

The Art of Organic Synthesis

The appeal of a problem in synthesis and its attractiveness can be expected to reach a level out of all proportion to practical considerations, whenever it presents a clear challenge to the creativity, originality, and imagination of the expert in synthesis.

E.J. Corey

The synthetic chemist is more than a logician and a strategist; he is an explorer strongly influenced to speculate, to imagine and even to create. These added elements provide the touch of artistry which can hardly be included in a cataloguing of the basic principles of synthesis, but they are very real and extremely important.

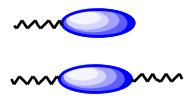
E.J. Corey

In my work, I have always tried to conjugate truth and beauty. But when I was forced to choose, I usually chose beauty.

Hermann Weyl

When I am working on a problem, I never think about beauty. I think only of how to solve the problem. But when I have finished, if the solution is not beautiful, I know it is wrong.

Buckminster Fuller



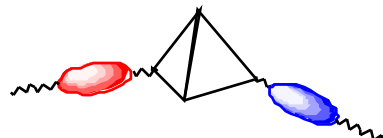
Calamitic



Banana-shaped



Swallow-tailed



Pyramidal or Bowl-shaped Core

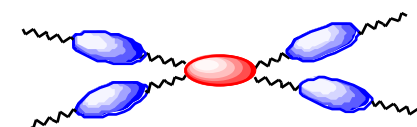


Tetra-catenar



Poly-catenar

Some Template Structures for Calamitic Liquid Crystals



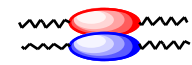
Tetramer with Flat Core



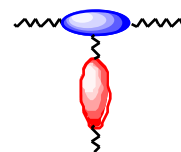
Linear Dimers and Trimers etc



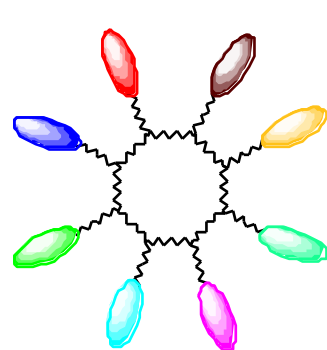
Laterally-connected



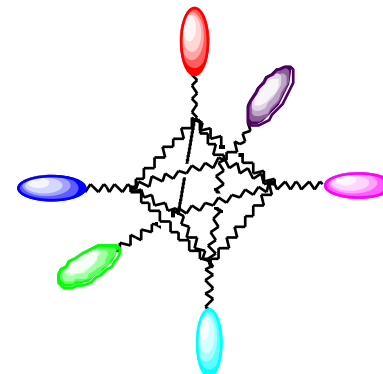
Siamese Twins



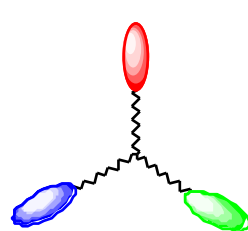
T-shaped



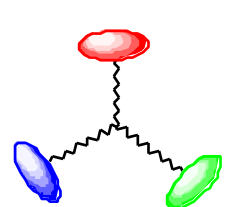
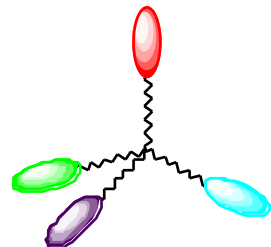
Cyclic Systems



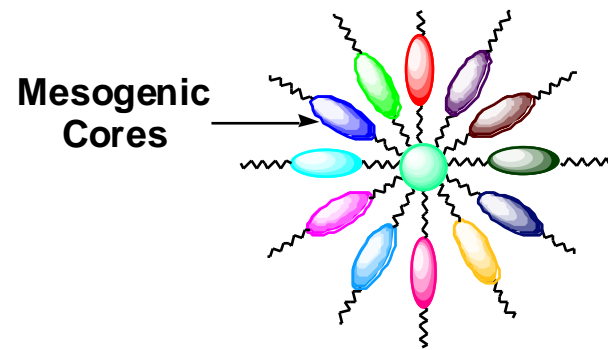
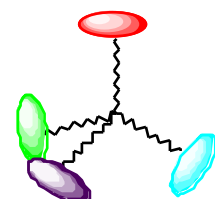
Cage Systems



Terminal Trimers and Tetramers etc



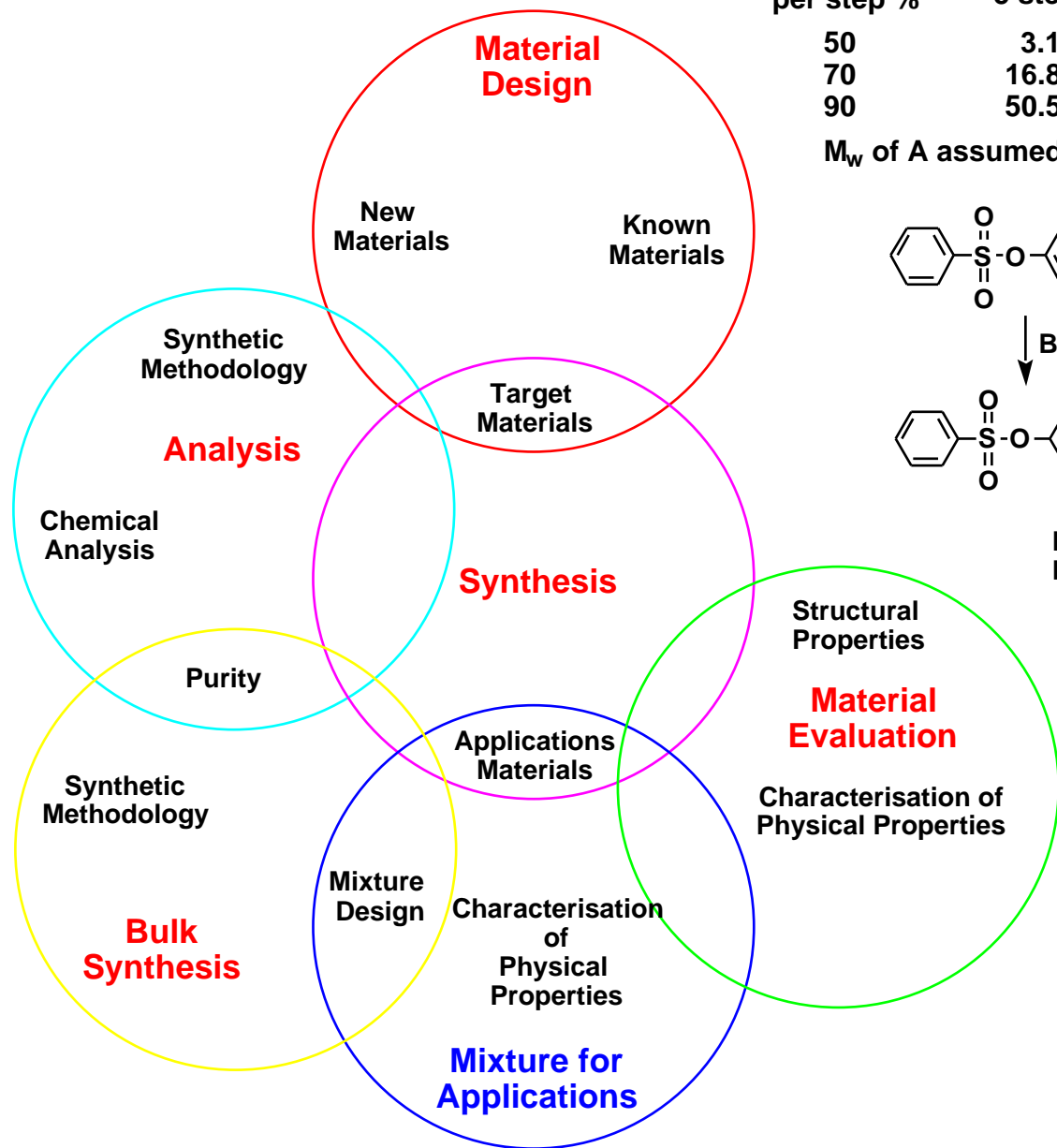
Lateral Trimers and Tetramers etc



Mesogenic Cores

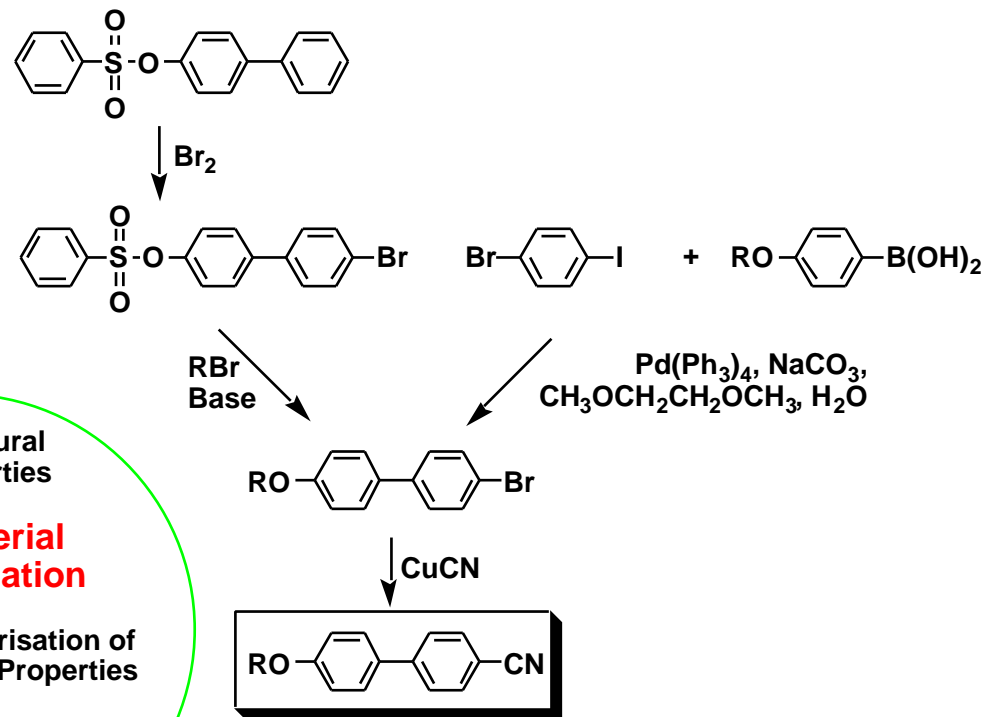
Dendrimers

Synthetic Strategies for Materials



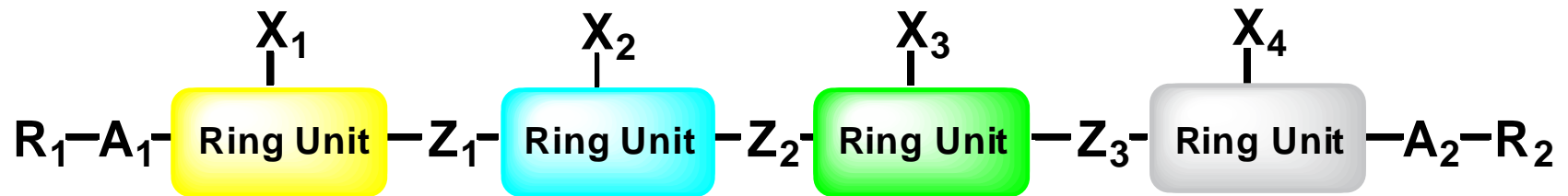
Average Yield per step %	Overall yield %			*Grams of starting material		
	5 steps	10 steps	15 steps	5 steps	10 steps	15 steps
50	3.1	0.1	0.003	16	512	16384
70	16.8	2.8	0.5	3	18	105
90	50.5	35.4	21.1	0.8	1.4	2.4

M_w of A assumed to be 1/2 M_w of product *for 1 gm of product



General Synthetic Procedures

General Structure of a Calamitic (rod-like) Liquid Crystals

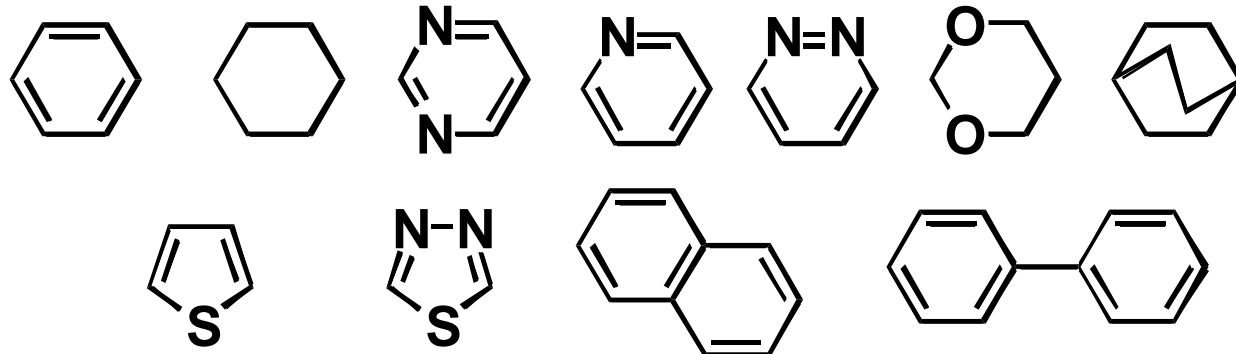


R = Alkyl, alkoxy, carbonyl, silyloxy, ethyleneoxy, chiral hydrocarbons etc

Z = direct link, COO, CH₂CH₂, CH=CH, CH₂O, COS, CF=CF, —C≡C— etc

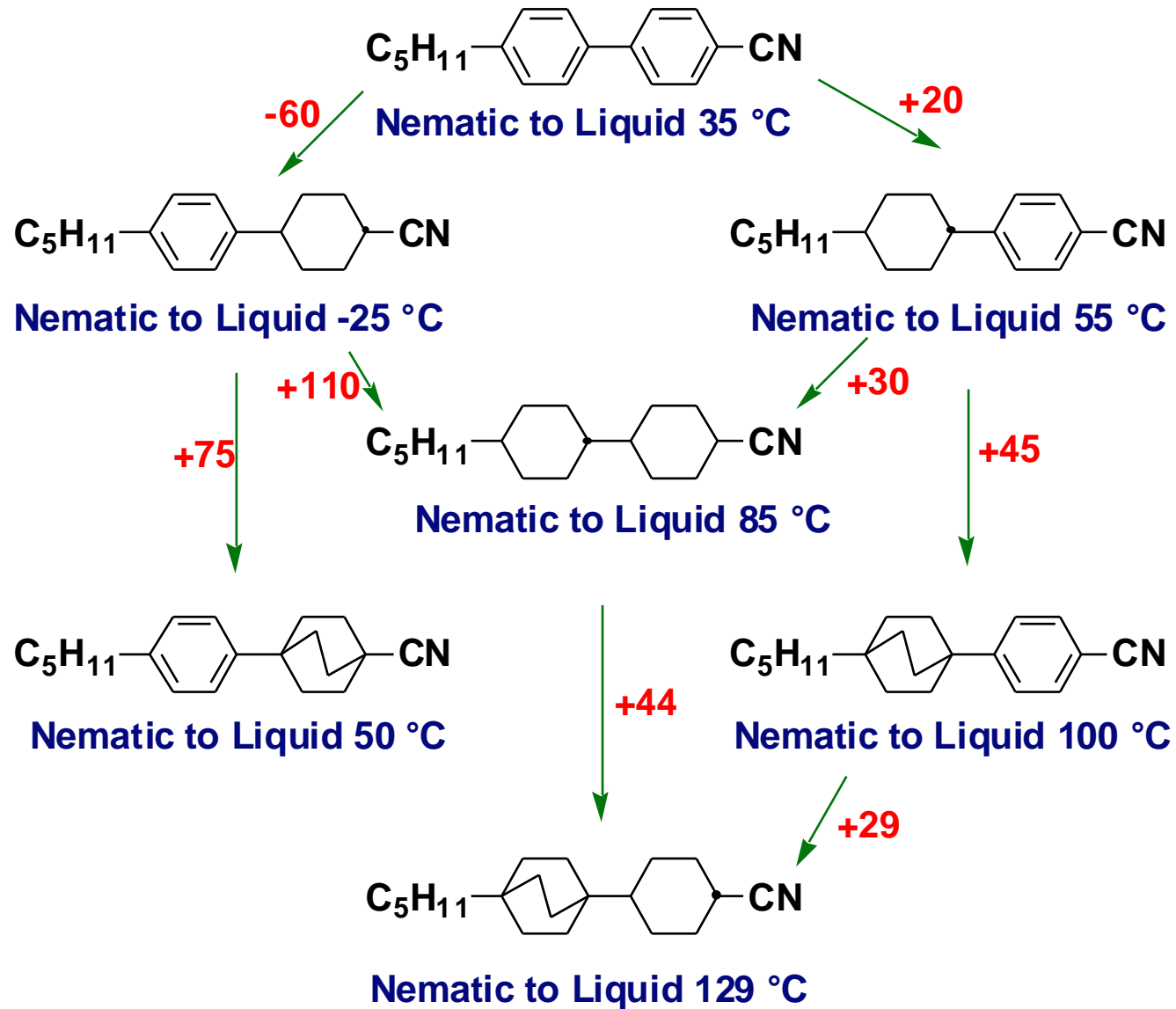
X = CN, F, Cl, Br, CH₃ etc

Ring Unit



Effects of Molecular Structure on Mesophase Formation

Effect of Ring Structures on Nematic Phases



General Reactions:

Etherifications, Friedel-Crafts, Esterifications, De-alkylations, Diazotisations, Halogenations, Hydrogenations, Sharpless Epoxidations, Hydroborations, Suzuki Coupling Reactions, Zinc Coupling Reactions etc

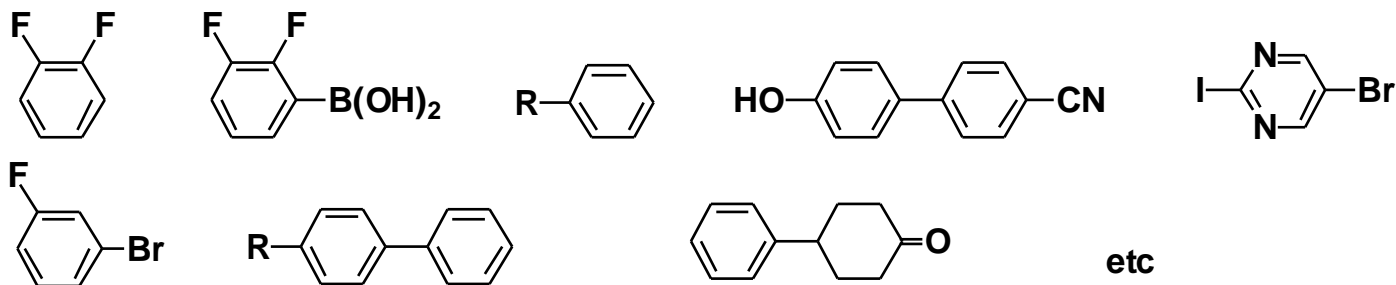
Commercial Liquid Crystals Available:

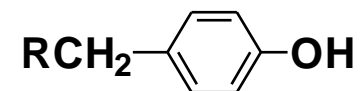
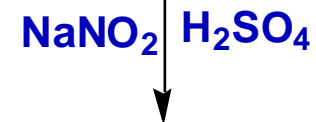
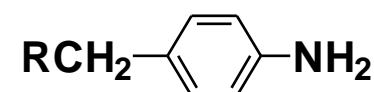
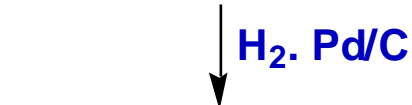
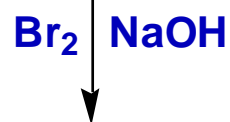
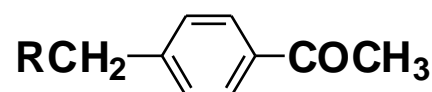
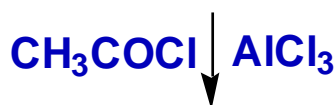
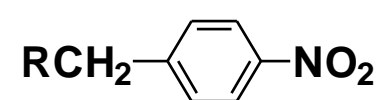
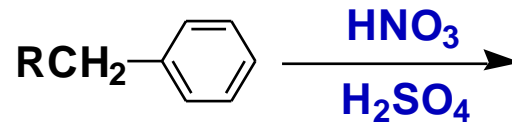
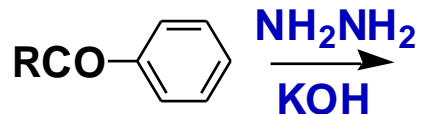
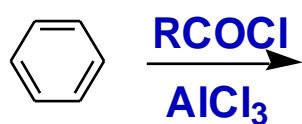
Very few single liquid crystal components available, some from China some from Germany (Synthon and Clariant), some from the UK (Kingston Chemicals) - small companies!

Generally E Merck (the biggest supplier of liquid crystals) do not supply single components - mostly mixtures are sold.

Other suppliers - Chisso and Dianippon Inc - again mostly mixtures available.

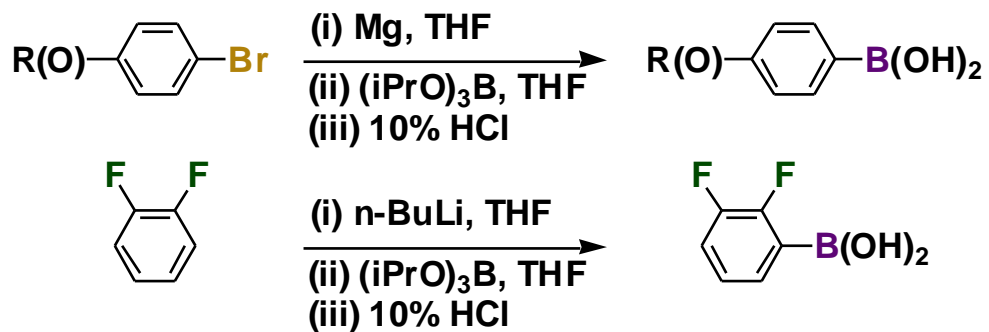
Typical Substrates Available





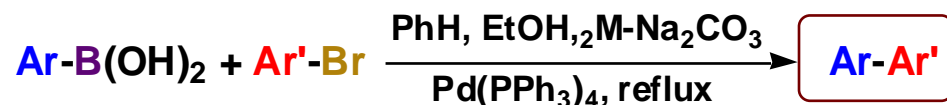
Standard Stock Materials

Versatile Synthetic Procedure for the Preparation of Core Systems

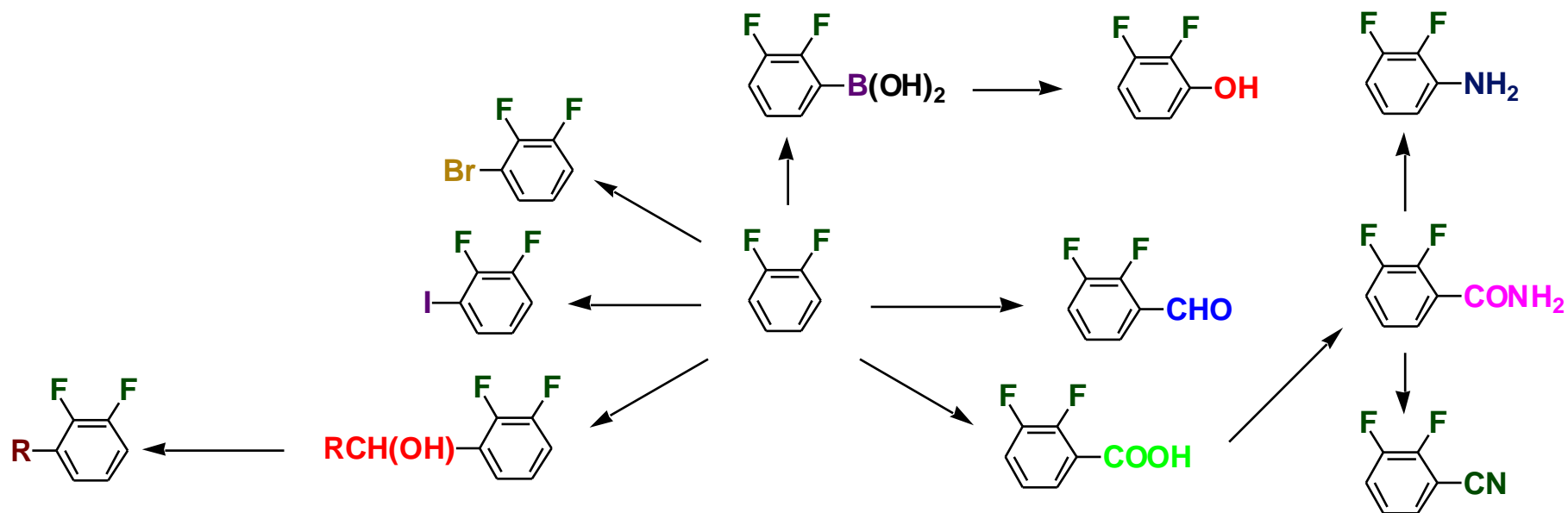


Boronic acids are easily purified, stable in air, stable to moisture, and can be stored

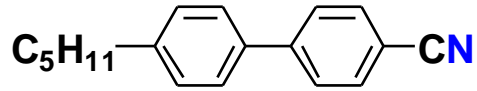
Coupling:



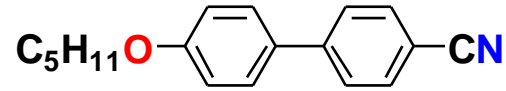
Excellent yields, no homocoupling tolerates many functional groups



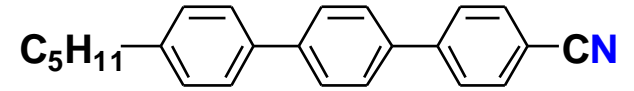
Typical Nematic Materials for TN and STN Displays



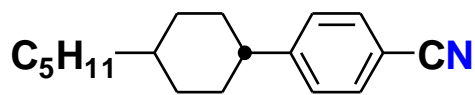
K 24 N 35 I



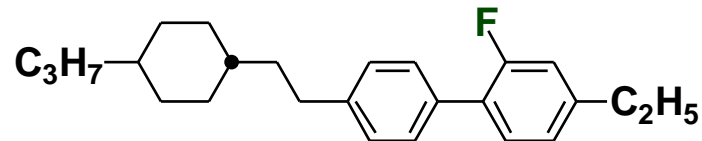
K 48 N 68 I



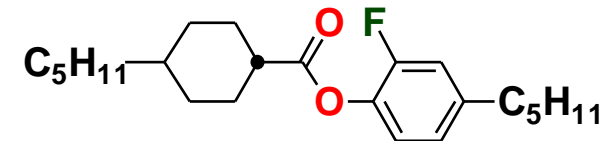
K 130 N 239 I



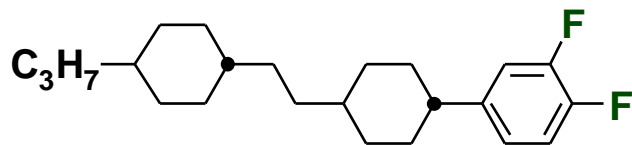
K 31 N 55 I



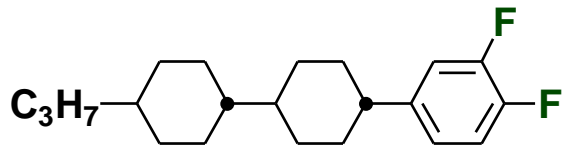
K 27 N 97 I



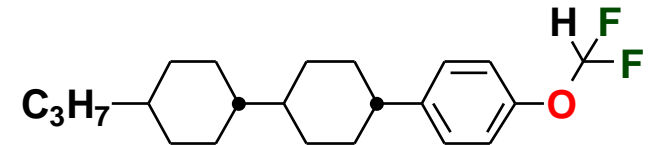
K 17 N 37 I



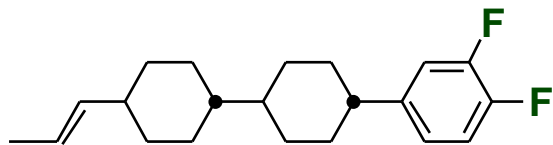
K 36 N 105 I



K 44 N 118 I



K 52 S_B 69 N 174 I



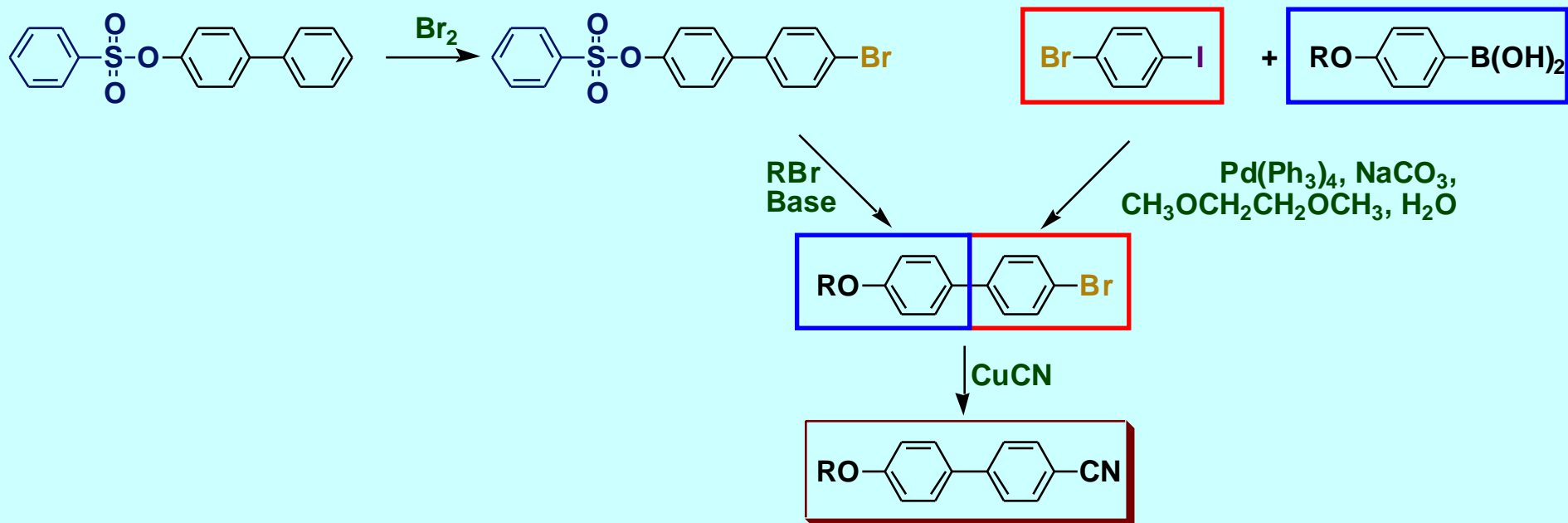
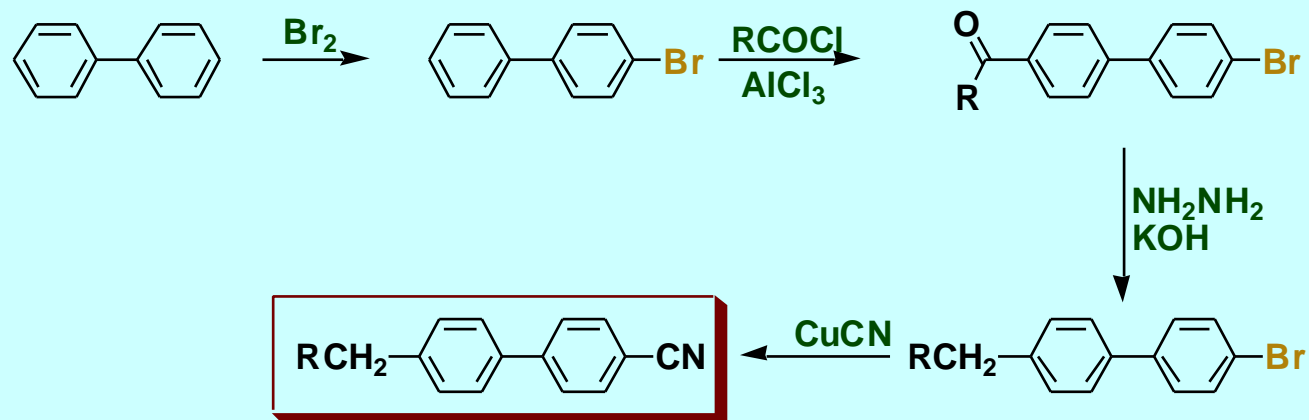
K 49 S_x 65 N 159 I

Synthesis of Nematic Materials with Positive Dielectric Anisotropy

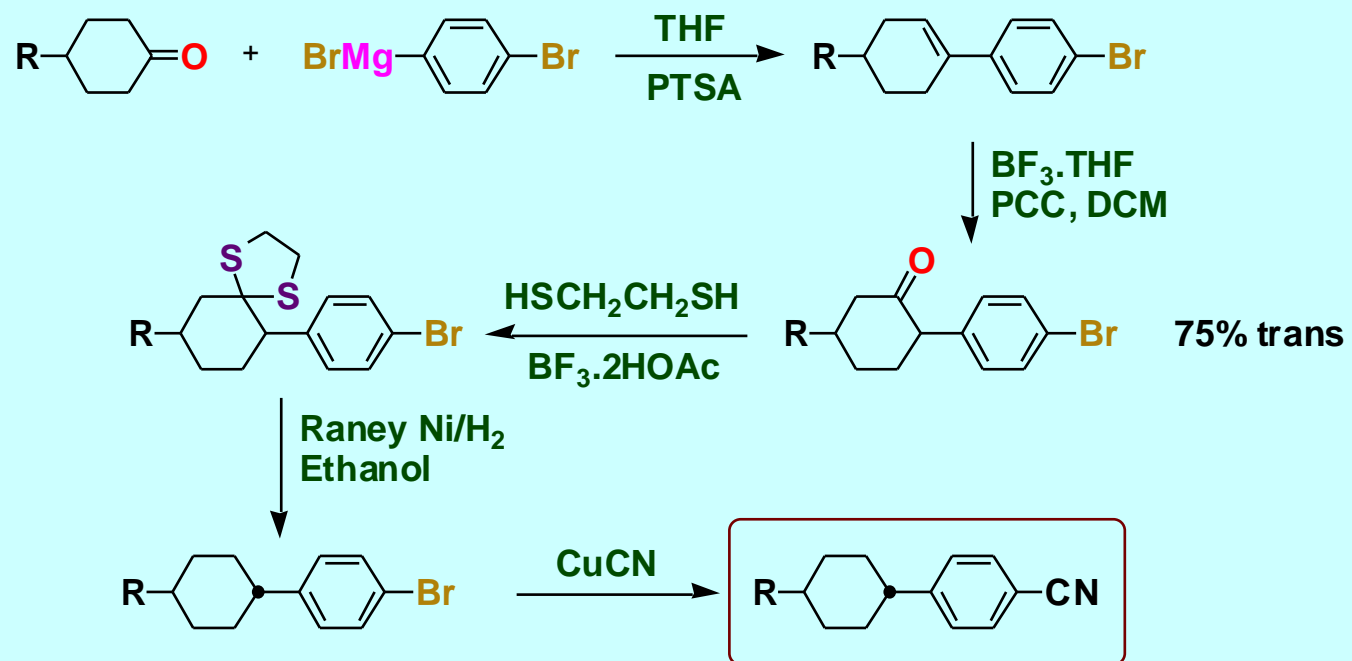
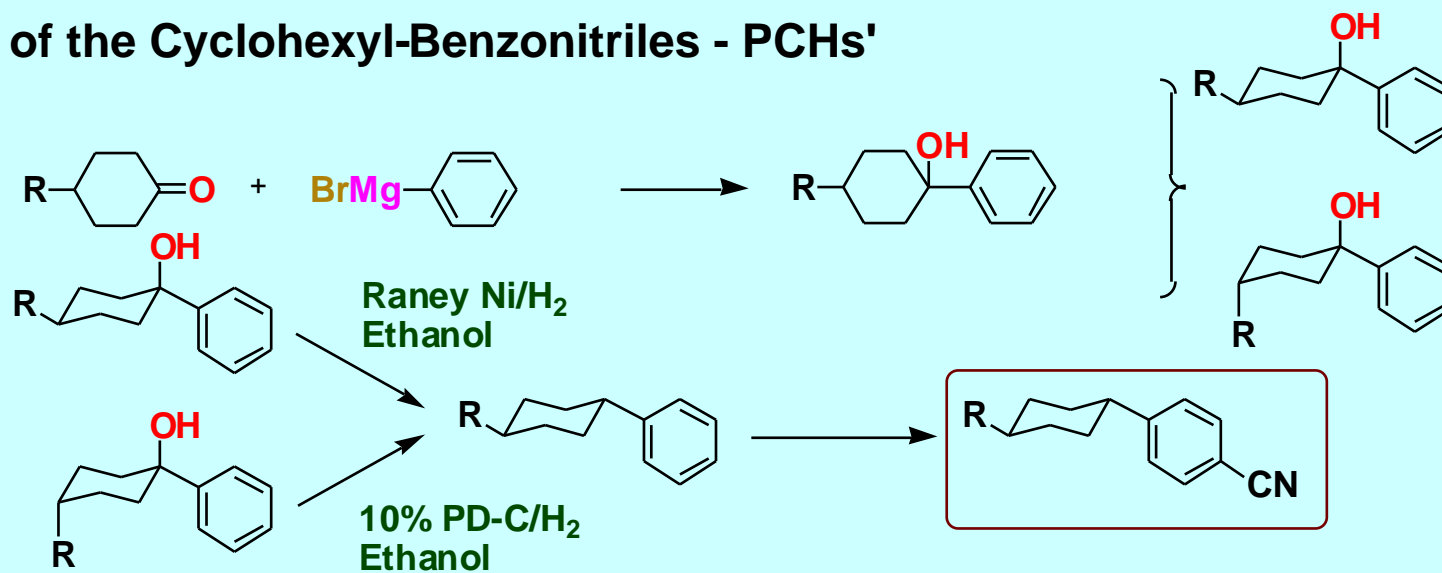
Synthesis of Core Rings Systems

- 1. Biphenyls**
- 2. Phenyl-Cyclohexanes**
- 3. Phenyl-Dioxanes**
- 4. Phenyl-Bicyclooctanes**
- 5. Phenyl-Pyrimidines**
- 6. Fused Rings Systems**

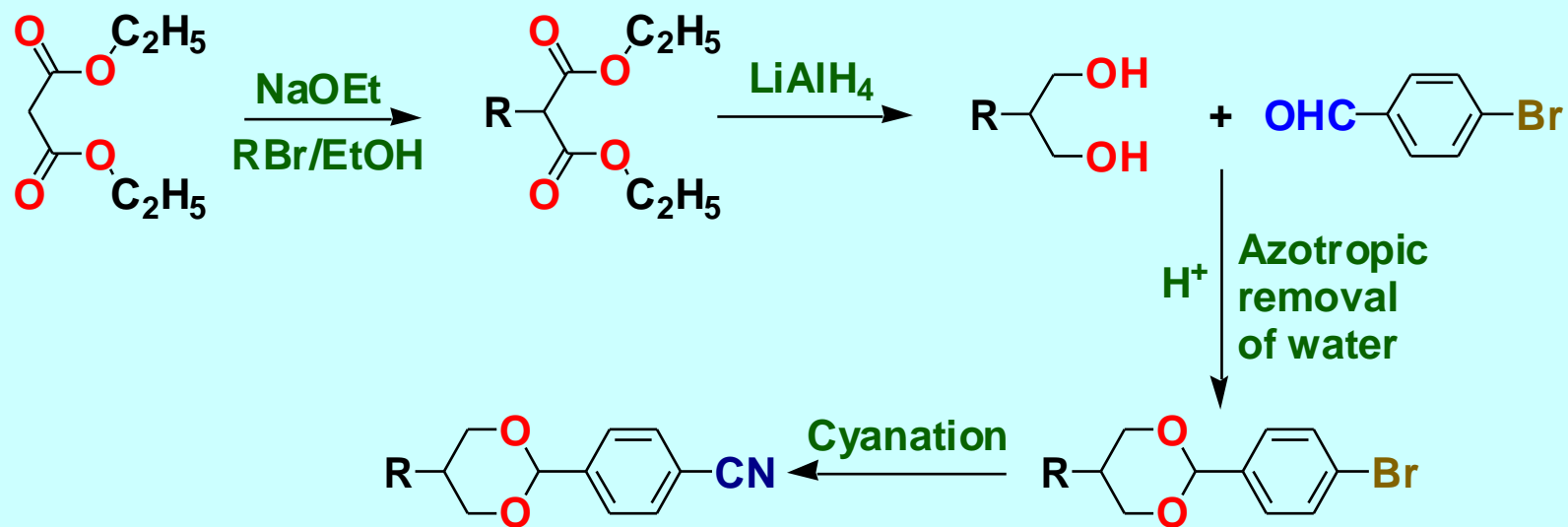
Synthesis of Cyano-Biphenyls



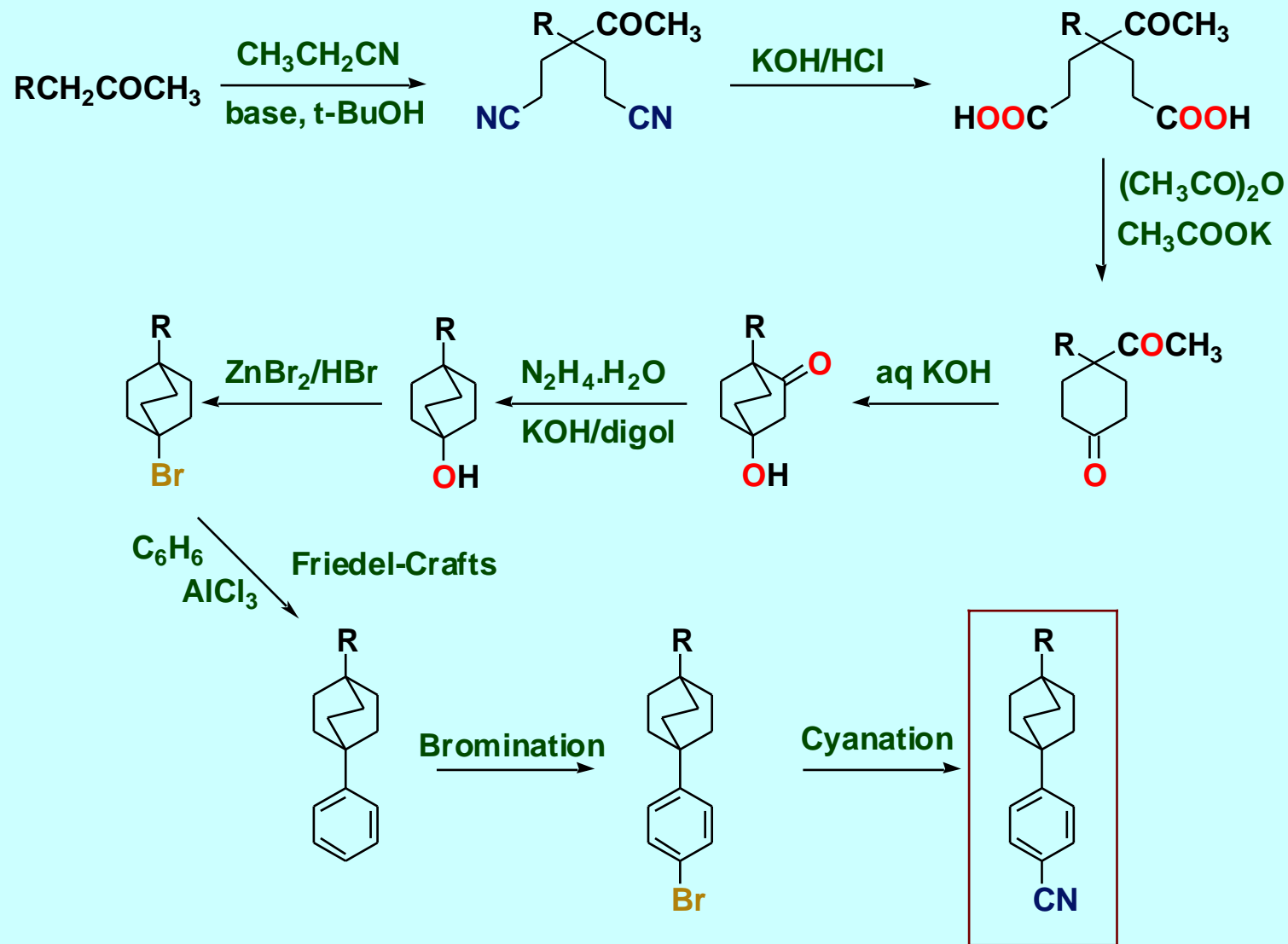
Synthesis of the Cyclohexyl-Benzonitriles - PCHs'



Synthesis of Dioxanyl Systems etc

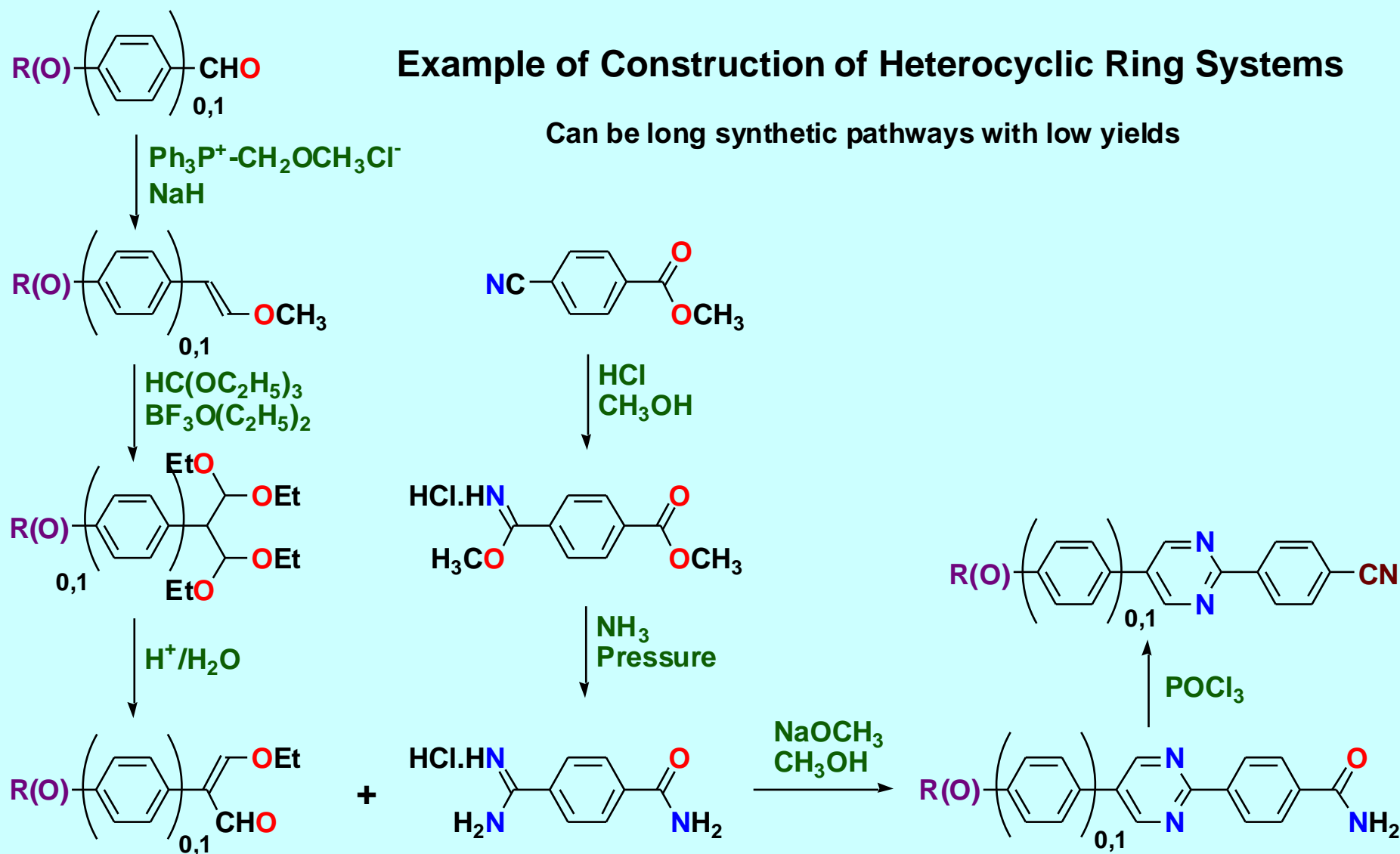


Synthesis of Bicyclo[2.2.2]octanes

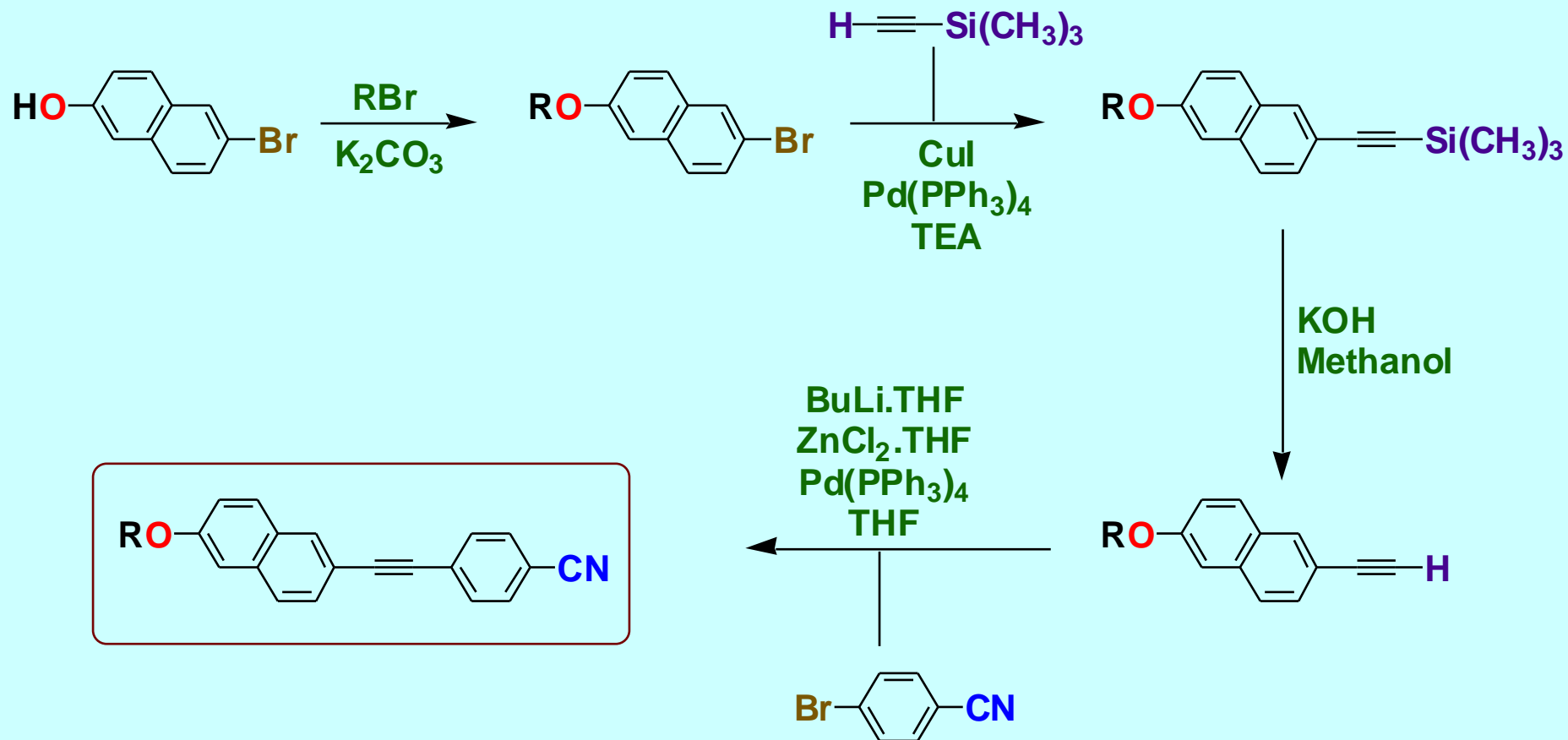


Example of Construction of Heterocyclic Ring Systems

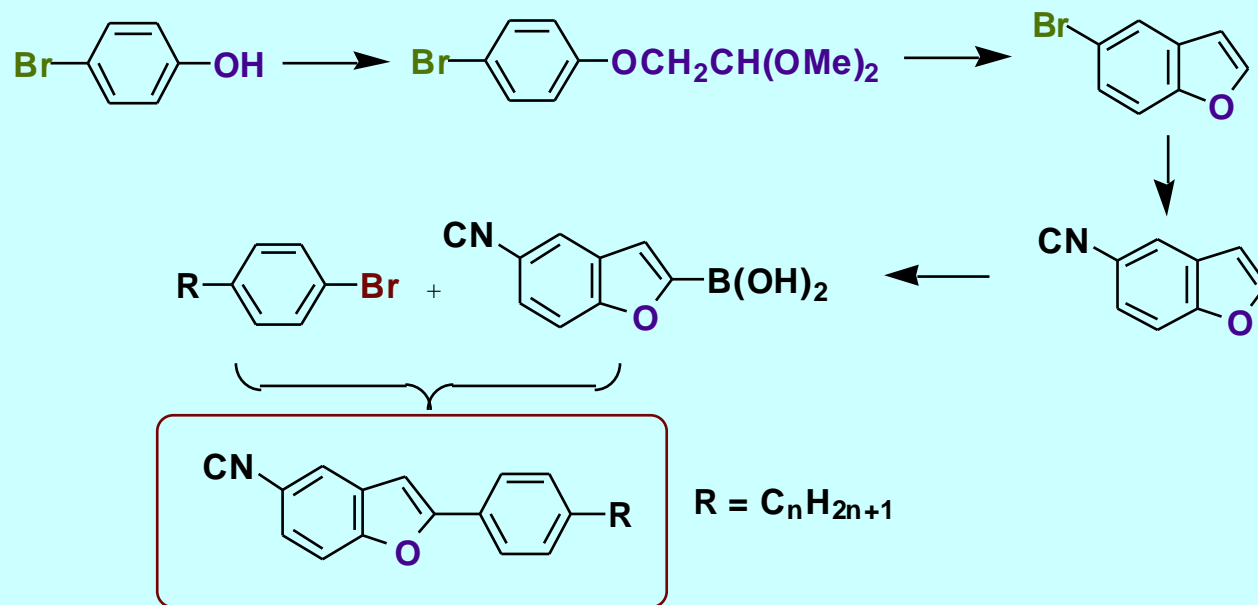
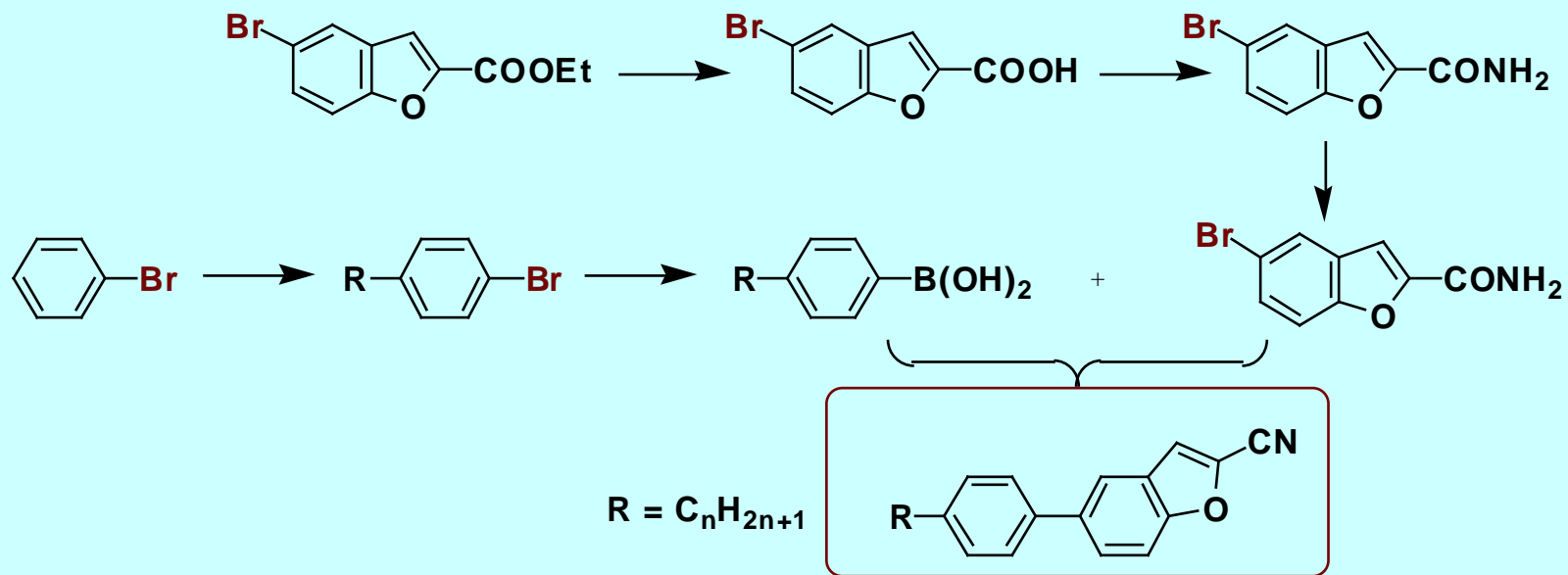
Can be long synthetic pathways with low yields



Synthesis of Fused Ring Systems



Synthesis of Fused Ring Systems

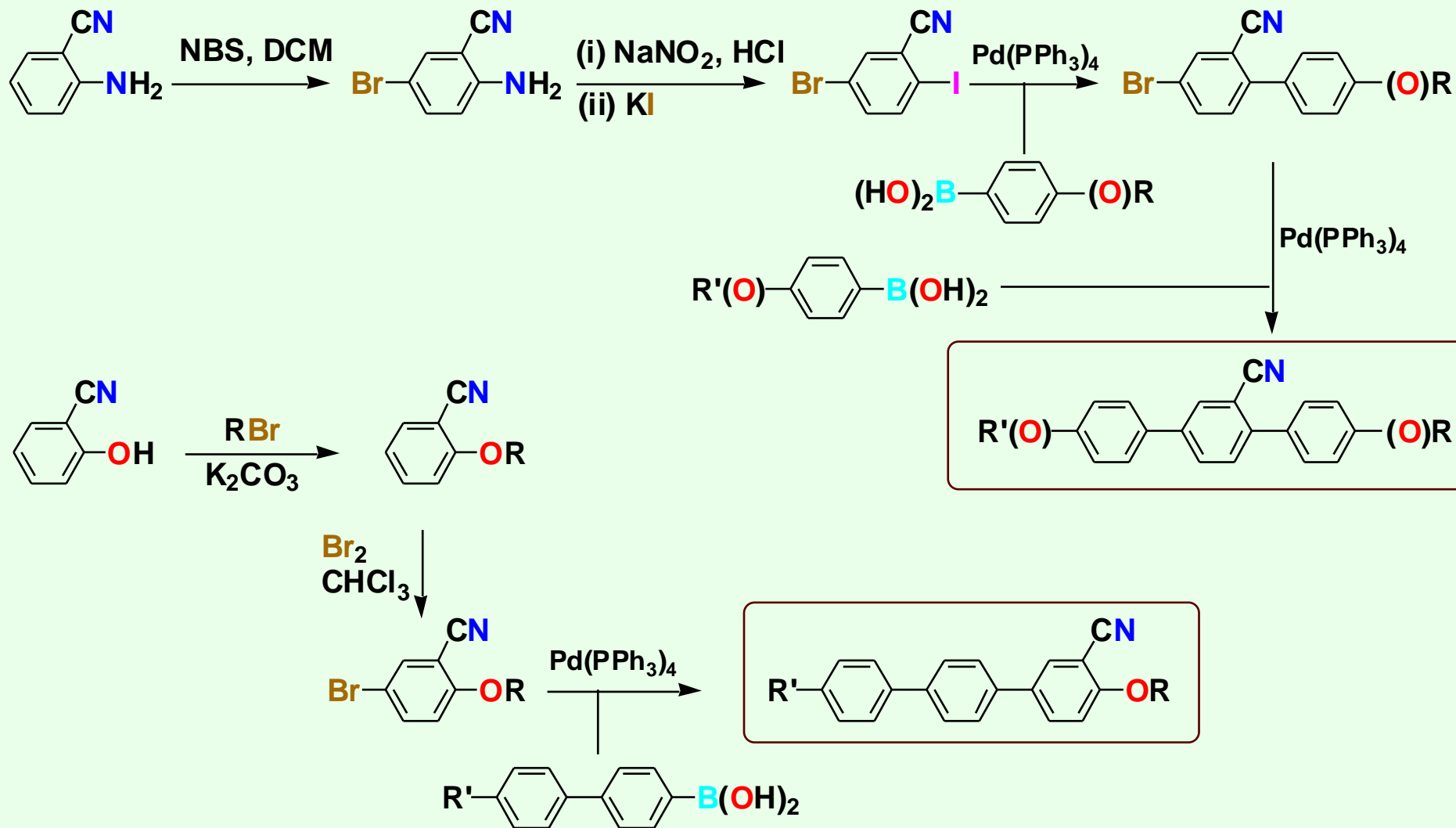


Synthesis of Nematic Materials with Negative Dielectric Anisotropy

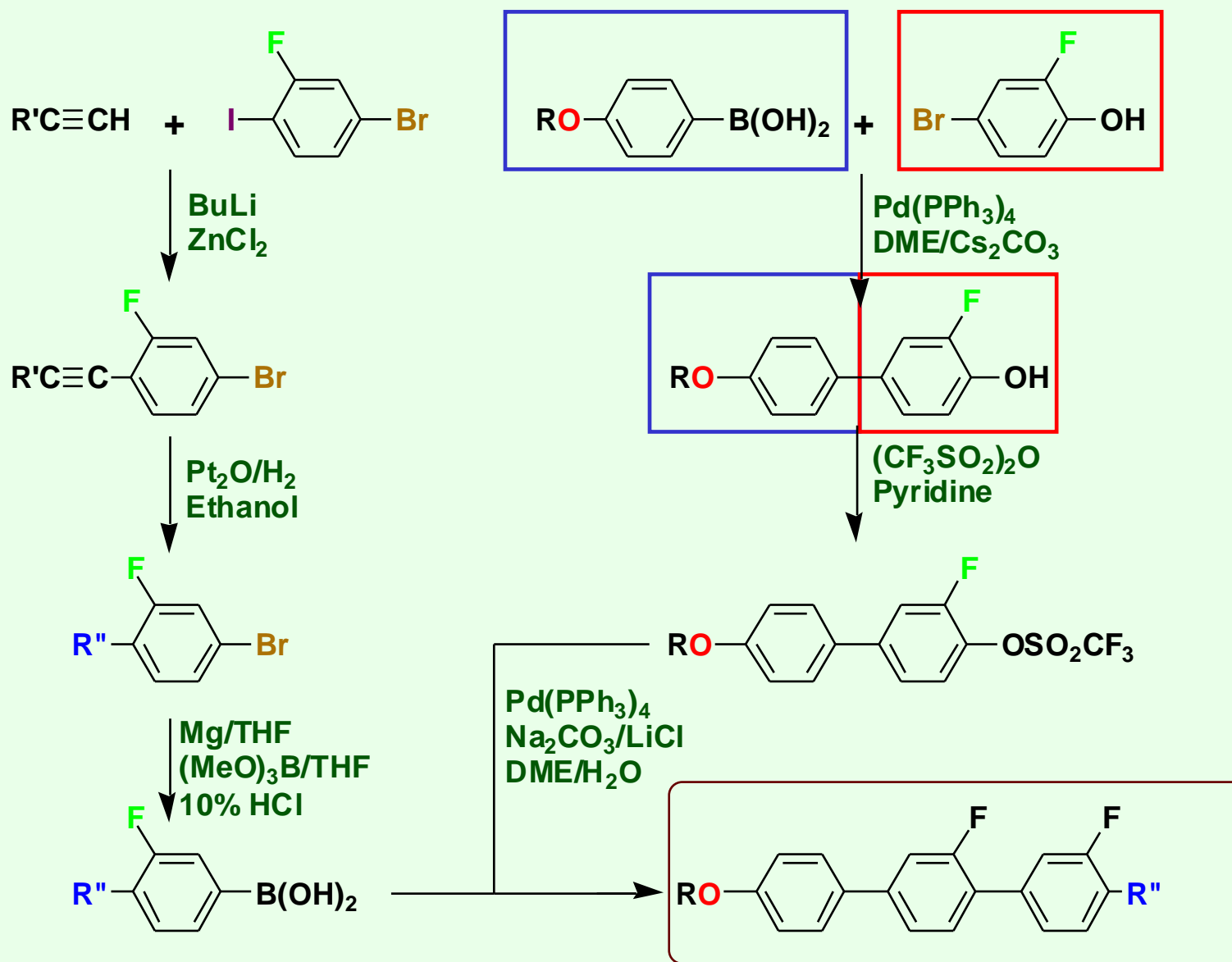
Synthesis of Laterally Substituted Core Rings Systems

- 1. Cyano-Terphenyls**
- 2. Fluoro-Terphenyls**
- 3. Difluoro-Terphenyls**
- 4. Difluorophenyl-Pyrimidines**
- 5. Difluorophenyl-Cyclohexanes**
- 6. Fluoro-Cyclohexanes**

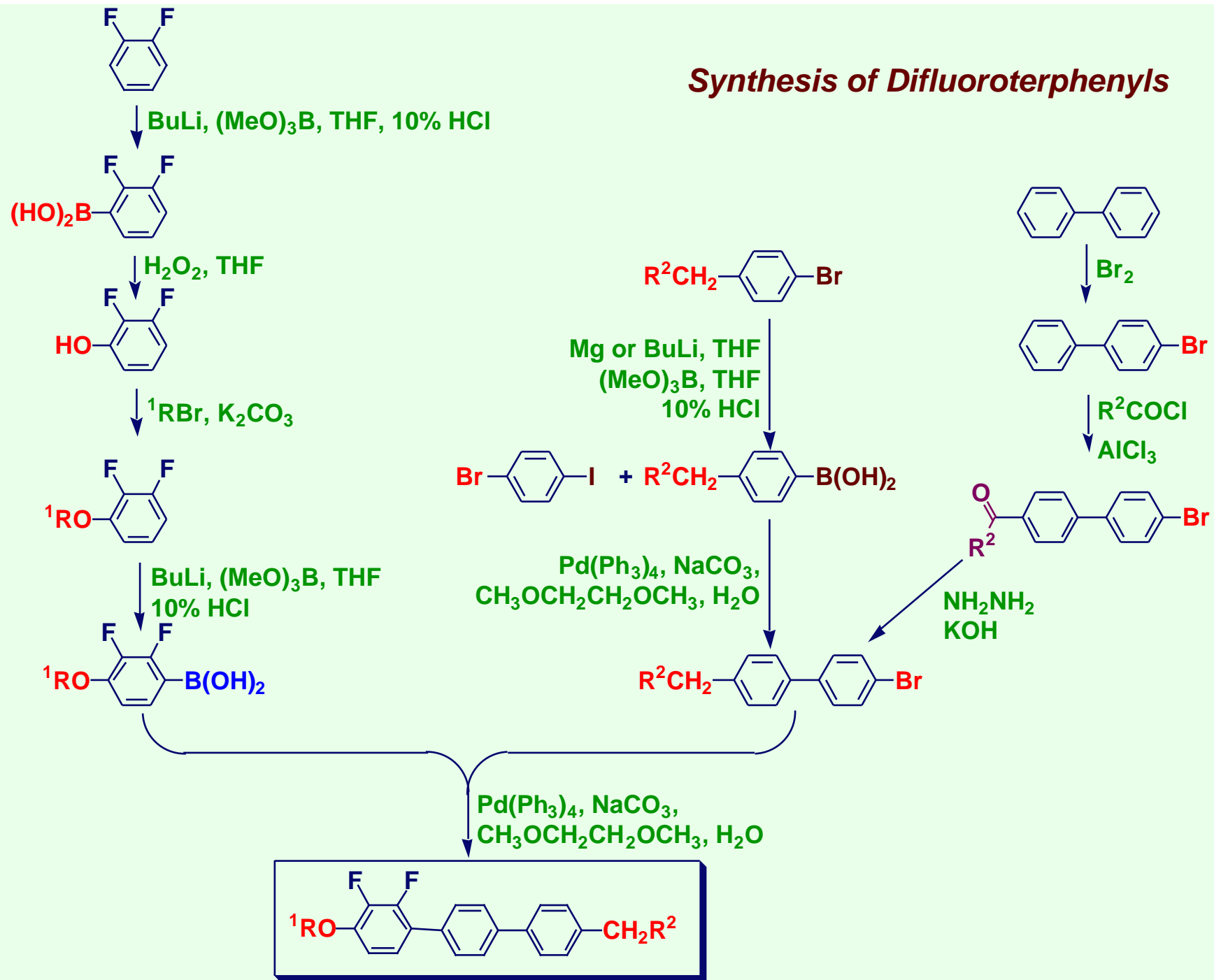
Synthesis of Lateral Cyano-substituted Terphenyls

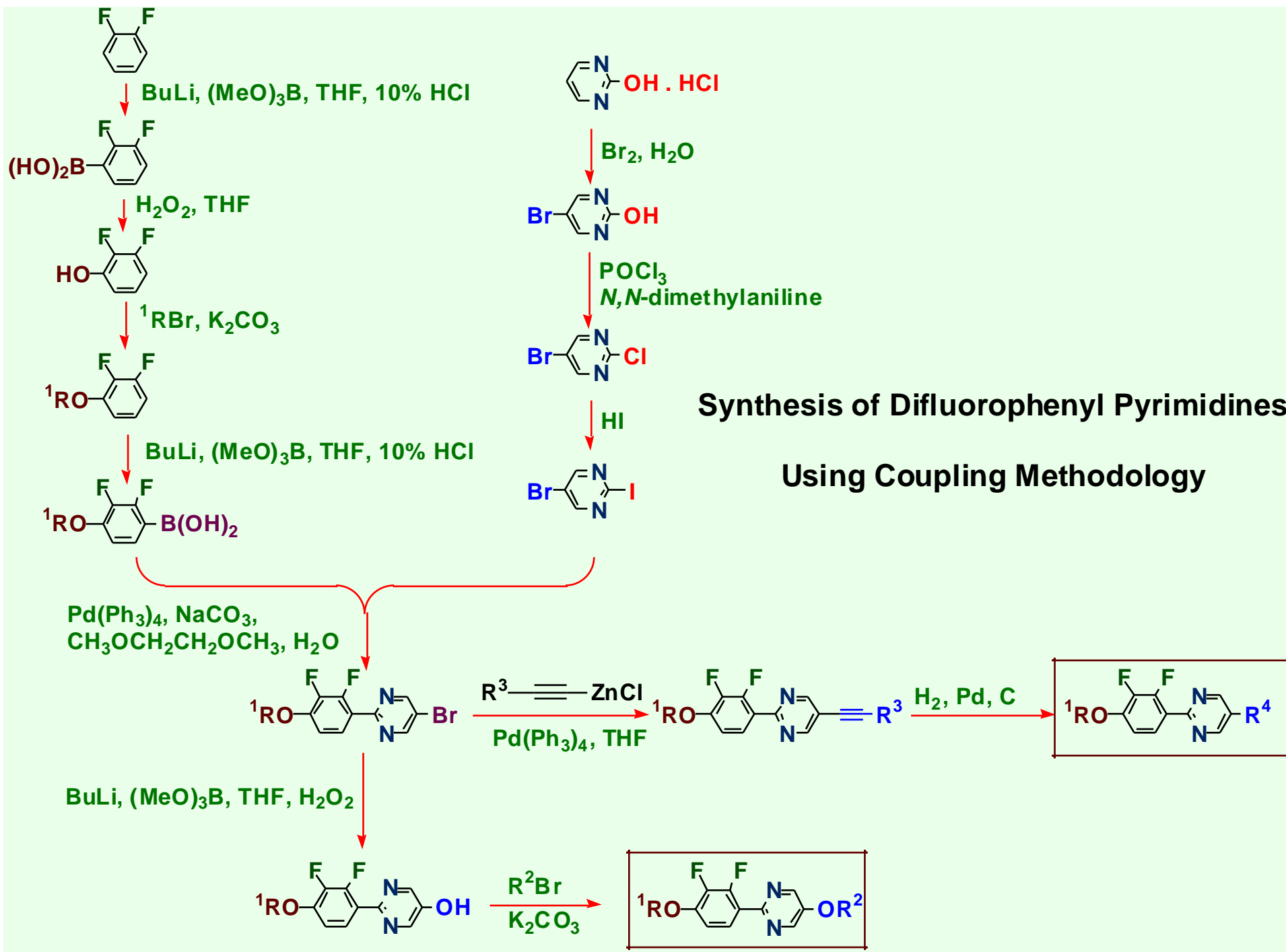


Cross-Coupling Reactions in the Synthesis of Fluoro-substituted Liquid Crystals

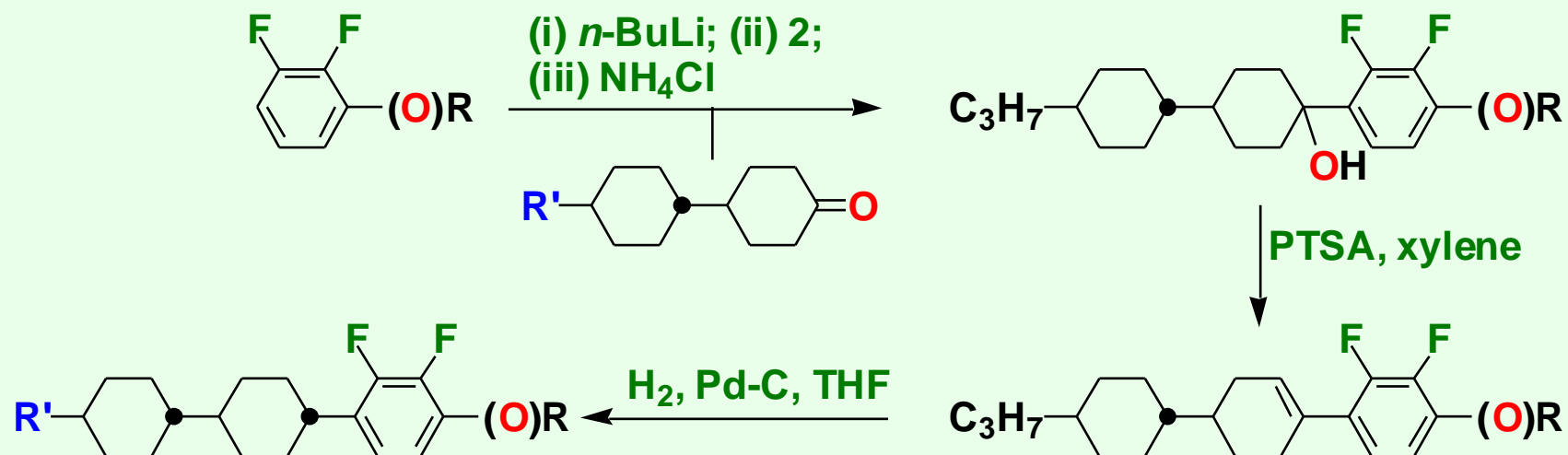


Synthesis of Difluoroterphenyls





Synthesis of Directly-linked Bicyclohexyl-2,3-difluorophenyls

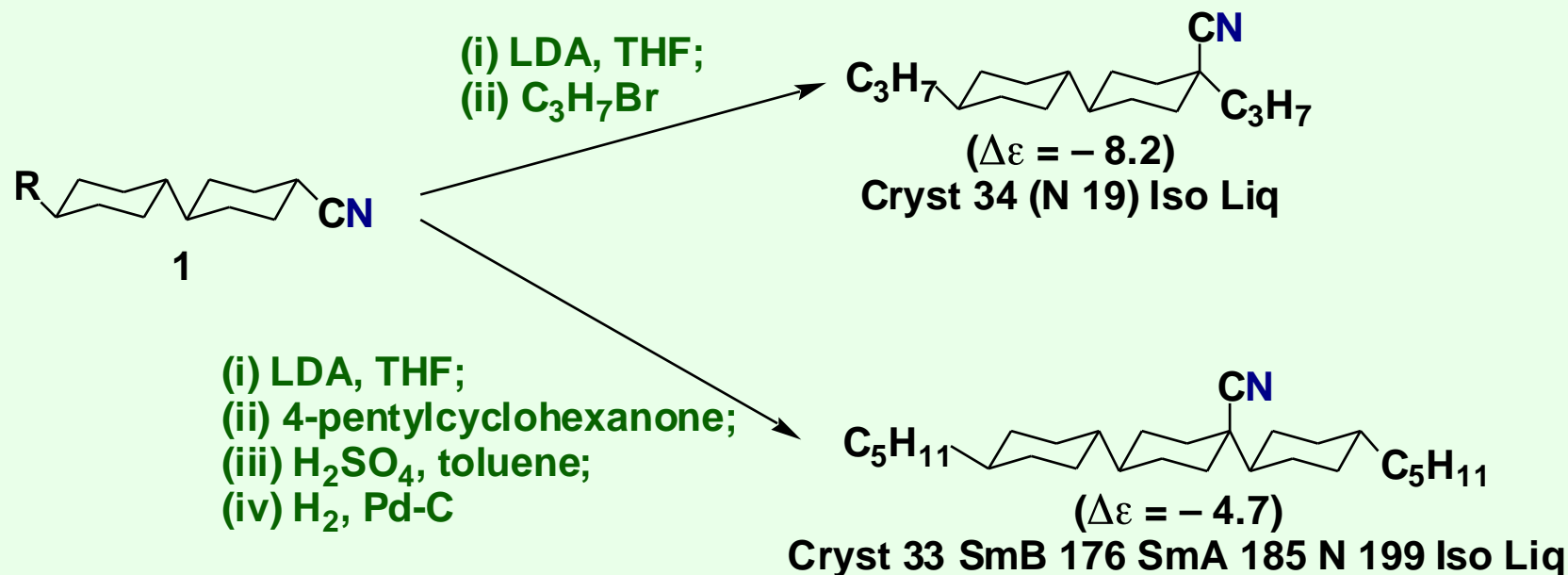


$\text{R}' = \text{C}_3\text{H}_7$, $(\text{O})\text{R} = \text{OC}_2\text{H}_5$ Cryst 79 (S_B 78) N 185 Iso Liq ($\Delta\varepsilon = -5.9$)

$\text{R}' = \text{C}_3\text{H}_7$, $(\text{O})\text{R} = \text{CH}_3$ Cryst 67 N 145 Iso Liq ($\Delta\varepsilon = -2.7$)

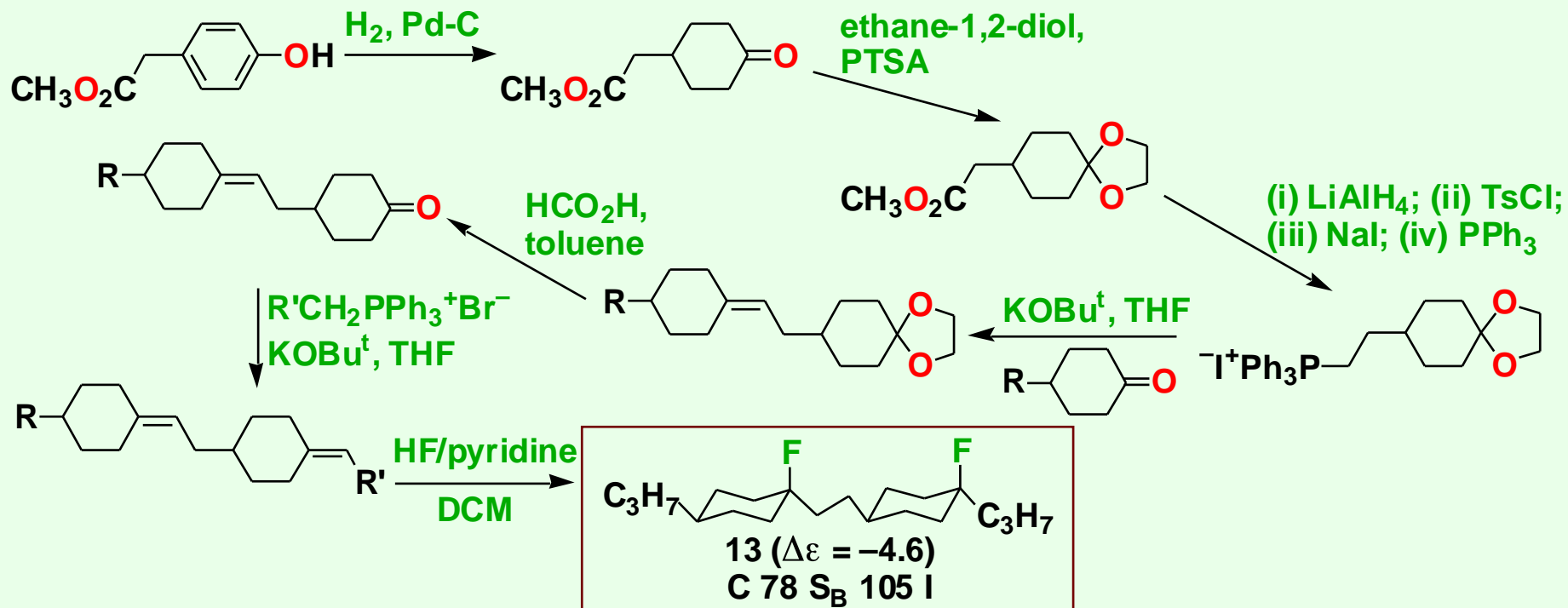
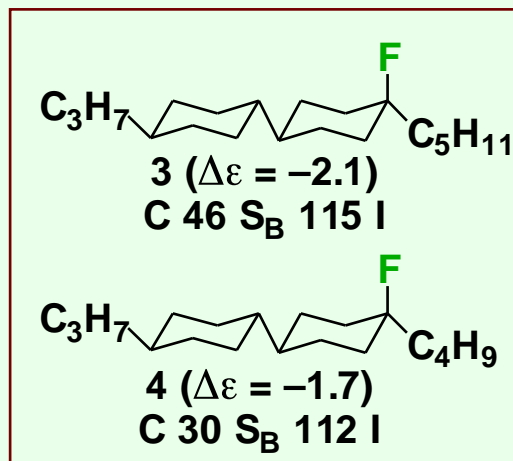
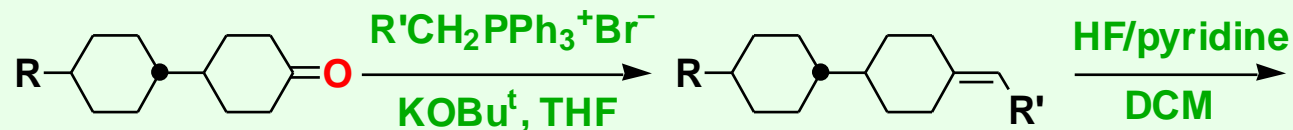
Developed by Merck as strong negative $\Delta\varepsilon$ nematic materials for ECB-TFT applications
 both have strong negative $\Delta\varepsilon$, especially upper compound due to the ether oxygen
 the lower compound has a lower viscosity due to lack of ether oxygen
 short terminal chains minimise smectic character and minimise viscosity
 excellent voltage holding ratios (VHRs)

Synthesis of Axial Cyano-substituted Cyclohexanes



Originally developed for positive contrast guest-host displays which require negative $\Delta\epsilon$
 other analogues originally developed as S_C host materials for ferroelectric mixtures
 cyclohexane systems have a strong tendency towards orthogonal smectic phases (S_B and S_A)
 axial cyano depresses mp and smectic phase stability, and generates some nematic character
 cyano group is slightly shielded by the core structure strong negative $\Delta\epsilon$, but poor solubility,
 high viscosity, and poor voltage holding ratios (VHRs)

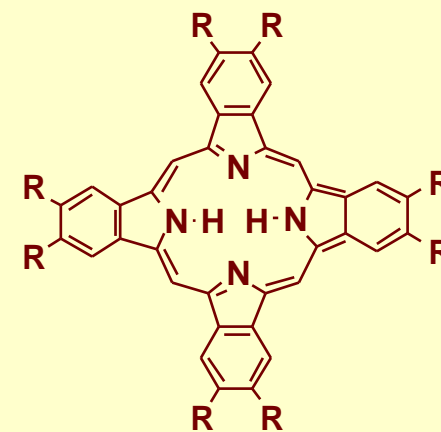
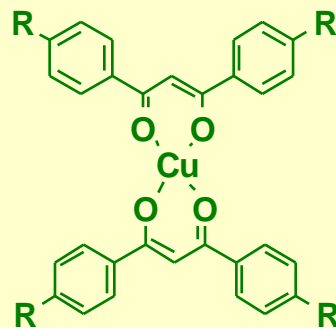
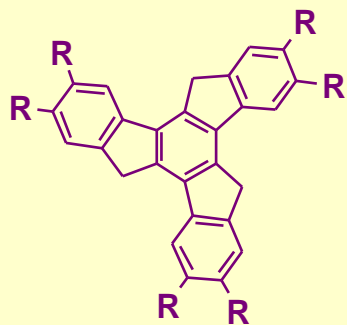
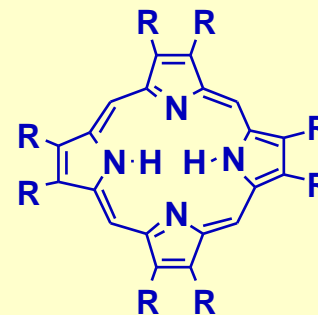
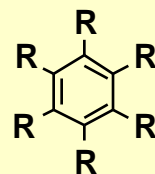
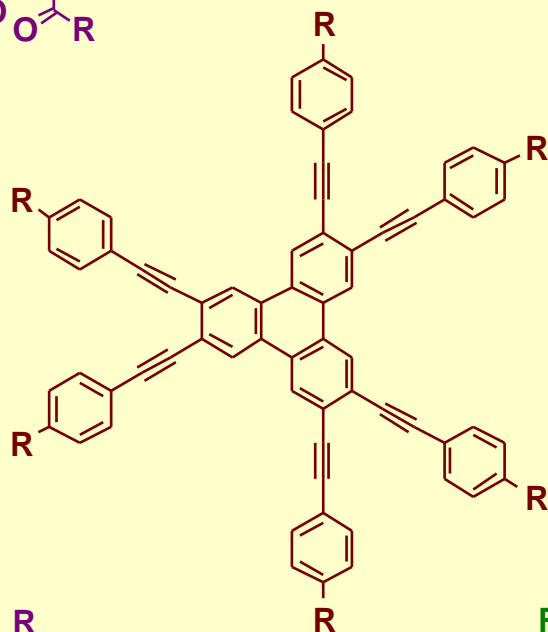
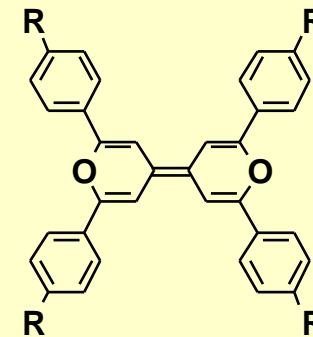
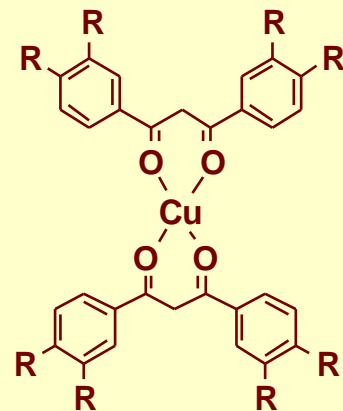
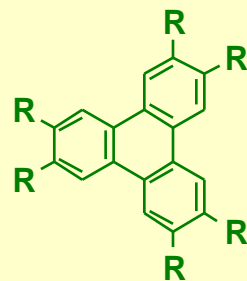
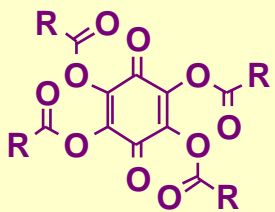
Synthesis of Axial Fluoro-substituted Cyclohexanes



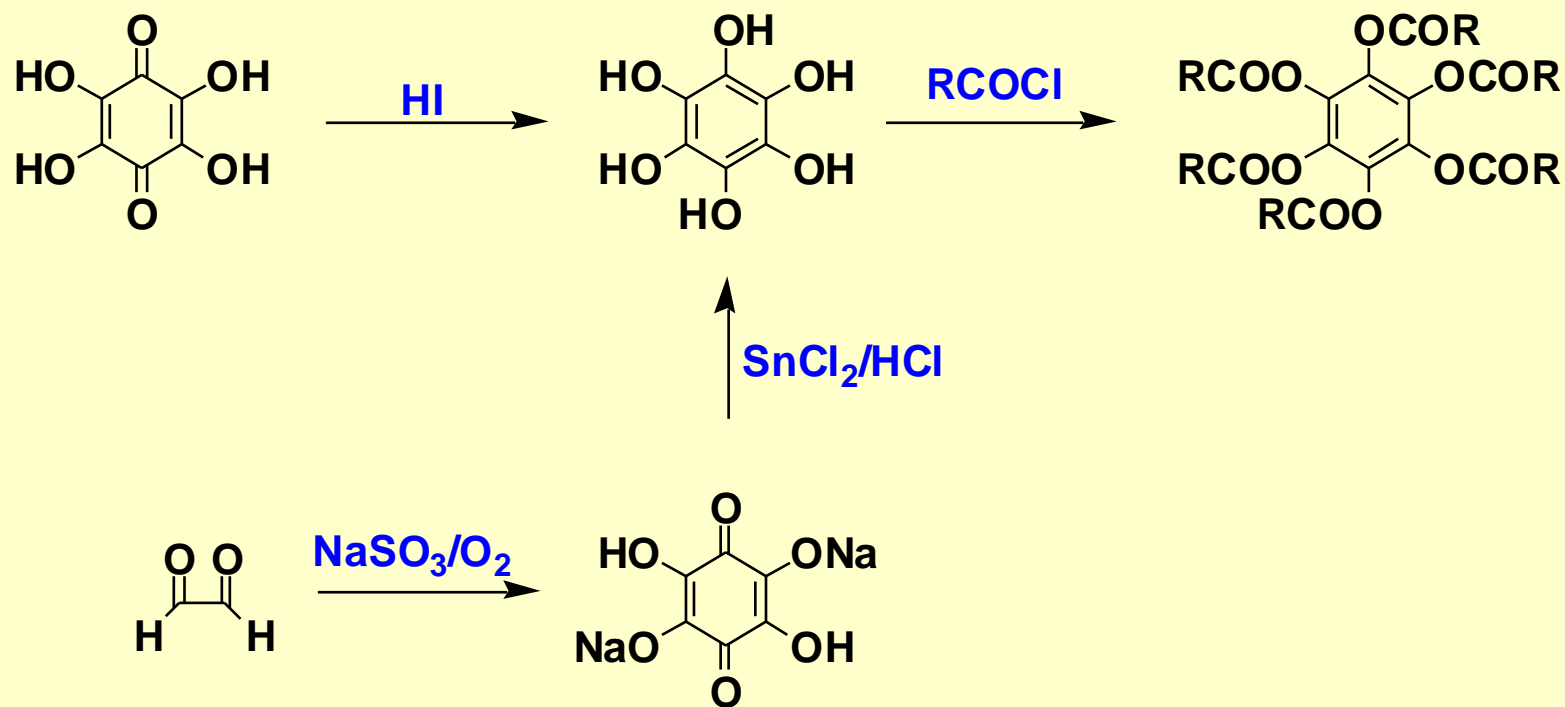
Synthesis of Discotic Liquid Crystals

- 1. Synthesis of Hexa-substituted Benzenes**
- 2. Synthesis of Triphenylenes**
 - Symmetrical**
 - Unsymmetrical**
- 3. Synthesis of Multi-ynes**
- 4. Synthesis of Truxenes**

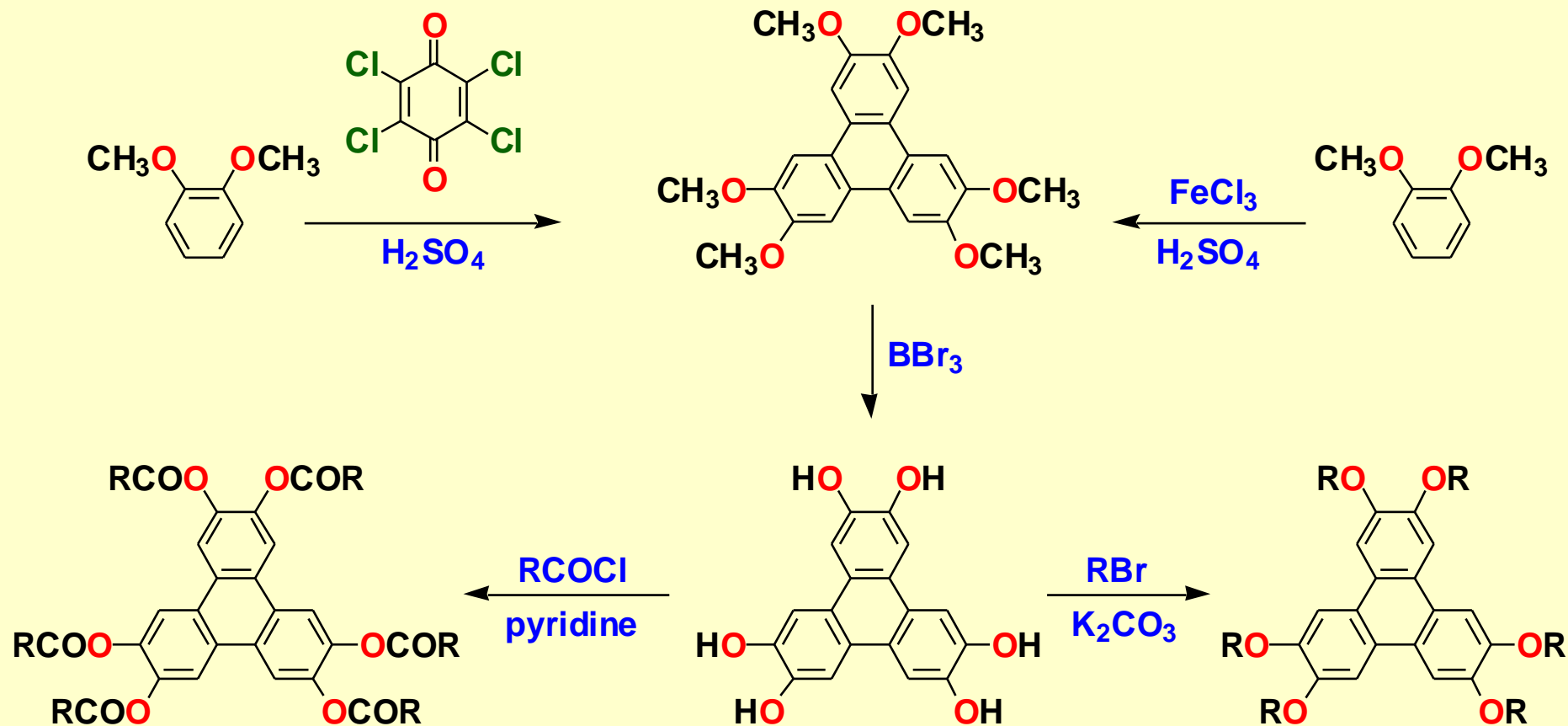
Discotic Liquid Crystals have Core-units Based Primarily on Fused Ring Systems



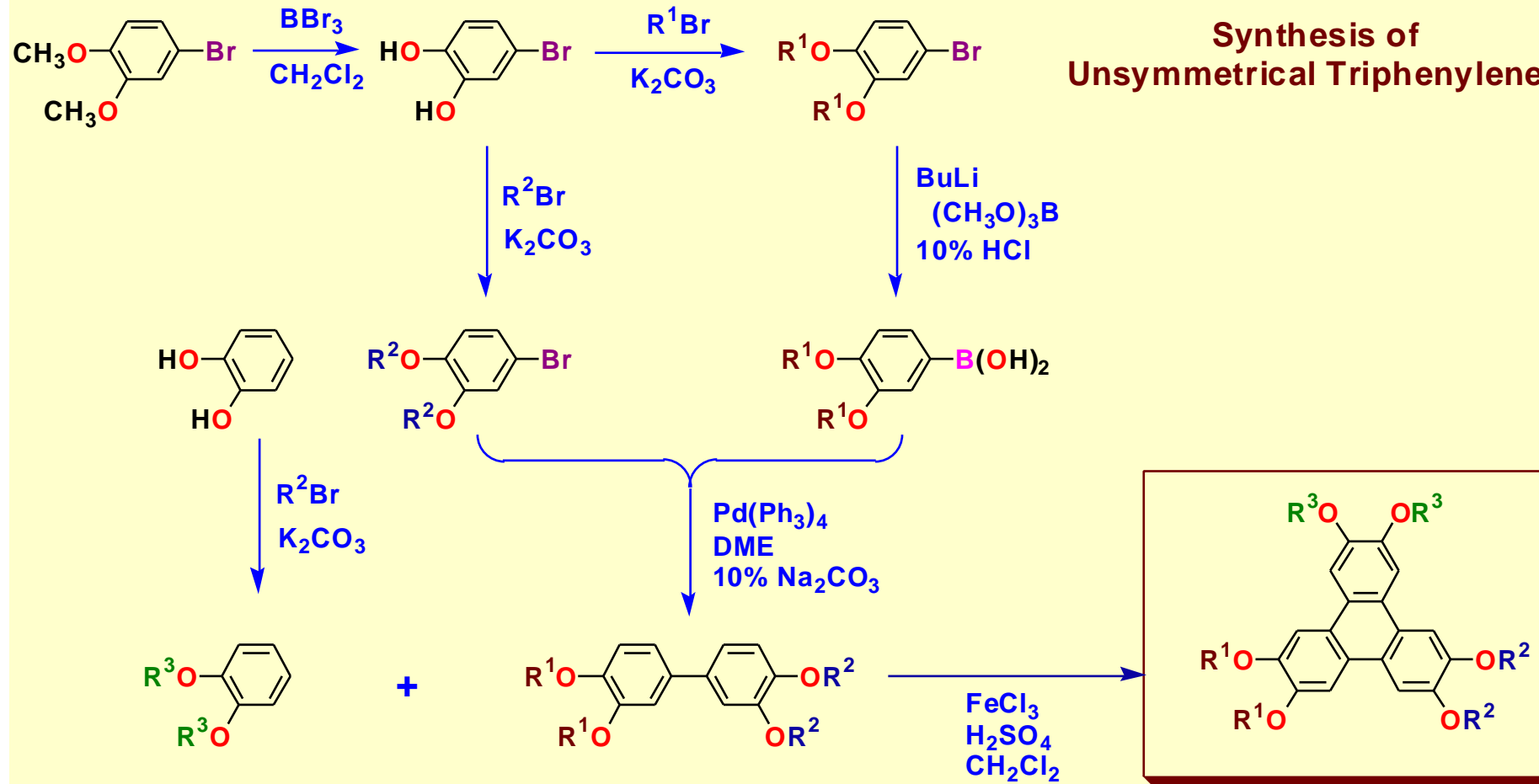
Synthesis of the First Columnar Liquid Crystals



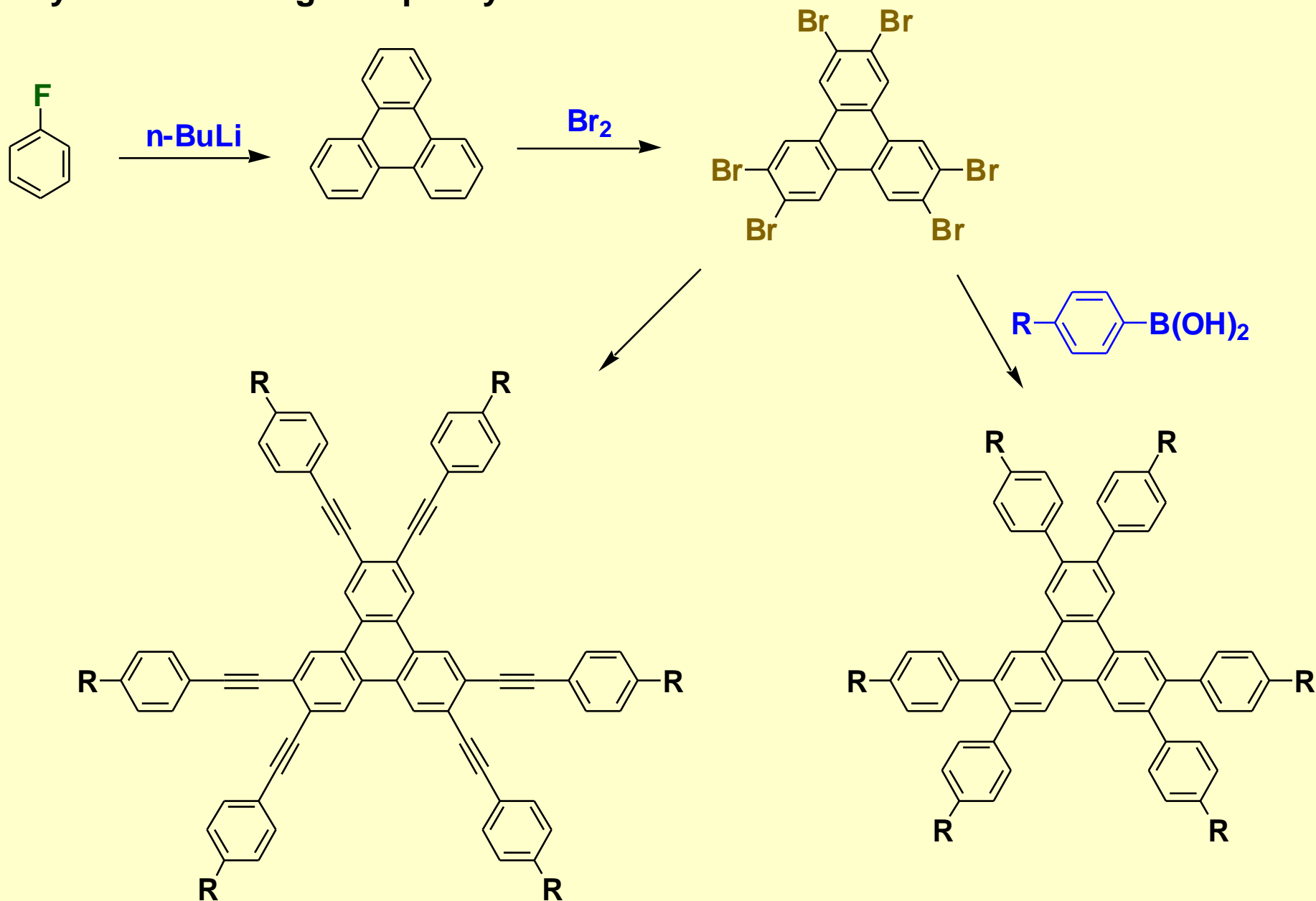
Synthesis of Triphenylenes



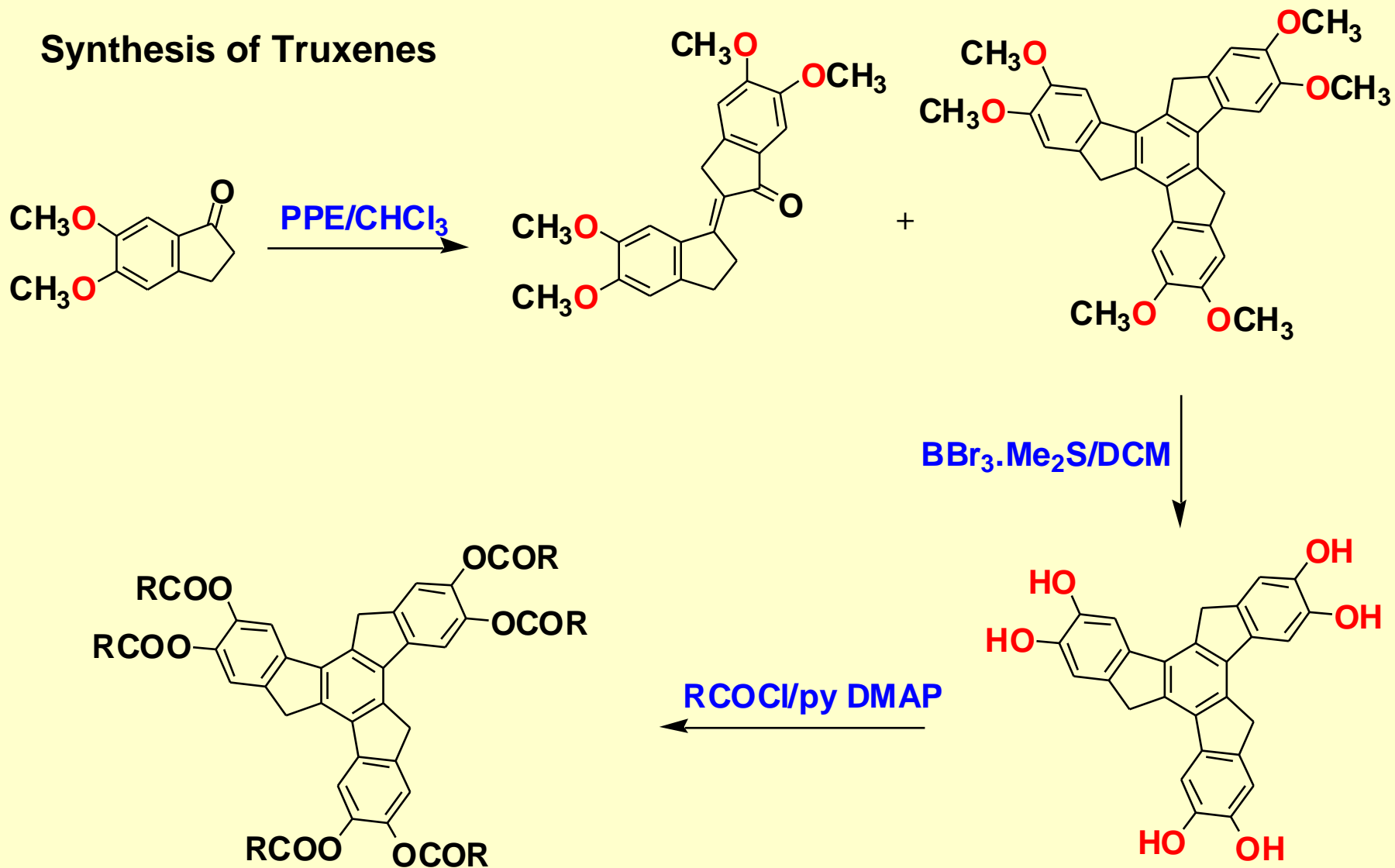
Synthesis of Unsymmetrical Triphenylenes



Synthesis of Larger Triphenylenes



Synthesis of Truxenes



Synthesis of Chiral Materials

1. Using Chiral Substrates

Problems of Optical Purity

Problems of Racemization

2. Syntheses of Chiral Substrates

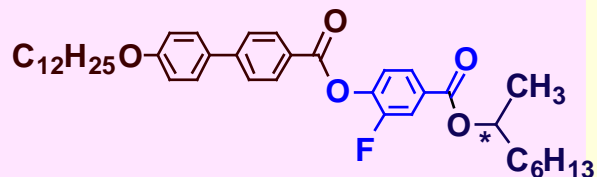
3. Resolution for Intermediates

4. Asymmetric Synthesis

Effect of:

1. Method of Measurement
2. Improvement in Identification
3. Change in Chemical Purity
4. Optical Purity

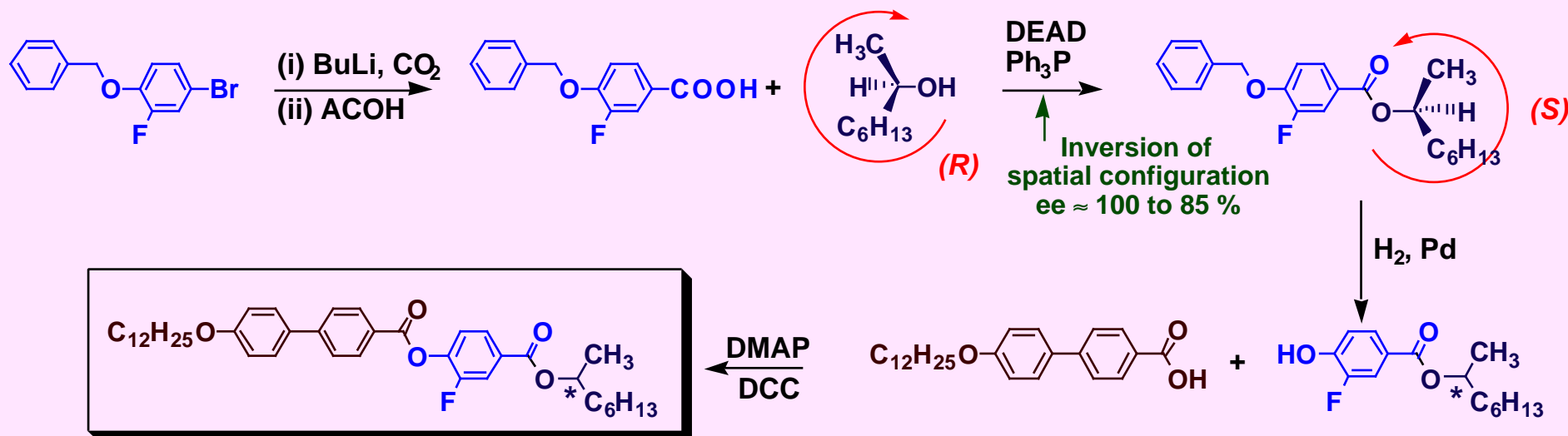
For: 12F1m7

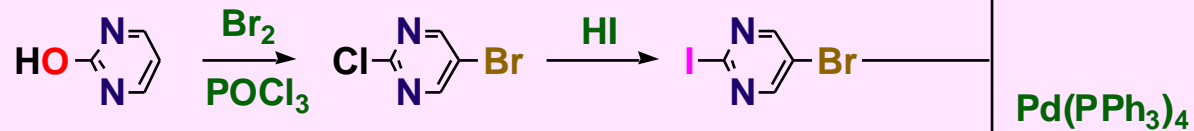
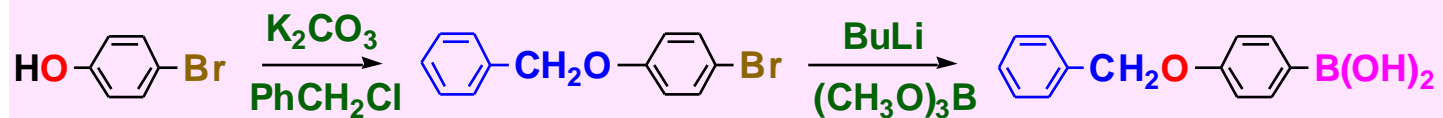


Iso Liq to SmA*	SmA* to SmC*	SmC* to SmC* γ	SmC* to FiLC	FiLC to AF	SmC* γ to SmC*A	
101.0	80.2	67.9			61.2	1986 Goodby: Microscopy 1992 Nishiyama: DSC 1992 Nishiyama: Cell
100.0	78.8	63.8			?	
101.0	80.0	64.0			47.0	
105.7	90.7	82.0			78.3	1994 Seed
105.7	90.7	82.0			78.3	1995 Robinson: Thesis
105.7	93.0		90.0	83.5	78.3	1997 Panarin: Phys Rev
105.0	88.6				75.0	1998 Parghi

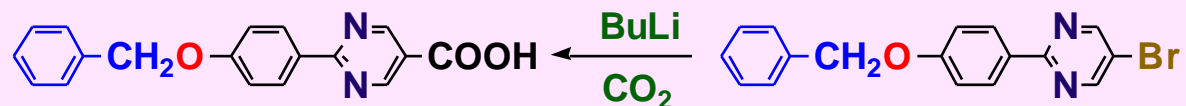
Improvement in Phase Identification Change in Chemical Purity Variation in Method of Study

Synthetic Procedure

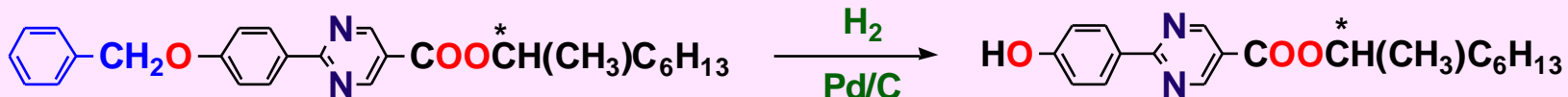
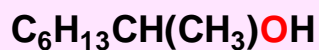




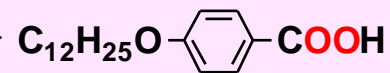
$\text{Pd}(\text{PPh}_3)_4$



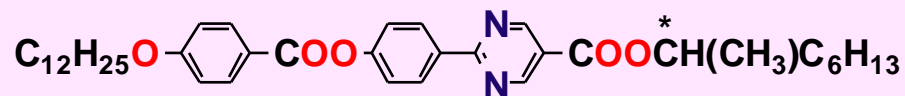
DEAD
 PPh_3

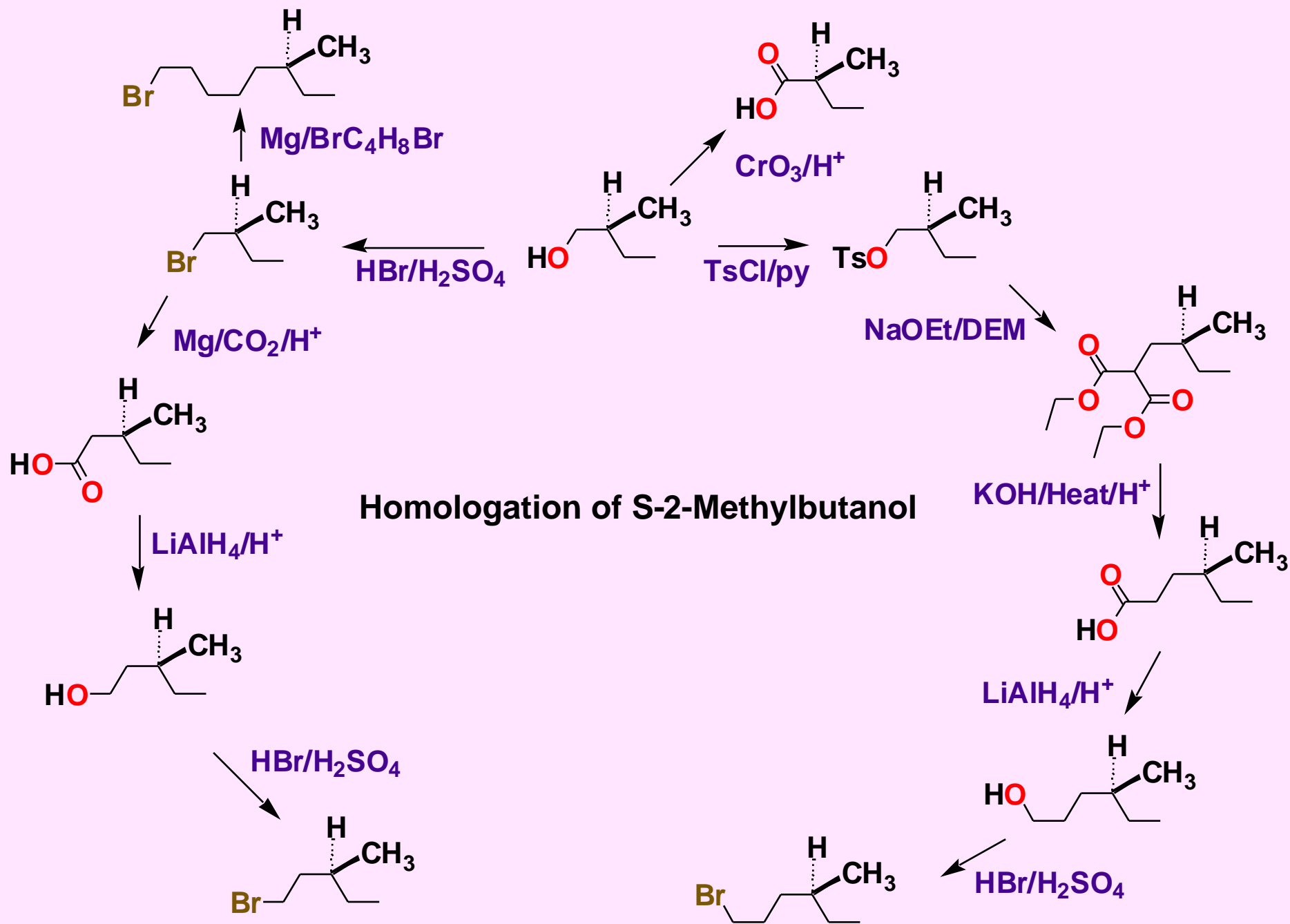


DCC
 DMAP

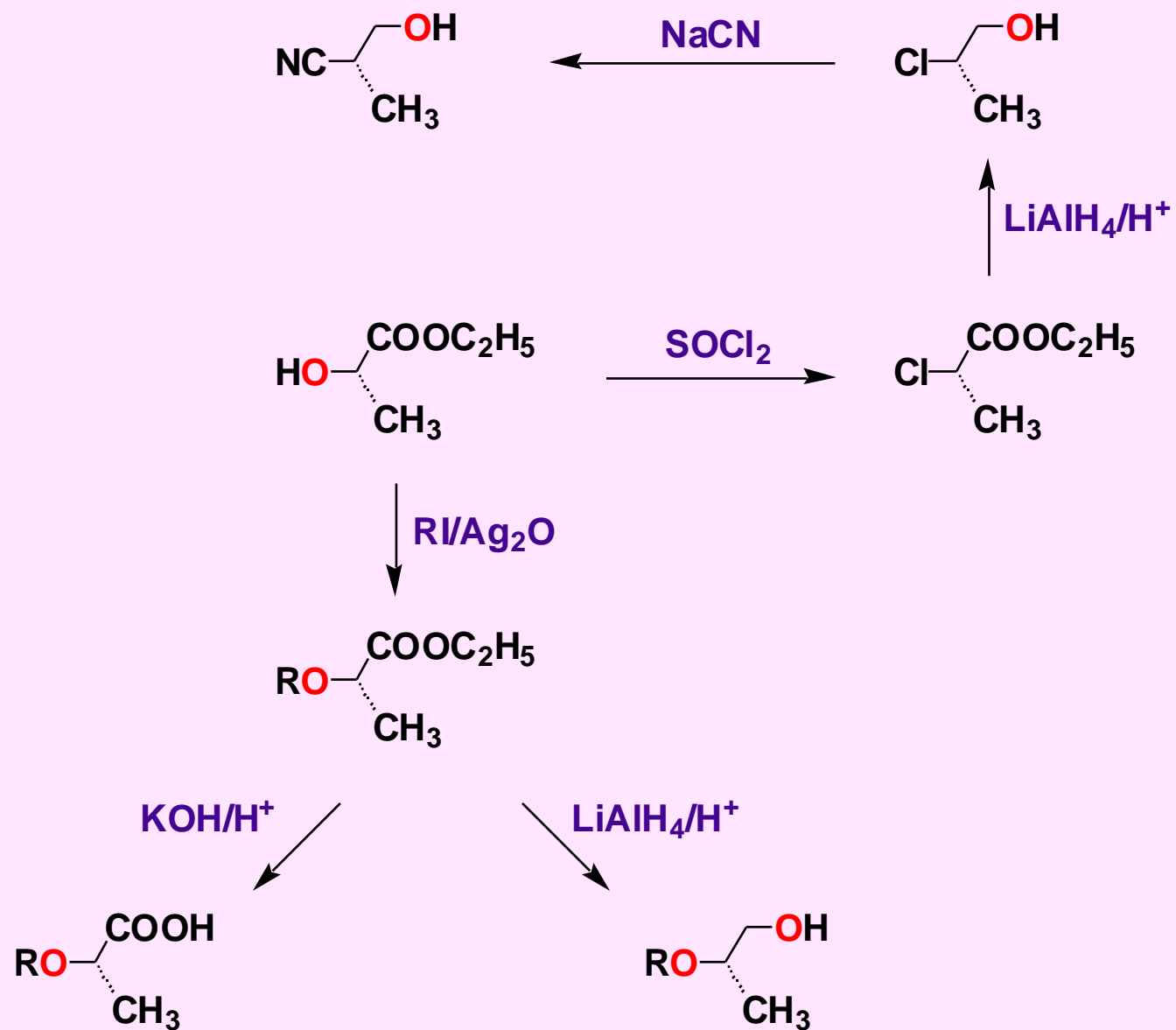


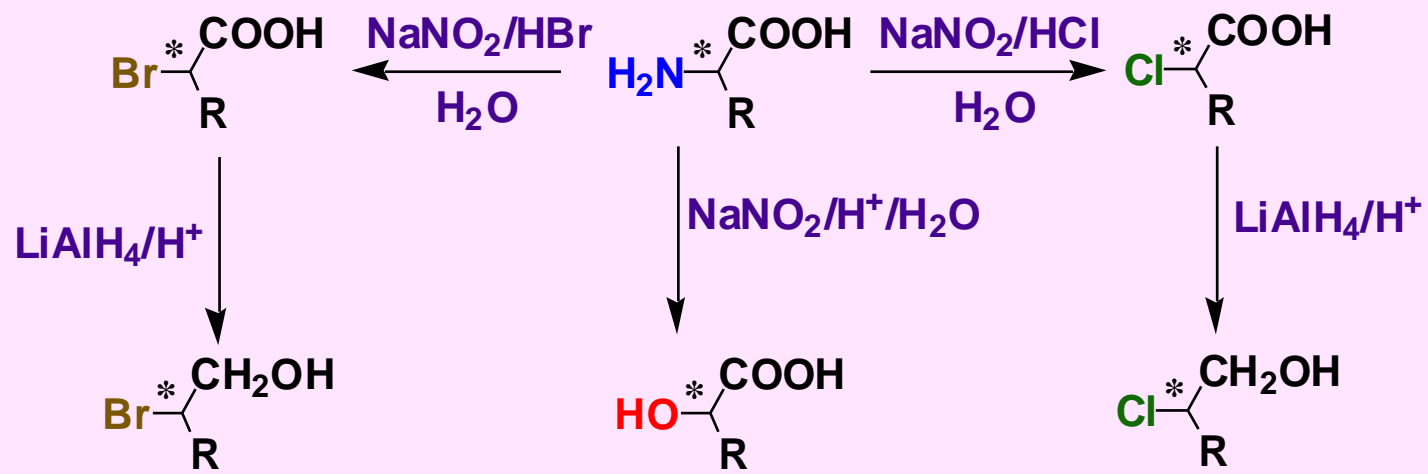
Synthesis of a TGBC_A Material



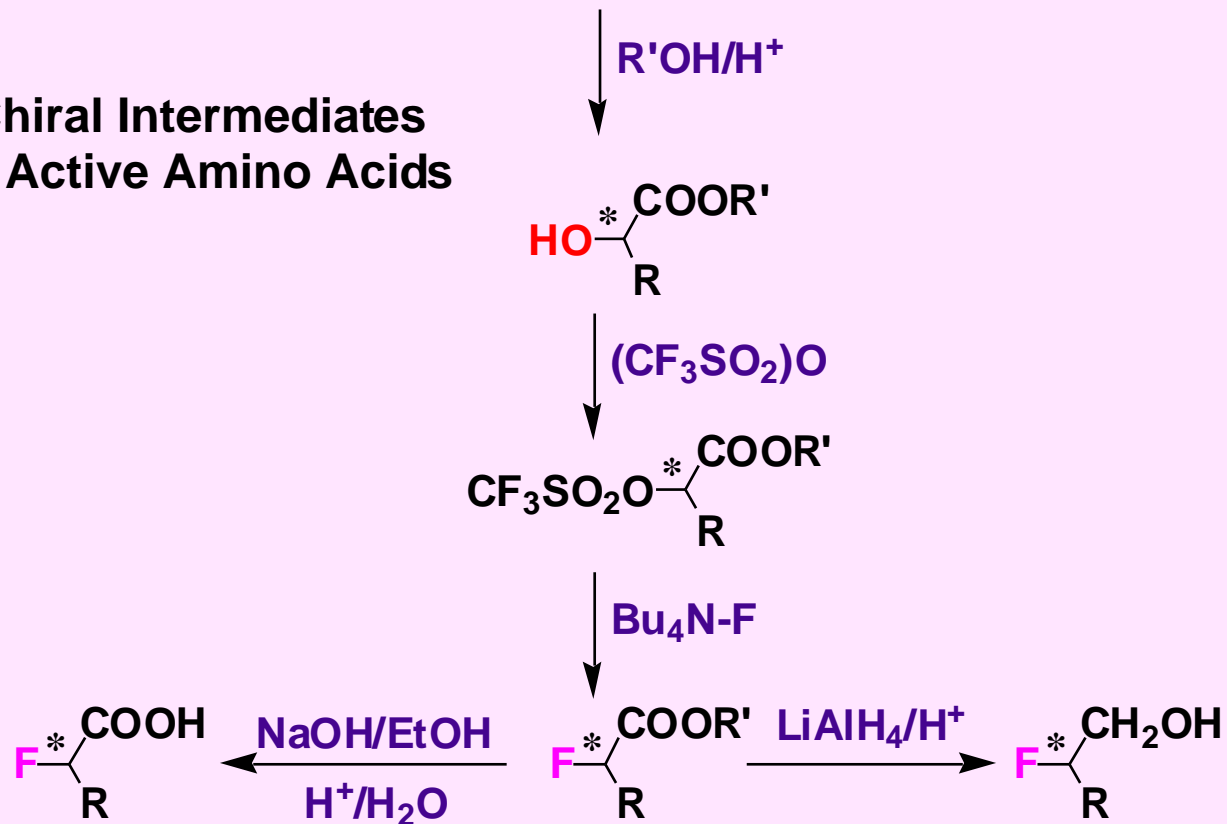


Derivatization of S-Ethyl Lactate

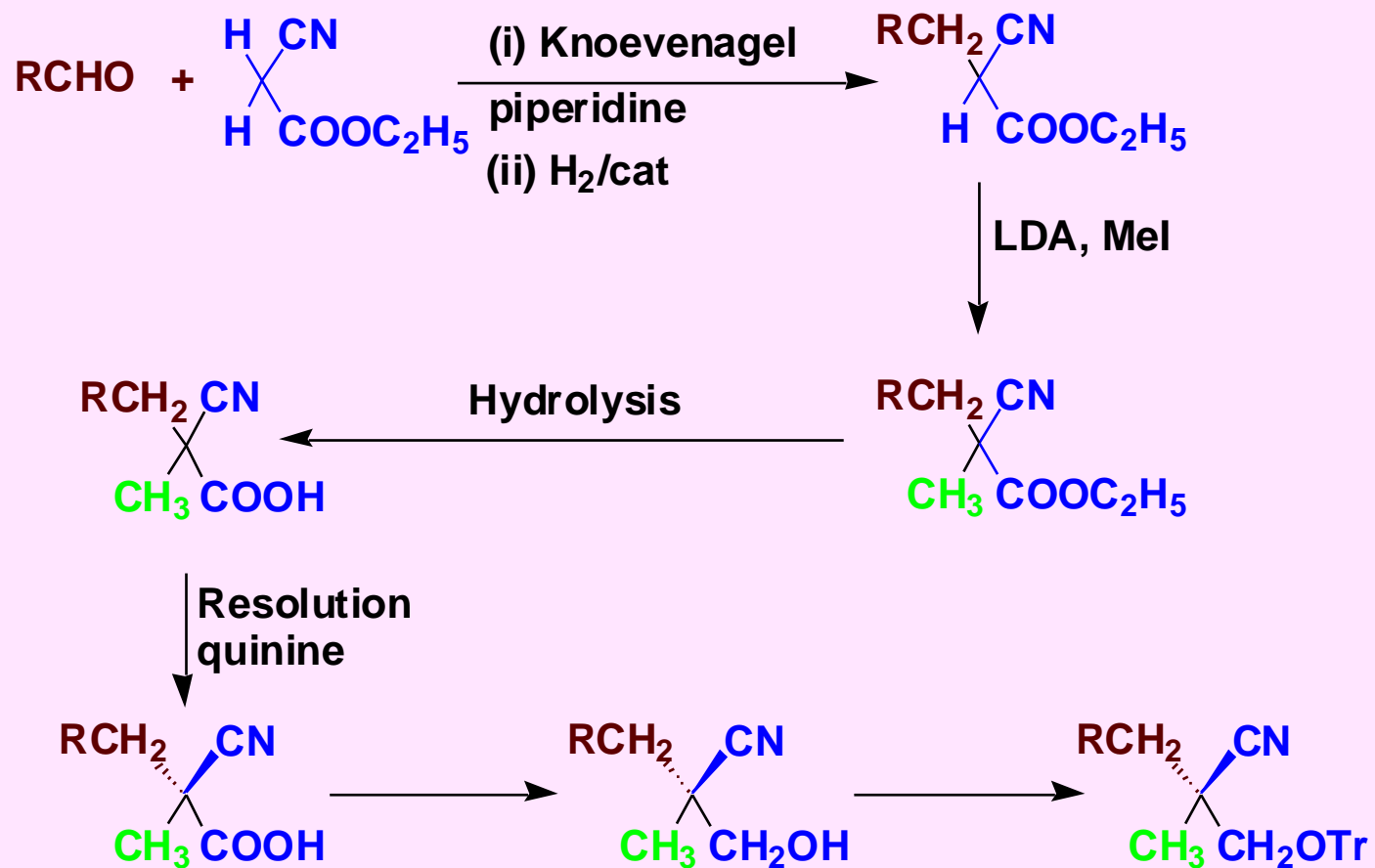




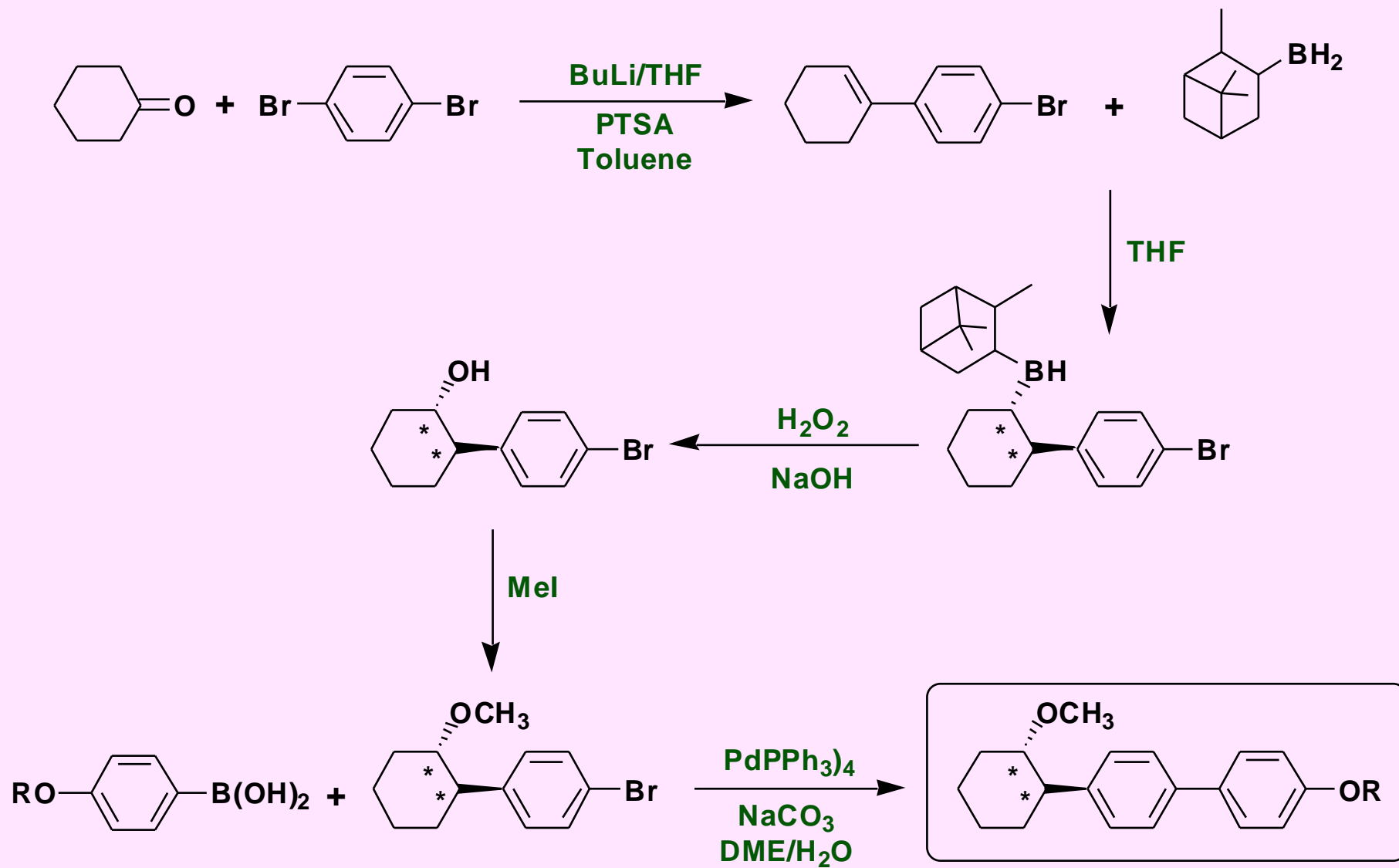
**Synthesis of Chiral Intermediates
from Optically Active Amino Acids**



Chiral Systems via Resolution

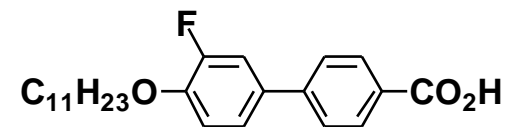
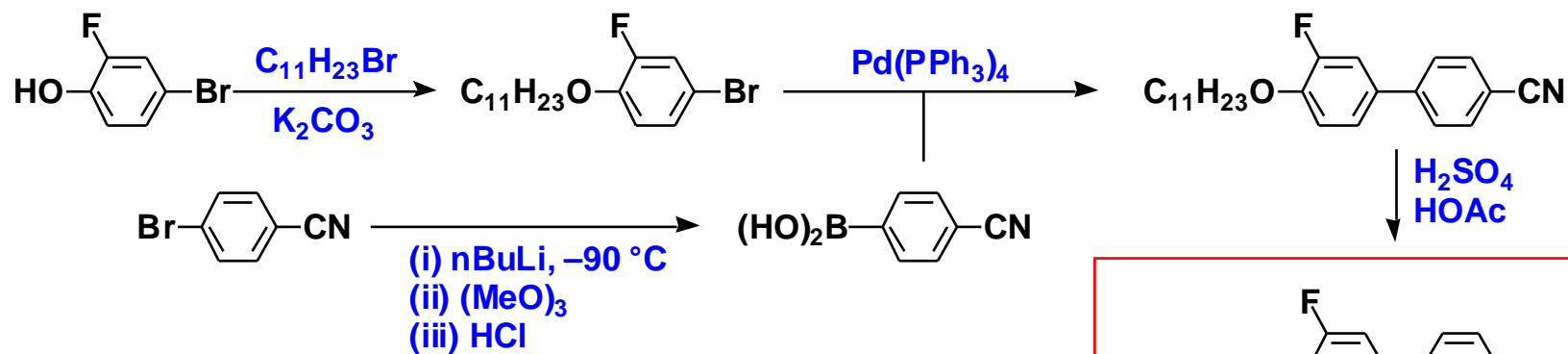
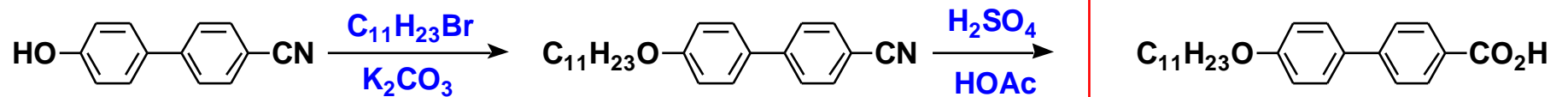


Asymmetric Synthesis using Brown's Chiral Hydroboration Method

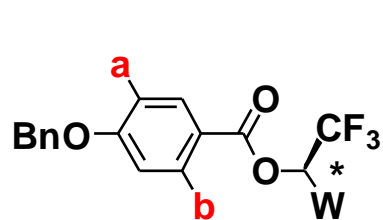
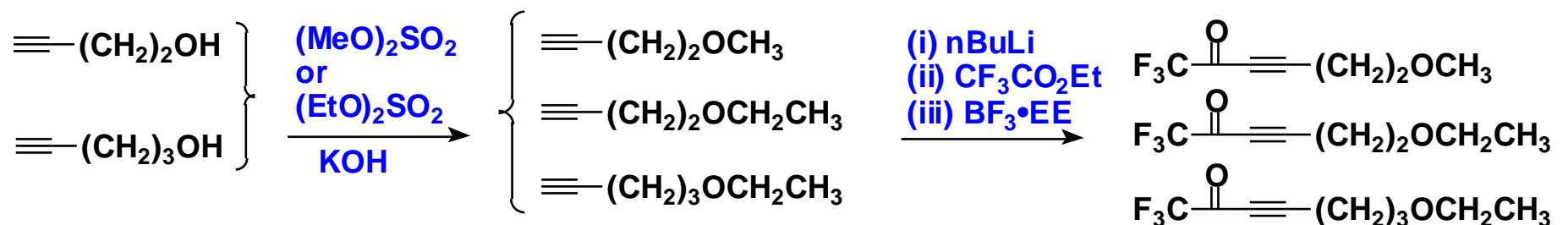


**Synthesis Using
All of the Techniques**

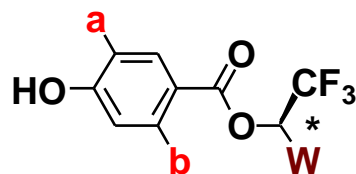
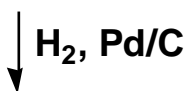
Synthesis of Acids



Synthesis of Phenols

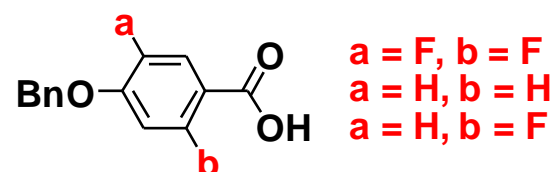


$a = \text{F}, b = \text{F}$
 $a = \text{H}, b = \text{H}$
 $a = \text{H}, b = \text{F}$



$a = \text{F}, b = \text{F}$
 $a = \text{H}, b = \text{H}$
 $a = \text{H}, b = \text{F}$

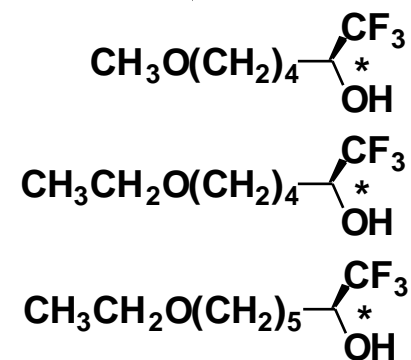
$W = (\text{CH}_2)_4\text{OCH}_3$
 $W = (\text{CH}_2)_4\text{OCH}_2\text{CH}_3$
 $W = (\text{CH}_2)_5\text{OCH}_2\text{CH}_3$



$a = \text{F}, b = \text{F}$
 $a = \text{H}, b = \text{H}$
 $a = \text{H}, b = \text{F}$

$\xleftarrow{\text{DEAD, PPh}_3, \text{THF}}$

\downarrow
 (i) (-)-DIP chloride
 (ii) $\text{H}_2, \text{Pd/C}$



Synthesis of Protected Hydroxybenzoic Acids

