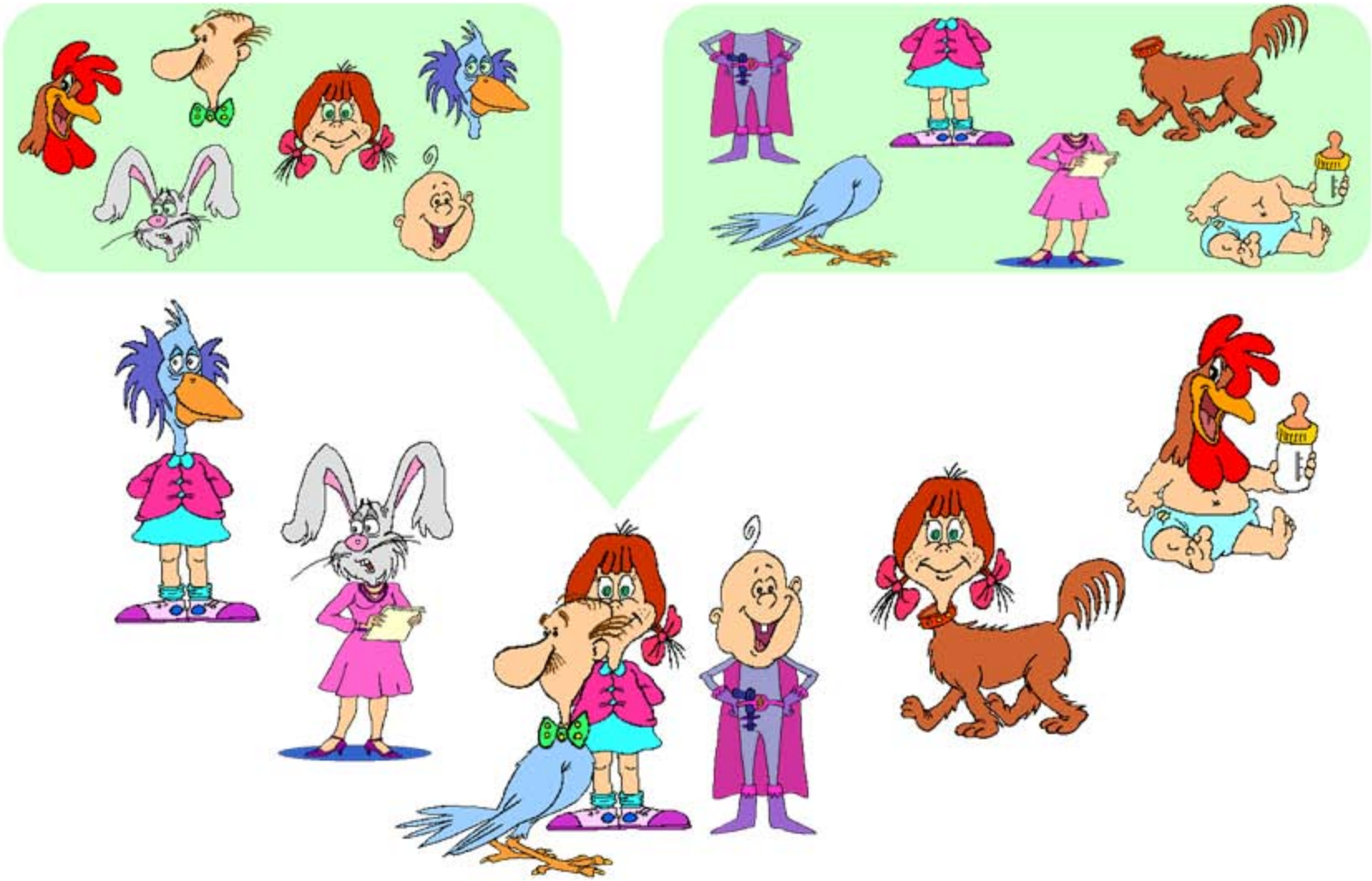
-Then where? chemical waste

-Then where? fumes

-Then where? Practical uses

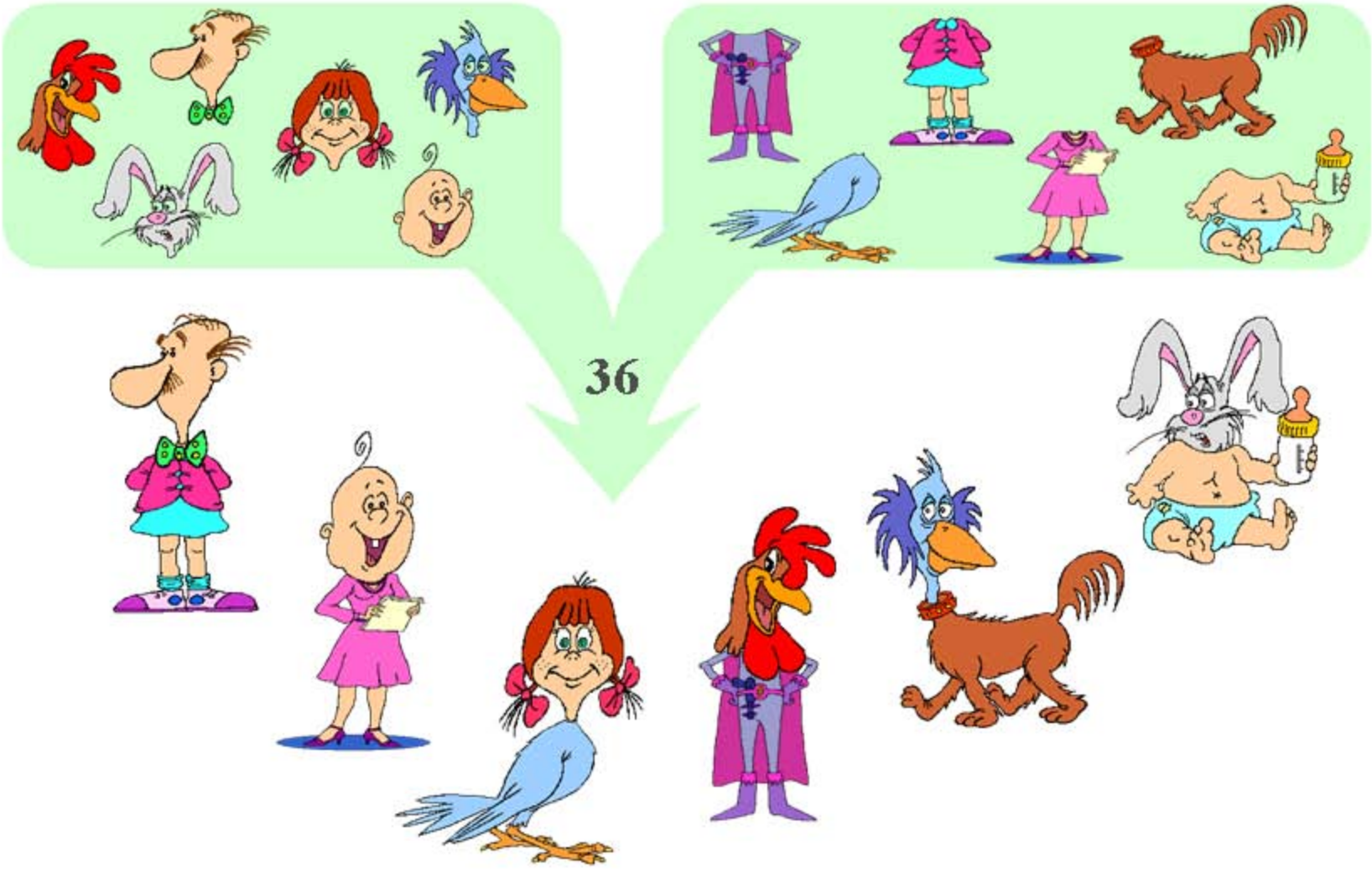
- drug testing
- property screening
- many other applications

• New Approach: Combinatorial synthesis



From: Mario Geysen, UVA Chemistry

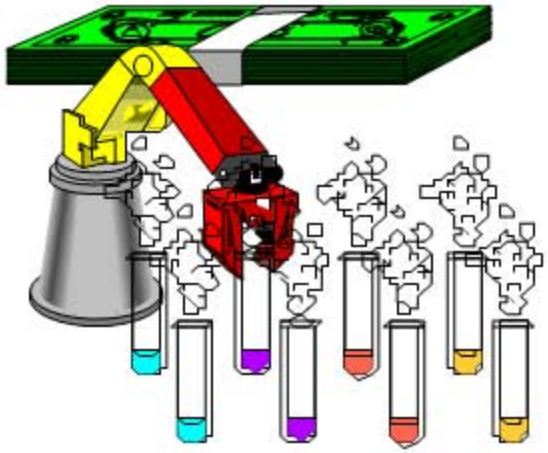
•New Approach: Combinatorial synthesis



From: Mario Geysen, UVA Chemistry

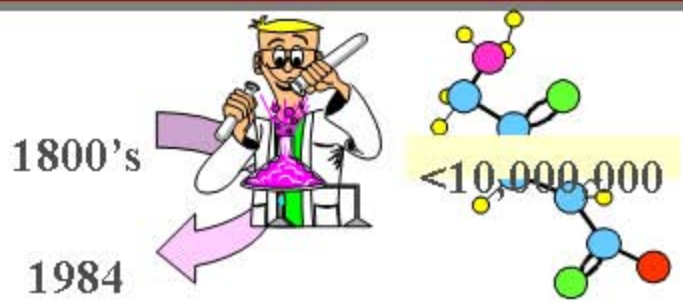
•Manual vs robots: costs involved

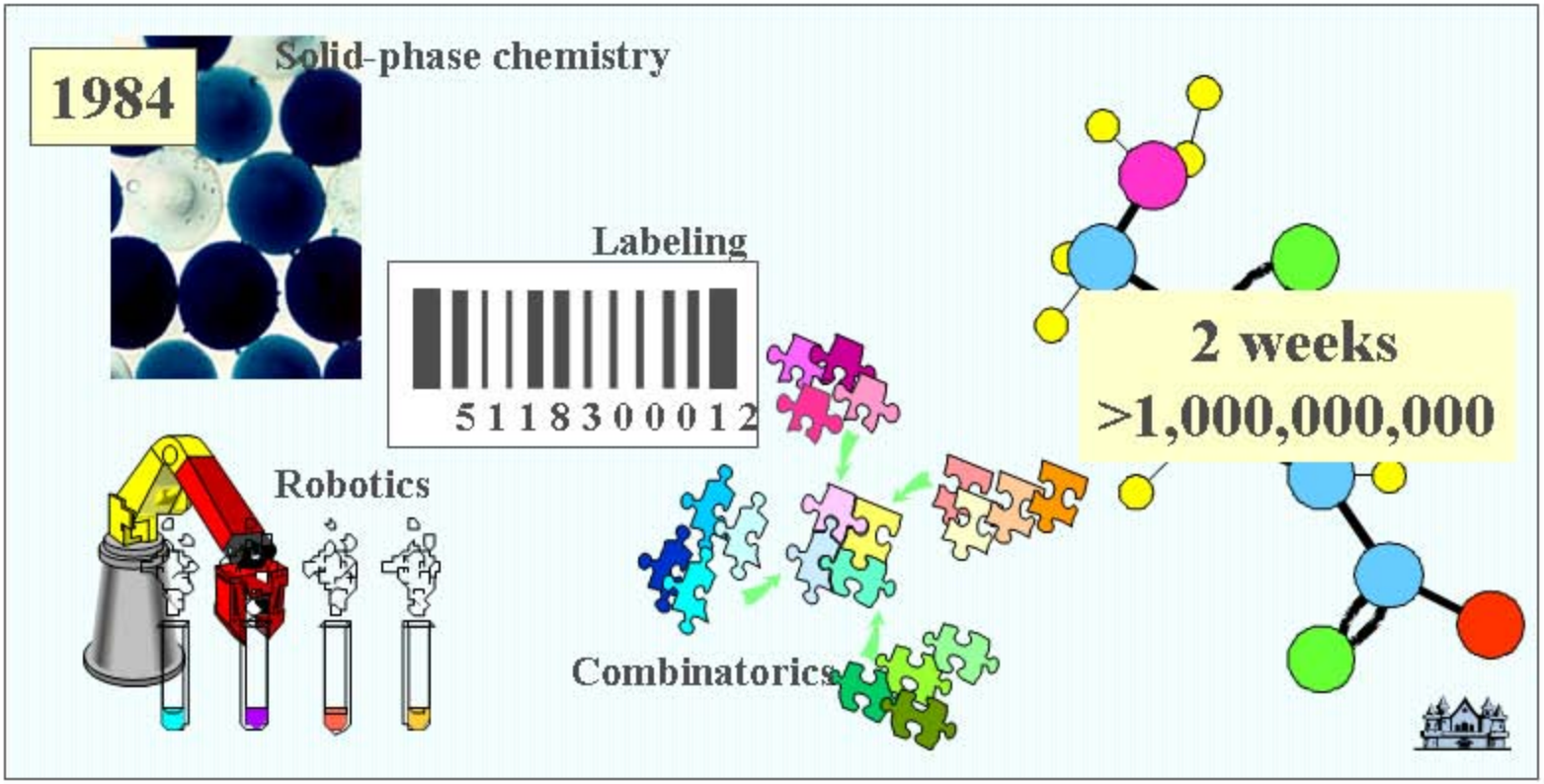
OR



From: Mario Geysen, UVA Chemistry

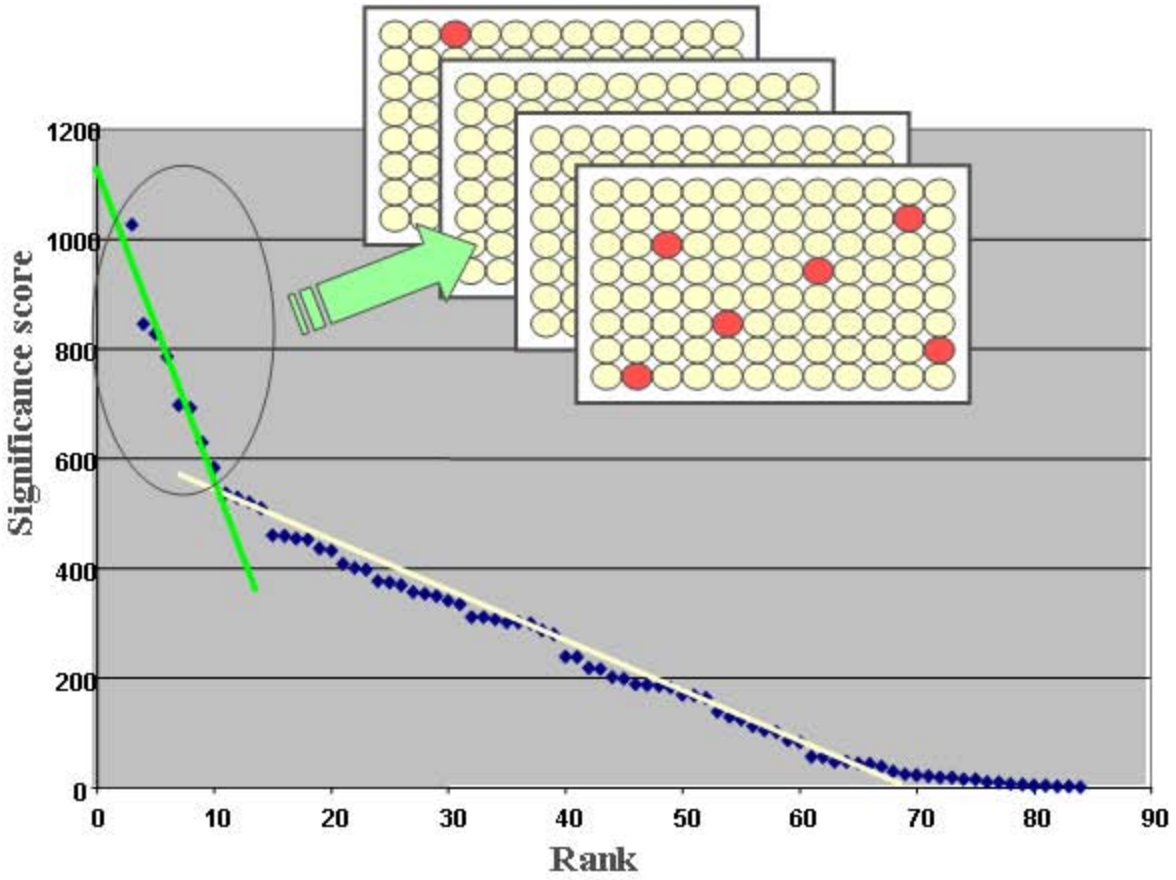
•1st Combinatorial chemical library

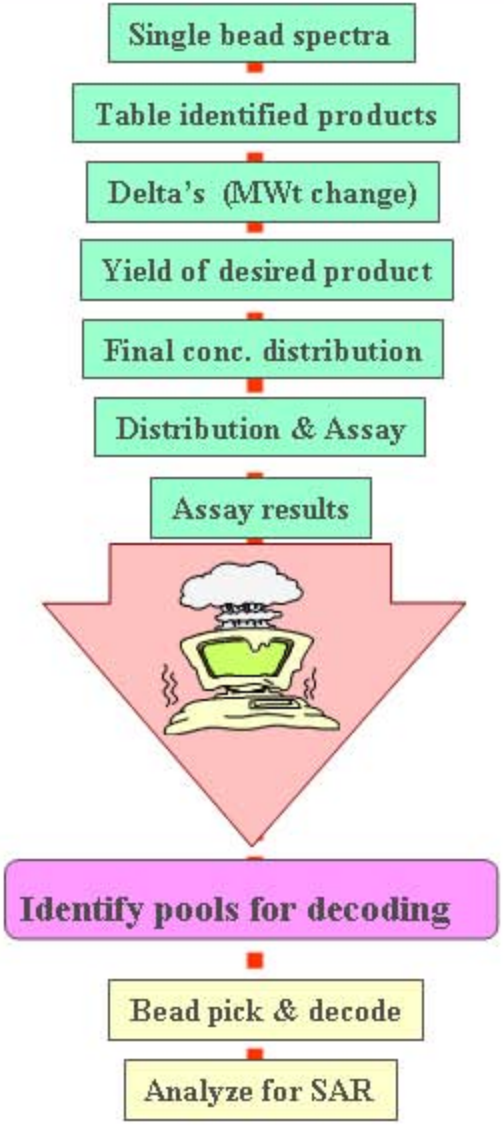




From: Mario Geysen, UVA Chemistry

•High throughput screening





From: Mario Geysen, UVA Chemistry

- Combinatorial synthesis laboratory

- Robot and multi-well trays