UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO

FACULTY OF CHEMISTRY

ORGANIC CHEMISTRY DEPARTAMENT

COMPENDIUM OF EXPERIMENTS FOR ORGANIC CHEMISTRY III (1506)

SEMESTER 2026-2

Organic Chemistry III Lab (1506)

Semester 2026-2

M. en C. Ana Adela Sánchez Mendoza

Dr. J. Oscar Humberto Pérez Díaz

Q. Irene Sara Audelo Mendez

Los experimentos de Aminación Reductiva y Olefinación de Wittig se desarrollaron con fondos del **PAPIME No. PE204623**

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El presente manual es una actualización y modificación del previo elaborado por:

M.C. Ana Adela Sánchez Mendoza

Dr. Diego Isaac Martinez Bourget.

Coordinador del Laboratorio de Química Orgánica III

1506 – Química

QUIMICA ORGÁNICA III (1506)

PROGRAMA DE PRÁCTICAS

Semestre 2026-2 **12 Enero 2026**

Semana	No	No. Práctica	Días Festivos
02 - 06 Feb	**1**	**Bienvenida, reglamento, forma de evaluación**	**Lun 02 Feb**
09 - 13 Feb	**2**	**Taller presencial de RMN ^{13}C**	
16 - 20 Feb	**3**	Nitrocompuestos I: **Reducción *Quimioselectiva* 4-nitroacetofenona**	
23 – 27 Feb	**4**	Nitrocompuestos II: **Reducción de Zinin**	
02– 06 Mar	**5**	Aminas I: **Colorantes azoicos**	
09 – 13 Mar	**6**	Aminas II: **Aminación reductiva / Acetilación**	
16 – 20 Mar	7	Compuestos Azufrados I: **Sulfanilamida I**	**Lun 16 Mar**
23 - 27 Mar	**8**	Compuestos Azufrados II: **Sulfanilamida II**	
30 Mar – 3 Abr	**--**	**Semana Santa**	
06 – 10 Abr	**9**	Carbonilos I: **Síntesis de Iminas**	
13 – 17 Abr	**10**	**Seminario RMN**	
20 – 24 Abr	**11**	Carbonilos II: **Condensación aldólica / benzoínica I**	
27 Abr – 01 May	**12**	Carbonilos III: **Condensación benzoínica II**	**Vie 01 May**
4 – 8 May	**13**	Carbonilos IV: **Síntesis de Oximas**	**Mar 05 May**
11 – 15 May	**14**	Carbonilos V: **Olefinación de Wittig**	**Vie 15 May**
18 – 22 May	**15**	**Evaluación experimental**	

Dr. Diego Isaac Martinez Bourget.
Coordinador de Laboratorio de Química Orgánica III (1506)

EXPERIMENT 1

NITRO COMPOUNDS I

CHEMOSELECTIVE REDUCTION OF 4-NITRO ACETOPHENONE

I. Objectives.

a) To perform a chemoselective reduction of nitro/carbonyl compounds.
b) To obtain 1-(4-nitrophenyl)-ethanol.
c) To employ synthesis techniques based on Green Chemistry principles.

II. Background information.

There are different reducing agents, each of which has the ability to reduce one or several functional groups; however, there are others that are capable of selectively reduce certain functionalities. This is the case of $NaBH_4$, which is highly selective for the carbonyl group, while $SnCl_2$ is highly selective for reducing -NO_2 groups.

III. Reagents.

Reagents	Amount	Reagents	Amount
4-nitroacetophenone	0.25 g	$NaBH_4$	0.25 g
10% HCl solution	2 mL	CH_2Cl_2	5 mL
Na_2SO_4	As needed		

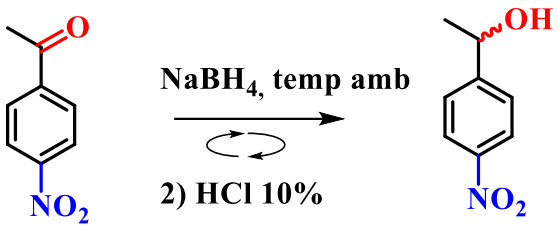
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Magnetic stirring bar ¼ ´´	1	Three fingers clamp	1
Water pump with hoses	1	T destilation adapter 14/23	1
Elution chamber with lid	1	Microscale three fingers clamp	1
Spatula	1	10 mL graduated cylinder	1
Glass vial	2	Pewter bowl	1
Glass funnel	1	Water condenser with hoses	1
50 mL separatory funnel stopper	1	20 mL beaker	1
10 mL round flat-bottom flask	1	Watch glass	1
25 mL Erlenmeyer flask	2	Weighing device	1
Porcelain mortar and pestle	1	Bent distilling adapter 14/23	1

V. Reaction and molar relationship.



	4-nitroacetophenone	$NaBH_4$	1-(4-nitrophenyl)-ethanol
Molar mass (g/mol)			
Mass (g)			
mmol			
Chemical equivalents			
Physical propieties			

VI. Experimental procedure.

In a 30 mL porcelain mortar, place 0.25 g of 4-nitroacetophenone, then add 0.25g $NaBH_4$. Next, vigorously mix the two solids using a pestle for 10 minutes (an oil formation will be observed). Once mixing time is complete, add 2 mL of CH_2Cl_2 to the mortar and pour the liquid into a 20 mL beaker. Wash the interior of the mortar three more times, each time with 1.5 mL of dichloromethane, and combine all washings inside the same beaker. Finally, wash with 3 mL of water and combine this volume with the dichloromethane washings. Transfer all the contents of the beaker into a separation funnel and add 2 mL of 10% v/v HCl solution. Carefully separate the phases, isolate the aqueous phase, and wash the organic phase again with 2 mL of water. Combine the aqueous phases for disposal. Dry the organic phase with anhydrous sodium sulfate and transfer it to a previously weighed 10 mL round-bottom flask equipped with a magnetic stirrer. Wash the beaker containing the damp Na_2SO_4 with an additional 2 mL of CH_2Cl_2 and add it to the rest of the CH_2Cl_2 solution. At this stage, take a sample of the reaction mixture and perform a TLC (Thin Layer Chromatography) using a Hex:AcOEt (6:4) eluent mixture. Evaporate the CH_2Cl_2 solution containing the product to dryness. Remove the magnetic stirring bar, weigh the obtained oil-like liquid, and determine the reaction yield.

To transfer it into the product vial, dissolve the product in 0.5 mL of CH_2Cl_2 and deposit it into the respective container.

VII. Questions

1. Write the formula of three aromatic compounds that may be susceptible to a reduction reaction with sodium borohydride.

2. What is the purpose of washing the CH_2Cl_2 organic phase with HCl and water solution?

3. What might happen if you wash with excess acid and water?

4. Mention and briefly describe another method of obtaining alcohols through reduction.

VII. Biliografic references.

1. J. Isaac-García., J.A. Doblado. Experimental Organic Chemistry: Laboratory Manual. Academic Press, Elsevier, 2016.
2. J.C. Gilbert, S. F. Martin. Experimental Organic Chemistry. 5ª ed. Brooks/Cole. Laboratory series for Organic Chemistry. CENGAGE Learning, USA, 2010.
3. Bruice, Paula Yurkanis. Química Orgánica, 5a. Ed., Pearson-Prentice Hall, México, 2008.
4. Wade, L. G., JR., Química Orgánica, 7a. Ed., Pearson-Prentice-Hall, México, 2014.
5. Carey Francis A. Química Orgánica, 9a. Ed. McGraw-Hill, México, 2014.

VIII. Apendix I. Prior knowledge.

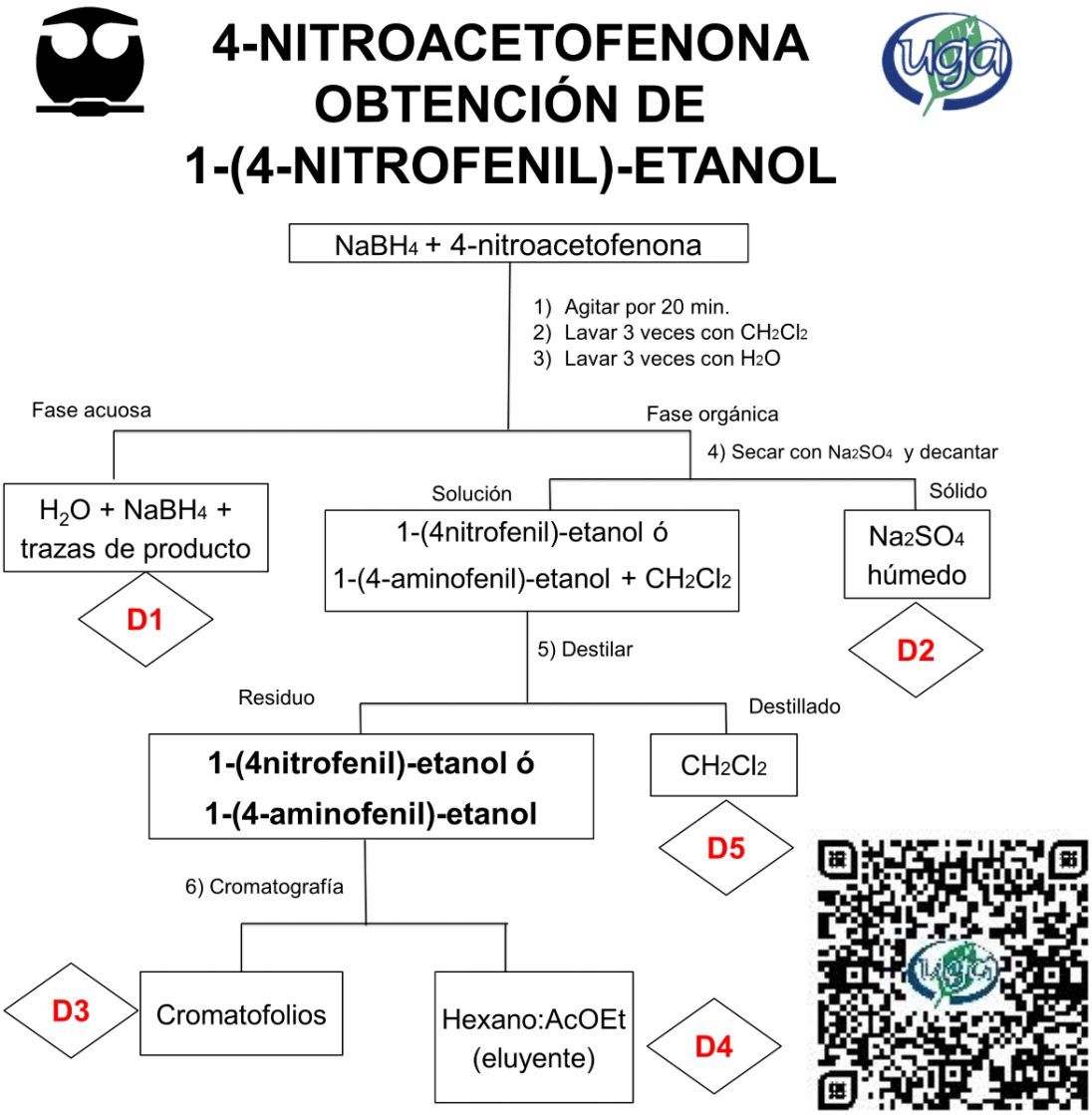
1. Differences between chemo, regio, and stereoselectivity.
2. Selective reducing agents for the carbonyl group.
3. Reaction mechanism of carbonyl reduction using $NaBH_4$.
4. Solid-state reactions / solvent-free conditions.
5. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

IX. Apendix II
Preparation of regents

10% HCl solution (1 L)

Measure 100 mL of concentrated hydrochloric acid (HCl) using a graduated cylinder, and slowly add it into a 1000 mL volumetric flask containing 880 mL of distilled water. Finally, fill up the flask to the mark with distilled water. Ensure the volumetric flask is placed in an ice bath, gently agitate until homogenized, then proceed to pour it into the storage container. Important: DO NOT reverse the order of addition. Wear a lab coat, gloves, and safety goggles. The solution releases heat.

X. Waste management.



D1: Verificar la presencia del reductor y destruirlo, desechar la solución neutra al drenaje.
D2 Y D3: Enviar a incineración
D4: Recuperar el disolvente para su reutilización.

Scheme 1. QR / Flowchart of 1- (4-nitrophenyl)-ethanol synthesis and its waste management.

EXPERIMENT 2

NITRO COMPOUNDS II

ZININ REDUCTION / SYNTHESIS OF *m*-NITRO ANILINE

I. Objectives.

1. To perform a selective reduction of nitro compounds.
2. To obtain *m*-nitroaniline from *m*-dinitrobenzene and to separate them based on their acid-base characteristics.

II. Background information.

The nitro compounds are organic compounds that display one or more nitro groups (**NO_2**), which is one of the functional groups most commonly found in explosive compounds. These types of functionalities are among several functional groups commonly referred to as explosophores.

The nitro group is a strongly electron-withdrawing group; due to this, the C-H bonds adjacent to the **NO_2** group exhibit acidic characteristics. Similarly, based on this electron-withdrawing property, the nitro group in aromatic compounds is responsible for slowing down reactions of the electrophilic aromatic substitution (EAS) type. However, conversely, it accelerates SNAr (nucleophilic aromatic substitution) reactions.

Natural nitro compounds are extremely rare; just to cite a few examples: chloramphenicol, 3-nitropropionic acid, 2-nitrophenol, which exhibit activities such as antibiotics or pheromones. Nitro compounds are invariably synthesized in the laboratory through nitration reactions. However, the greatest significance of nitro compounds lies in being raw materials for obtaining amines, which are synthesized by reducing the nitro group of these organic compounds.

III. Reagents.

Sodium sulfide Na_2S	0.25 g	Sulfur S_8	0.1 g
m-Dinitrobenzene	0.175 g	NH_4OH	As needed
10% HCl solution	5 mL	Hexano / AcOEt	3 mL

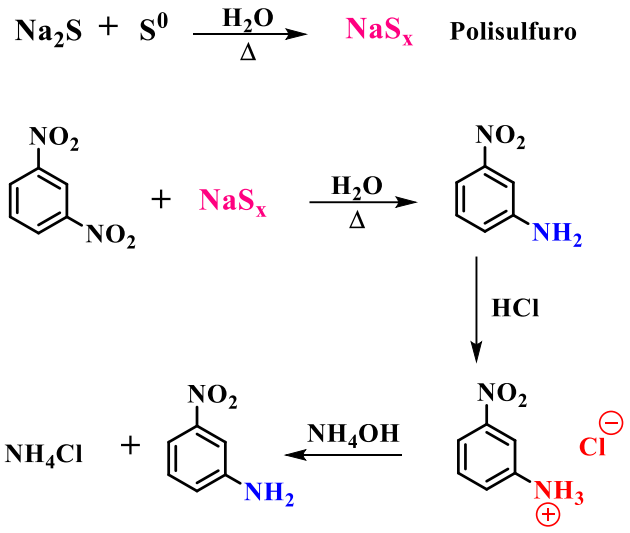
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Glass stirrer	1	125 mL Erlenmeyer flask	1
Magnetic stir bar ¼ ´´ & ½´´	2	25 mL Kitasato flask with hose	1
Elution chamber with lid	1	Three fingers clamp	1
Spatula	1	Microscale three fingers clamp	1
Glass vial	1	10 mL graduated cylinder	1
Glass funnel	1	5 mL graduated pipette	1
Glass vial	2	Pewter bowl	1
Büchner funnel	1	50 mL beaker	1
50 mL separatory funnel stopper	1	Watch glass	1
25 mL Erlenmeyer flask	2	Weighing devicel	1
50 mL Erlenmeyer flask	1		

V. Reaction and molar relationship.



	Sodium sulfide / Sulfur	*m*-dinitrobenzene	*m*-nitro aniline
Molar mass (g/mol)			
Mass (g)			
mmol			
Chemical equivalents			
Physical propieties			

VI. Experimental procedure.

Inside the fume hood, prepare a solution of sodium polysulfide by placing 30 mL of water in a 50 mL beaker and adding 0.25 g of sodium sulfide. Then, add 0.1 g of finely powdered sulfur. Heat this solution with magnetic stirring until complete dissolution of sulfur occurs. If the volume decreases to less than 25 mL, add hot water to maintain a constant volume of 25 mL of solution, and transfer this solution to a separation funnel.

In a 125 mL Erlenmeyer flask equipped with a magnetic stirrer, place 0.175 g of m-dinitrobenzene and 25 mL of water. Heat this mixture to boiling. Once the solution is boiling, and while maintaining magnetic stirring, slowly add dropwise the sodium polysulfide solution. After the addition of sodium polysulfide is complete, allow the mixture to continue boiling for an additional 20 minutes (do not let the reaction mixture dry out; if necessary, add hot water to maintain a constant volume of 25 mL).

Once the heating period is completed, the solution is allowed to cool to room temperature and then further cooled in an ice bath. The resulting solid is vacuum-filtered and washed with ice-cold water until the wash water becomes slightly yellow. In a 20 mL beaker, prepare 5 mL of a 10% HCl solution.

The obtained solid is transferred into a 25 mL Erlenmeyer flask, followed by the addition of 5 mL of 10% HCl solution. Heat the mixture to boiling to dissolve the m-nitroaniline, leaving sulfur and any unreacted m-dinitrobenzene suspended. Gravity filtration is performed, and the solids are discarded in the designated waste container.

The filtrate is cooled, and a concentrated solution of ammonium hydroxide is added drop by drop until an alkaline pH is reached, precipitating *m*-nitroaniline. This compound is then vacuum-filtered and purified through simple recrystallization using water. Determine the melting point of the obtained solid, weigh the final product to calculate its yield, and perform thin-layer chromatography of the reaction, comparing the starting material against the product. Use a hexane:ethyl acetate mixture (8:2) as the eluent.

VII. Questions.

1. Write a plausible mechanism for the reaction carried out.
2. How did you obtain sodium polysulfide?
3. How did you remove the unreacted *m*-dinitrobenzene and precipitated sulfur?
4. How did you regenerate the purified amine in the end?
5. What is the toxicity of sodium sulfide, sodium polysulfide, *m*-dinitrobenzene, and *m*-nitroaniline?

VIII. Bibliographic references.

1. Ávila, G.; García, C. *et al* Química Orgánica. Experimentos con un Enfoque Ecológico **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
2. March, J., March's Advanced Organic Chemistry, Reactions, Mechanisms and Structure **2007**, Wiley, John and Sons Incorporated, 6ta Edición, Estados Unidos de Norteamérica.
3. *Org. React*. 20, 455-481.
4. Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry **1996**, Prentice Hall 5ta. Edición, Estados Unidos de Norteamérica.

IX. Apendix I. Prior knowledge.

a) Different reducing agents to obtain amines from nitro compounds.
b) Most commonly used selective reducing agents for nitro groups in the laboratory.
c) Importance of the Zinin reaction among synthetic methods for amines.
d) Reduction of nitro compounds in alkaline medium and the products that can be isolated from this reaction.

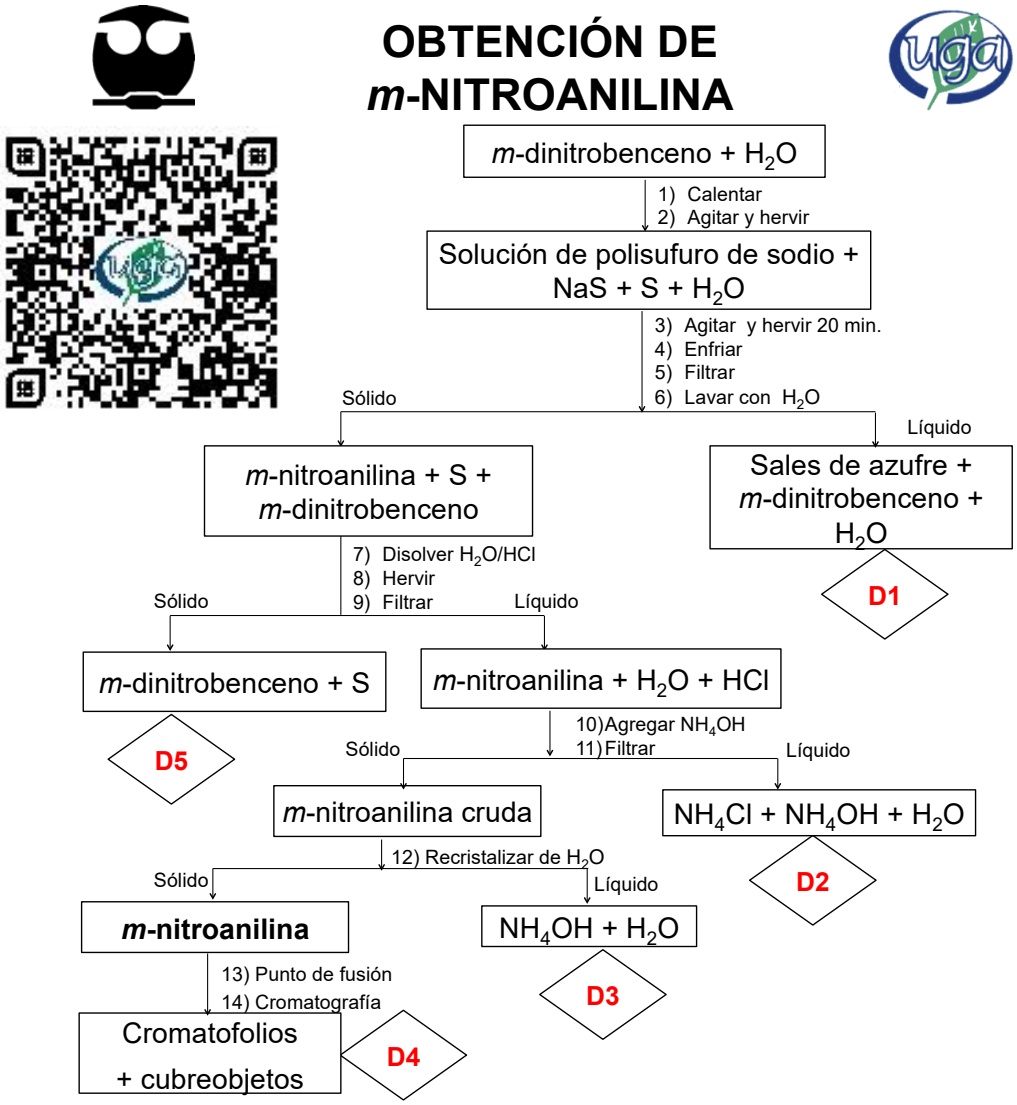
e) Effect of substituents on the regioselectivity of the Zinin reduction.
f) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Apendix II. Preparation of reagents.

10% HCl solution (1 L)

Measure 100 mL of concentrated hydrochloric acid (HCl) using a graduated cylinder, and slowly add it into a 1000 mL volumetric flask containing 880 mL of distilled water. Finally, fill up the flask to the mark with distilled water. Ensure the volumetric flask is placed in an ice bath, gently agitate until homogenized, then proceed to pour it into the storage container. Important: DO NOT reverse the order of addition. Wear a lab coat, gloves, and safety goggles. The solution releases heat.

XI. Waste management.



.**D1:** Filtrar los sólidos y la solución adsorber con carbón activado, el líquido resultante debe neutralizarse y los residuos sólidos se envían a incineración.
D2 : Revisar pH y desechar neutro al drenaje.
D3: Adsorber sobre carbón activado, revisar pH y desechar neutro. Residuos sólidos mandar a incineración.
D4: Enviar a incineración

Scheme 2. QR / Flowchart of *m*-nitro aniline synthesis and its waste management.

EXPERIMENT 3

AMINES I

DIAZONIUM SALTS / SYNTHESIS OF DIAZOIC DYES: METHYL ORANGE

I. Objectives.

a) To illustrate in the laboratory, the coupling reactions of diazonium salts.
b) To obtain azo dyes through the diazotization and coupling reactions of diazonium salts of sulfanilic acid.
c) To dye various fibers with the synthesized diazo dyes.

II. Background information.

Azo dyes are aromatic organic compounds that exhibit the functional group Ar-N=N=Ar, owing to significant electron delocalization between sp2 hybridized atoms and high p bond conjugation along this type of compound. Due to these delocalization and electronic conjugation phenomena, azo compounds display intense and vibrant colors, typically ranging from yellow to red, although blue hues are also present. Many of these diazo compounds serve as paints, fiber dyes, and others as pH indicators.

The obtaining of these diazo compounds is usually achieved through reactions called coupling reactions, where aryl-diazonium salts, acting as strong electrophiles, are obtained through SEAr-type reactions.

III. Reagents.

N,N-dimethylaniline	0.06 mL	Sulfanilic acid	0.1 g
Sodium nitrite $NaNO_2$	0.03 g	Concentrated HCl	Drops
NaOH solution 10%	As needed	Ethanol	10 mL

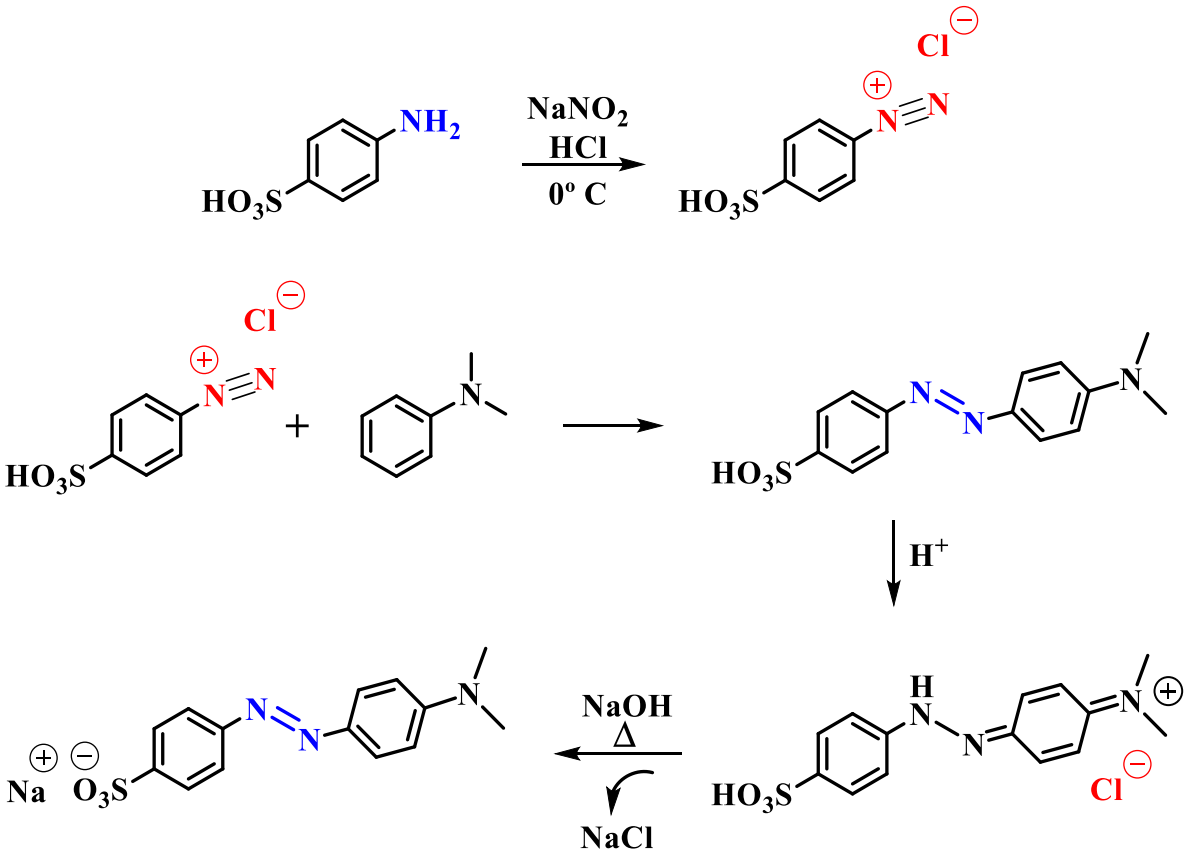
IV. Equipment.

Fisher-Johns melting point apparatus	Hot plate magnetic stirrer
Analytical Balance	

Glasswere for each team

Glass stirrer	1	Three-finger clamp with nut	1
Magnetic stir bar ½´´	1	1 mL graduated pipette	2
Glass funnel	1	5 mL graduated pipette	1
Porcelain Büchner funnel with extension	1	10 mL graduated cylinder	1
Spatula	1	Pewter bowl	1
25 mL Erlenmeyer flask	2	Termomether -10 a 260º C	1
50 mL Kitasato flask with hose	1	20 mL beaker	1
Weighing vessel	1	30 mL beaker	1
Microscale three-finger clamp with nut	1	Glass watch	1

V. Reaction and molar relationship.



	Sulfanilic acid	Dimethylaniline	$NaNO_2$	Orange methyl
Molar mass (g/mol)				
Mass (g)				
Density (g/mL)				
mmol				
Chemical equiv				
Physical properties				

VI. Experimental procedure.

N,N-dimethylaniline: Must be worked in a ventilated area. The use of gloves, safety glasses and appropriate clothing is recommended for handling it. In case of direct contact, rinse with water for several minutes, even while using gloves.

In a 25 mL beaker, place 0.1 g of sulfanilic acid, 0.06 mL of dimethylaniline (1-2 drops), and 0.05 mL of concentrated hydrochloric acid (1-2 drops). Also, add 5 mL of water, and cool this reaction mixture within an ice-salt bath until it reaches a temperature of 0 – 5º C.

In another 20 mL beaker, prepare 1 mL of sodium nitrite solution by cooling 1 mL of distilled water and 0.03g of sodium nitrite; keep the solution below 5º C.

Add dropwise, within an ice bath and with constant manual stirring, the sodium nitrite solution into the solution of dimethylaniline and sulfanilic acid, prepared earlier. Once the addition is complete, stir the mixture until it reaches room temperature. The reaction mixture will acquire a reddish-purple color. Stir until it reaches room temperature and maintain it for 10 minutes.

After this time, add dropwise with manual stirring a 10% NaOH solution until pH=10. Subsequently, heat the reaction mixture with constant stirring and remove the beaker when it begins to boil. Allow it to cool to room temperature for a few minutes, then cool it within an ice bath and vacuum filter the solid.

Wash the filtrate with ice-cold water (2 x 5 mL), dry the solid, and proceed to weigh its mass to determine the % yield. Methyl orange will precipitate as the sodium salt.

Staining tests.

In a 30 mL beaker, place 10 mL ethanol and prepare a 1% solution of the dye. Add small pieces of different fibers such as cotton, wool, or silk (preferably white). Boil the fabrics for 5 minutes, then rinse the fabric pieces with water. Observe and record the results.

VII. Questions.

1) Explain, why are aromatic diazonium salts relatively stable.
2) How is the decomposition of diazonium salts prevented?
3) What pH difference is required for the coupling reaction of diazonium salts to be optimal for substrates containing phenols and amines in their structure?
4) What is a dye, and what is the mechanism by which a dye colors fiber?

VIII. Bibliographic references.

1. Ávila, G.; García, C. *et al Química Orgánica. Experimentos con un Enfoque Ecológico* **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
2. Vogel, A. I., *Vogel's Textbook of Practical Organic Chemistry* **1996,** Prentice Hall, 5ta. Edición, Estados Unidos de Norteamérica.
3. Williamson Kenneth, *Macro and Microscale Organic Experiments* **2010**, Cengage Learning Brooks/Cole, 6ta Edición, Estados Unidos de Norteamérica.
4. Brewster R.Q., Vanderwerf C.A., McEwen W.E, *Curso Práctico de Química Orgánica* **1970**, Editorial Alhambra, 2da Edición, México.
5. Bruice Paula Yurkanis, *Química Orgánica* **2008**, Pearson-Prentice Hall, 5ta Edición, México.
6. Carey Francis A. *Química Orgánica* **2014**, McGraw-Hill, 9ena Edición, México.

IX. Appendix I. Prior knowledge

1. Reductive Amination Reaction.
2. Reaction mechanism for the reduction of imines.
3. Different reducing agents used in reductive amination, benefits and cons, and costs.
4. Acetylation reaction of amines
5. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Appendix II. Preparation of reagents.

10% NaOH solution (1L)

Weigh 100 g of sodium hydroxide (NaOH) and pour it into a 1000 mL volumetric flask containing 500 mL of distilled water within an ice bath. Gently stir the solution, and slowly fill the flask to a final volume of 1000 mL (1 L). The solution releases heat.

XI. Waste management.

OBTENCIÓN DE ANARANJADO DE METILO

D1: Lleve a sequedad. Almacene el sólido para su incineración.

Scheme 3. QR / Flowchart of orange methyl synthesis and its waste management.

EXPERIMENT 4

AMINES II

REDUCTIVE AMINATION / ACETYLATION

I. Objectives.

a) To illustrate the Reductive Amination reaction in the laboratory.
b) To synthesize a secondary amine from imine synthesis and reduction reactions.
c) To carry out the acetylation of the secondary amine obtained by Reductive Amination.
d) To use synthesis techniques based on Green Chemistry.

II. Background information.

The synthesis of amines by alkylation of the amino group is a difficult method to control since poly-alkylation is normally favored.

An alternative for the synthesis of amines that works efficiently in most cases is Reductive Amination, which consists of obtaining imines from aldehydes and ketones with amines, which subsequently undergo a reduction reaction with some reducing agent. suitable, thus achieving the synthesis of secondary and tertiary amines, avoiding the undesirable problem of multiple alkylation. It is possible to start with a primary amine and carry out two successive Reductive Amination reactions to efficiently obtain tertiary amines of your choice.

III. Reagents.

o-Vanillin	0.39 g	*p*-Toluidine	0.27 g
$NaBH_4$	0.07 g	EtOH	10 mL
Glacial acetic acid	1 mL	Acetic anhydride	1 mL

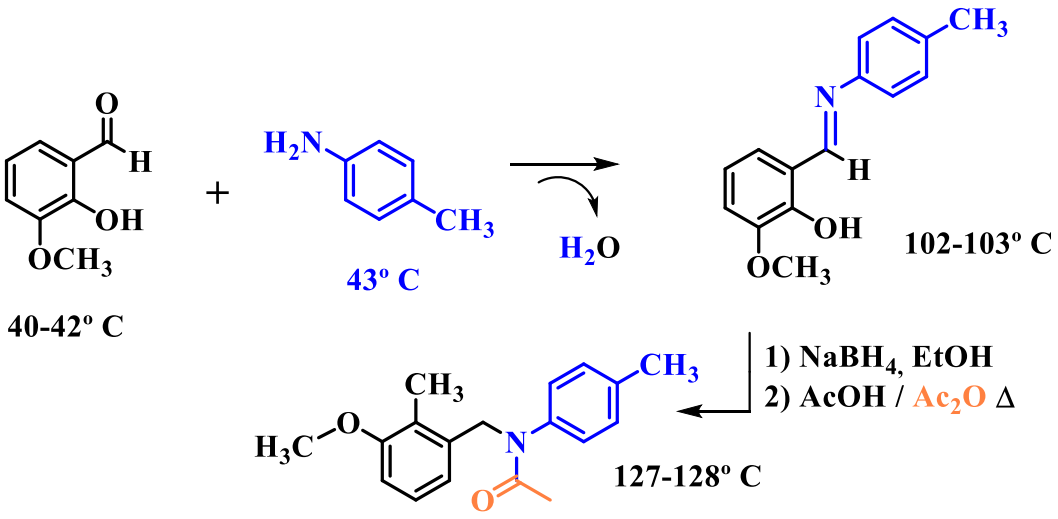
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team.

Glass stirrer	1	Plastic Büchner funnel with extension	1
Magnetic Stir bar ½´	1	10 mL graduated cylinder	1
Elution chamber with lid	1	Thermometer -10-260º C	1
Spatula	1	30 mL beaker	1
Glass vial	2	100 mL beaker	2
50 mL Kitasato flask with hose	1	Watch glass	1
Three fingers clamp	1	Weighing device	1
Pewter bowl	1		

V. Reaction and molar relationship.



	o-Vainilline	*p*-Toluidine	$NaBH_4$	AcOH	Ac_2O	Amide
Molar mass						
Mass (g)						
Density (g/mL)						
mmol						
Chemical equiv						
Melting point	40 -42° C	43° C	400°			**127-128°**

VI. Experimental procedure.

p-Toluidine: **Toxic, it must be worked in a ventilated area. The use of gloves, safety glasses and appropriate clothing is mandatory for handling it. In case of direct contact, rinse with water for several minutes, even while using gloves.**

In a 30 mL beaker, add 0.39 g of *o*-vanillin and 0.27 g of *p*-toluidine on opposite sides of the beaker, slowly and gently mix both solids and observe what happens. The two initial reagents give rise to a bright orange product that is initially visible only where the 2 reagents come into contact; Following this observation, the reagents should be mixed vigorously with a glass rod evenly.

The low melting point of the reactants and the heat generated by the mechanical friction of both reactants will cause them to melt quickly; However, 5 minutes after vigorous stirring, a bright orange solid will be observed, which corresponds to the corresponding imine. The % yield is practically quantitative and the product is quite pure. (melting point: 102-103° C) Save some of this solid to determine its respective melting point and apply it in the final TLC.

The imine will subsequently be reduced to an amine by the action of $NaBH_4$ and its subsequent acetylation with Ac_2O.

The reduction of the imine is completed by adding 10 mL of ethanol to the beaker and also adding a magnetic stirring bar, heating this solution gently (60º C), and adding 0.07 g (1.85 mmol) of $NaBH_4$ in small portions. Slowly, the imine is partially soluble in ethanol, but the amine is practically soluble in ethanol, so after about 10 minutes after adding all the $NaBH_4$, the alcoholic solution turns beige indicating the total reduction has been completed. the imine in the respective amine, take the pH of the solution.

The next step is the chemoselective acetylation of the corresponding amine, take the reaction mixture into the hood and then, 1 mL of glacial acetic acid is added to the alcoholic solution, to neutralize the excess $NaBH_4$ (measure pH). Next, 1 mL of Ac_2O is added and the reaction is gently heated to 65-70º C for 10 min. While you heat the amine solution with acetic anhydride, place 50 mL of distilled water in a beaker to cool down it; really cold water will be needed.

Pour the reaction mixture into a 100 mL beaker. Once the reaction time is over, it is allowed to cool to room temperature and placed on the stirring grid. The amide precipitates when 40 mL of ice water is added.

The solid formed is filtered under vacuum, the mass is quantified and its % yield is determined. Perform a TLC using Hex: AcOEt (7:3) as eluent, using a little *o*-vanillin, and *p*-toluidine as initial standards as well as the intermediate imine and the final product and finally determine the melting point of the product obtained (point theoretical fusion 127-128º C).

VII. Questions.

a. Explain what is the role of water in the reaction?

b. Why is it not feasible to recrystallize the intermediate imine?

c. What is the gas that is released in the exothermic reaction?

d. Justify the change in melting points between the intermediate imine and the final secondary amine.

VIII. Bibliografic references.

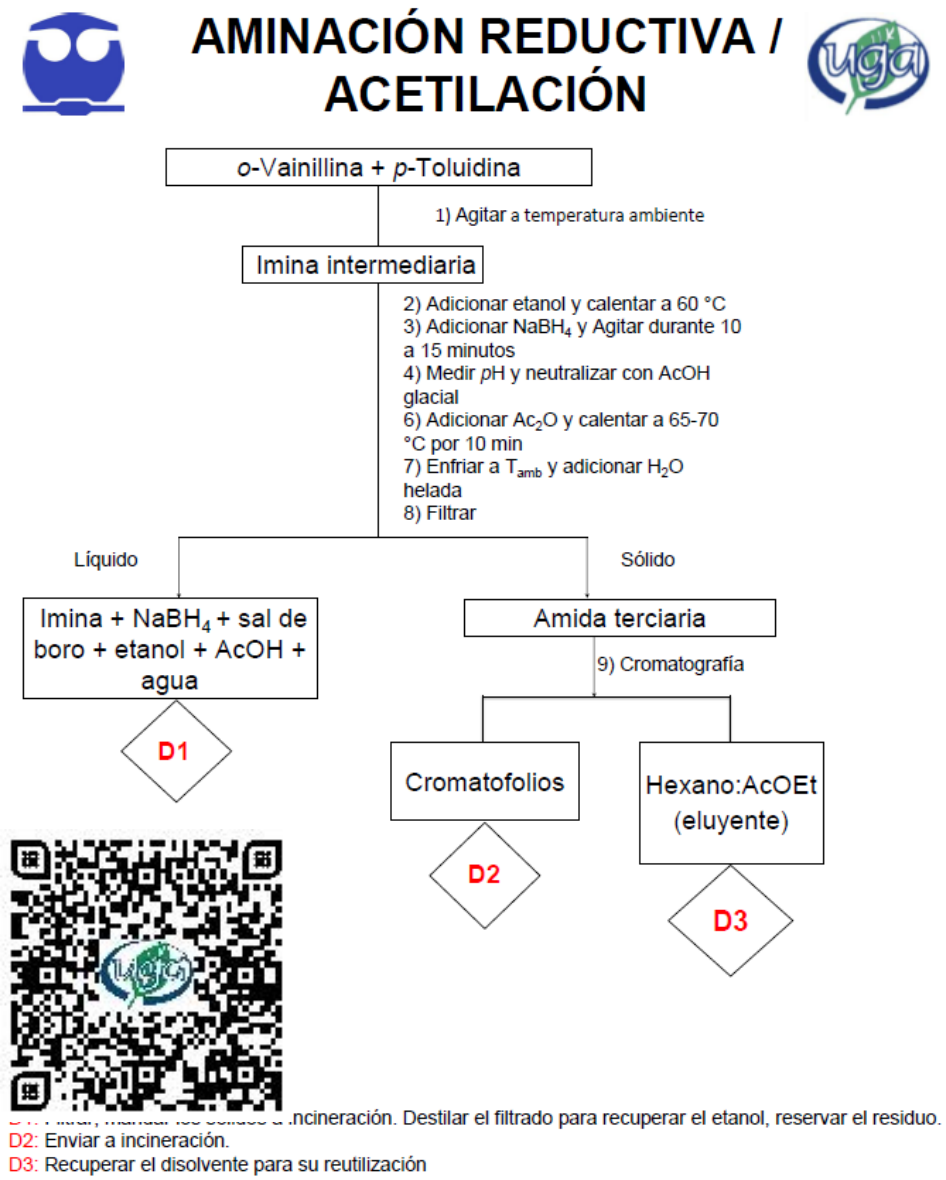
1. Touchette, K. M.; Reductive Amination: A Remarkable Experiment, for the Organic Laboratory, *Journal of Chemical Education* **2006**, 83, (6), 929-930.
2. Merle, W. C.; Ciszewski, J: T.; Bhatti, M. M.; Swanson, W. F.; Wilson, A. M.; A Simple Secondary Amine Synthesis: Reductive Amination Using Sodium Triacetoxyborohydride, *Journal of Chemical Education* **2000**, 77, (2), 270-271.
3. León-Cedeño, F.; Experiencias en la Implementación de las Técnicas de Química Verde, *Anuario Latinoamericano de Educación Química*, XXIV, **2008-2009**, 133-143.
4. Menche, D.; Arikan, F.; Li, J.; and Rudolph, Directed Reductive Amination of β-Hydroxy-ketones: Convergent Assembly of the Ritonavir/Lopinavir Core, *Organic Letters* **2007**, 9, 267-270.
5. Abdel-Magid, F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; and Shah, R. D.; Reductive Amination of Aldehydes and Ketones with Sodium Triacetoxyborohydride. Studies on Direct and Indirect Reductive Amination Procedures, *Journal of Organic Chemistry* **1996**, 61, 3849-3862.

6. Cho, T.; and. Kang, S. K.; Direct and Indirect Reductive Amination of Aldehydes and Ketones with Solid Acid-Activated Sodium Borohydride under Solvent-Free Conditions, *Tetrahedron* **2005**, 61, 5725- 5734.

IX. Appendix I. Prior Knwolegde

1. Reductive Amination Reaction.
2. Reaction mechanism for the reduction of imines.
3. Different reducing agents used in reductive amination, benefits and cons, and costs.
4. Acetylation reaction of amines
5. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

IX. Waste manegement.



Scheme 4. QR / Flowchart of reductive amination/acetylation synthesis and its waste management.

EXPERIMENT 5

AMINES III:

HINSBERG´S METHODOLOGY FOR AMINES IDENTIFICATION

I.Objetives.

a) To separate and identify mixtures of primary, secondary, and tertiary amines by Hinsberg's method.
b) To understand the basis and the reactions that form Hinsberg's method.

II. Background information.

Hinsberg's reagent, the alternative name for benzenesulfonyl chloride, is named after the German chemist Oscar Hinsberg, who used it for the first time in 1890 for the detection and distinction of primary, secondary, and tertiary amines in the presence of alkaline solutions (NaOH/KOH). This reagent is an organosulfur compound with a colorless oily liquid appearance soluble in organic solvents. This reagent carries out reactions with compounds showing O-H and N-H bonds which are natural reagents in the preparation of sulfonamides (reaction with amines) and sulfo-esters (reaction with alcohols).

Primary amines form a soluble sulfonamide salt, subsequent acidification of this salt will precipitate a primary amine. While the secondary amines will react directly to obtain an insoluble sulfonamide. Finally, tertiary amines will not react with Hinsberg's reagent and will remain insoluble. However, after acidification, the tertiary amines will form soluble ammonium salts.

III. Reagents.

Reagents	Amount	Reagents	Amount
Aniline	0.5 mL	Triethylamine	0.5 mL
N-methyl aniline	0.5 mL	Benzenesulfonyl Chloride	4 mL
N,N-diethyl aniline	0.5 mL	10% HCl solution	As needed
Ethylendiamine	0.5 mL	5% NaOH solution	40 mL

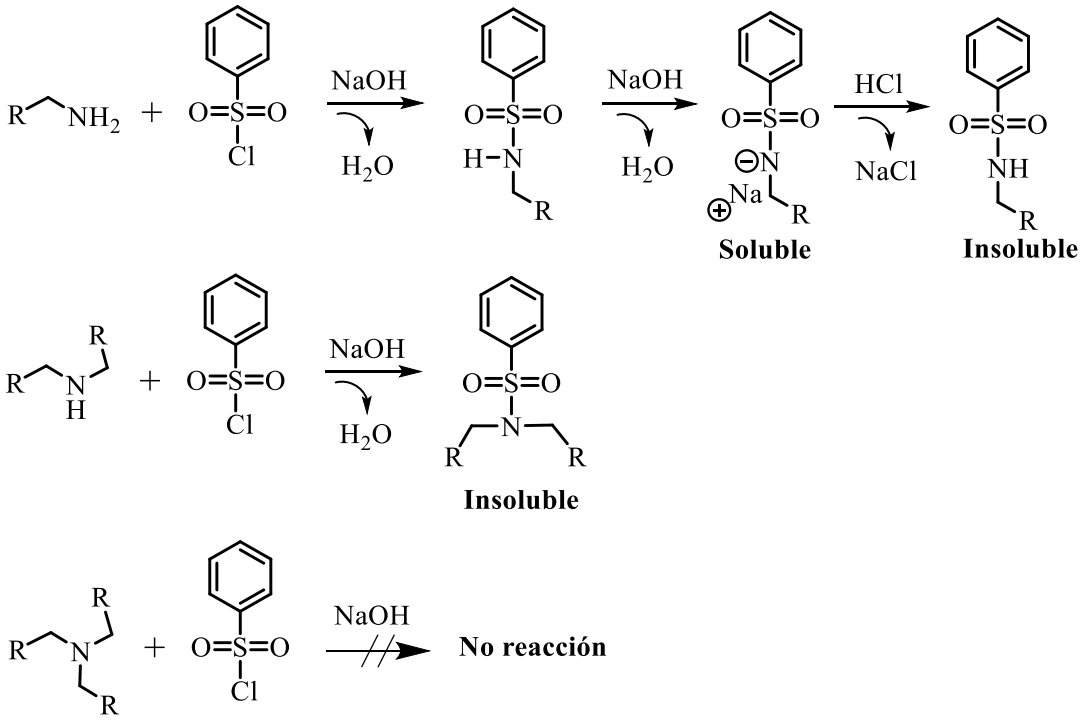
IV. Equipment

Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Glass stirrer	1	Three-finger clamp w/clamp holder	1
Büchner funnel with extension tube	1	10 mL graduated cylinder	1
Separating funnel 50 mL w/ stopper	1	400 mL glass beaker	1
Rack	1	Cork stopper for the test tube	1
Kitasato flask with hose	1	Test tubes	20
Test tube clamp	1	Watch glass	1

V. Reaction.



VI. Experimental procedure.

N,N-diethylaniline / N-methylaniline: **Must be worked in a ventilated area. The use of gloves, safety glasses and appropriate clothing is recommended for handling it. In case of direct contact, rinse with water for several minutes, even while using gloves.**

In a test tube place 0.3 g (approximately 6 drops) of the amine or a mixture of them. Add 5 mL of 5% sodium hydroxide and 0.5 mL (approximately 8 drops of benzenesulfonyl chloride). Cap the tube with a cork stopper and shake vigorously. Uncap the tube and heat it in a water bath for 5 to 10 minutes. Cool under running water, allow to stand and observe. If other phase(s), solid(s) or liquid(s), appear and remain after dilution with 10 mL of water, then separate them from the aqueous phase, by filtration or extraction as appropriate. Acidify the aqueous phase with 10% HCl up to pH=3, if a precipitate or other phase appears, this will indicate the presence of a primary amine.

Mix the phases other than the aqueous phase and add 10% HCl up to pH=3, (measure with pH paper). If there is no dissolution, it indicates secondary amine, if the dissolution is total, it indicates the presence of tertiary amine. If the dissolution is partial, this indicates the presence of both types of amines. Verify the presence of tertiary amines separating the secondary amine that was not dissolved and alkalinizing the soluble portion in the acid-aqueous phase with 10% NaOH. The appearance of another different phase from the aqueous one will confirm the presence of tertiary amine.

* The Hinsberg's test fails for some amines containing - OH, - NO2, and – COOH groups, as they behave as primary amines, although they are not.

VII. Questions.

1. How does a primary amine behave when treated with Hinsberg's reagent?
2. What is the behavior of a secondary amine when treated with Hinsberg's reagent?
3. How does a tertiary amine behave with Hinsberg's reagent?
4. Investigate how it is possible to separate a mixture of primary, secondary, and tertiary amines quantitatively by applying this method.
5. Investigate the method of hydrolysis of sulfonamides, with the aim of recovering the corresponding amines.

VII. Bibliografic references.

1. Ávila, G.; García, C. *et al* Química Orgánica. Experimentos con un Enfoque Carey F. A.; Giuliano R. M. *Química Orgánica* **2014**, Editorial McGraw Hill, 9na Edición, México.
2. Pavia Donald L. *Introduction to Organic Laboratory Techniques: A Microscale Approach* **2006**, Editorial Cengage Learning, 4ta Edición, Estados Unidos de Norteamérica.
3. Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry* **1996**, Editorial Prentice Hall, UNAM,
4. Mayo, D. W.; Pike, R. M; Trumper, P. K. *Microscale Organic Laboratory* **1994**, 3era Edición, Editorial John Wiley & Sons Inc. Estados Unidos de Norteamérica.
5. Shriner R.L., Fuson R.C. & Curtin D.Y. *Identificación Sistemática de Compuestos Orgánicos*.**1966**, Editorial Limusa Wiley, 1er Edicion, México.

   Streiwieser, Andrew Introduction to Organic Chemistry **1998**, Editorial Prentice Hall, 4ta Edición, Estados Unidos de Norteamérica.

VIII. Appendix I. Prior knowledge

1. Chemical properties of primary, secondary, and tertiary amines.
2. Behavior of primary and secondary amines when treated with chlorides of carboxylic acids and chlorides of sulfonic acids.
3. Behavior of tertiary amines when treated with Hinsberg's reagent.
4. Solubility behavior of sulfonamides in acidic and basic aqueous solutions.
5. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

IX. Appendix II. Preparation or reagents

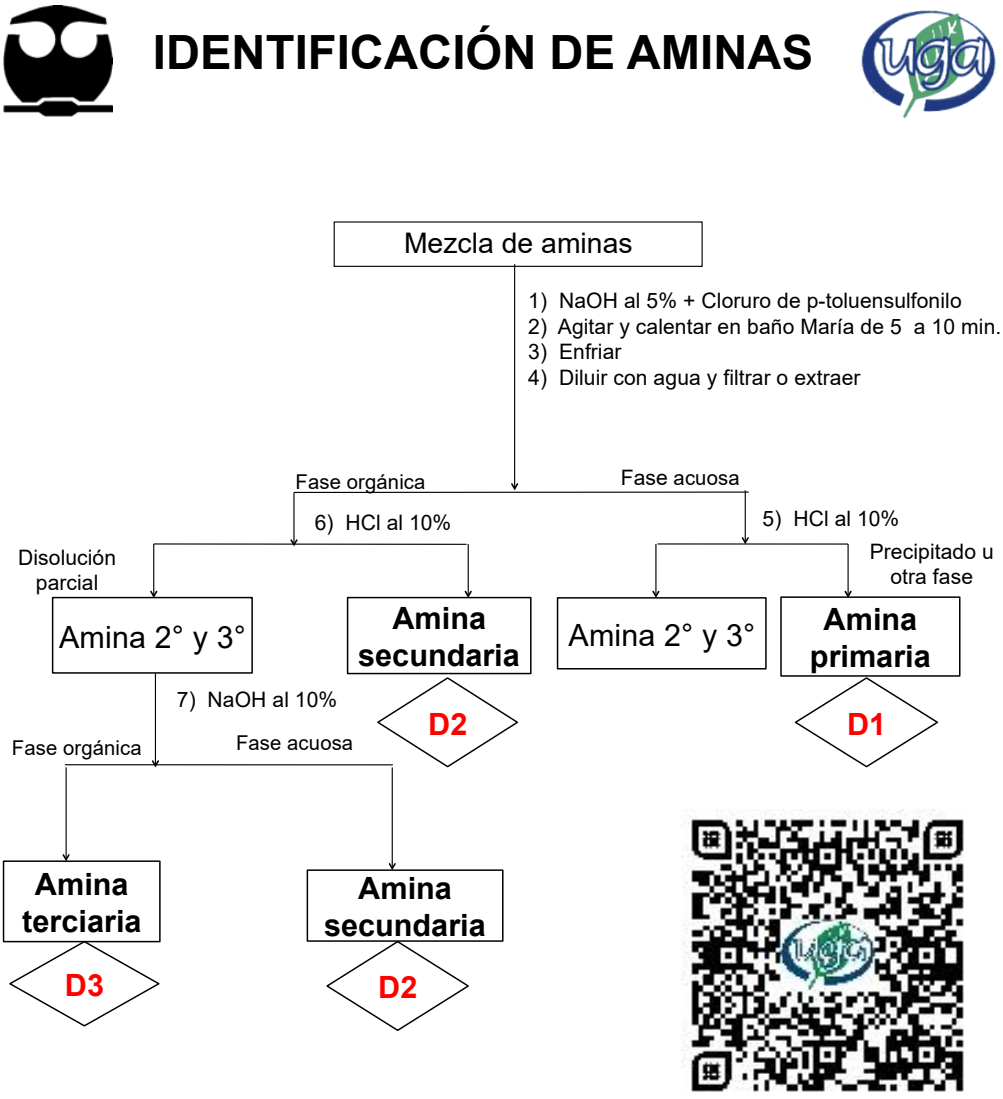
10% HCl solution (1 L)

Measure with a graduated cylinder 100 mL of concentrated hydrochloric acid (HCl) and add it slowly into a 1000 mL volumetric flask containing 880 mL of distilled water, finally add distilled water until it reaches the gauged mark, the volumetric flask should be in an ice bath, shake gently until homogenized, proceed to pour into the container where it will be stored. Important: DO NOT invert the order of addition, use gown, gloves, and safety glasses. CAUTION: The solution releases heat.

5% NaOH solution (1L)

Weigh 50 g of sodium hydroxide (NaOH) and pour it into a 1000 mL volumetric flask containing 500 mL of distilled water in an ice bath, gently shake the solution, and slowly fill the flask to a final volume of 1000 mL (1L). CAUTION: The solution releases heat.

X. Waste management.



D1, D2 y D3: Medir pH, neutralizar, adsorber con celita durante 15 minutos, filtrar y desechar.

Scheme 5. QR / Flowchart of Hinsberg´s amine identification and its waste management.

EXPERIMENT 6A

ORGANIC SULFUR COMPOUNDS I

SYNTHESIS OF SULFANYLAMIDE I

I. Objectives.

a) To illustrate a chlorosulfonation reaction on an aromatic ring.
b) To carry out the preparation of a sulfonyl chloride intermediate derived from acetanilide.
c) To perform a nucleophilic substitution on sulfonic acid chloride.

II. Background information.

Sulfur is located in the second period of the periodic table of elements and belongs to the oxygen family, that is why virtually any organic functional group that shows oxygen, there is also its counterpart with the sulfur atom, such is the case of thiols, thioethers, thioketones. In addition, there are other functional groups very unstable for the oxygen atom (tricoodinated oxygen), for instance: sulfoxides, sulfinyl imines, sulfonium ylides, and finally other functional groups with a higher degree of oxidation for the sulfur atom such as sulfones and sulfamides.

Normally sulfur chemistry is linked to bad odors, however, many sulfur compounds lack an unpleasant aroma, on the contrary, they show pleasant aromas such as the aroma of grapefruit (thioterpineol) or the sweetener saccharin.

III. Reagents.

Reacgent	**Amount**	**Reagent**	**Amount**
Acetanilide	1.0 g	Chlorosulfonic acid	3.5 mL
Ammonium hydroxide	7 mL	33% NaOH dissolution	15 mL

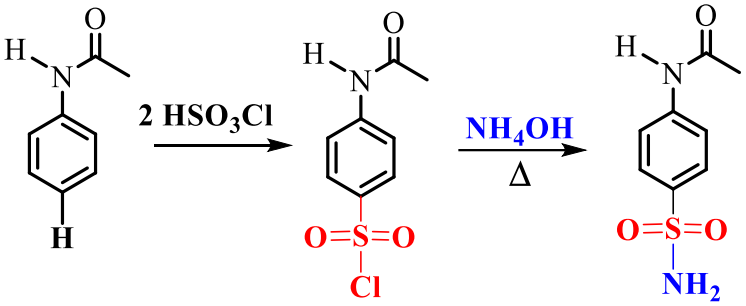
IV. Equipment.

Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team.

Glass stirrer	1	Three fingers clamp with holder	1
Electric water bath	1	10 mL gratuated pìpelte	1
Glass funnel	1	10 mL gratuated cylinder	1
Büchner funnel with extensión	1	Pewter bowl	1
Spatula	1	Plastic container for ice bath	1
50 mL Erlenmeyer flask	2	50 mL glass beaker	1
125 mL Erlenmeyer flask	1	150 mL glass beaker	1
125 mL Kitasato flask with tubing	1	400 mL glass beaker	1
Weighing vessel	1	Watch glass	1
Mono-filled stopper for 50 mL flask w/ release tube and trap hose			1

V. Reaction and molar relationship.



	Acetanilide	Chlorosulfonic acid	*N*-acetyl sulfanyl chloride
Molar weight (g/mol)			
Mass (g)			
Density (g/mL)			
mmol			
Chemical equiv			
Physical properties			

VI. Experimental procedure.

Chlorosulfonic acid: **It is a very corrosive compound, pH<1. Using gloves, safety glasses and lab coat is mandatory. It can cause severe burns to the skin and eyes. It reacts violently to water. In case of contact with the substance, remove the gloves and contaminated clothing and wash off with plenty of water for 3 – 5 minutes, then rinse the area with a $NaHCO_3$ 10% dissolution**.

To carry out the chlorosulfonation reaction, the material to be used must be completely dry and take place inside the fume hood.

In a 50 mL Erlenmeyer flask place 1.0 g of dry acetanilide, gently heat the acetanilide using the heating rack until the acetanilide melts (**Figure 1**). Once melted, stop heating, and spread the freshly melted acetanilide over the lower walls of the Erlenmeyer flask until solidifies again. Cool the Erlenmeyer flask with the freshly melted acetanilide in an ice bath and fit a gas trap with a 33% NaOH solution as shown below (**Figure 2**).

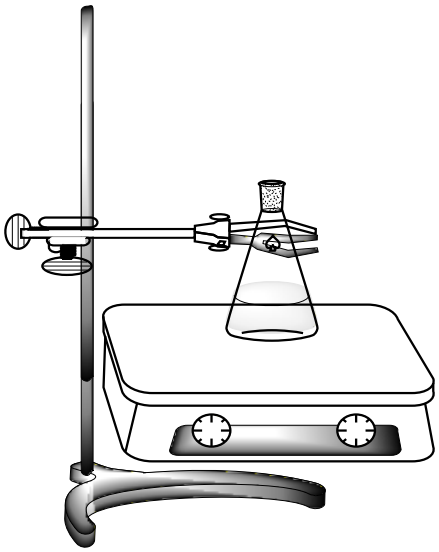


Figure 1. Melt representation of acetanilide on the walls of the Erlenmeyer flask.

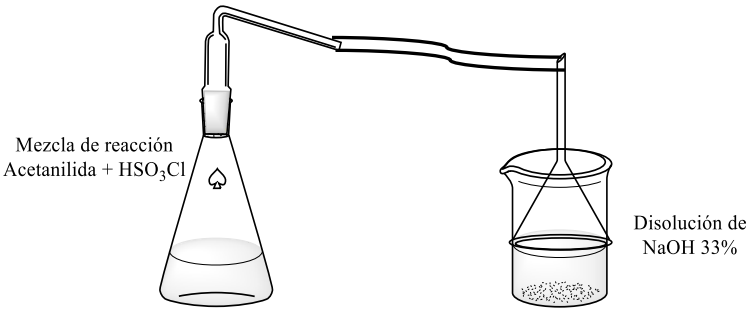


Figure 2. Gas trap (HCl) for the synthesis of N-acetyl sulfanylium chloride.

Using nitrile gloves, carefully add in a single operation 3.5 mL of chlorosulfonic acid (which should be inside the fume hood in a burette with Teflon stopcock) to the Erlenmeyer flask containing the freshly melted acetanilide (which remains inside an ice bath), once finished adding the chlorosulfonic acid, connect the gas trap and remove the flask from the ice bath to allow the reaction to start, gently shake the flask occasionally to promote the maximum reaction of the chlorosulfonic acid with the acetanilide on the flask walls, so that the HCl(g) is released at a fast rate, **if the release of the hydrogen chloride is violent, put the flask back into an ice bath**.

After a total of 10 minutes, only a few grains of acetanilide remain unreacted, at this point carefully heat the reaction flask in a water bath for a further 10-15 minutes (or until gas release ceases). Inside the hood, and with extreme care, pour the contents of the flask, drop by drop, and with continuous stirring over 30-40 grams of water ice contained in a 150 mL beaker, the reaction is very violent and a substantial amount of HCl(g) is released.

Use the glass rod to stir the reaction mixture inside the glass beaker. Wash the interior of the Erlenmeyer flask with ice water to remove the excess of chlorosulfonic acid and remaining acetanilide. It continues shaking with the glass rod until obtaining a suspension of a granular white solid of *N*-acetylsulfanyl chloride. Separate the obtained solid by vacuum filtration and wash it with cold water until the wash water shows a pH value of pH=5-6. Handle the wash water carefully as it contains a concentrated mixture of HCl-H_2SO_4.

Transfer the freshly filtered *N*-acetylsulfanyl chloride solid to a 125 mL Erlenmeyer flask, then add 17 mL of freshly prepared NH_4OH solution (7 mL of concentrated NH_4OH and 10 mL of distilled water).

Gently heat this solution over the heating plate by placing a short-stemmed glass funnel inside the neck of the Erlenmeyer flask, stirring this reaction mixture for about 5-10 minutes, taking care that the solution does not dry out completely.

Once the heating time is finished, remove the heating, and allow it to reach room temperature, later it cools this dissolution inside a bath of ice to favor the maximum precipitation of the solid, immediately filters to the vacuum, and washes the solid with cold water until the wash water shows pH=7.

Dry the solid obtained and save it for the next session (End of the part A).

VII. Questions.

a) What product would you expect if instead of acetanilide, aniline was used? Explain on scientific grounds.
b) Draw, develop, and explain the reactions that occur between chlorosulfonic acid and water.
c) What reaction takes place between *N*-acetylsulfanyl chloride and NH_4OH?

VIII. Bibliografic referenses.

1) Ávila, G.; García, C. *et al Química Orgánica. Experimentos con un Enfoque Ecológico* **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
2) Pavia Donald L., I*ntroduction to Organic Laboratory Techniques: A Microscale Approach* **2006**, Cengage Learning Brooks/Cole Laboratory Series, 4ta. Edición, Estados Unidos de Norteamérica.
3) Vogel, A. I., *Vogel's Textbook of Practical Organic Chemistry* **1996**, Prentice Hall, 5ta. Edición, Estados Unidos de Norteamérica.
4) Williamson Kenneth, *Macro and Microscale Organic Experiments* **2010**, Cengage Learning Brooks/Cole, 6ta Edición, Estados Unidos de Norteamérica.
5) Brewster R.Q., Vanderwerf C.A., McEwen W.E*., Curso Práctico de Química Orgánica* **1970**, Editorial Alhambra, 2da Edición, México.
6) Bruice Paula Yurkanis, *Química Orgánica* **2008**, Pearson-Prentice Hall, 5ta Edición, México.
7) Carey Francis A. *Química Orgánica* **2014**, McGraw-Hill, 9ena Edición, México.
8) Wade, L. G., JR., *Química Orgánica* **2014**, Pearson- Prentice Hall, 7ma. Edición México.

IX. Appendix I Prior knowlegde.

a) Reaction mechanism of the Chlorosulfonation reaction of aromatic compounds.
b) Behavior of aniline and acetanilide against the Chlorosulfonation reaction.
c) Main applications of aromatic chlorosulfonates.
d) Nucleophilic Substitution reactions on the chloride of the synthesized chlorosulfonil acid.
e) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

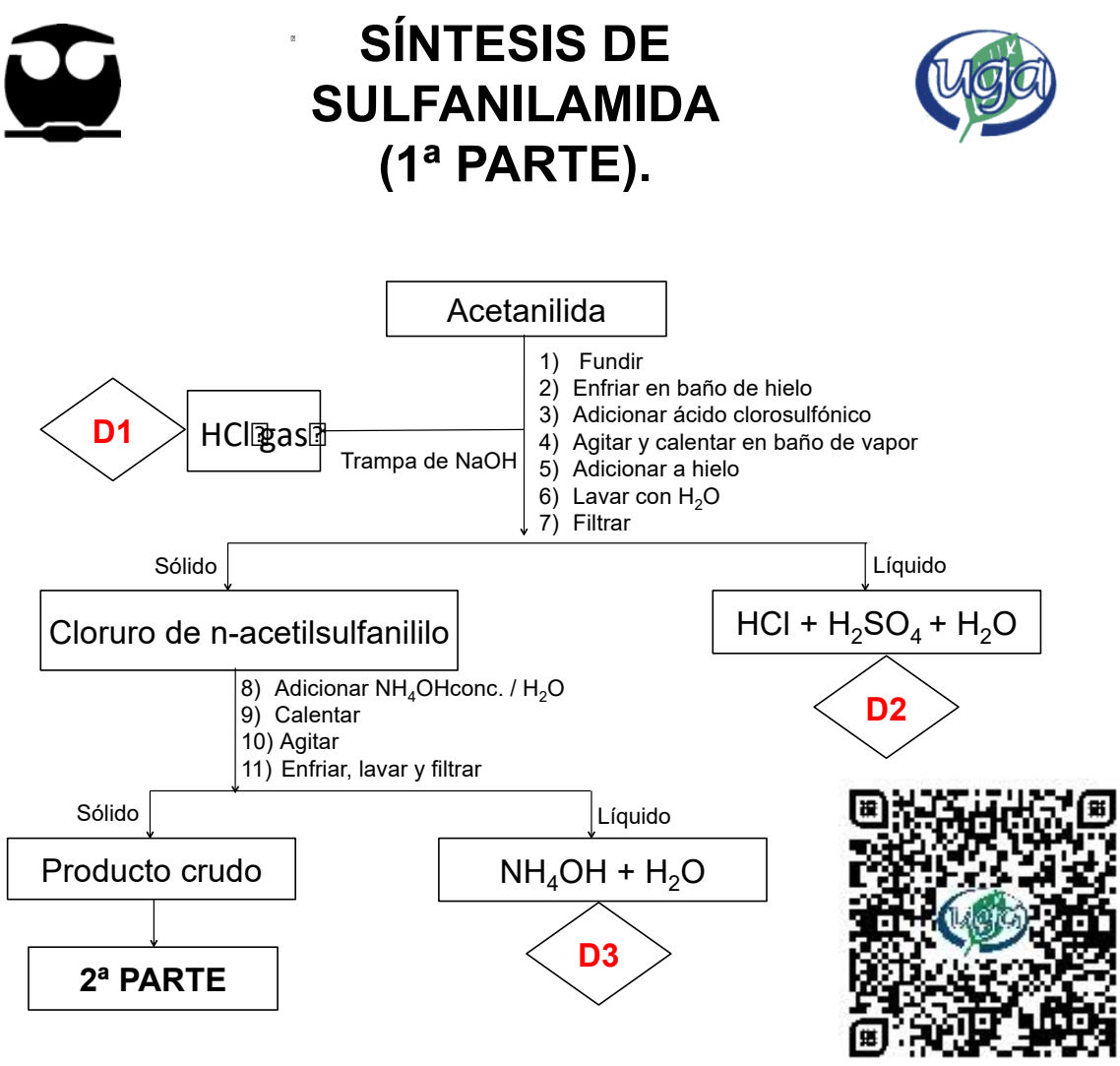
XI. Appendix II

Reagent preparation.

33% NaOH solution

Weigh 330 g of sodium hydroxide (NaOH) and pour into a 1000 mL volumetric flask containing 500 mL of distilled water and placed in an ice bath, shake the solution gently, slowly fill the flask to a final volume of 1000 mL (1L). The solution releases heat, prepare it in an ice bath.

XII. Waste management.



D1 y D2: Verificar el pH, neutralizar, filtrar si es necesario y desechar por el drenaje..
D3: Neutralizar con precaución y con agua-hielo, desechar con abundante agua.

Scheme 6. QR / Flowchart of sulfanylamide synthesis and its waste management.

EXPERIMENT 6B

ORGANIC SULFUR COMPOUNDS II

SYNTHESIS OF SULFANYLAMIDE II

I. Objectives.

a) To perform a hydrolysis reaction of an sulfonamide.
b) To obtain sulfayilamide, which is a product with historical pharmacological activity.

II. Background information.

Sulfanilamide is an antibiotic drug, which was widely used and sprayed on the wounds of soldiers during World War II by the Allies, which drastically reduced mortality rates due to infections compared to earlier wars such as World War I. Current antibiotics have relegated sulfanilamide to being a drug used only for vaginal yeast infections.

With this drug, a whole generation of antibiotics colloquially called sulfas was initiated and developed. Approximately 3% of the world's population is allergic to sulfas. Currently, sulfonamides are present in several drugs such as diabetes mellitus drugs, anticonvulsants, diuretics, highly selective analgesics, and some antibiotics such as sulfamethoxazole.

III. Reagents.

Reagents	Amount
15% Hydrochloric acid	25 mL
Sodium bicarbonate	As needed

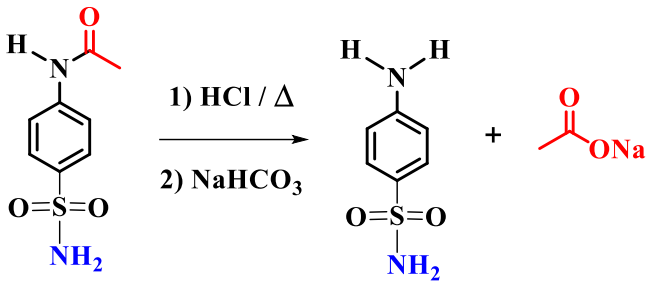
IV. Equipment.

Analytical balance	Hot plate magnetic stirrer
Melting point apparatus	UV light lamp

Glasswere for each team.

Glass stirrer	1	125 Kitasato flask with hose	1
Magnetic stirring bar ½´	1	Weithing device	1
Elution chamber with lid	1	Three finger clamp	1
Glass funnel	1	5 mL graduated pipette	1
Plastic Büchner funnel	1	10 mL graduated cylinder	1
Spatula	1	Pewter bowl	1
Glass vial	1	50 mL beaker	1
25 mL Erlenmeyer flask	2	Glass watch	1
125 mL Erlenmeyer flask	1		

V. Reaction and molar relationship.



	N-acetyl sulfanyl chloride	HCl 15%	Sulfanylamide
Molar mass (g/mol)			
Mass (g)			
Density (g/mL)			
mmol			
Chemical equivalents			
Physical propieties			

VI. Experimental procedure.

Pour the full dry product previously synthesized into an 125 mL Erlenmeyer flask provided with a magnetic stirring bar and add slowly 25 mL of a solution of 15% HCl, places this reaction to boiling on a heating plate with magnetic agitation during a lapse of 30 minutes, verifying continuously that the reaction does not dry up, in case of being necessary it adds more water to maintain constant a volume of 25 mL.

Finished this time of reaction, it withdraws the flask from the heating and allows it to warm up for a few minutes, immediately it cools the flask under the jet of the water faucet, if turbidity is observed in the interior of the flask when lowering the temperature, it is due to return to the heating in the plate for about 5 minutes more. If such turbidity is not shown, it carefully adds solid $NaHCO_3$ and with permanent agitation until obtaining a pH=8. When the requested pH has been reached, cool the reaction mixture inside an ice bath to favor the precipitation of the solid, if necessary, induce precipitation by scraping the walls of the vessel and vacuum filter the formed solid. Weigh the formed solid and determine its % crude yield.

Recrystallize the filtered solid from water as the ideal solvent, dry the solid well, quantify the final recrystallized mass, determine its melting point, and perform a thin layer chromatography (TLC) using hexane: ethyl acetate (1:1) as eluent.

VII. Questions.

a) What reaction takes place on “diamide” when it is boiled in the presence of aqueous HCl?
b) What is the basis for the selective hydrolysis of the carboxylic amide on the sulfamide?
c) Why is it necessary to add $NaHCO_3$?
d) Why is it so important that the final solution has a *pH*=7? What would happen if the solution were left at *pH*=6?

VIII. Bibliografic references.

a) Ávila, G.; García, C. *et al* Química Orgánica. Experimentos con un Enfoque Ecológico **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
b) Pavia Donald L., Introduction to Organic Laboratory Techniques: A Microscale Approach **2006**, Cengage Learning Brooks/Cole Laboratory Series, 4ta. Edición, Estados Unidos de Norteamérica.
c) Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry **1996**, Prentice Hall, 5ta. Edición, Estados Unidos de Norteamérica.
d) Williamson Kenneth, Macro and Microscale Organic Experiments **2010**, Cengage Learning Brooks/Cole, 6ta Edición, Estados Unidos de Norteamérica.
e) Brewster R.Q., Vanderwerf C.A., McEwen W.E, Curso Práctico de Química Orgánica **1970**, Editorial Alhambra, 2da Edición, México.
f) Carey Francis A. Química Orgánica **2014**, McGraw-Hill, 9ena Edición, México.
g) Wade, L. G., JR., Química Orgánica **2014**, Pearson- Prentice Hall, 7ma. Edición México.

IX. Appendix I. Prior knowledge.

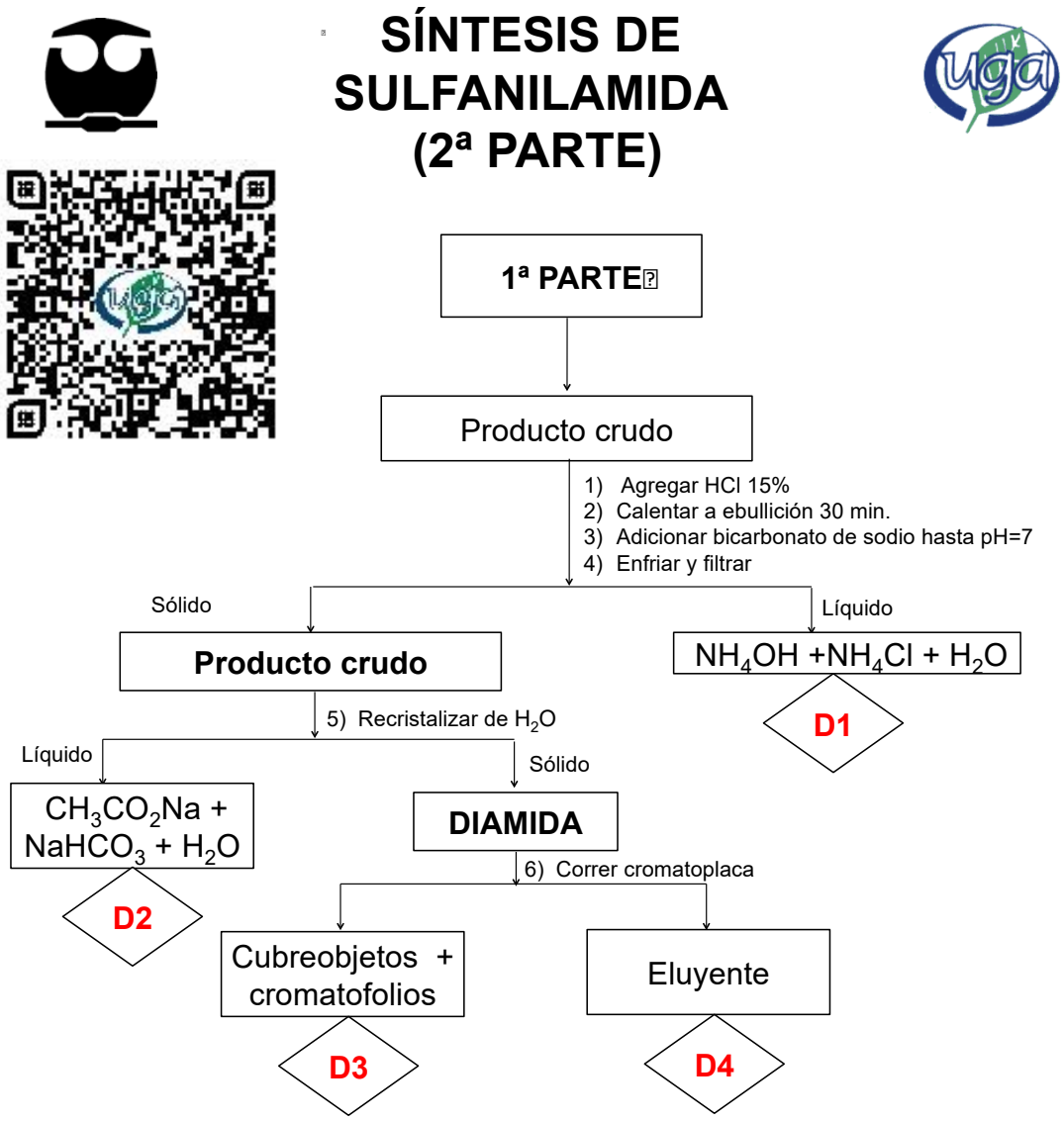
a) Nucleophilic substitution reactions on chlorosulfonic acids.
b) Hydrolysis of amides from carboxylic acids.
c) Hydrolysis of sulfamides (amides of sulfonic acids).
d) General application of sulfas in general.
e) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Appendix II. Preparation of reagents.

15% HCl solution (1L)

Measure with a graduated cylinder 150 mL of concentrated hydrochloric acid (HCl) and add it slowly into a 1000 mL volumetric flask containing 830 mL of distilled water, then add distilled water, the volumetric flask should be in an ice bath, shake gently until homogenized, proceed to pour into the container where it will be stored. Important: DO NOT invert the order of addition, use gown, gloves, and safety glasses. CAUTION: The solution gives off heat.

XI. Waste management.



D1: Neutralizar con precaución con hielo agua y en la campana. Filtrar los sólidos y enviar a incineración.
D2: Solución ácida. Se filtra y desecha neutra o puede usarse para neutralizar.
D3: Se mandan a incineración.
D4: Recuperar el disolvente para su reutilización.

Scheme 7. QR / Flowchart of sulfanylamide hydrolisis and its waste management.

EXPERIMENT 7

CARBONYLS I

SYNTHESIS OF IMINES

I. Objetives.

a) To ilustrate a carbon-nitrogen (iminium) doble bond formation reaction to produce an imine.
b) To obtain *N*- ((*E*)-phenylmethylene) aniline, *N*-benzylidenaniline.

II. Background information.

Imines are compounds that contain a C=N double bond, which can contain substituents on both carbon and nitrogen, which can be identical or different. Imines result from typical condensation reaction between a carbonyl compound and NH3 or a primary amine, the resulting compounds with ammonia are not thermodynamically stable, while those formed with primary amines are stable, and highly stable if the substituent on the nitrogen is an aromatic ring, and they are usually called *Schiff Bases*.

Although the imine synthesis method is usually reversible and requires long reaction times, acid catalysis and dehydrating agents or even azeotropic removal of water are usually used to promote the completion of the synthesis. The generic names given to imines are: aldoimines and ketoimines depending on whether they come from condensation with aldehyde or ketones respectively.

III. Reagents.

Benzaldehyde	0.45 mL	Ethanol	6 mL
Aniline	0.4 mL	Hexane / Ethyl acetate	5 mL

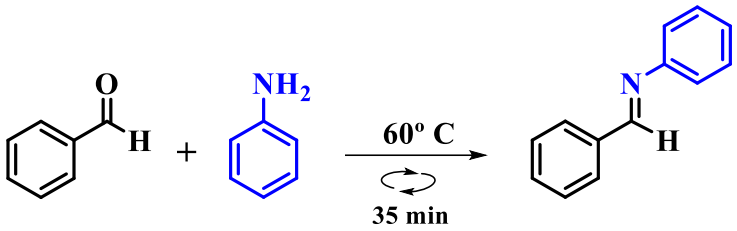
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Magnetic stir bar	1	Microscale three fingers clamp	1
Elution chamber with lid	1	10 mL graduated cylinder	1
Spatula	1	Pewter bowl	1
Glass vial	1	Air condenser 14/23	1
Plastic Büchner funnel	1	20 mL beaker	1
10 mL round flat-bottom flask	1	50 mL beaker	1
25 mL Erlenmeyer flask	2	Termometer from -10º to 200º C	1
50 mL Kitasato flask with hose	1	Watch glass	1
Three fingers clamp	1		

V. Reaction and molar relationship.



	Benzaldehyde	Aniline	*N*-Benzylidenaniline
Molar mass (g/mol)			
Mass (g)			
Volume (mL)			
Density (g/mL)			
mmol			
Chemical equivalents			
Physical propieties			

VI. Experimental procedure.

Before to carry out the reaction, prepare and mantain a water bath at 60º C into a 50 mL beaker; on the other hand cool approximately 8-10 mL of ethanol inside an ice-NaCl bath, which must be really cold to be used later. In a 10 mL round flat-bottom flask fitted with magnetic stirring bar add 0.45 mL of benzaldehyde, then add 0.4 mL of freshly distilled aniline dropwise (turbidity forms inside the reaction flask). Inmediately place the reaction flask into the water bath at a constant temperatura of 60º C and place an air condenser and leave the reaction at that temperature for 35 minutes.

Once the reaction time is over, cool the reaction to room temperatura, then pour the reaction mixture into a 20 mL beaker containing 3 mL of cold ethanol, rinse the reaction flask with 1 or 2 mL of cold ethanol, and place the beaker in the ice bath for 5-10 minutes. If after this period there has been no precipitate, induc crystalization by scraping the walls of the beaker. Filter the solid under vacuum on the Büchner funnel, perform 2 washes with 1 mL of cold ethanol each. Dry the product, quantify the mass obtained so that you can determine the % reaction yield, determine the melting point and perform a TLC, using diluted standars of benzaldehyde and aniline, with 8:2 mixture of eluents (Hex: EtOAc).

VII. Questions.

1) How does pH affect your reaction? What pH range is optimal for this reaction?
2) What product would be obtained if pyrrolidine were used instead of aniline?
3) Explain whether aliphatic aldehydes can form imines by this methodology?
4) Why is the product not recrystallized?

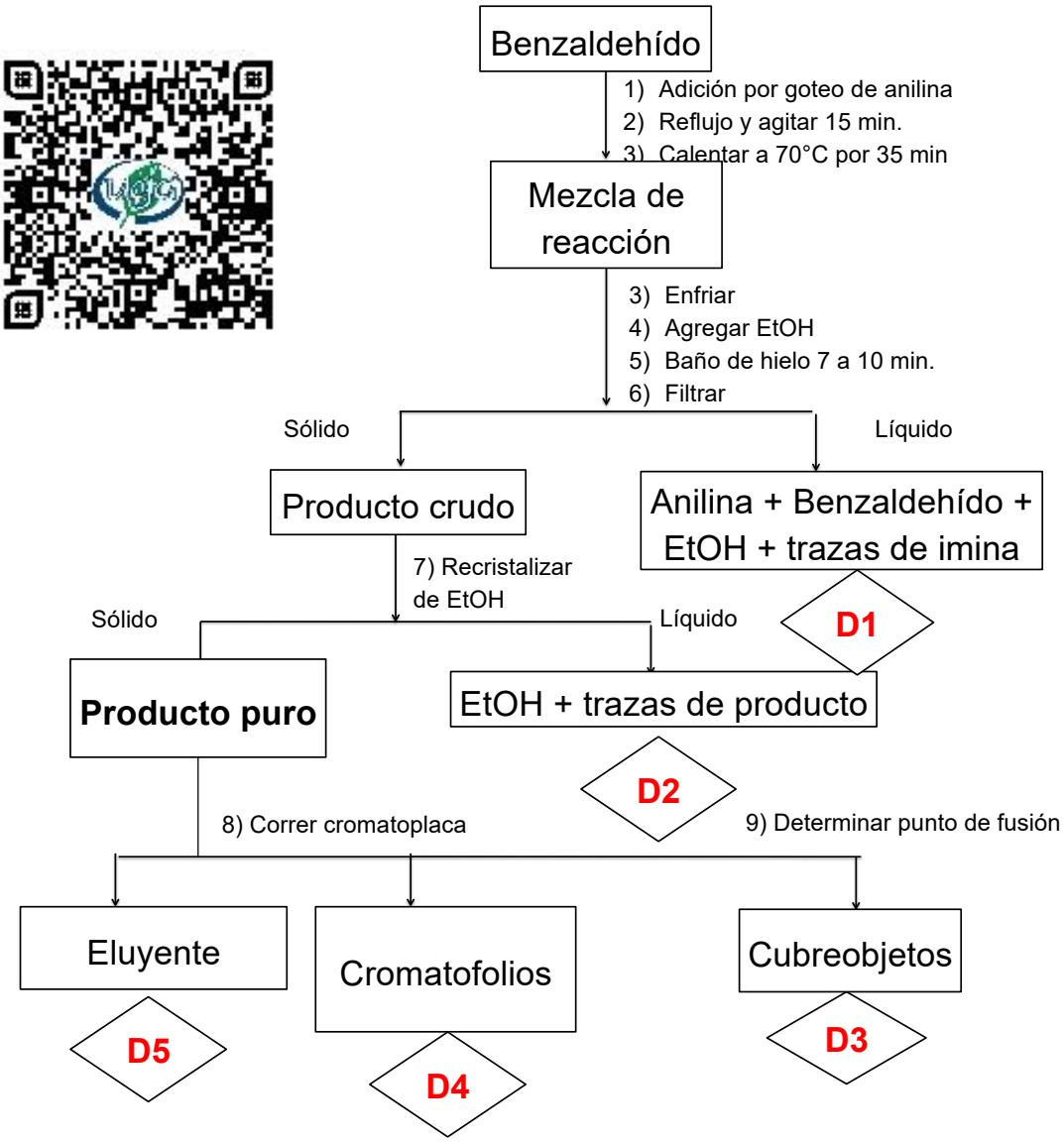
VIII. Bibliographic references.

1. Carey F. A.; Giuliano R. M. Química Orgánica **2014**, Editorial McGraw Hill, 9na Edición, México.
2. Kenneth, W. Macro and Microscale Organic Experiments **2010**, Editorial Cengage Learning, 6ta Edición, Estados Unidos de Norteamérica.
3. Ávila, G.; García, C. *et al* Química Orgánica. Experimentos con un Enfoque Ecológico **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
4. Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry, **1996**, Prentice Hall 5a. Edición, Estados Unidos de Norteamérica.
5. Pavia Donald L., Introduction to Organic Laboratory Techniques: A Microscale Approach, **2006**, Cengage Learning, Brooks/Cole Laboratory Series 4a. Edición, Estados Unidos de Norteamérica.

IX. Apendix I. Prior knowledge.

1) Characteristics of imines and enamines.
2) Optimum pH for imine synthesis.
3) Nucleophilic addition reaction to carbonyl group.
4) Reaction of the carbonyl grupos with primary and secondary amines.
5) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Waste management



D1 y D2: Adsorber sobre carbón activado, filtrar y neutralizar. Residuos sólidos enviar a incineración.
D3 y D4: Se empaqueta y se manda a incineración por separado.
D5: Recuperar el eluyente para su reutilización.

Scheme 8. QR/Flowchart of imine synthesis and its waste management.

EXPERIMENT 8

CARBONYLS II

ALDOL CONDENSATION

I. Objetives.

1) To understand the reaction conditions that allow aldol condensation.
2) You will perform a “crossed aldol condensation” focusing on the reaction conditions and reagent addition.
3) To illustrate a carbonyl condensation reaction.

II. Background information.

Aldehydes and ketones that show alpha hydrogens to the carbonyl group undergo aldol condensation reactions with relative ease, due to the intrinsic acidity that these hydrogens show, these aldol condensation reactions are catalyzed by strong bases and to a lesser extent by acids.

The reaction typically known as aldol condensation is actually two consecutive reactions, the first corresponds to the nucleophilic addition to a second carbonyl group, this reaction is called: aldol addition, and the product of this reaction is known β–hydroxy aldehyde or β-hydroxy ketone, this product formed can easily carry out a dehydration reaction, either thermally or catalyzed by acid or alkaline medium, the product of this second reaction (dehydration) is the final product of the aldol condensation reaction and is called: α,β-unsaturated carbonyl. The formation of this π-conjugated system is precisely the driving force of the spontaneous dehydration reaction, since the final product is thermodynamically very stable.

Specifically, when two different carbonyls are mixed, a mixture of different product is carried out; this reaction is known as cross-aldol condensation. However, when a carbonyl lacking alpha hydrogens and a carbonyl with alpha hydrogens are mixed in presence of a catalyst a directed cross-aldol condensation reaction is carried out.

III. Reagents.

Acetone	0.2 mL	Ethanol	20 mL
Benzaldehyde	0.3 mL	NaOH	0.15 g
Aqueous solution of HCl 1:1	1 mL	Hexane	4 mL
Ethyl acetate	1 mL		

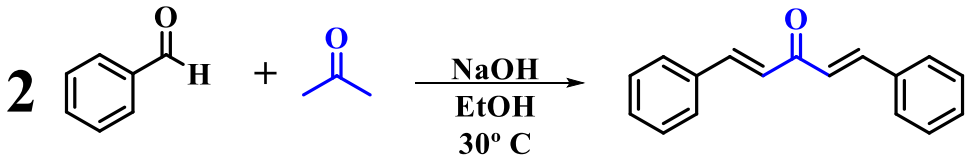
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Glass stirrer	1	Three fingers clamp	1
Magnetic stir bar	1	Microscale three fingers clamp	1
Elution chamber with lid	1	10 mL graduated cylinder	1
Glass funnel	1	Pewter bowl	1
Glass vial	1	20 mL beaker	1
Büchner funnel	1	50 mL beaker	1
Spatula	1	100 mL beaker	1
25 mL Erlenmeyer flask	2	Termometer from -10º to 350º C	1
50 mL Kitasato flask with hose	1	Watch glass	1

V. Chemical reaction and molar relationship.



	Benzaldehyde	Acetone	*E,E*-Dibenzylidenacetone
Molar mass (g/mol)			
Mass (g)			
Density (g/mL)			
mmol			
Chemical equivalents			
Physical propieties			

VI. Experimental procedure.

On a beaker (10 mL) prepare a solution of 0.15 g of NaOH in 2 mL of H_2O. Into an Erlenmeyer flask (10 mL) add 6 mL of EtOH and 0.5 mL of benzaldehyde. Add the NaOH solution to the benzaldehyde solution, the reaction mixture is left under stir and heated up at 30°C, followed by the addition of 0.2 mL of acetone dropwise. The mixture is left under the same conditions for 30 min (temperature MUST NOT increase above 30 °C).

Thereafter, the reaction is cooled down in an ice bath. The solid form is filtered and washed with cold water (until the water shows a pH = 7). The product is purified by crystallization in EtOH. If red/orange color is observed add HCl (1:1) until pH = 7. After the purification is done, weigh the product and calculate the reaction yield. Measure the melting point and perform a TLC analysis, do not forget to compare the pure product to the starting material (use hexane/EtOAc 4:1 as eluent).

VII. Questions.

1) Why is the order of addition of the reagents so important?
2) What would happen if the NaOH solution was added fisrst to the acetone instead of the benzaldehde?

3) Why only a single product was observed and not a mixture?
4) Why H_2O is lost "easily" under basic conditions during the addition process?
5) What is the main purpose of washing with H_2O until reach pH = 7 prior to crystallization?
6) Which methods were used to corroborate the authenticity of the product and its purity?
7) What is the characteristic of protons *α* to a carbonyl group, investigate their pKa value?
8) Why the final product is *α*,*β*-unsaturated compound and not the aldol?
9) Why the temperature must not be above 30° C?

VIII. Bibliographic references.

1. Ávila A. J. G. et al, Química Orgánica: Experimentos con un enfoque ecológico 2ª edición, UNAM, Dirección General de Publicaciones y Fomento Editorial, **2009**, pág. 343-350.
2. Kenneth, W. Macro and Microscale Organic Experiments **2010**, Editorial Cengage Learning, 6ta Edición, Estados Unidos de Norteamérica.
3. Pavia Donald L., Introduction to Organic Laboratory Techniques: A Microscale Approach, **2006**, Cengage Learning, Brooks/Cole Laboratory Series 4a. Edición, Estados Unidos de Norteamérica.
4. Bruice, P. Y., Química Orgánica 5ª edición, Pearson Educación, México **2008**, pág. 352-353.
5. Carey F. A.; Giuliano R. M. Química Orgánica **2014**, Editorial McGraw Hill, 9na Edición, México.
6. McMurry, J., Química Orgánica 8ª edición, Cengage Learning, México, **2012**, pág. 877-890.
7. Morrison, R. T. y Boyd, R. N., Química Orgánica 5ª edición, Addison-Wesley Iberoamericana, Boston Massachusetts, **1988**, pág. 864-871.
8. Solomons, T. W. G., Química Orgánica 2ª edición, Limusa-Wiley, México, **1999**, pág. 487-900.
9. Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry, **1996**, Prentice Hall 5a. Edición, Estados Unidos de Norteamérica.
10. Wade, L. G., JR., Química Orgánica **2014**, Pearson- Prentice Hall, 7ma. Edición México.

IX. Apendix I. Prior knowledge.

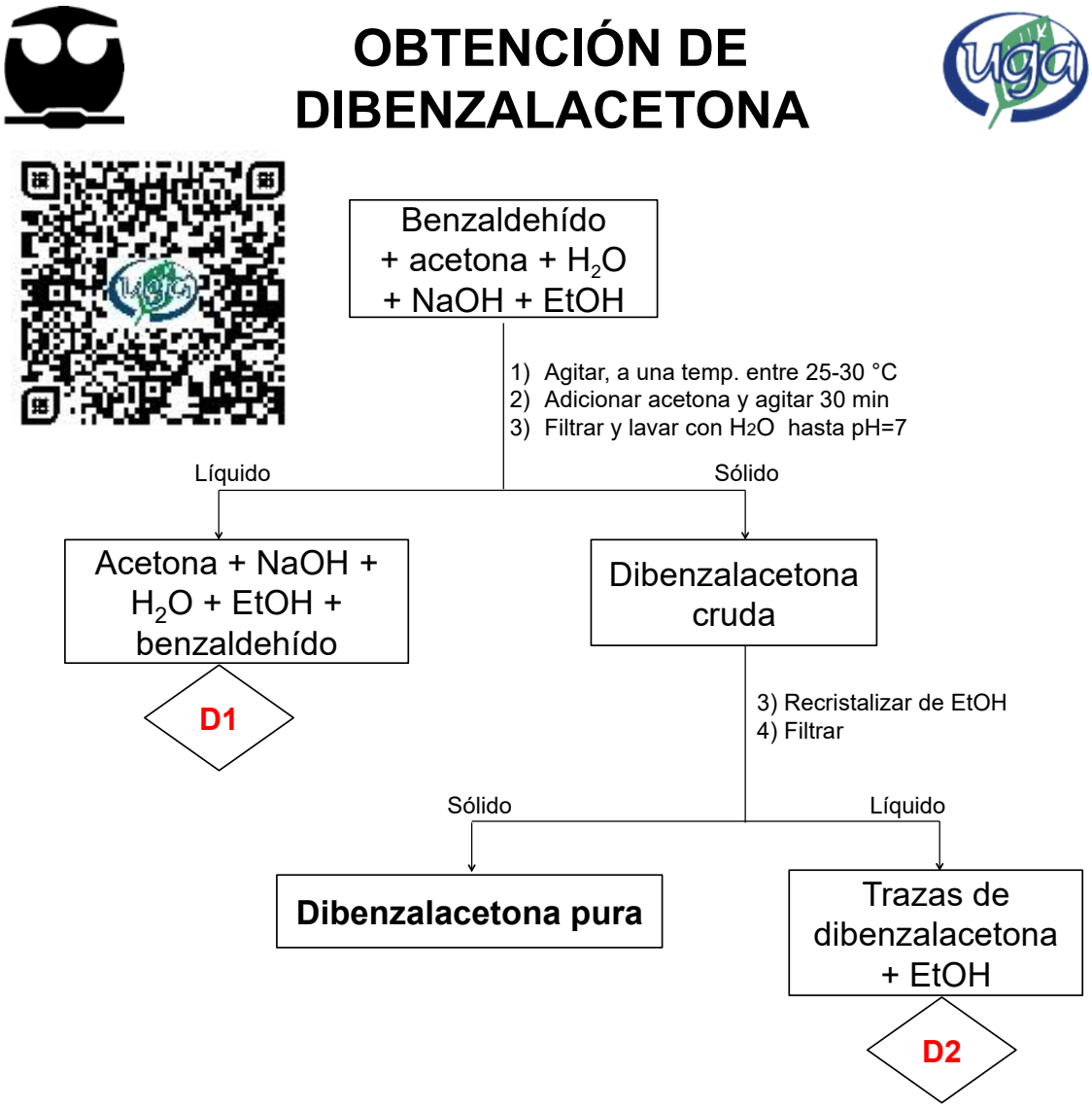
1. Nucleophilic addition reactions to the carbonyl group.
2. Aldol condensation reactions, reaction conditions and products.
3. Cross-directed and crossed aldol condensation.
4. Relevance of the products obtained through this type of reaction.
5. Importance of π delocalization in π-conjugated carbonyl systems.
6. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Apendix II. Preparation of reagents.

HCl (1:1) solution preparation

Measure 50 mL of water on a graduated cylinder and cool it down in an ice bath. Dropwise add concentrated HCl (Perform this inside the fumehood).

XI. Waste Treatment.



D1 Y D2: Neutralizar, adsorber si tiene color, filtrar y desechar. (Enviar el sólido a incineración).

Scheme 9. QR/ Flow chart of aldol condensation synthesis and its waste management.

EXPERIMENT 9

CARBONYLS III

BENZOIN CONDENSATION

I. Objectives.

1. To perform a reaction with aldehydes showing the polarity inversion of the carbonyl group after a nucleophilic addition.
2. Illustrate a carbon–carbon bond formation to produce α-hydroxyketones.
3. Obtain benzoin through a condensation reaction.

II. Background information.

Benzoin condensation is a dimerization reaction without the loss of a water molecule. This reaction has generated interest as it shows the polarity inversion of the carbonyl group, usually an electrophile, behaving as a nucleophile (carbanion stabilized by inductive effect).

The reaction must be catalyzed by a strong nucleophile such as cyanide or a *N*-hetrocyclic carbene (*NHC*) under basic conditions. This reaction occurs between aromatic aldehydes producing acyloins (α-hydroxyketones) which can be used as precursors for the generation of heterocyclic compounds.

III. Reagents.

Reagent	Amount	Reagent	Amount
Benzaldehyde	0.5 mL	NaOH	0.25 g
Thiamine hydrochloride	0.8 g	Ethanol	10 mL

IV. Equipment.

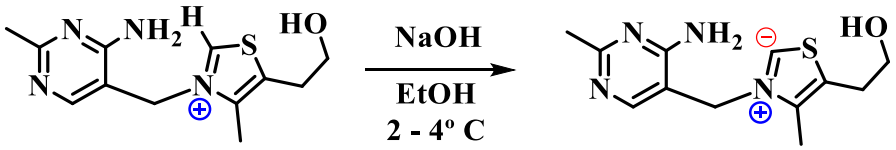
Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

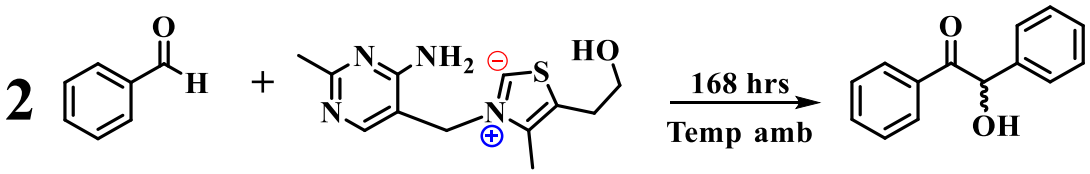
Glasswere for each team. **The student must bring a 10 mL vial for the 1st session**.

1st Session			
Spatula	1	10 mL cylinder	1
Weithing device	1	Pewter bowl	1
1 mL pippete	1	10 mL beaker	1
5 mL pippete	1		
2nd Session			
Glass stirrer	1	25 mL Erlenmeyer flask	2
Magnetic stirring bar ½´	1	50 mL Kitasato flaskwith hose	1
Elution chamber with lid	1	Three fingers clamp	1
Büchner funnel with extention	1	10 mL graduated cylinder	1
Glass funnel	1	Pewter bowl	1

Spatula	1	20 mL beaker	1
Glass vial	1	Glass watch	1

V. Chemical reaction and molar relationship.





	Benzaldehyde	Thiamine HCl	NaOH	Benzoine
Molar mass (g/mol)				
Mass (g)				
Volume (mL)				
Density (g/mL)				
mmol				
Chemical equiv				
Physical propieties				

VI. Experimental procedure.

First session.

A 10% solution of NaOH (1 mL) is added to a 20 mL beaker. Separately, in a 10 mL vial 0.18 g of Thiamine-HCl is dissolved in 1.0 mL of distilled water and 5 mL of ethanol. The vial is cooled down using an iced bath (ice + NaCl) for 5-10 min. The mixture is left under stirring and once it reaches 2-4 °C the 10% NaOH solution (previously prepared) is added dropwise over 10 min, until a pH = 10-11 is observed (check the pH when the solution has a volume of 8 mL). Thereafter, 0.5 mL of benzaldehyde is added, the reaction is mixed manually (verify that the pH is always around 10 to 11, if it is lower keep adding more NaOH). Close the vial with a proper cap and cover it with aluminum foil. Placed the vial in a dark area and leave it until the next lab session.

Second session.

Without the aluminum foil, cool down the vial in an iced bath (ice + NaCl) for 5-10 min. If you have not observed crystals, try to induce the crystallization by scratching the walls of the vial. The solid formed is isolated by suction filtration, the product is washed using cold water (3 mL) and cold ethanol (3 mL). Record the mass of the crude, the product is purified by recrystallization using ethanol/water. Isolate the product and quantify the final mass and melting point. Finally, a TLC is performed (eluent: EtOAc).

VII. Questions.

1) What is the benzoin condensation?
2) Which catalyst are you using?
3) What is the relevance of using NaOH 10%?
4) What is meant by green chemistry and its principles?
5) Would you consider that the reaction performed fulfills the principles of green chemistry? Explain.
6) Will the aliphatic aldehydes react to form acyloins? What would it be the conditions?

VIII. Bibliografic refences.

1. Carey F. A.; Giuliano R. M. Química Orgánica **2014**, Editorial McGraw Hill, 9na Edición, México.
2. Kenneth, W. Macro and Microscale Organic Experiments **2010**, Editorial Cengage Learning, 6ta Edición, Estados Unidos de Norteamérica.
3. Ávila, G.; García, C. *et al* Química Orgánica. Experimentos con un Enfoque Ecológico **2009**, Dirección General de Publicaciones y Fomento Editorial, UNAM, 2da Edición, México.
4. Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry, **1996**, Prentice Hall 5a. Edición, Estados Unidos de Norteamérica.
5. Pavia Donald L., Introduction to Organic Laboratory Techniques: A Microscale Approach, **2006**, Cengage Learning, Brooks/Cole Laboratory Series 4a. Edición, Estados Unidos de Norteamérica.
6. Wade, L. G., JR., Química Orgánica **2014**, Pearson- Prentice Hall, 7ma. Edición México.
7. Bruice Paula Yurkanis, Química Orgánica **2008**, Pearson-Prentice Hall, 5ta Edición, México.

IX. Appendix I. Prior knowledge.

a) Condensation reactions of aromatic aldehydes.
b) Benzoin condensation, reaction conditions and catalysts used.
c) Applications of benzoin condensation in organic chemistry.
d) Green chemistry definition and its principles.
e) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Appendix II. Preparation of reagents.

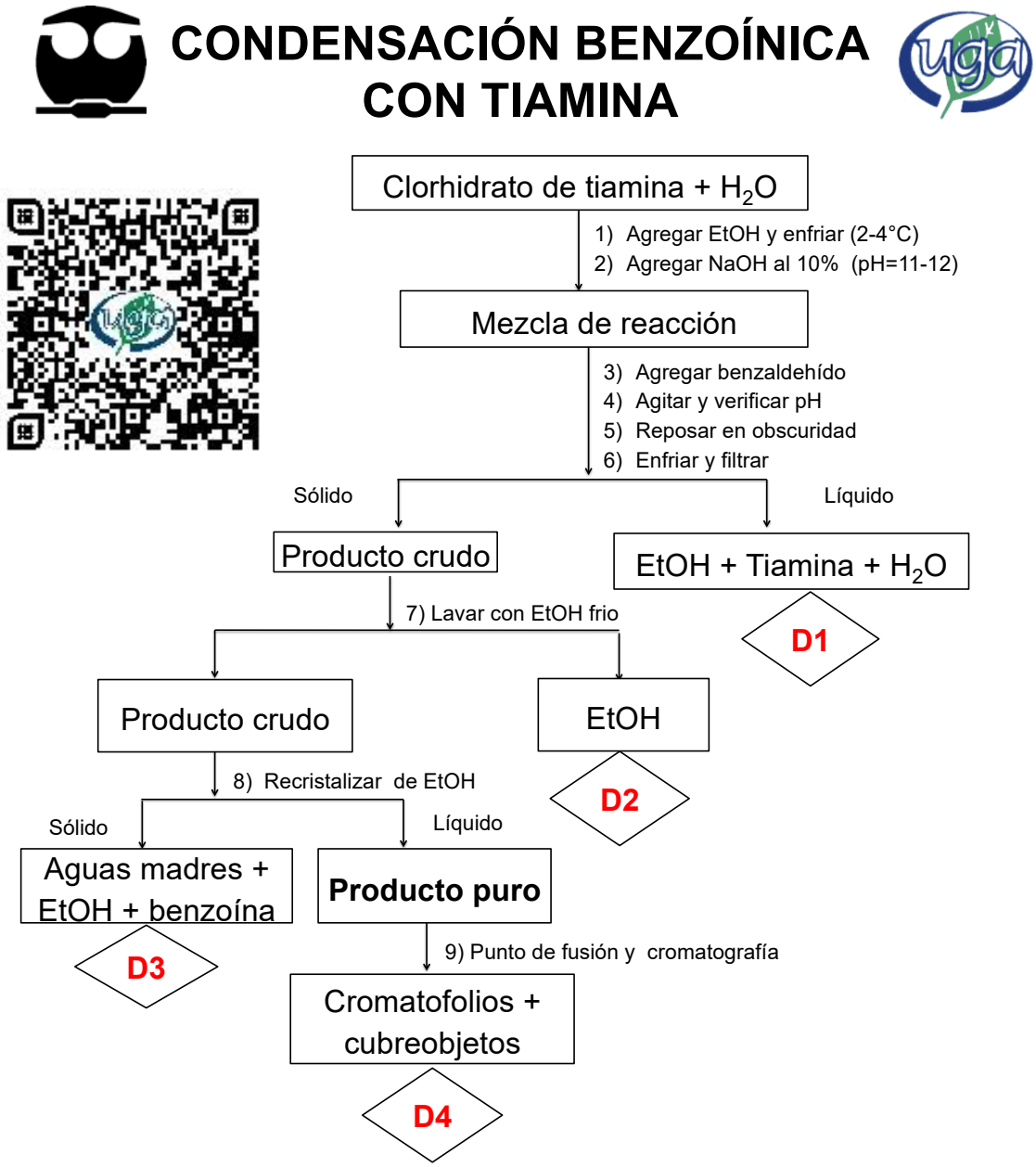
10% NaOH solution (1 L)

In a 1000 mL volumetric flask, 500 mL of distilled water is added, thereafter 100 g of NaOH is added. The solution is stirred. Slowly, add distilled water until 1000 mL mark is reached. The solution gives off heat, place the solution into an ice bath.

50% HCl solution (1L)

In a 1000 mL volumetric flask, 480 mL of distilled water is added, thereafter using a graduated cylinder 500 mL of concentrated HCl is measured and added to the 1000 mL volumetric flask. Slowly, add distilled water until 1000 mL mark is reached. The solution must be prepared into an ice bath.

XI. Waste management.



Scheme 10. QR/Flow chart of benzoin condensation synthesis and its waste management.

EXPERIMENT 10

CARBONYLS IV

SYNTHESIS OF OXIMES

I. Objetives.

a) To illustrate a reaction to form an oxime R′RC=N–OH.
b) To synthesize acetophenone oxime.

II. Backgrounf information.

Oximes are compounds that can be obtained through a condensation reaction of hydroxylamine and aldehyde (aldoxime) or a ketone (ketoxime). Oximes show two different stereoisomers; however, the trans isomer is the more thermodynamically stable.

Oximes have generated interest due to their versatile structures and application in the medical and biological fields. Moreover, oximes show two nucleophilic atoms, nitrogen, and oxygen, whereas carbon is considered electrophilic. Oximes are more stable than imines towards hydrolysis, however, both compounds can be reduced to produce amines.

Oximes IR spectra shows 3 characteristic absorption bands: 3600 cm^{-1} (O-H), 1665 cm^{-1} (C=N) y 945 cm^{-1} (N-O).

III. Reagents.

Acetophenone	0.6 mL	Ethanol	9 mL
Hydroxylamine hydrochloride	0.43 g	Hexane	9 mL
Sodium acetate	0.63 g	Ethyl acetate	1 mL

IV. Equipment.

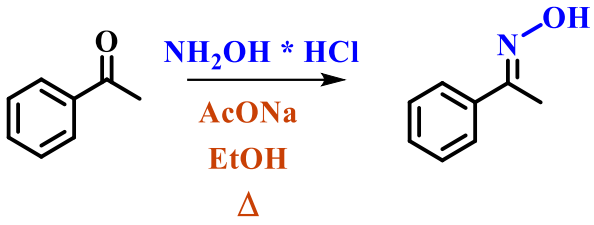
Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team.

Glass stirrer	1	Weitghing device	1
Magnetic stirring bar 1/4´´	1	Three fingers clamp	1
Water pump with hoses	1	Microscale three fingers clamp	1
Elution chamber with lid	1	10 mL graduated cylinder	1
Bent distilling adapter 14/23	1	Water condenser with hoses	1
Büchner funnel with extention	1	Pewter bowl	1
Glass funnel	1	Plastic ice container	1
Spatula	1	T destilation adapter 14/23	1
Glass vial	1	Glass stopper 14/23	1
25 mL flat-bottom round flask	1	30 mL beaker	1

25 mL Erlenmeyer flask	2	Glass watch	1
50 mL Kitasato flask with hose	1		1

V. Chemical reaction and molar relationship



	Acetophenone	$NH_2OH*HCl$	AcONa	Oxime
Molar mass (g/mol)				
Mas (g)				
Volume (mL)				
Density (g/mL)				
mmol				
Chemical equiv				
Physical propieties	202º C BP	152º C MP	324º C	55-60º C MP

VI. Experimental Procedure.

A flat bottom flask (25 mL) is charged with a magnetic stirring bar, 0.6 mL of acetophenone, 0.43 g of $NH_2OH*HCl$, 0.63 g of sodium acetate, and 9 mL of ethanol. The reaction mixture is left under reflux for 30 min.

After the appropriate time, a distillation is performed until 1 mL of solution is observed. Discard the ethanol in the organic waste container. The reaction mixture is let to reach room temperature, thereafter, is transferred to a 30 mL beaker, which containing 10 mL of cold water. The beaker is then placed into an ice bath for 5 min to maximize the solid formation. The product is isolated by vacuum filtration and washed with cold water (2 x 5 mL).

The mass of the crude product is recorded, make sure to save oxime for the melting point (MP) and TLC. Recrystallize the remaining product using hexane. Determine the yield and MP of the purified product. A TLC is performed (eluent Hexene:EtOAc 9:1) for the acetophenone, crude, and purified product.

VII. Questions.

a) Does the oxime synthesis need acidic conditions? Justify.
b) How many isomers are expected? Which is more stable? Why?
c) What conditions are required to reduce an oxime to obtain a primary amine?
d) Give some examples where oximes are used to form other products.

VIII. Bibliografic references.

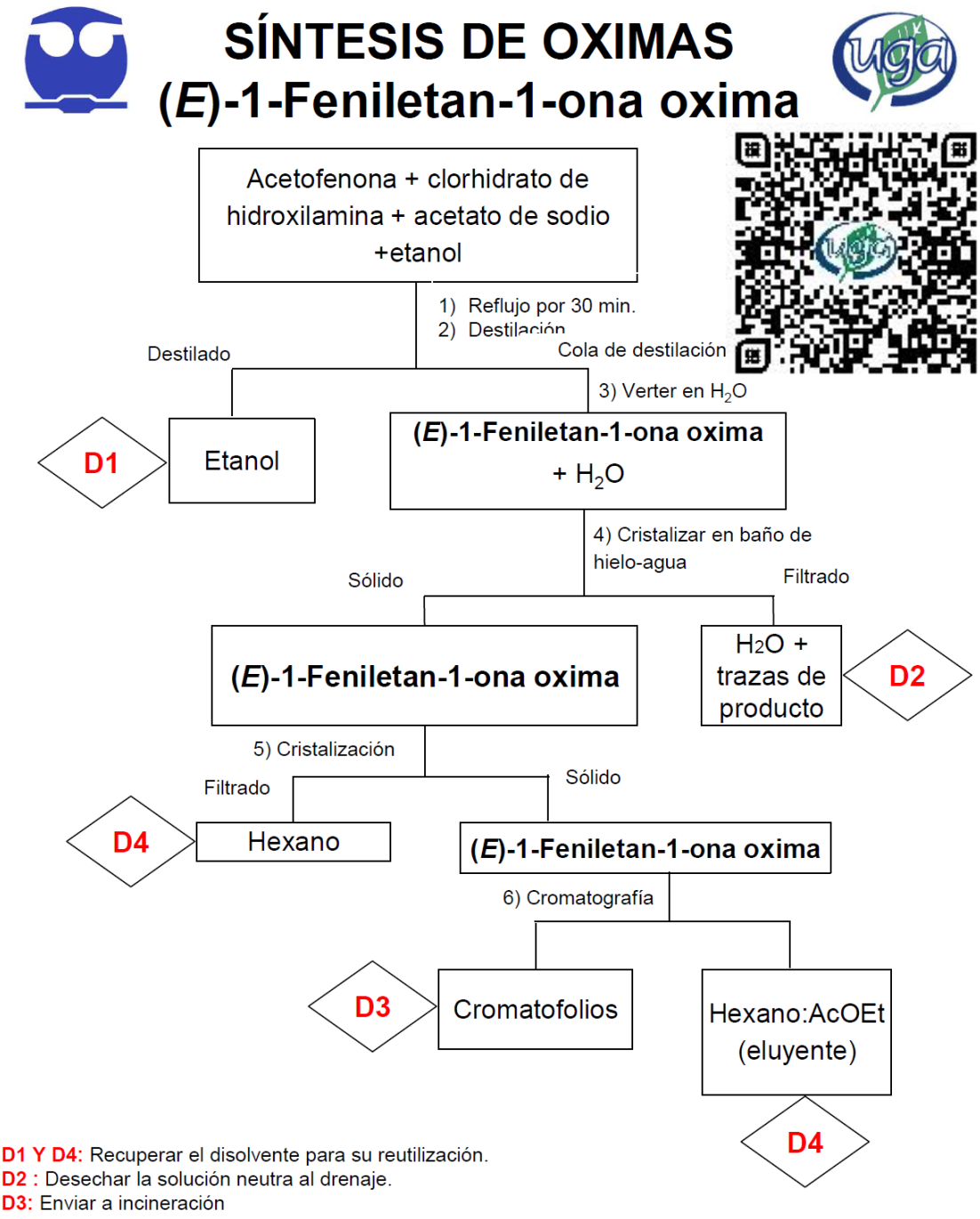
1) Carey F. A.; Giuliano R. M. *Química Orgánica* **2014**, Editorial McGraw Hill, 9na Edición, México.

2) Wade, L. G., JR., *Química Orgánica* **2014**, Pearson- Prentice Hall, 7ma. Edición México.
3) Verma, A; Goyal, N. Modification and optimization of a two-step oxidation-oxime experiment for pophomore level laboratory course. *J. Chem Educ*. **2020**, 97, 11, 4123-4126.

IX. Appendix I. Prior Knowledge.

1) Structure and reactivity of oximes.
2) Reaction mechanism for the synthesis of oximes.
3) Chemical reaction conditions to reduce oximes.
4) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products.

X. Waste management.



Scheme 11. QR/Flow chart of oxime synthesis and its waste management.

EXPERIMENT 11

CARBONYLS V

WITTIG OLEFINATION

I. **Objectives.**

1) To exemplify the synthesis of alkenes through the Wittig reaction in which a carbonyl is reacted with a phosphonium ylide.

2) To perform a Wittig reaction in an aqueous medium, considered sustainable chemistry.

3) To confirm the configuration of the alkene obtained by spectroscopic analysis of the product by ^{1}H NMR.

II. **Background information**.

In general terms, Wittig olefination is an organic chemical reaction in which an aldehyde/ketone is reacted in the presence of a triphenylphosphonium ylide, to give an alkene as a product and triphenylphosphine oxide as a byproduct.

This reaction was named after the German chemist Georg Wittig who first described it in the mid-1950s, and later received the Nobel Prize in Chemistry in 1979.[1]

Conventional reaction conditions for the selective formation of alkenes with the *E* configuration use stabilized ylides and aldehydes, and are most of the time carried out in organic solvents such as toluene, DMF, or DMSO. If aldehydes are used, the geometry of the double bond of the alkene formed is easily predicted, if unstabilized ylides are used, the *Z* configuration of the alkene is obtained with high selectivity, on the other hand, if the ylide is stabilized (from esters or ketones) the alkene *E* is obtained with high selectivity.

Historically, the methodologies to carry out the Wittig reaction had used dangerous reagents and relatively complicated procedures to be taught in the teaching laboratory at the undergraduate level, however, now a days with modern laboratory techniques, the Wittig synthesis has been able to be carried out. At the undergraduate level with quite simple and safer procedures.

The use of water as a solvent in the Wittig reaction has already been used previously, using modified phosphonium salts soluble in water, allowing this type of reaction to be considered within the scope of green chemistry.[2]

III. Reagents.

4-nitro benzaldehyde	0.6 mL	Ethyl bromoacetate	0.9 mL
Triphenylphosphine	1.45 g	Concentrated NH_4OH	5 mL
Saturaded $NaHCO_3$ solution	10 mL	10% $NaHSO_3$ solution	10 mL
Saturaded NaCl solution	10 mL	Ethanol	15 mL

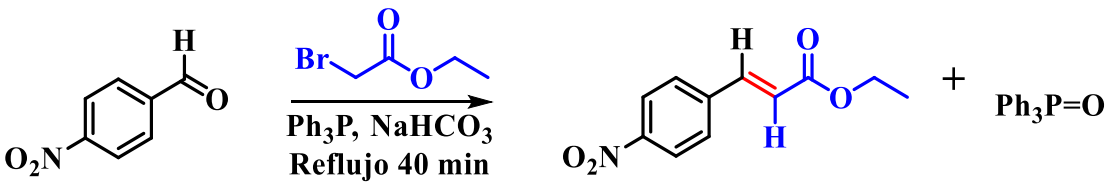
IV. Equipment.

Fisher-Johns melting point apparatus	UV light lamp
Analytical Balance	Hot plate magnetic stirrer

Glasswere for each team

Magnetic stirring bar ½ ´´	1	Three fingers clamp	2
Water pump	1	Microscale three finger clamp	1
Elution chamber with lid	1	10 mL graduated cylinder	1
Plastic Büchner funnel	1	Pewter bowl	1
Glass funnel	1	Plastic container for ice	1
Gas trap	1	Water condenser with hoses	1
Spatula	1	Microscale vacuum destilation adapter w/ olive	1
25 mL flat-bottom round flask		Separating funnel 50 mL with stopper	1
125 mL flat-bottom round flask	1	30 mL beaker	2
50 mL Erlenmeyer flask	3	50 mL beaker	1
50 mL Kitasato flask with hose	1	Glass vial	2
125 mL Kitasato flask	1	Glass watch	1
Weighing device	1		

V. Reaction and molar relationship



	4-nitro benzaldehyde	Ethyl bromoacetate	Triphenylphosphine	Ethyl 4-nitrocinamate
Molar mass (g/mol)				
Mass (g)				
Density (g/mL)				
Volume (mL)				
mmol				
Physical propieties				MP 136–137º C

Tear liquid

VI. Experimental procedure.

Ethyl bromoacetate:, lachrymatory compound. Wear gloves, glasses and a lab coat. Keep away from ignition sources, keep container tightly closed.

In case of contact with the substance, remove gloves and contaminated clothing, wash with plenty of water for 3-5 minutes and transport the person to fresh air and leave them there for a period of 3-5 minutes.

Into a 25 mL flat-bottomed ball flask fitted with a magnetic stirring bar, add 1.45 g of triphenylphosphine, 10 mL of saturated $NaHCO_3$ solution, and 0.6 grams of *p*-nitrobenzaldehyde. Adapt a water condenser in the reflux position, above the water condenser adapt a vacuum T with an olive/glass stopper that will act as a gas trap, the hose must reach a Kitasato flask that contains 5 mL of concentrated NH_4OH inside, carefully check that the glass tube is totally immersed into the NH_4OH, cover the union of the hose and gas trap with parafilm (**Figure 3**).

Once the entire system is assembled, uncover the water condernser and quickly add in a single operation 0.9 mL of ethyl bromoacetate (Caution Tearmliquid), taking care of to not touch the walls or the reaction flask, once it was poured, adapt the water condenser once again and reflux the reaction mixture for 30 minutes with vigorous stirring the resulting heterogeneous mixture, the reaction proceeds at the interface.

After the reaction time finished, remove the flask from heating and allow it to cool to room temperature. Transfer the contents of the ball flask into a 50 mL separating funnel, and perform multiple extractions with 15 mL of AcOEt (3X5 mL), combine all the organic phases, and discard the aqueous phase at the end.

Wash the organic phase with 10 mL of 10% $NaHSO_3$ solution, reserve the organic phase; The organic phase is then washed again with 10 mL of brine (saturated NaCl solution), reserving the organic phase. The organic phase is dried over Na_2SO_4 until excess water is removed.

The organic phase, previously dried with Na_2SO_4, is poured into a 125 mL ball flask with the help of a filtration funnel and a cotton swab, rinse the Na_2SO_4 previosly used with 3 mL of AcOEt, then evaporate the solvent at vaccum (a brown solution will remain in the flask). Cool the solution in an ice bath, a yellow-brown solid should form upon cooling add 6 mL of ice-cold ethanol and dissociate the solid with the help of a spatula, the desired product will precipitate.

The triphenylphosphine oxide (byproduct) remains dissolved in the ethanol, while the product crystallizes slowly when the solution is cooled, filtered under vacuum, and ashed the crystals with 6 mL ice-cold ethanol (in 2 washes of 3 mL each). Quantify the mass obtained, determine the melting point of the crude product, and perform a TLC of the

product against *p*-nitro benzaldehyde as a raw material reference, using Hex: AcOEt 8:2 as eluent.

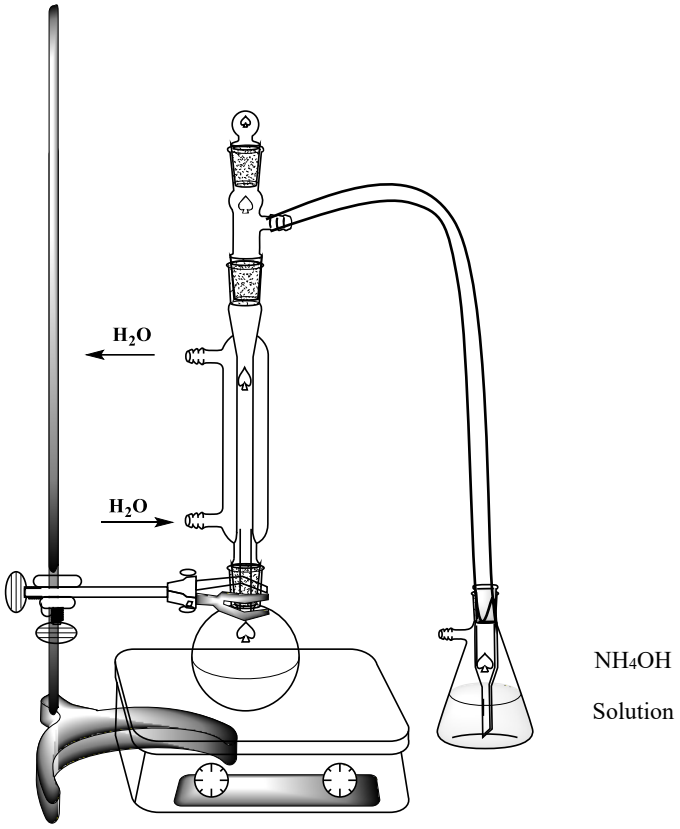


Figure 3. System for the Wittig reaction.

VII. Questions.

1. Why is the alkene with *E* configuration mainly obtained?
2. What role do the $NaHSO_3$ and NaCl washes have in the reaction mixture?
3. What information does the chromatoplate made provide you?
4. How could you confirm that the alkene with *E* configuration was obtained?
5. Justify on scientific bases why triphenylphosnine oxide is soluble in ethanol and the product is not.

VIII. Bibliografic references.

1. a) Wittig, G.; Schönllkopf, U. *Chem. Ber*. **1954**, 87(9), 1318-1330. b) Wittig, G. *Science* **1980**, 210(4470), 600-604
2. a) El Batta, A.; Jian, C.; Zhao, W.; Anness, R.; Cooksy, A.L.; Bergdahl, M. *J. Org Chem.* **2007**, 74(14), 5244-5259. b) Leung, S.H.; Angel, S.A. *J. Chem. Educ*. **2004**, 81(10), 1492-1493. c) Wu, J.; Li, D.; Zhang, D. *Synth. Commun.* **2007**, 35(19) 2543-2551. d) Kelly, M.J.B.; Fallot, L.B.; Gustafson, J.L.; Bergdahl, M. *J. Chem. Educ*. **2016**, 93(9), 1631-1636.
3. McMurry, J. Organic Chemistry 2023, Editorial Openstax, 10ma Edición, Estados Unidos de Norteamérica.
4. Bruice, Paula Yurkanis Química Orgánica 2008, Editorial Prentice Hall, 5ta. Edición, México.
5. Carey Francis A. Química Orgánica 2014, Editorial McGraw-Hill, 9na. Edición, México.

IX. Appendix I. Prior knowledge

1. Characteristics of Phosphorus Ylides.
2. Conventional reaction conditions of the Wittig reaction.
3. Wittig olefination reaction mechanism.
4. Selectivity of the conformation of the alkenes obtained by the Wittig reaction and the reaction conditions to obtain the E and Z isomers.
5. Other olefination methods: Julia, Horner-Wadsworth-Emmons, Tebbe reagent.
6. Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products

X. Apendix II. Preparation of reagents

Saturated $NaHCO_3$ solution (1L)

Weigh 150 g of sodium bicarbonate ($NaHCO_3$) and pour it into a 1 L beaker containing 1000 mL of distilled water and shake until completely dissolved. Once dissolved, pour into a container labeled Saturated Baking Soda.

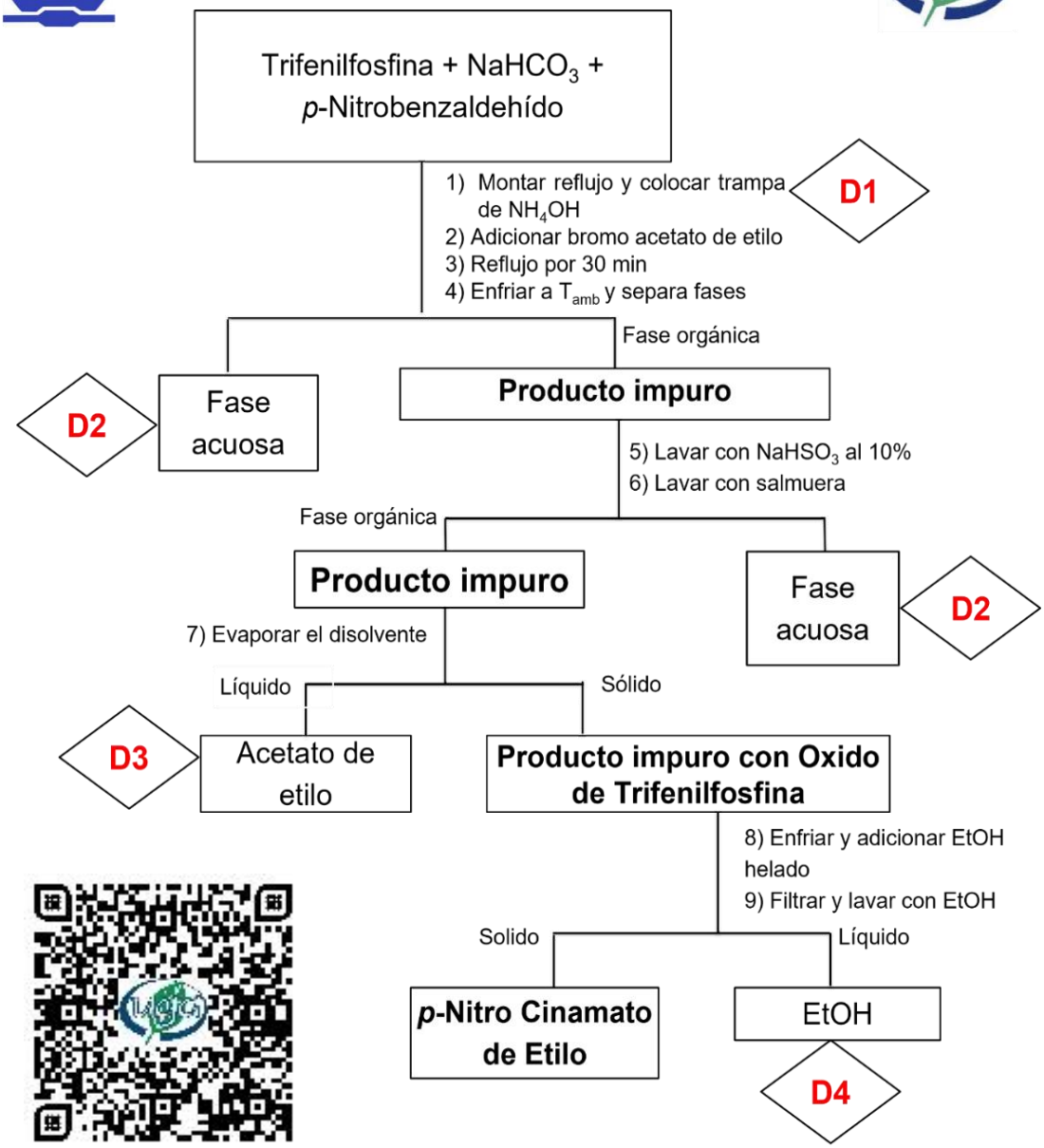
$NaHSO_3$ solution 10% (1L)

Weigh 100 g of $NaHSO_3$ and add it to the inside of a 1000 mL volumetric flask, add 800 mL of water and shake until completely dissolved, then make the volume to 1000 mL with distilled water, and pour into a container labeled $NaHSO_3$ 10%. (Sodium bisulfite).

Saturated NaCl Solution / Brine (1L)

Weigh 350 grams of NaCl and add them to the inside of a beaker containing 1000 mL of distilled water, stir until completely dissolved, then pour into a container labeled Brine or Saturated NaCl Solution.

XI. Waste management.



D1 Y D2: Desechar neutro.

Scheme 12. QR/Flow chart of Wittig olefination and its waste management

EXPERIMENT 12

CARBONYLS VI

CARBONYL IDENTIFICATION

I. Objectives.

a) Identify the carbonyl group in aldehydes and ketones.
b) Distinguish between an aldehyde and a ketone through characteristic drop tests.

II. Background infomation.

The intrinsic physical and chemical reactivity of organic molecules is primarily grounded in the presence of specific functional groups or "chemical families." Functional groups are clusters of atoms that remain constant both in their spatial arrangement and connectivity, and it is due to this regularity that they impart physical and chemical properties similar to the chemical structures in which they appear in their hydrocarbon skeleton.

The typical reactions of each functional group occur within the group of atoms that form that functional group, and it is these reactions that allow for the qualitative identification of molecules.

Due to the high reactivity it exhibits, the carbonyl group has a series of tests that facilitate its identification. However, several of these reactions are not exclusive to the carbonyl group. This is why, with the advent of spectroscopic techniques, these spot tests have gradually been disappearing.

III. Reagents.

Benzaldehyde	1 mL	Butan-2-one	1 mL
Formaldehyde	1 mL	Acetonphenone	1 mL
Propanaldehyde	1 mL	Metyl isobutyl ketone	1 mL
Glucose	1.0 g	Dibutylketone	1 mL
10% NaOH solution	16 mL	H_2CrO_4 solution	2 mL
2,4-DNFH solution	16 mL	5% $AgNO_3$ solution	8 mL
25% NH_4OH solution	8 mL	KI-I_2 solution	10 mL
1,4-Dioxane	As needed	HNO_3 concentrated	As needed

IV. Glasswere for each team

Electric Water bath	1	Test tube clamp	1
Büchner funnel	1	Three fingers clamp	2
Spatula	1	Pewter bowl	1
Test tube rack	1	Test tubes	10
50 mL Kitasato flask	1	400 mL beaker	1

V. Experimental procedure.

General important instructions.
Before conducting each test, the tubes and materials to be used must be clean. When using reagents, be careful not to contaminate them.
Use the specified amounts of reagents and substances in each test, as an excess may lead to misinterpretation.

1) **Carbonyl group identification**.
Add approximately 0.2 mL of the substance and add 2 mL of 2,4-dinitrophenylhydrazine solution (2,4-DNPH). If no precipitate forms, gently heat the tube in a water bath for 5 minutes, then allow it to cool and induce crystallization, you can place it into an ice bath. If no precipitation occurs, add 1-2 drops of ice-cold water and cool within an ice bath. The formation of an orange precipitate indicates the presence of a carbonyl group in the molecule and is considered a positive test.

b) **Chromic acid test**.
Positive reaction for aldehydes and α-hydroxyketones, negative for ketones.
Dissolve a drop or 10 mg of aldehyde in 1 mL of acetone. Add several drops of Jones reagent (CrO_3/H_2SO_4). A positive result is indicated by the formation of a green or blue precipitate of $Cr3^+$ salts.
With aliphatic aldehydes, the solution becomes cloudy within 5 seconds, and a characteristic precipitate appears in 30 s. Aromatic aldehydes usually require 30 to 90 seconds for precipitate formation. Ketones do not change coloration, as no REDOX reaction occurs.

c) **Tollens test**.
Positive reaction exclusively for aldehydes, negative for ketones.
This reagent should be used freshly prepared.
Perform only in the case of obtaining a positive result with chromic acid.
In a clean test tube, place 2 mL of a 5% silver nitrate solution, one to two drops of 10% sodium hydroxide, and dropwise with agitation, a 25% ammonium hydroxide solution, just until the silver oxide that precipitated dissolves, avoiding any excess.
To the above reagent, add 0.1 g of the substance or 2 drops if it is liquid, shake and heat gently in a water bath, letting the tube stand. The formation of a silver mirror indicates a positive test. After completing the test, wash the test tube with nitric acid (Caution, dangerous reagent). Collect the resulting silver nitrate in a container to recover the silver.

d) **Haloform (Iodoform) test**.
Positive reaction for methyl ketones and alcohols of the structural type R-CH(OH)-CH_3, (R=H, alkyl, aryl). The only aldehyde that gives a positive test is acetaldehyde.
In a test tube, place 0.1 g of the substance or 2 to 3 drops if it is liquid and 2 mL of water. If the substance is not soluble in it, add 2-3 mL of dioxane. Add 1 mL of 10% NaOH dropwise and, while stirring, a triiodide solution (I_2/KI) just until the dark brown color of iodine persists.
Heat the mixture in a water bath for 2 minutes. If during this time the brown color disappears, add a few more drops of the triiodide solution until the color does not disappear after 2 minutes of heating.

Decolorize the solution by adding 3 to 4 drops of 10% NaOH, dilute with water almost to fill the tube, let it cool, and separate the iodoform by filtration.

VI. Questions.

1. Draw and balance each of the reactions that were carried our.
2. Investigate which reagent is selective for the identification of the carbonyl group in aldehydes and ketones.
3. How did you distinguish an aldehyde from ketone?
4. What is the Tollens reagent reaction and in what cases is it carried out?
5. What is the haloform reaction and in what cases is it carried out?
6. In a table, indicate the results of the reactions conducted with each of the studied substrates.

VII. Bibliografic references.

1. Pavia Donald L. Introduction to Organic Laboratory Techniques: A Microscale Approach **2006**, Cengage Learning, Brooks/Cole Laboratory Series, 4th Edition, United States of America.
2. Willimson Kenneth Macro and Microscale Organic Experiments **2010**, Cengage Learning, 6th Edition, United States of America.
3. Vogel, A. I., Vogel's Textbook of Practical Organic Chemistry **1996**, Prentice Hall, 5th. Edition, United States of America.
4. Shriner, R. L., Fusson R.C. y Curtin D.Y. Identificación Sistemática de Compuestos Orgánicos **1966**, Editorial Limusa-Wiley, 1st Edition, Mexico.
5. Bruice, Paula Yurkanis Organic Chemistry **2016**, Prentice Hall, 5th Edition. United States of America.
6. Carey Francis A. Organic Chemistry **2019**, McGraw-Hill, 11th Edition, United States of America.

VIII. Appendix I. Prior Knowledge.

1) Identification reactions of the carbonyl group (2,4-DNPH).
2) Principle and mechanism of aldehyde oxidation aldehídos (Jones, Tollens).
3) Principle and mechanism of methyl ketone oxidation (Haloform).
4) Physical, chemical and toxicological properties (CRETIB, Corrosive, Reactive, Explosive, Toxic, Flammable and Biologically Infectious) of reagents and products

IX. Appendix II. Preparation of reagents.

10% NaOH Solution (1L).

Weigh 100 g of sodium hydroxide (NaOH) and pour it into a 1000 mL volumetric flask containing 500 mL of distilled water within an ice bath. Gently stir the solution and slowly fill the flask up to a final volume of 1000 mL (1L). The solution releases heat.

2,4-DNPH Solution (1L).

Weigh 20 g of 2,4-dinitrophenylhydrazine and pour it into a 1000 mL Erlenmeyer flask, add 800 mL of methanol; the solution will become cloudy. Subsequently, slowly add 40 mL of concentrated H_2SO_4, stirring carefully until homogeneity is achieved, the solution should become completely translucent.

5% $AgNO_3$ Solution (100 mL).

Weigh 5.o of $AgNO_3$ and empty it into a 100 mL volumetric flask, fill with distilled water to 100 mL.

H_2CrO_4 Solution (500 mL).

Weigh and dissolve 100 g of CrO_3 in 300 mL of distilled water. Then, slowly add 100 mL of concentrated H_2SO_4, gently stirring until the solution is complete. The reagent should be prepared on the same day. Exothermic reaction, use lab coat, gloves, and safety goggles.

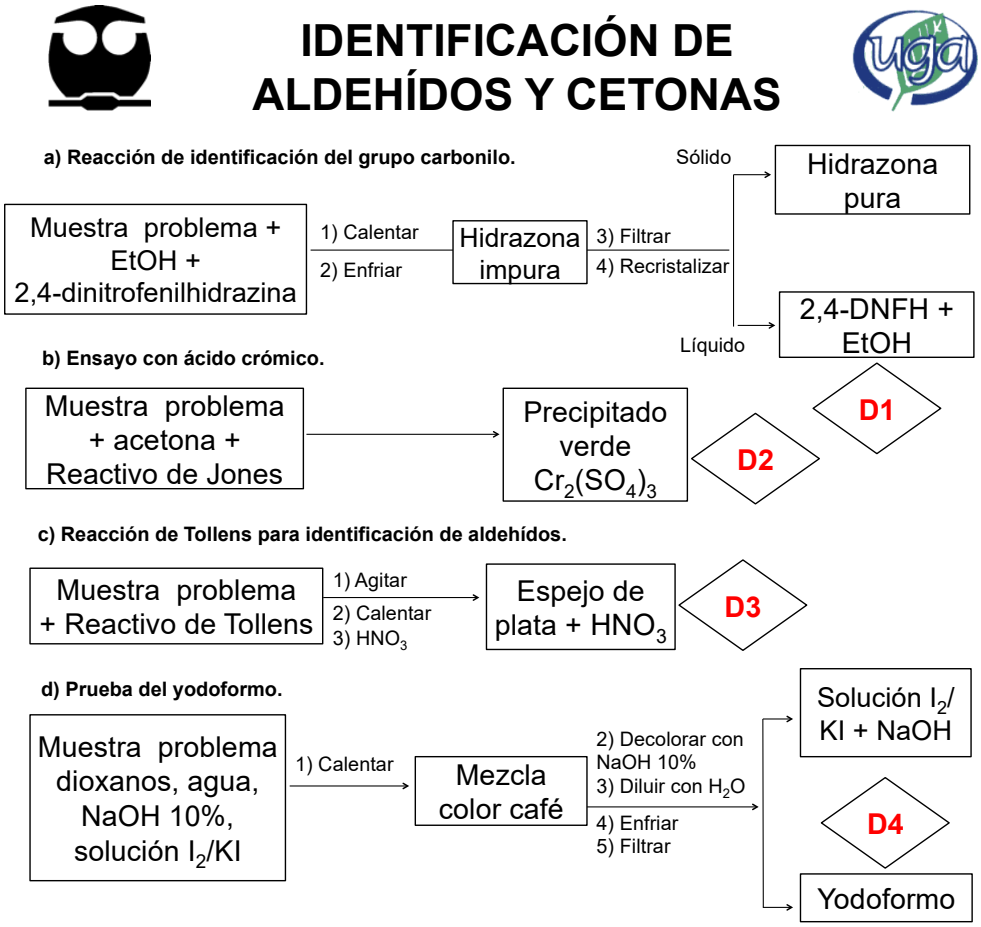
25% NH4OH Solution (1 L)

Add 250 mL of concentrated NH4OH to a 1 L volumetric flask and fill with distilled wáter to 1000 mL.

KI-I_2 Solution (1 L).

Weigh 200 g of KI and 100 g of I_2, add to a 1000 mL beaker, and add 800 mL of water. Stir until the solution is complete.

X. Waste management.



D1: Adsorber con carbón activado hasta eliminar color, desechar la solución neutra al drenaje. Enviar a incineración el carbón utilizado.
D2: Agregar bisulfito de sodio para pasar todo el Cr^{6+} a Cr^{3+}. Precipitar con NaOH. Filtrar el precipitado ($Cr(OH)_3$). Repetir la operación hasta no tener precipitado. Desechar la solución neutra al drenaje. El sólido debe enviarse a confinamiento.
D3: Para precipitar en pH:1, agregar NaCl, filtrar, volver a agregar NaCl. Cuando no haya precipitado adsorber, neutralizar y desechar.
D4: Filtrar el sólido y enviar a incineración. Adsorber la solución sobre carbón activado, neutralizar y desechar por el drenaje. Enviar a incineración el carbón utilizado.

Scheme 13. QR/Flow chart carbonyl identification and its waste management

CASE ANALYSIS
CARBONYL GROUP CHEMISTRY IN ORGANIC SYNTHESIS

Objetive

Evaluate and analyze a real synthetic problem and provide possible solutions with scientific bases.

Background information.

Polymers are macromolecules composed of many units called monomers, which is the fundamental unit of the macromolecule, which is repeated along the chain *n* times through covalent bonds.

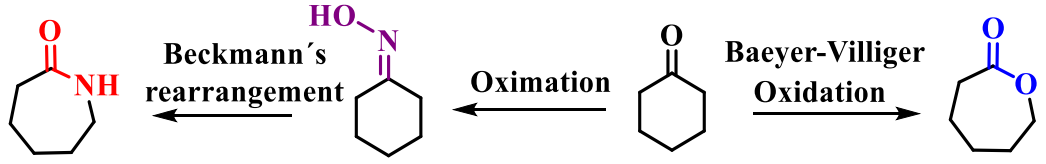
Polymers exist in nature, examples are starch, cellulose, lignin, proteins, nucleic acids, etc. A very basic division classifies them as degradable and non-degradable. During the 1990s, non-degradable polymers were demonized; however, this type of polymer is of great importance and usefulness, such is the case of plumbing pipes. PVC (which are normally used to transport fecal waste in our homes, it would not be pleasant if they degraded after 5 years), what is important to highlight is the excessive use of non-degradable polymers, such as the case of low-density polyethylene.

There are a couple of polymers of great current importance, one is nylon 6,6 which is widely used in the production of clothing, ropes or more solid objects such as utensil handles, another polymer is caprolactone, which when it is polymerized, it can be used in the production of implants and/or surgical sutures for use in humans.

Problematic.

At the plant of the UNIVEX company located in Salamanca Guanajuato, Mexico, which specializes in the synthesis of ε-caprolactam, the chemist from new products development department was fired and before leaving the facilities as revenge he deleted all the files of synthetic methods and the experiment logbook disappeared. Therefore, as you are newly hired in the company, you will have to start from scratch to propose synthetic routes of ε-caprolactam from cyclohexanone. Likewise, they are interested in obtaining ε-caprolactone also from the same ketone.

A basic synthesis scheme is shown below to obtain both cyclic compounds from the common raw material: cyclohexanone.



ε-Caprolactame

ε-Caprolactone

The glassware, solvents and reagents in the new products laboratory at the UNIVEX plant are shown below.

Ethyl acetate	Anhydrous sodium sulfate	HCl 37%
Dichloromethane	Molecular sieve 3Å	H_2SO_4 98%
Ethyl ether	Silica gel	HNO_3 70%
Tetrahydrofuran	Sodium chloride	H_3PO_4 85%
Benzene	K_2CO_3	*m*-CPBA Acid
Dichloromethane	$NaHCO_3$	*p*-toluenesulfonic acid
Acetone	NH_4OH	CH_3CO_2H Glacial
Acetonitrile	NaH_2PO_4	Peracetic acid
Methanol	NaOH pellets	H_2O_2
Ethanol	Calcium chloride	Water ice
iso-Propyl alcohol	$NH_2OH \cdot HCl$	Dry ice
n-Butanol	*n*-BuLi	Distilled water
H_2	$LiAlH_4$	Benzophenone
Metallic sodium	$NaBH_4$	N_2

25, 50, 100 mL flat bottom ball flasks	Liebig condenser (Condenser Straight)
Vigreaux Columns	Magnetic stirring bars
Magnetic stirrers with heating plates	Glass beakers of 10, 20, 50, 100, 200 mL
Glass test tubes of 20, 50, 100 and 150 mL	Erlenmeyer flasks of 20, 50, 100, 150 and 200 mL
Glass funnels	Distillation head T bend
Alcohol thermometers from -20 - 110 ºC	Thermometer holder
Dean-Stark Traps	Distillation collectors
100, 250 mL extraction funnel	Watch glasses
Kitasato flask 50, 100, 200 mL	Büchner funnels
Filter paper	pH indicator paper strips
Pipettes of 1, 5, 10 mL	Drying tube
Stainless steel spatulas	Glass stirring rods
Claisen collectors	Test tubes plastic racks
Test tubes	Analytical balance
Clamps 3 prong fingers with laboratory stand clamp holder	TLC Elution chambers with lid
UV light lamp	Aspirator Vacuum Pump

Methodological Issues.

1. Investigate reaction conditions to obtain ε-caprolactone from cyclohexanone, propose a methodology based on the reagents available to obtain this chemical compound. You must consider melting points, boiling points, densities, etc. of the final product.

2. On a scientific basis, do you justify the choice of your methodology to obtain ε-caprolactone?

3. Describe this methodology step by step (as if it were an experiment for the Organic chemistry III course 1506 laboratory) until obtaining the final product and suggesting a purification method. You must analyze the solubility, density of the reactants, intermediates, and products, etc. Show the detailed reaction mechanism of the transformation of cyclohexanone into ε-caprolactone.

4. Show the detailed reaction mechanism of the transformation of cyclohexanone into ε-caprolactone.

5. Investigate reaction conditions to obtain ε-caprolactam from cyclohexanone, propose a methodology based on the reagents available to obtain this chemical compound. You must consider melting points, boiling points, densities, etc. of the final product.

6. On a scientific basis, do you justify the choice of your methodology to obtain ε-caprolactame?

7. Describe this methodology step by step (as if it were an experiment for the Organic chemistry III course 1506 laboratory), until obtaining the final product and suggesting a purification method. You must analyze the solubility, density of the reactants, intermediates, and products, etc.

8. Show the detailed reaction mechanism of the transformation of cyclohexanone into ε-caprolactam.

9. What effect would the use of a Dean Stark trap have on obtaining the cyclohexanone oxime? Justify your answer with scientific bases.

10. Perform the calculations and species variation tables, starting with 5 grams of cyclohexanone, for both ε-caprolactone and ε-caprolactam.

Bibliography.

1. Stevens, E.S. (**2002**), Green Plastics: an introduction to the new science of biodegradable plastics, USA. Princeton University Press, pp. 95-97, 128-129.

2. Rawesh, K.; Sneha, S.; Prangya, P.D.; Ahmed, A.F.; Biswajit, C. Catalysis Reviews, **2019**, 61.4.

3. Chen, J.; Zhao.X.; Zhang, G.; Chen, B.; Cai, W. Chinese Journal of Chemical Engineering, **2013**, *21*, 1404.

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