

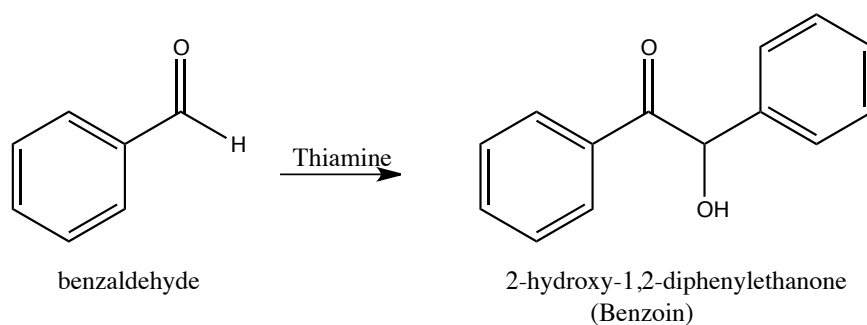
Benzoin condensation catalyzed by thiamine (n°38)

1. INTRODUCTION

1.1) Purpose

The objective of this experiment is to synthesize benzoin from the benzaldehyde, using thiamine hydrochloride.

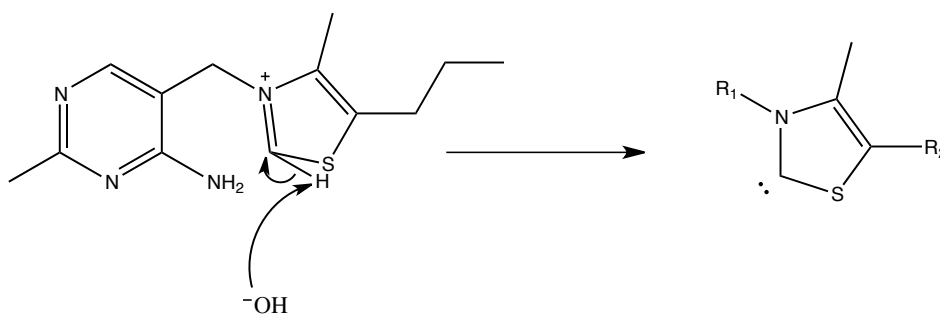
1.2) Scheme



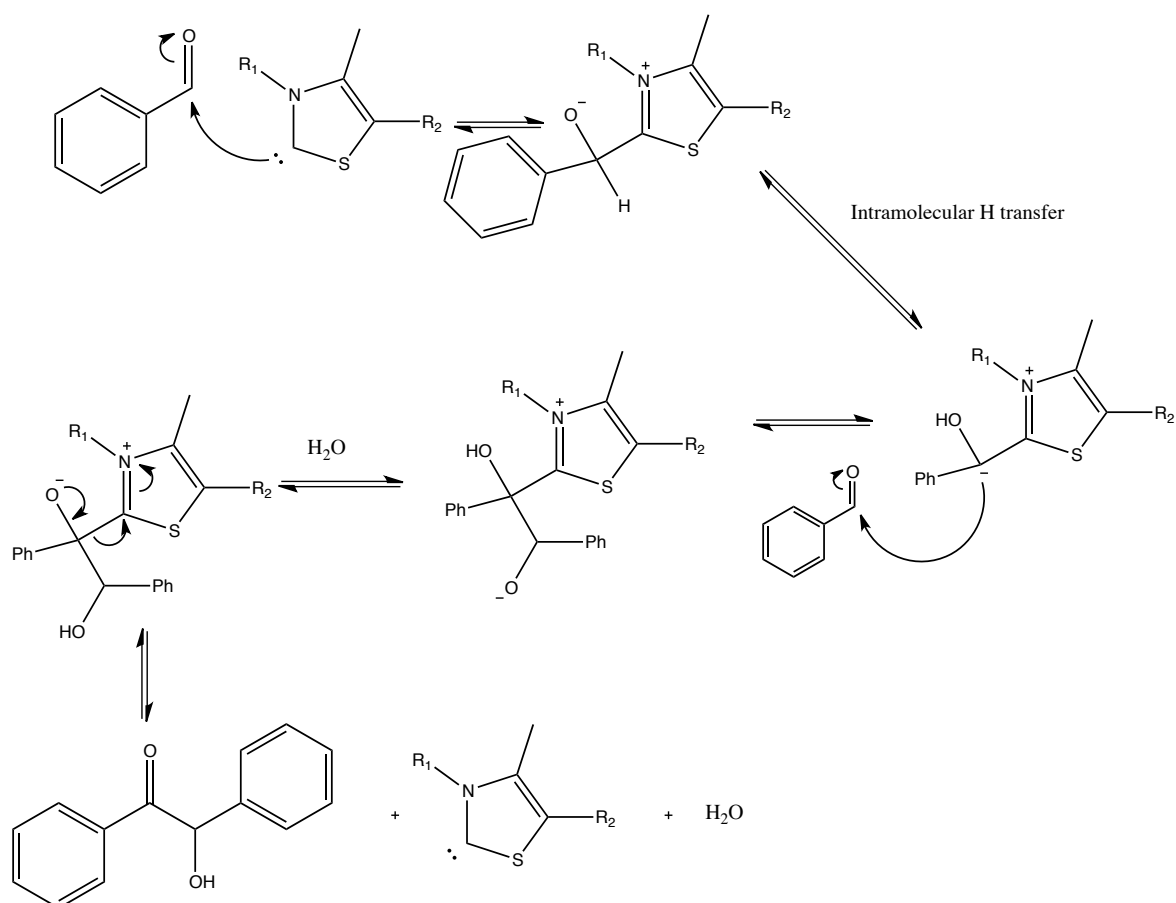
1.3) Mechanism

Step 1: Deprotonation of the thiamine:

NaOH attacks thiamine and deprotonates it. It is a condensation, since a molecule of H₂O is released. There is a formation of a carbene, which is very reactive.



Step 2: nucleophile attack of the benzaldehyde by the deprotonated thiamine:



2. PROCEDURE

2.1) Reaction

Reagents	molar mass [g/mol]	wt/vol taken	n [mmol]	equivalence
Thiamine chloride	300.81	3.55 g	0.012	1
Benzaldehyde	106.12	20.0 mL	0.196	16.33

In a 100mL twin neck round bottom flask, 3.5g of thiamine hydrochloride were dissolved in 8mL of water. Then, 35mL of EtOH at 95% were added and the solution was cooled down to 0°C. Into the agitated solution, first were added slowly 7mL of cold NaOH 3M and then 20mL of benzaldehyde. The mixture was heated at 60°C for 90 min. The solution was cooled down naturally then with an ice bath until crystallization.

2.2) Isolation

The obtained crystals were washed with water and then recrystallized in ethanol.

3. DISCUSSION AND RESULTS

3.1) Observations

When the mixture of thiamin, water and EtOH was cooled down, a white precipitate was formed.

The final product is almost pearly white and "spiky" crystals.

Its fusion temperature is 134.7-136.2 °C which is in agreement with the values given by the protocol: 134-136 °C.

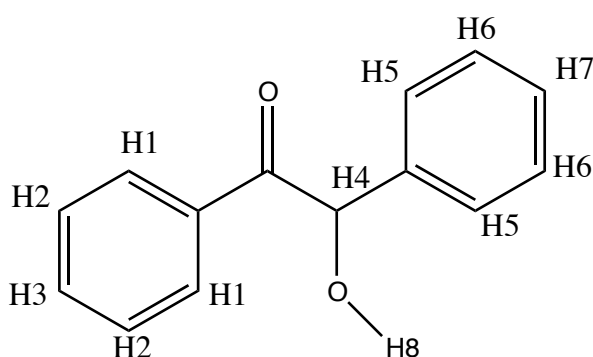
3.2) Yield

molar mass [g/mol]	n_{th} [mmol]	n_{exp} [mmol]	yield [%]
212.24	196	44.1	23%

9.3679g of product were obtained after recrystallization. This represents a 23% yield. The protocol said that the mass should be 10g (48%) but actually 10g represent 24% of yield (taking benzaldehyde as the limiting reagent). So the result is satisfying.

4. SPECTROMETRY DATA

4.1) NMR 1H ($CDCl_3$, 400MHz)



bond	shift δ [ppm]	multiplicity	hydrogen
C-H	7.92	multiplet	benzene H1
C-H	7.55-7.27	multiplet	benzene H2, H3, H5, H6, H7
C-H	5.97	doublet	H4
O-H	4.57	doublet	H8

δ 7.92 (m, 2H) ; δ 7.55-7.27 (m, 8H); δ 5.97 (d, J=6.0 Hz, 1H); δ 4.57 (d, 6.0 Hz, 1H)

There is a problem with the multiplet corresponding to δ 7.55-7.27 ppm because the integral should show only 8 hydrogens, but actually shows 9. The problem could be the solvent (CDCl_3) that would have been left in the product.

4.2) IR (neat, cm^{-1})

3404; 1679; 1263; 1204; 1092; 1068; 977; 753; 696; 673

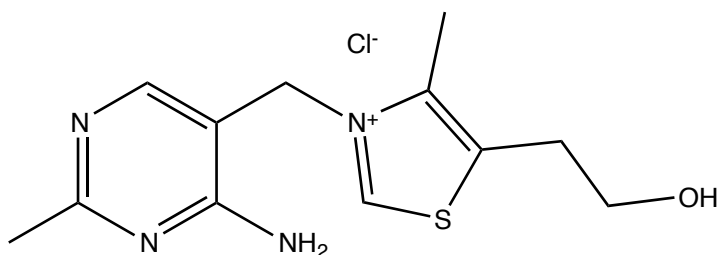
We can clearly see major peaks: one at 3404 cm^{-1} , corresponding to the O-H stretch and another at 1679 cm^{-1} , corresponding to the C=O stretch of an aldehyde.

Therefore the IR confirms that it is the expected product.

5. QUESTIONS

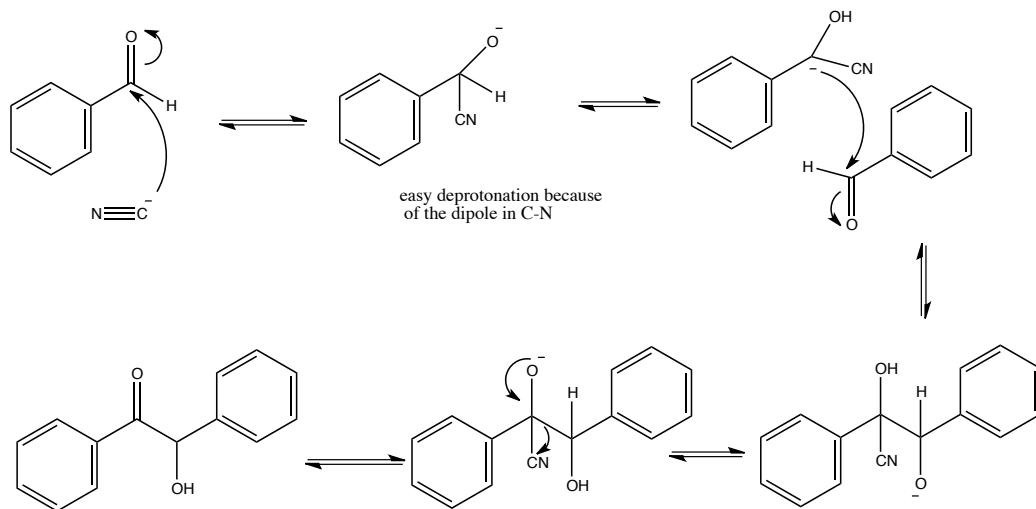
1) *What is the thiamine formula and what is its action mechanism in the reaction of benzoin condensation?*

See "mechanism". Thiamine is a catalyst; it is regenerated each time a benzoin molecule is synthesized.



3-((4-amino-2-methylpyrimidin-5-yl)methyl)-5-(2-hydroxyethyl)-4-methylthiazol-3-ium chloride

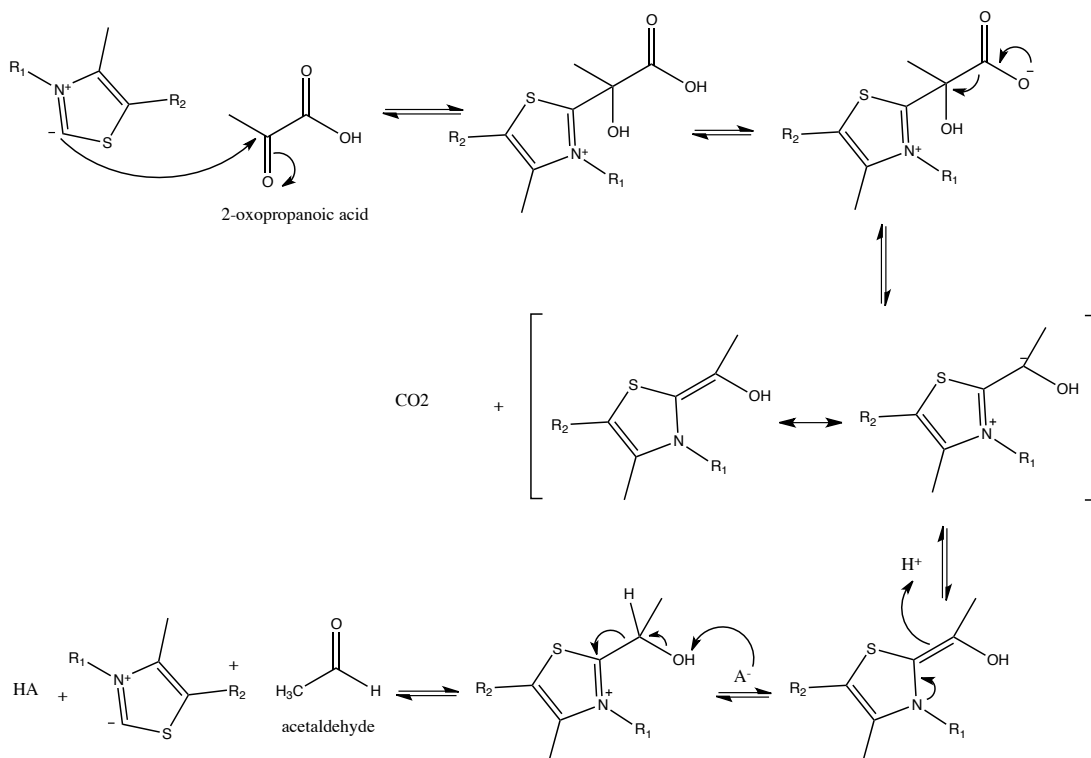
2) *Show how cyanide can replace thiamine in this reaction.*



It is the same mechanism as the one with thiamine. So cyanide can also be used as a catalyzer. [3]

- 3) *The pyruvate decarboxylase is an enzyme depending on the thiamine which catalyses the decarboxylation of pyruvic acid to acetaldehyde. Write a mechanism for this transformation and note down the bibliographic reference.*

The mechanism is an oxidative decarboxylation, with a release of CO₂. [4]



6. REFERENCES

[1] *Travaux Pratiques de Chimie Organique 3^{ème} Semestre*, **21 Novembre 2011 - 16 Mars 2012**, 38

[2] Silverstein, Bassler, Morrill, *Spectrometric identification of organic compounds*

[3] *Organic chemistry lessons*, Dr. A. Zumbuehl, p.52

[4] Vollhart-Schore, *Traité de chimie organique*, 5^{ème} édition, **2009**, p.1080

7. ANNEXES

IR spectrum, NMR spectrum