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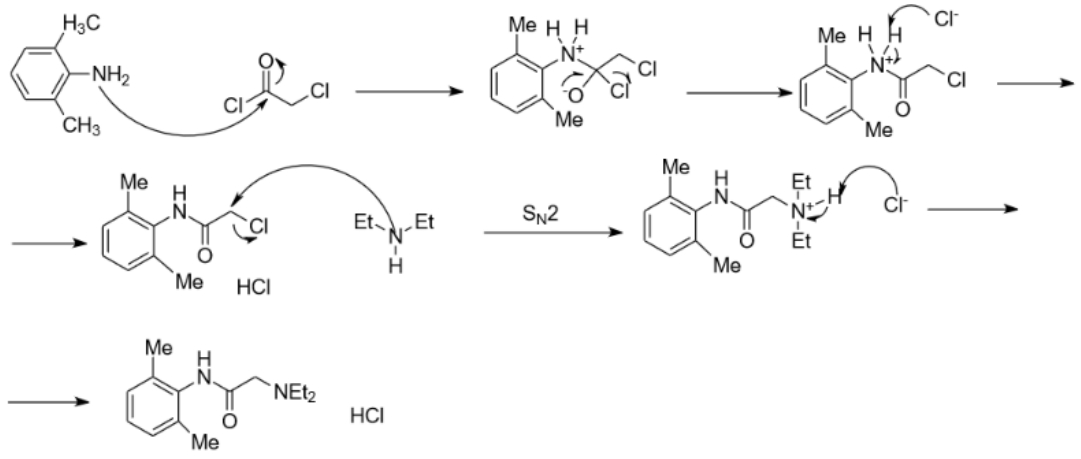
EXPERIMENTATION IN ORGANIC CHEMISTRY	**Practice number:**
FAMILY, FIRST NAME: Mirane Florencio Zabaleta	**DATE:** 30/04/2020

A	**MAIN FEATURES IN THE PRACTICE**
A.1	Main objective of the practice

To learn how is Lidocaine synthesized in the lab, an important medication. Working on a nucleophilic substitution reaction.

A.2	Mechanism of the reaction



A.3	Dangerous reagents	Preventive Measures; H and P phrases
	2,6-Dimethylaniline	H302 + H312 + H332: Nocivo en caso de ingestión, contacto con la piel o inhalación. H315: Provoca irritación cutánea. H335: Puede irritar las vías respiratorias.
	Glacial acetic acid	H226: Flammable liquid and vapor. H314: Causes severe skin burns and eye damage. H402: armful to aquatic life
	Chloroacetyl chloride	H301Toxic if swallowed. H311Toxic in contact with skin. H314Causes severe skin burns and eye damage.

	Sodium acetate (%5)	H319: Causes serious eye irritation. P264: Wash {hands} thoroughly after handling. P280: Wear {protective gloves/protective clothing/eye protection/face protection}
	Toluene	H225: Highly flammable liquid and vapour. H304: May be fatal if swallowed and enters airways. H315: Causes skin irritation
	Diethylamine	H317: May cause an allergic skin reaction H318: Causes serious eye damage H402: Harmful to aquatic life.
	HCl	H290: May be corrosive to metals. H314: Causes severe skin burns and eye damage. P260: Do not breathe dusts or mists.
	KOH	H302: Harmful if swallowed H314: Causes severe skin burns and eye damage H402: Harmful to aquatic life.
	Na_2SO_4(anhy.)	H315: Causes skin irritation [Warning Skin corrosion/irritation]. H318: Causes serious eye damage [Danger Serious eye damage/eye irritation].
	Pentane	H361f: Suspected of damaging fertility. H373: May cause damage to organs through prolonged or repeated exposure. H411: Toxic to aquatic life with long lasting effects.

A.4 Experimental procedure

Amidation:

1. 2,6,-Dimethylaniline is placed in a round bottom flask and glacial acetic acid is added. Then, chloroacetyl chloride is carefully added too.
2. -After that, the mixture is heated for 5min at 45ºC.
3. Then Sodium Acetate is added while stirring and the suspension is cooled down to 10ºC in an ice-water solution.
4. Next, is vacuum-filtered so as to split the precipitate formed before. This solid is washed with water so as to eliminate any rest of acetic acid.
5. Finally, we let the solid dry completely during the night.

Nucleophilic substitution reaction:

6. Just take one gram of the compound obtained and dissolved in toluene. Then the corresponding diethylamine is added.
7. Then we connect the condenser and leave it under reflux for an hour.
8. After that we have to take it to the extraction funnel and HCl is added. The funnel is shaken and the aqueous phase collected.
9. The organic phase is washed again with HCl and the new aqueous phase is extracted with the other one and the organic one separated in an Erlenmeyer flask.
10. The aqueous solution is cooled down to less than 10ºC and KOH is added slowly until a precipitate, Lidocaine, is formed. A bit more is added to assure the complete precipitation. Let it warm to room temperature.
11. The solution is placed again in the separation funnel and pentane is added. We extract the aqueous phase and the organic one is washed with water. This is repeated five times.
12. The last organic phase is dried with Na_2SO_4, the liquid is filtered and finally the solvent is eliminated in the rotavapor.

<table>
<tr><td>B</td><td colspan="5">RESULTS</td></tr>
<tr><td rowspan="4">B.1</td><td>Molecular formula:
$C_{10}H_{12}ClNO$</td><td>M.W. (g/mol):
197,66</td><td>Density:
-</td><td>State:
solid</td><td>Color:
White/brown</td></tr>
<tr><td colspan="2">Theoretical weight or volume of the final product:
$g = 0{,}0203 \times 197{,}66 = 4{,}012g$

Measured experimental weight or volume of the final product:
%90 of the starting product.</td><td colspan="3">Theoretical melting point or boiling point (ºC):
• Boiling point: 316,8±30,0ºC
• Melting point: 150-151ºC</td></tr>
<tr><td>Molecular Formula:
$C_{14}H_{22}N_2O$</td><td>M.W. (g/mol)
234,34</td><td>Density
•</td><td>State:
Solid</td><td>Color:
White or slightly yellow</td></tr>
<tr><td colspan="2">Theoretical weight or volume of the final product:
$g = 0{,}00506 \times 234{,}34 = 1{,}18g$

Measured experimental weight or volume of the final product:
$g = 1g$</td><td colspan="3">Theoretical melting point or boiling point (ºC):
• Boiling point: 181ºC
• Melting point: 68,5ºC</td></tr>
<tr><td>B.2</td><td colspan="5">Yield. Analysis of the results</td></tr>
<tr><td></td><td colspan="5">
<table>
<tr><th>Reagent</th><th>g</th><th>MW</th><th>mol</th><th>δ</th><th>mL</th></tr>
<tr><td>$C_8H_{11}N$</td><td>2,46</td><td>121,18</td><td>0,0203</td><td>0,984</td><td>2,5</td></tr>
<tr><td>$C_2H_2Cl_2O$</td><td>2,56</td><td>112,94</td><td>0,0227</td><td>1,42</td><td>1,8</td></tr>
<tr><td rowspan="2">$C_{10}H_{12}ClNO$</td><td>3,611</td><td rowspan="2">197,66</td><td>0,0183</td><td rowspan="2">•</td><td>•</td></tr>
<tr><td>1</td><td>0,00506</td><td>•</td></tr>
<tr><td>$C_4H_{11}N$</td><td>1,06</td><td>73,14</td><td>0,0145</td><td>0,706</td><td>1,5</td></tr>
<tr><td>$C_{14}H_{22}N_2O$</td><td>1</td><td>234,34</td><td>0,00427</td><td>•</td><td>•</td></tr>
</table>

In the first reaction, the amidation reaction, we have a limitant reactant that will be 2,6-Dimethylaniline. So, there will be a surplus of Chloroacetyl chloride.
If we obtain the %90 of the starting product, the grams weighted will be the next:
$$g = \frac{90}{100} \times 0{,}0203 \times 197{,}66 = 3{,}611g$$
In the next reaction we have another limitant reactant, α-chloro-2,6-dimethylacetanilide. So, we will have a surplus of diethylamine.
$$\%yield_{Lidocaine} = \frac{0{,}00427}{0{,}00506} \times 100 = \%84{,}39$$
</td></tr>
</table>

B.3	Spectroscopic Data:

NMR spectroscopy:

α-chloro-2,6-dimethylacetanilide

- ^{1}H NMR:
  δ 7,92 we have a brought singlet that belongs to the H attached to the N.
  δ 7,20-7,02 is a multiplate that belongs to the H in the aromatic ring.
  δ 4,20 a singlet that belongs to the CH_2 hydrogens, between the chlorine and the carbonyl group.
  δ 2,22 we have another singlet that belongs to both methyl groups.
- ^{13}C NMR:
  δ 164,6 belongs to the carbonyl group.
  δ 135,4 belongs to both 4ºC attached to the methyl groups.
  δ 132,8 belongs to the carbon in meta position to the methyl groups.
  δ 128,3 belongs to the 2ºC in ortho position to de methyl groups.
  δ 127,9 it has to do with the 4ºC attached to the N.
  δ 42,8 it belongs to the carbon next to the chlorine.
  δ 18,3 it has to do with the methyl groups.
- IR:
  We have two interesting signals, one of them is around 3200 wavenumbers that refers to the N-H bond. We also have some small peak from 1750-1900 that belong to the aromatic ring that this presence can also be seen in the pointing peak at 1540. Apart from that we have also a pointing peak at 1640 that has to do with the carbonyl group.

Lidocaine

Most of the signals above appear in the spectroscopy of lidocaine in the same place.

- ^{1}H NMR:
  δ 8,93 we have a brought singlet that belongs to the H attached to the N.
  δ 7,09 this singlet should be a multiplate as it belongs to the hydrogens of the aromatic ring.
  δ 3,22 the singlet belongs to the CH_2 hydrogens between carbonyl and the ethylamine.
  δ 2,69 a quadruplet that belongs to the ethyl groups of the amine.
  δ 2,24 a singlet that belongs to both methyl groups.
  δ 1,14 a triplet that also belongs to the ethyl groups of the amine.
- ^{13}C NMR:
  δ 170,3 it belongs to the carbon of the carbonyl group.
  δ 135,1 belongs to the C4º that are attached to the methyl groups.
  δ 134,0 it has to do with the C4º next to the amine.
  δ 128,2 belongs to the carbon in meta position to the methyl groups.
  δ 127,1 belongs to the 2ºC in ortho position to de methyl groups.
  δ 57,5 it has to do with the 2ºcarbone between the carbonyl and the amine.
  δ 49,0 it belongs to the ethyl groups, exactly to the C next to the amine.
  δ 18,6 it has to do with the C of the methyl groups.

δ 12,7 it has to do with the ethyl group but in this case with the CH3 in the corner.

- IR:
  We have a big peak that is quite width that refer to the N-H at 3120 wavenumbers. We also have the small peak mentioned in the last IR that had to do with the aromatic ring and the pointing peak can also be seen but at 1600. We can also see the peak that belongs to the carbonyl.

B.4	Conclusions

I've learned more about the synthesis of the lidocaine, which is an important medicine used quite regularly by dentist. I've also acquired some interesting theoretical concepts as how is the process of any reaction done in the lab; First, we will start with the set up, then we would monitorize the reaction so as to know when we have finished. After that, we would do the work up so as to get rid of the reagents we don't want continued by the purification of the compound. Finally, we should do the characterization (NMR) to see if we have obtained the compound we wanted to.
Another interesting thing is the acid/basic extraction that in this case is a very useful technique.