

E28 EXTRACTION OF ORGANIC COMPOUNDS

Separation using acid-base properties, acylation

THE TASK

To use the acid/base properties of organic compounds to separate mixtures.

THE SKILLS

By the end of the experiment you should be able to:

- recognise how the common organic functional groups react with strong acids and bases,
- design separation strategies for organic compounds based on this,
- use a separating funnel safely.

OTHER OUTCOMES

- You will develop an appreciation of the techniques used in organic and pharmaceutical science to separate the compounds present in complex mixtures.

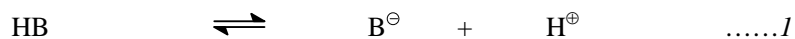
INTRODUCTION

The separation of pure components from a complex mixture is a problem that is central to practical organic chemistry, and one that cannot usually be solved by using variations in a single property such as boiling point, or solubility in a single solvent. However, by taking advantage of the presence of acidic and basic groups, it is sometimes possible to achieve clean separations of mixtures using a separating funnel, an organic solvent such as ether, and a sequence of extractions with strong acids and bases. This separation technique uses the property that charged species are soluble in water (a polar solvent) and neutral or uncharged species are soluble in organic (non-polar) solvents.

To understand this procedure fully, it is necessary to revise some acid/base theory as it applies in Organic Chemistry.

Acids

A typical acid, HB, can dissociate according to the following equation:



The equilibrium constant for this reaction is called the acid dissociation constant and is given by:

$$K_a = \frac{[\text{B}^{\ominus}][\text{H}^{\oplus}]}{[\text{HB}]}$$

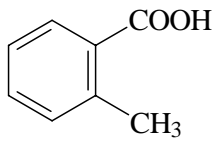
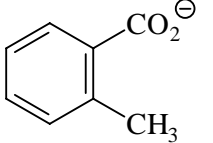
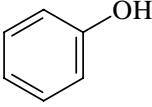
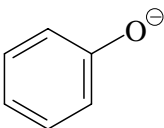
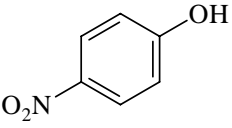
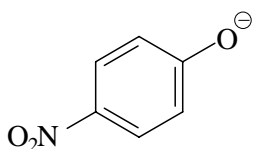
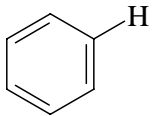
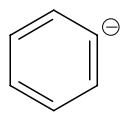
The stronger acids have the higher values of K_a . Indeed, for strong acids, reaction *I* proceeds essentially 100% to the right and thus K_a is very large. The vast majority of organic acids, however, have K_a values smaller than 10^{-3} M. In order to avoid dealing with these small numbers, it is common practice to tabulate acid strengths as $\text{p}K_a$ values.

$$\text{p}K_a = -\log_{10}K_a$$

The weakest acids have the smallest K_a values and hence have the largest $\text{p}K_a$ values. Conversely, the strong acids have the small $\text{p}K_a$ values.

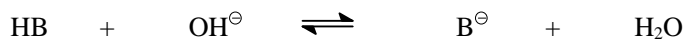
Any organic molecule that contains at least one hydrogen atom can be considered to be an acid. The vast majority of such compounds have pK_a values greater than 18 and have essentially no tendency to dissociate at all. Their importance as acids in organic chemistry is because of the reactions that their conjugate bases (which are very strong bases) undergo. Table E28-1 gives many examples of organic "acids" and their conjugate bases.

Table E28-1 Some Organic Acids and their Conjugate Bases

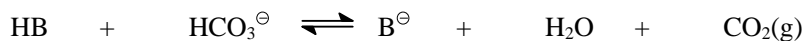
Acid	Class of compound (functional group)	K_a /M	pK_a	Conjugate base
CH ₃ COOH	carboxylic acid	$10^{-4.76}$	4.76	CH ₃ CO ₂ [⊖]
HCOOH	carboxylic acid	$10^{-3.74}$	3.74	HCO ₂ [⊖]
	carboxylic acid	$10^{-3.90}$	3.90	
	phenol	$10^{-9.98}$	9.98	
	phenol	$10^{-7.15}$	7.15	
CH ₃ CH ₂ OH	alcohol	10^{-18}	18	CH ₃ CH ₂ O [⊖]
H-C≡C-H	alkyne	10^{-25}	25	H-C≡C [⊖]
	arene (aromatic ring)	10^{-37}	37	
CH ₃ CH ₃	alkane	10^{-42}	42	CH ₃ CH ₂ [⊖]

Potentially, any acid can react with any base in a proton-transfer reaction. Whether or not any detectable reaction occurs is dependent on the relative strengths of the acid and base involved.

The hydroxide ion is a strong base and will undergo an acid/base reaction with any acid that has a pK_a less than 14, *viz.* the carboxylic acids and phenols. The reaction can be represented as:

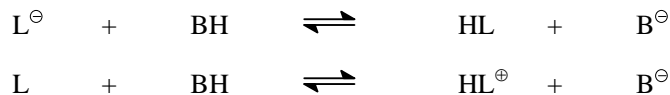


The hydrogencarbonate ion is a weaker base than the hydroxide ion and will only undergo reaction with relatively strong acids, specifically those that have pK_a values less than 6.35, *viz.* the carboxylic acids. The reaction can be represented as:



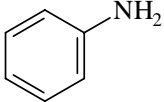
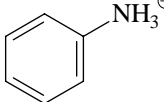
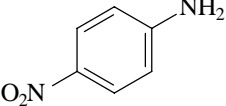
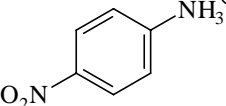
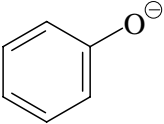
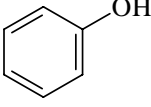
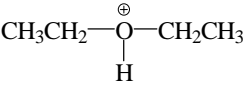
Bases

Just as any compound that contains a hydrogen atom can be thought of as an acid, any organic compound that contains a lone pair of electrons can be considered as a base. Such a species can potentially accept a proton from an acid according to one of the following equations.



Just as the relative strengths of acids are ranked, it is common practice to tabulate base strengths as pK_b values, or even more commonly as the pK_a values of the conjugate acids. The strongest bases have the smallest pK_b values and hence their conjugate acids have the largest pK_a values. Table E28-2 gives many examples of bases and their conjugate acids.

Table E28-2 Some Bases and their Conjugate Acids in Organic Chemistry

Base	Class of base	K_b /M	pK_b	Conjugate acid	pK_a of conjugate acid
NH_3	ammonia	$10^{-4.76}$	4.76	NH_4^{\oplus}	9.24
$\text{CH}_3\text{CH}_2\text{NH}_2$	aliphatic amine	$10^{-3.36}$	3.36	$\text{CH}_3\text{CH}_2\text{NH}_3^{\oplus}$	10.64
	aromatic amine (aniline)	$10^{-9.40}$	9.40		4.60
	aromatic amine (aniline)	$10^{-13.00}$	13.00		1.00
	phenoxide ion	$10^{-4.02}$	4.02		9.98
H_2O	water	$10^{+15.74}$	15.74	$\text{H}_3\text{O}^{\oplus}$	-1.74
$\text{CH}_3\text{CH}_2\text{OH}$	alcohol	10^{+16}	16	$\text{CH}_3\text{CH}_2\text{OH}_2^{\oplus}$	-2
$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$	ether	$10^{+17.5}$	17.5		-3.5
$\text{CH}_3\text{CO}_2^{\ominus}$	carboxylate ion	$10^{-9.24}$	9.24	CH_3COOH	4.76
OH^{\ominus}	hydroxide ion	$10^{+1.74}$	-1.74	H_2O	15.74
$\text{CH}_3\text{CH}_2\text{O}^{\ominus}$	alkoxide ion	10^{+4}	-4	$\text{CH}_3\text{CH}_2\text{OH}$	18
NH_2^{\ominus}	amide ion	10^{+20}	-20	NH_3	34
$\text{CH}_3\text{CH}_2^{\ominus}$	carbanion	10^{+28}	-28	CH_3CH_3	42

E28-4

Potentially, any base can react with any acid in a proton-transfer reaction. Whether or not any detectable reaction occurs is dependent on the relative strengths of the acid and base involved.

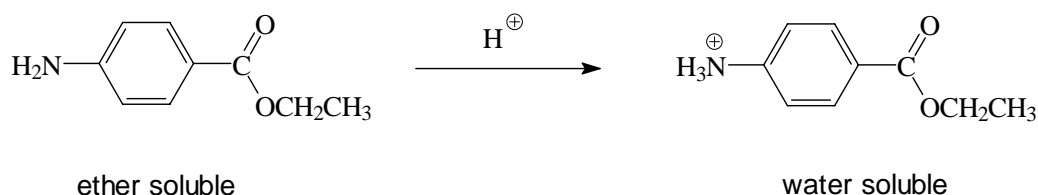
When the acid is strong (eg HCl), reaction will occur except with the weakest of bases, those with pK_b values greater than 15.74. All the bases listed in Table E28-2, except the alcohol and the ether, will react with 2 M hydrochloric acid to yield their conjugate acids.

Similarly, when the acid is water, which is a very weak acid, only the bases that are stronger than OH^\ominus (those with pK_b values less than -1.74) will react. When working with such species in the laboratory, special precautions must be taken to ensure that dry reaction conditions are maintained, often to the extent of excluding water vapour in the atmosphere. The bases in Table E28-2 that are stronger than OH^\ominus and hence unstable in the presence of water are $\text{CH}_3\text{CH}_2\text{O}^\ominus$, NH_2^\ominus and $\text{CH}_3\text{CH}_2^\ominus$.

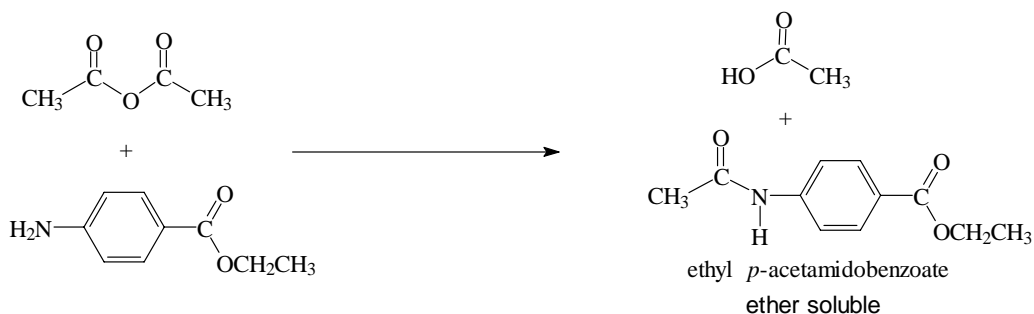
Extraction

The aim of this experiment is to separate a mixture of three aromatic, water-insoluble compounds using their acid/base properties. The compounds are an amine, a carboxylic acid and a neutral compound, and the separation depends upon the following properties.

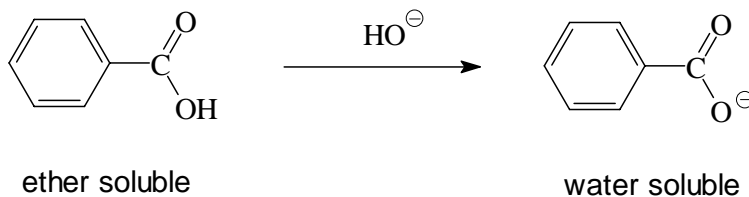
(1) The aromatic AMINE used is a weak base ($pK_b \sim 9$). The amine can be protonated by dilute hydrochloric acid (2 M) to form a charged species that is then extracted from ether into water.



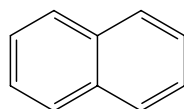
Amines are often oily compounds that slowly decompose. Hence, for isolation and storage purposes, they are usually converted to a more stable derivative - frequently an amide. On addition of a solution of sodium acetate (pK_a of acetic acid is 4.76) the aqueous solution is buffered to a point where a substantial proportion of the amine is unprotonated, and thus available for acetylation by acetic anhydride.



(2) The aromatic CARBOXYLIC ACID used is a weak acid ($pK_a \sim 4$) and so can be extracted from ether by 2 M NaOH. The carboxylate anion is water soluble and ether insoluble.



(3) The NEUTRAL compound is naphthalene, a low-melting solid (m.p. range 80-82 °C) that is soluble in ether, but insoluble in water. One of its uses is as mothballs.



naphthalene

SAFETY

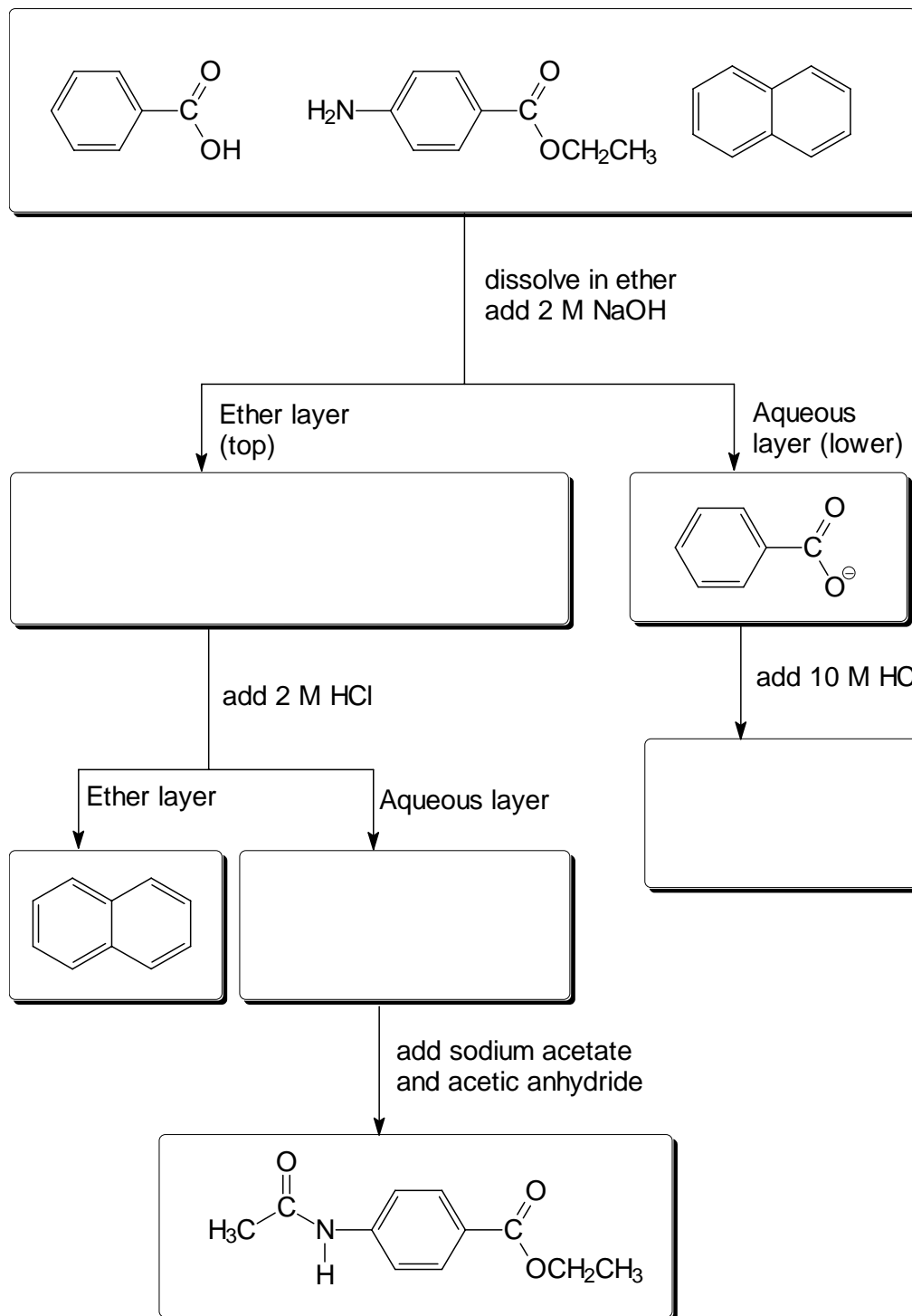
Materials	Nature
benzoic acid	
ethyl <i>p</i> -aminobenzoate	
ethyl <i>p</i> -acetamidobenzoate	
naphthalene	
sodium acetate	
acetic anhydride	
sodium hydroxide	
hydrochloric acid	
sodium sulfate	
diethyl ether	
ethanol	

Indicate, by signing, that you have understood the information in the safety table.

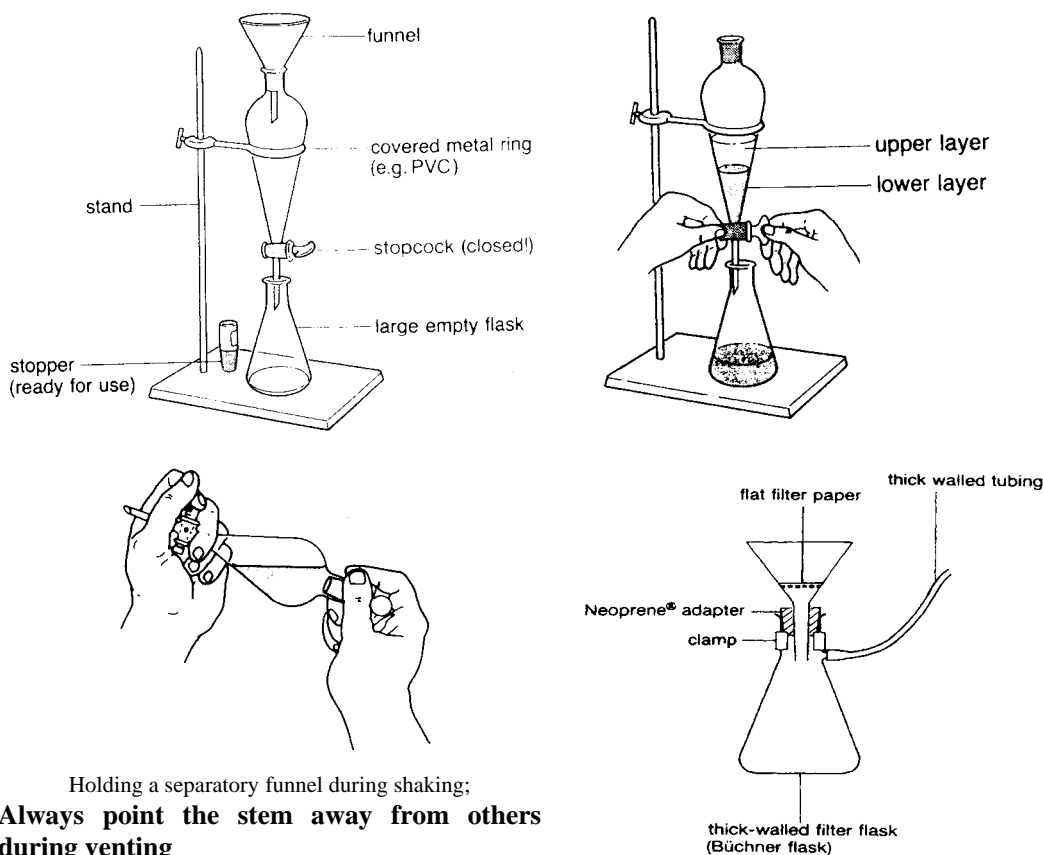
I understand the safety information	Demonstrator's Initials
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LAB-WORK

The sequence of operations is best summarised using a flow chart. Complete the chart.



1) Reread the instructions in Appendix A7 on how to use a separating funnel. Check the tap of your 250 mL separating funnel to ensure that it does not leak and the tap moves smoothly. Set up the funnel in a ring holder attached to the stand on your bench. Label three 100 mL conical flasks as CARBOXYLIC ACID, AMINE and NEUTRAL COMPOUND.



Holding a separatory funnel during shaking;

Always point the stem away from others during venting

2) Weigh out 4 g of the mixture which consists of naphthalene ($\approx 50\%$ by weight), benzoic acid ($\approx 25\%$ by weight) and ethyl *p*-aminobenzoate ($\approx 25\%$ by weight).

- Dissolve your mixture of compounds in ether, transferring the solution to the separatory funnel and using in total about 40 mL of ether.
- Add 10 mL of 2 M NaOH. Stopper the funnel well, invert (CARE! do not shake) and **immediately open the tap to release pressure** which develops as you shake the ether with the alkaline solution. Close the tap, shake briefly and re-open the tap to relieve pressure. Repeat this procedure twice and return the funnel to the stand and remove the stopper.
- When the layers have separated run out the alkaline solution (the lower layer) into the flask labelled CARBOXYLIC ACID.
- Re-extract the ether layer with 5 mL of NaOH solution and then 5 mL water adding these extracts to the flask. [Think about why these extractions are made.] Set aside the CARBOXYLIC ACID flask.

3) Use the same extraction procedure described above.

- Extract the ether with 2 M HCl (CARE! Do not use the 10 M HCl.) using 10 mL the first time and 5 mL the second and finally 5 mL water. Collect all the aqueous extracts (lower layers) in the flask labelled AMINE and set aside this flask also.
- The ether layer which contains the neutral compound should be poured out of the top of the separatory funnel into the flask labelled NEUTRAL COMPOUND. Take care to prevent any water droplets entering the flask. Add a spatulaful of anhydrous sodium sulfate (drying agent), swirl and cover the flask until you are ready to isolate the compound.

4) Take the flask labelled AMINE.

- Add 2 or 3 boiling chips and warm on a steam bath *in the fume hood* for a few minutes to boil off any ether dissolved in the aqueous solution.
- Add 5 g of sodium acetate ($\text{CH}_3\text{COONa}\cdot 3\text{H}_2\text{O}$) and then 1.5 mL of acetic anhydride from the dispenser stored in the fume hood. (Take your flask to the fume hood and transfer the acetic anhydride there.)
- Return the flask to your fume hood, mix the contents well and cool in an ice-bath with swirling. The *N*-acetyl derivative should crystallise within 5 minutes.
- After the contents are thoroughly cooled, take the flask back to your bench, collect the amide product using a Hirsch funnel (see diagram on previous page) and dry at the pump. Label a clean and dry 100 mL beaker with "AMIDE", weigh it and transfer your sample into it once the compound is dry.

What is the function of the sodium acetate?

Mass of AMIDE beaker and sample

g

Mass of AMIDE beaker

g

Mass of ethyl *p*-acetamidobenzoate

g

5) While the amide is crystallising take the CARBOXYLIC ACID flask to the steam bath in the fume hood, add a few boiling chips and boil off the dissolved ether.

- Cool the solution and cautiously add 5 mL of 10 M HCl, **slowly** with swirling. CARE!
- Cool in ice if necessary and collect the crystals using a Hirsch funnel. Wash with a little water and dry the crystals at the pump while you continue the rest of the experiment. Weigh a clean and dry 100 mL beaker labelled with "CARBOXYLIC ACID" and transfer your sample into it once the compound is dry.

What is the purpose of adding the hydrochloric acid?

Mass of CARBOXYLIC ACID beaker and sample	g
Mass of CARBOXYLIC ACID beaker	g
Mass of benzoic acid	g

6) Take the flask containing the NEUTRAL COMPOUND and filter the solution through a fluted filter paper (to remove the sodium sulfate) into a conical flask. Add a few boiling chips and boil off the ether on the steam bath in the fume hood. The residue should crystallise in the flask on cooling.

- Purify the compound by recrystallisation from ethanol (15-20 mL). See page E24-4 for full details on recrystallisation technique. Label a clean and dry 100 mL beaker with "NEUTRAL", weigh it and transfer your sample into it once the compound is dry.

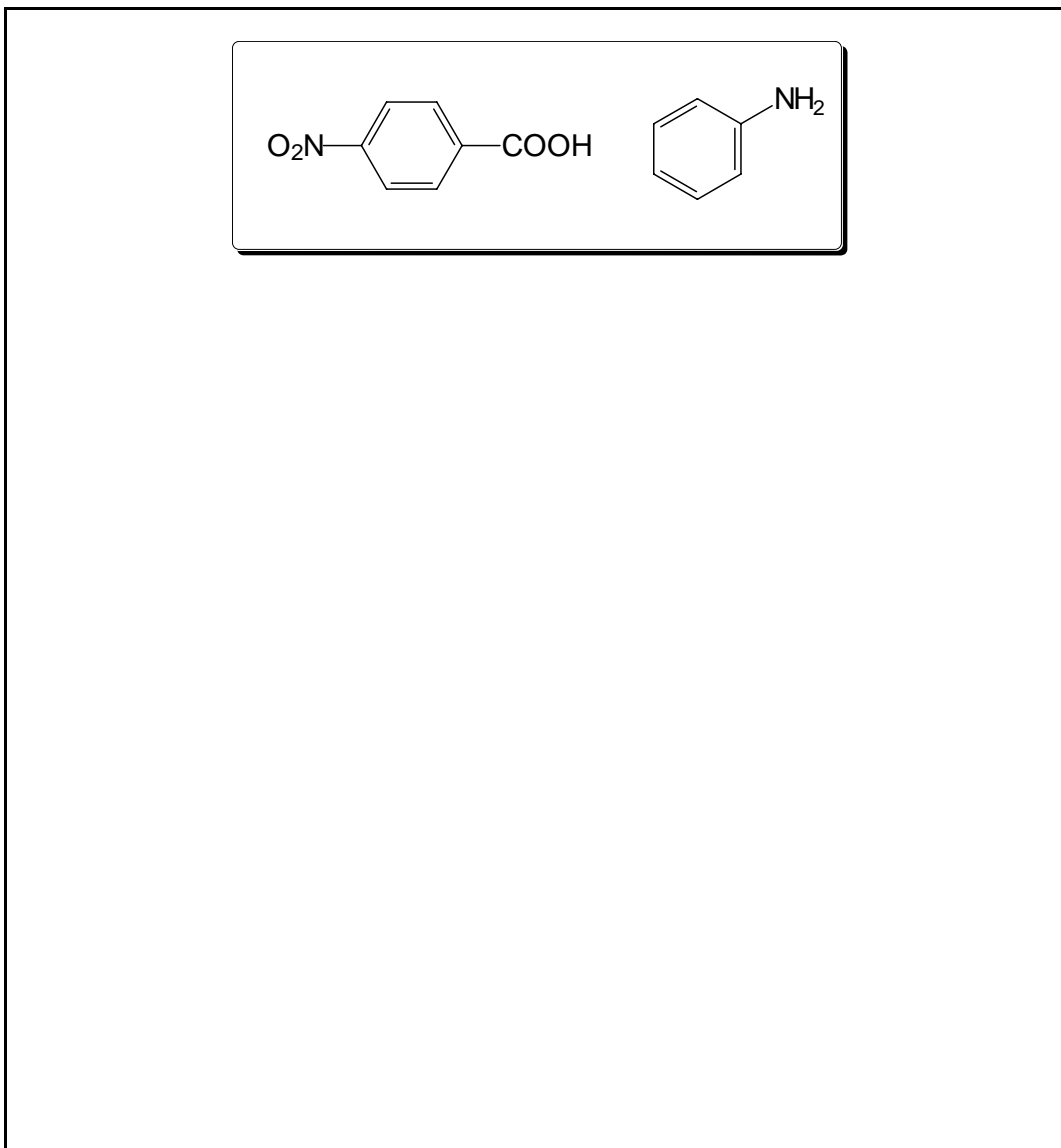
Mass of NEUTRAL beaker and sample	g
Mass of NEUTRAL beaker	g
Mass of naphthalene	g

Demonstrator's Initials	
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After all your compounds have been checked by your demonstrator, dispose of them in the appropriately marked containers in the fume hood.

POST-WORK

Complete the following flow chart to show how you would separate *p*-nitrobenzoic acid and aniline. (Hint: Both compounds are soluble in ether, but neither is soluble in water.)



Demonstrator's Initials	
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