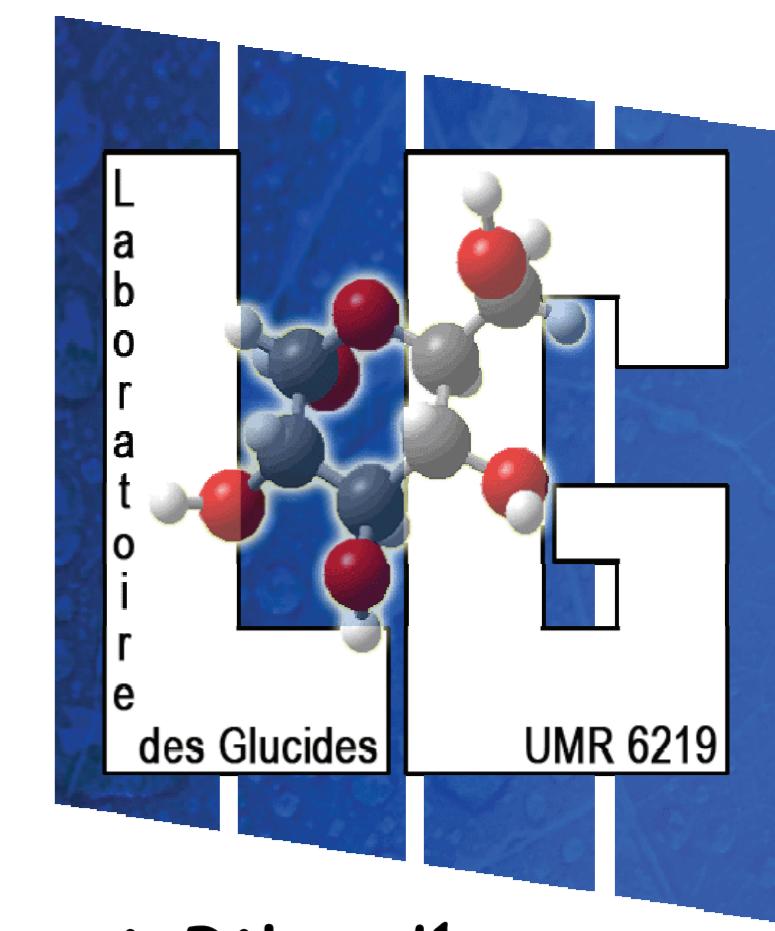


Chemo-Enzymatic Synthesis of Glycerolipidyl-Cyclodextrins



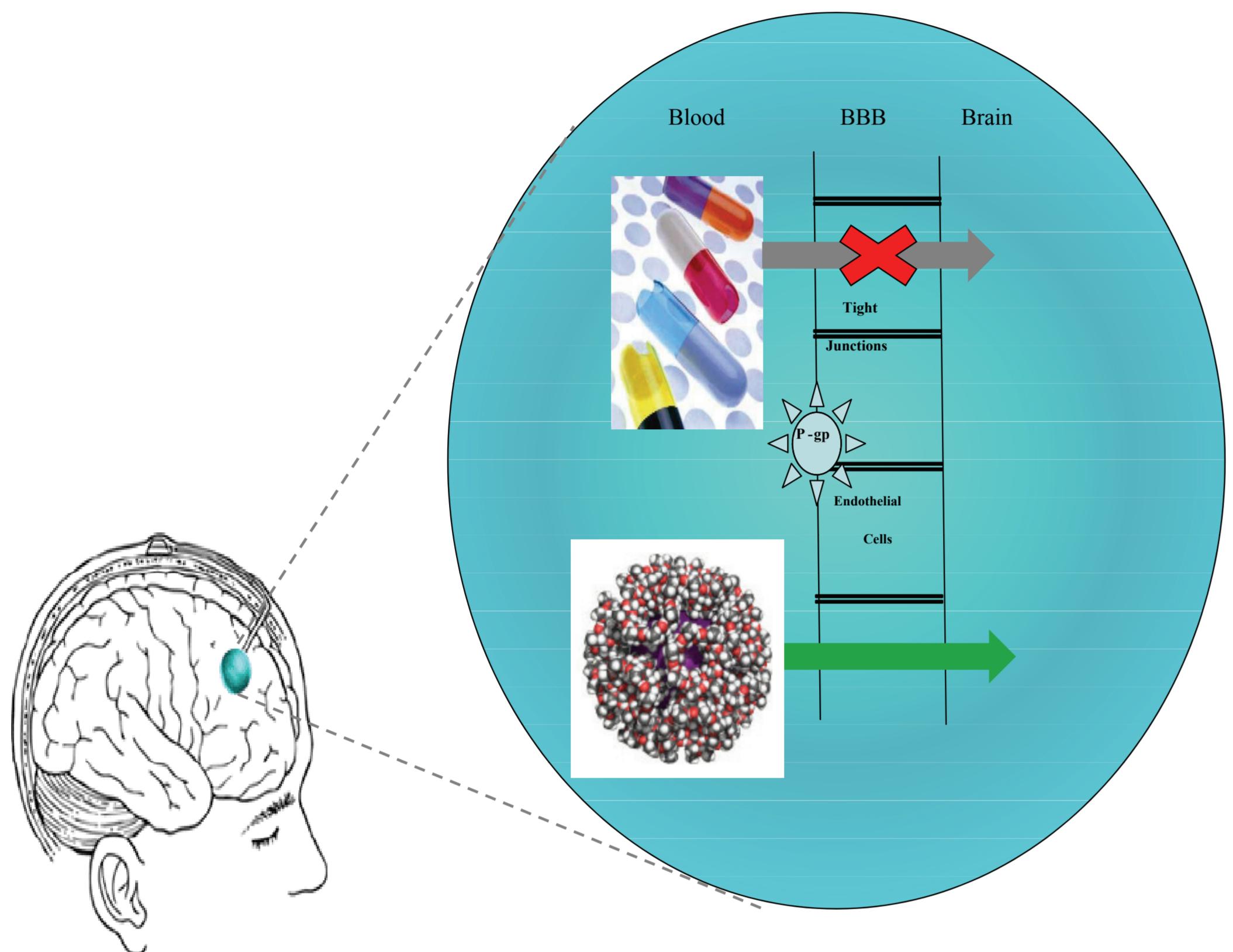
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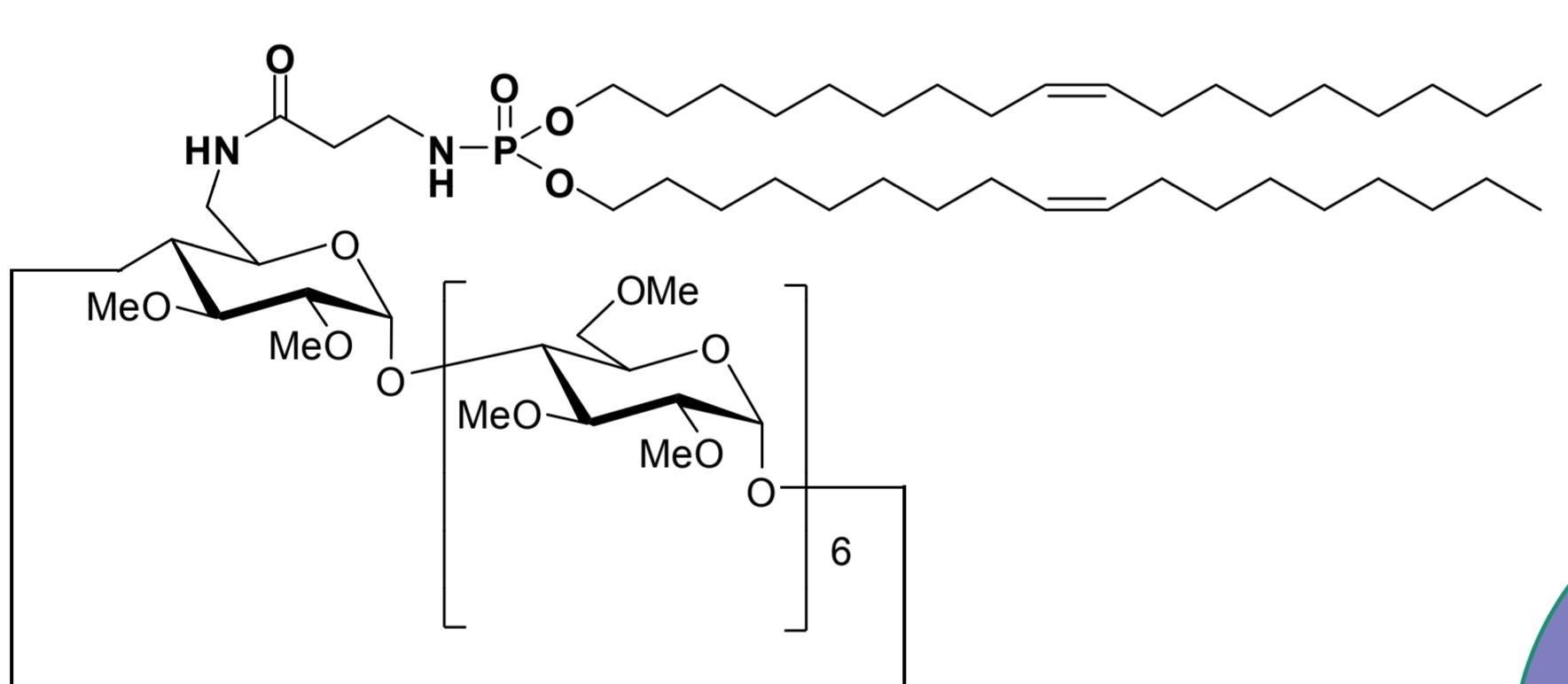
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Aim of this work : The formation of nanoparticles able to cross the BBB To improve the bioavailability of drugs.



A first family of amphiphilic cyclodextrins as nanovectors : liposphoramidyl-CDs



- > Nanoparticles (Np) formation by lipid film hydration method
- > Conversion of amphiphilic CD in Np : 84%

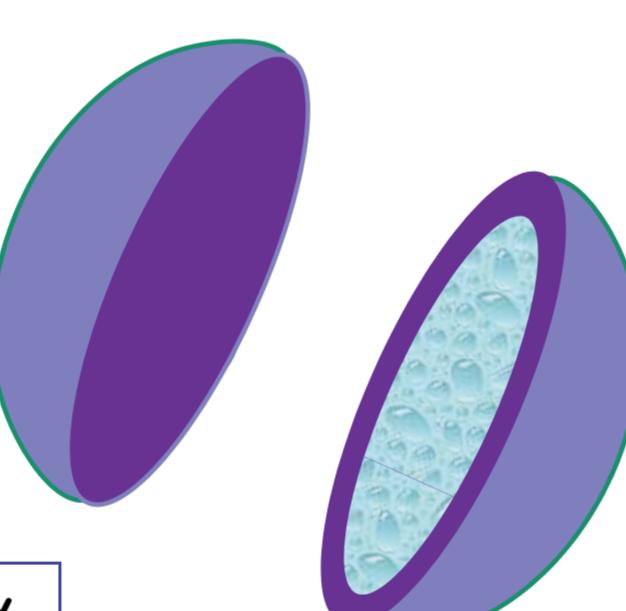
> Hydrodynamic Radius by DLS

	Radius (nm)	Polydispersity Index
Water	191±19	0,192
Glucose 5%	282±25	0,119
NaCl 0,9%	175±20	0,202
Phosphate Buffer	197±23	0,119

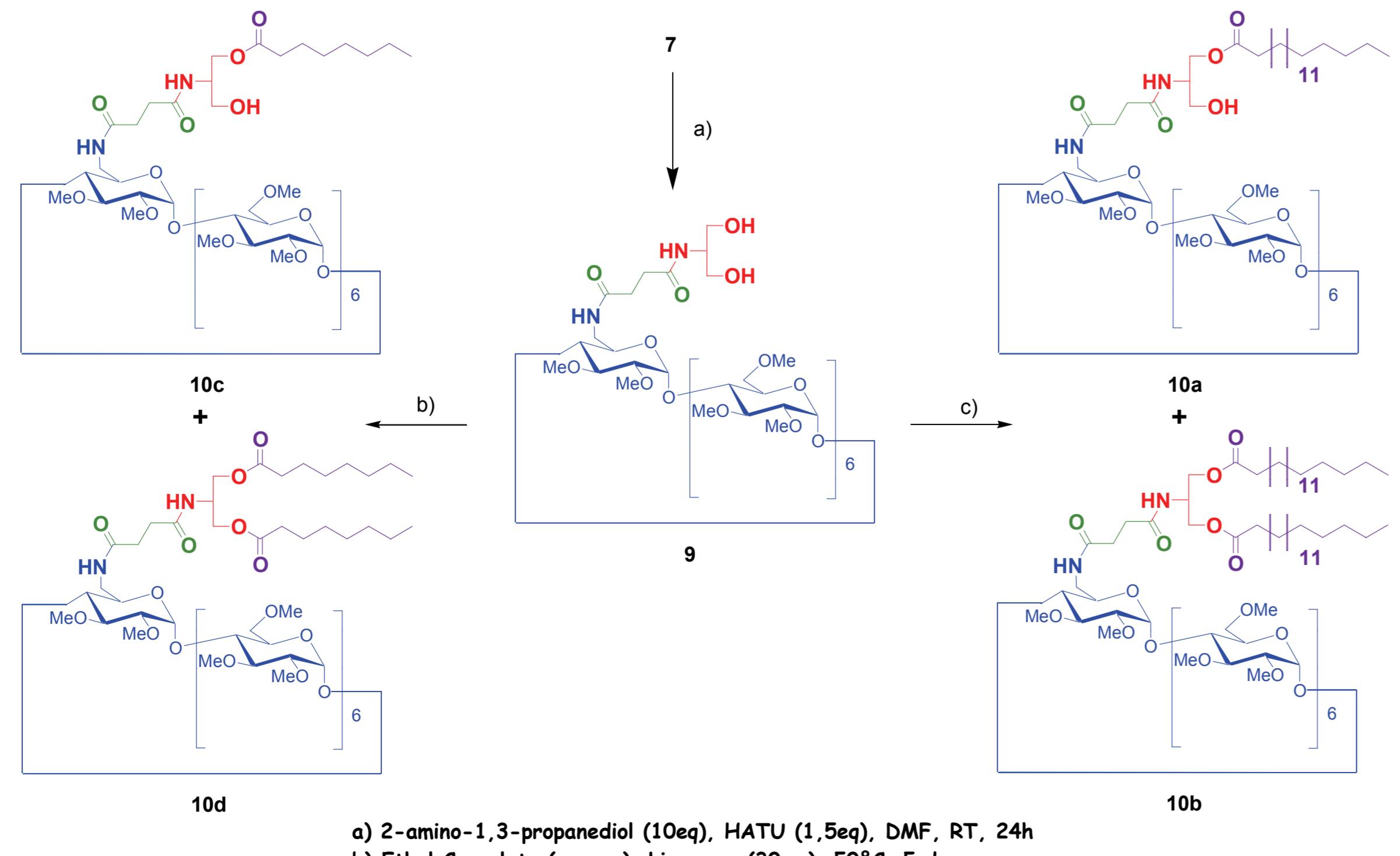
> BBB *in vitro* (LBHE Université d'Artois)

30% of CD has been found in the inner compartment of the BBB

Improvement of passage of N-Méthyl-Scopalamine ($\times 1,8$)

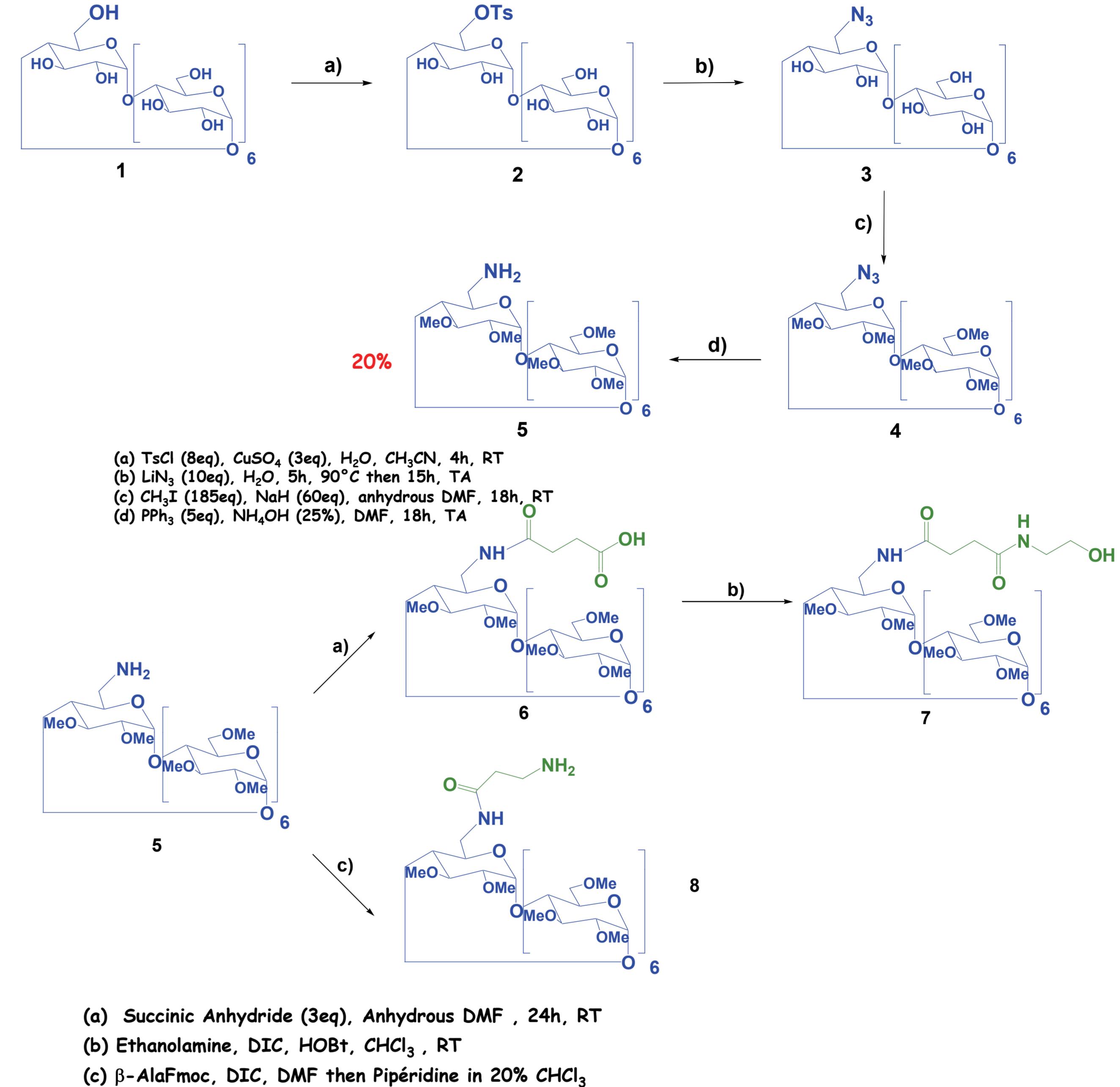


Glycerolipidyl-CD : The 2-amino-1,3-propanediol used as glycerol analogue and enzymatic O-acylation.



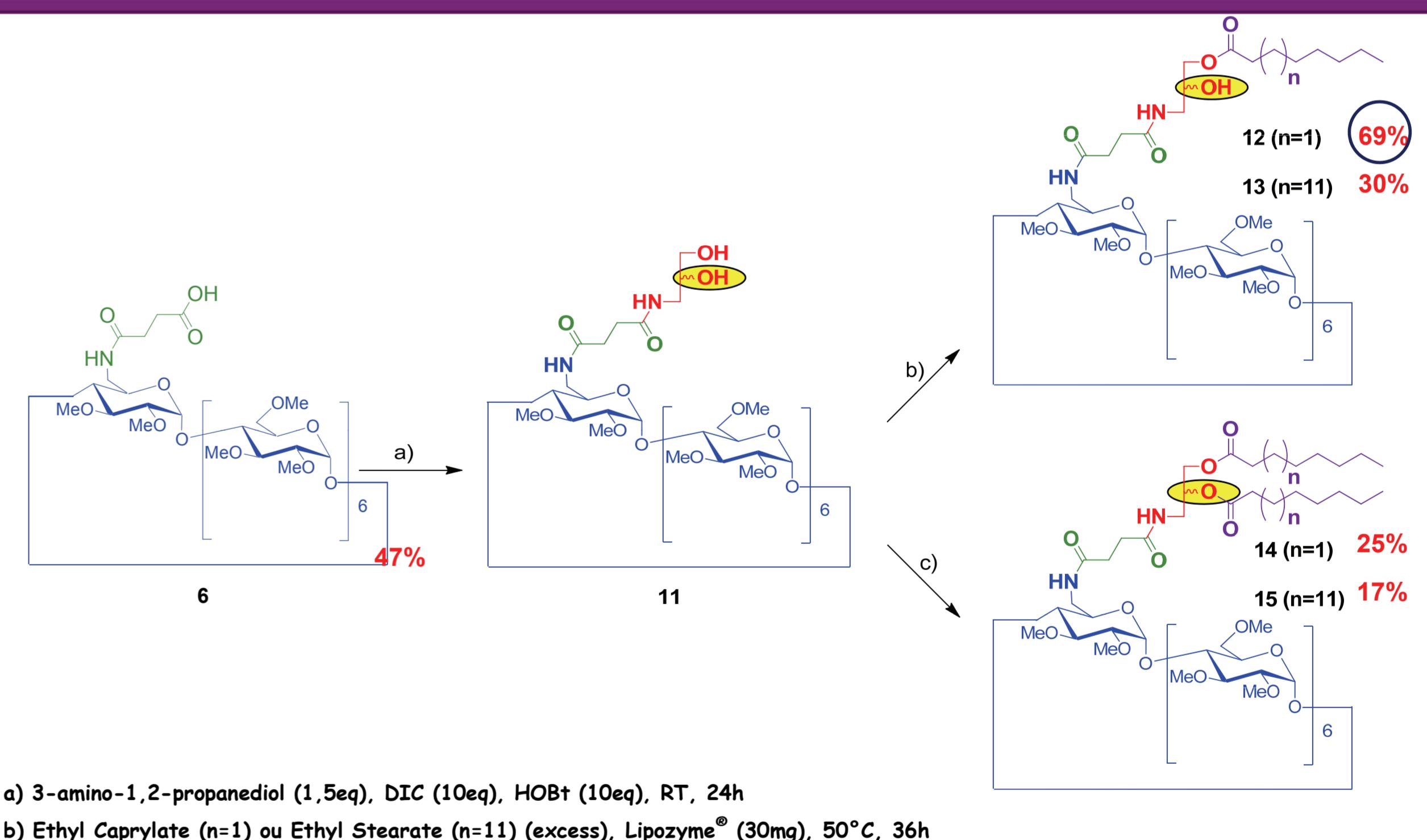
a) 2-amino-1,3-propanediol (10c), HATU (1,5eq), DMF, RT, 24h
b) Ethyl Caprylate (excess), Lipozyme (30mg), 50°C, 5 days
c) Ethyl Stearate (excess), Lipozyme (30mg), 50°C, 5days

Mono-substitution of CD : The synthesis of raw material with or without spacer arm.



(a) Succinic Anhydride (3eq), Anhydrous DMF, 24h, RT
(b) Ethanolamine, DIC, HOEt, CHCl₃, RT
(c) β-AlaFmoc, DIC, DMF then Pipéridine in 20% CHCl₃

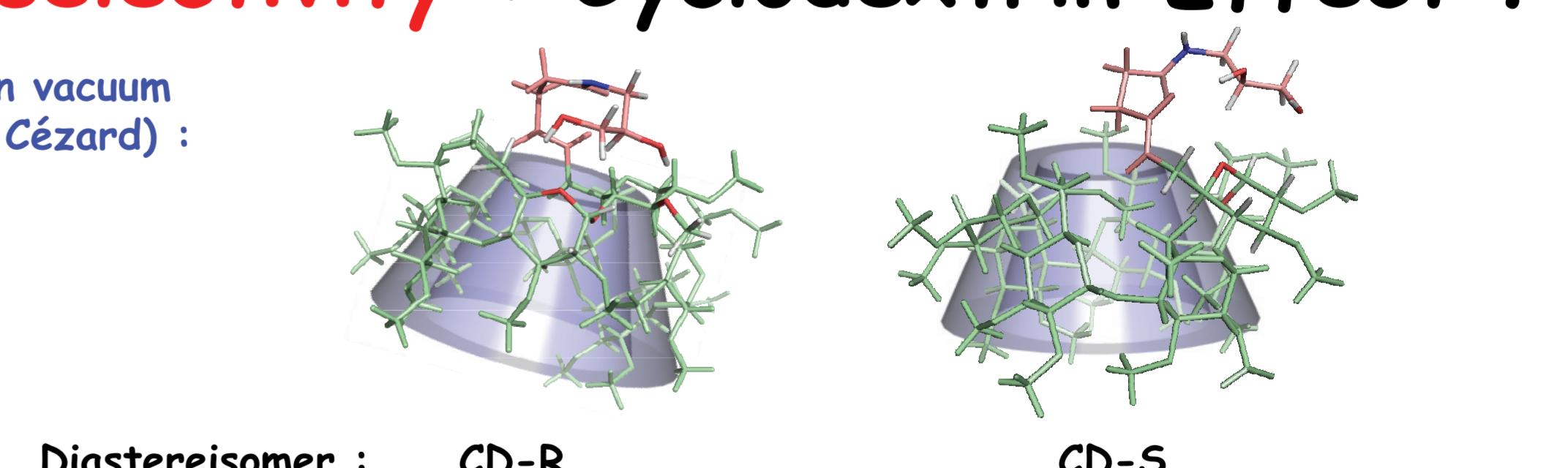
Glycerolipidyl-CD : The 3-amino-1,2-propanediol used as glycerol analogue and enzymatic O-acylation.



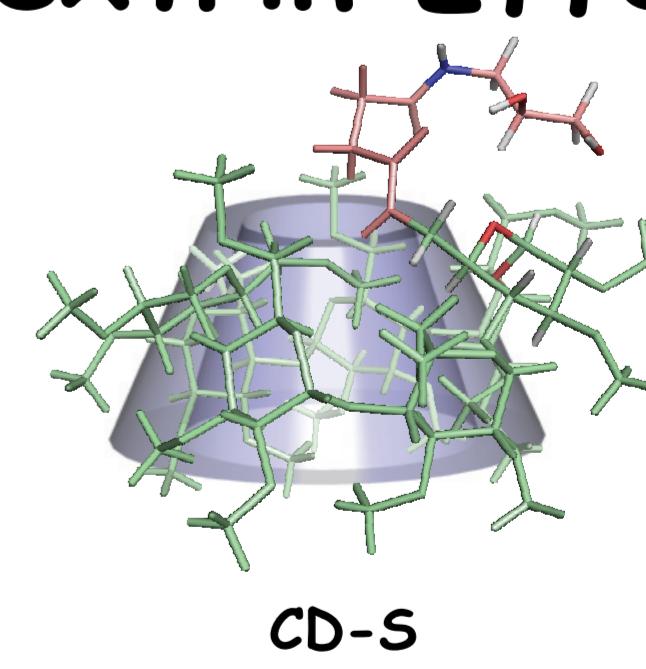
a) 3-amino-1,2-propanediol (1,5eq), DIC (10eq), HOEt (10eq), RT, 24h
b) Ethyl Caprylate (n=1) ou Ethyl Stearate (n=11) (excess), Lipozyme® (30mg), 50°C, 36h
c) Ethyl Caprylate (n=1) ou Ethyl Stearate (n=11) (excess), Lipozyme® (30mg), 50°C, 10days

Diastereoselectivity : Cyclodextrin Effect ?

> Modelling realized in vacuum
(Collaboration with C. Cézard) :



Diastereoisomer : CD-R



> For CD-R: H Bond between secondary alcohol of glycerol and O of glucopyranoside of CD which is closed to modified unit.
> For CD-S : arm goes out of the CD ring.
> 5 kcal difference energy between the most stable form of CD-R and CD-S.

Tensioactive properties :

Cyclodextrins	CAC	Cyclodextrins	CAC
	$1,1 \cdot 10^{-4} M$		$5,6 \cdot 10^{-5} M$
	$1,6 \cdot 10^{-4} M$		$4,9 \cdot 10^{-6} M$