PRACTICAL PROBLEMS

PROBLEM 1 (practical)

Nitration of phenacetine (4-ethoxyacetanilide) with nitric acid in acetic acid as solvent

Caution:

Both acetic acid and 65 % nitric acid attack the skin. If it happens, the skin must be rinsed with water immediately and washed with a saturated aqueous solution of sodium carbonate. Vapours of nitric acid damage the respiratory tract; moreover, nitric gases evolved in the reaction flask are very toxic.

The glass joints of the various apparatus must be only slightly greased.

Apparatus:

250 ml four-necked flask with laboratory stirrer, thermometer, reflux condenser with gas vent, water bath, Bunsen burner.

Preparation:

40 ml of acetic acid are placed with a glass syringe pipette in the four-necked round bottom flask. 2.0 g of phenacetine are then dissolved in the acetic acid. Also, 2.5 ml 65 % nitric acid are added by using a glass syringe pipette under an effective hood. This mixture is heated for five minutes in a water bath at 90 ^{o}C.

Isolation and purification:

The hot water bath is replaced by ice water. After ca. 10 minutes the gas vent is removed and ca. 120 ml of distilled water are added through the reflux condenser into the flask in order to dilute the original solution. Stirring is continued until a temperature of ca. 5 ^{o}C is reached.

The precipitated solid is filtered off and then washed with a total of 100 ml of cold water and finally dried at 60^{o} C for 2.5 hours in a drying oven.

Evaluation of the experiment:

a) Melting points:

The melting point of phenacetine and its reaction product are to be determined and recorded in the note book. The melting point of phenacetine is higher than 120^{o} C and that of the product is higher than 80^{o} C.

b) Thin-layer chromatogram:

The relative position of the spots of the starting compound and its reaction product must be recorded. In order to reach it, little portions of the both samples must be dissolved in 1-2 ml of acetone. The solutions must be placed on the plate by using a capillary tube. To develop the chromatogram, a mixture of 90 ml toluene, 25 ml acetone, and 5 ml acetic acid is used.

After drying the spots are circled with a pen. The R_f-values must be recorded.

c) Developing reagent:

The developed TLC-plate must be sprayed under a hood with the available reagent solution consisting of iron(III) chloride and potassium hexacyanoferrate(III).

Interpretation of the results:

1.1 Which nitration product(s) has (have) been formed? The discussion should focused on the relative position of the spots in your chromatogram; describe your arguments in the note book.

1.2 Explain why such "mild conditions" have been used here for the nitration reaction. Explain why the nitration reaction has proceeded in spite of these "mild conditions".

1.3 Explain the observed colour reaction of phenacetine with the developing reagent.

1.4 Make a brief proposal, how the filtrate should be prepared to avoid environmental damage.

Chemicals:

Acetic acid (analysis grade)

Nitric acid (analysis grade); *w* = 65 % by mass

Phenacetine (analysis grade)

Toluene (analysis grade)

Acetone (analysis grade)

Developing reagent: 100 ml solution
200 ml solution
700 ml distilled water.

SOLUTION

a) Melting points:
4-ethoxy-N-acetylphenylamin (phenacetine) : 135 ℃
4-ethoxy-2-nitroacetanilide : 103 ℃ (theoretic al value)

b), c) Documentation, Thin-layer chromatogram

Interpretation of the results:

1.1 The R_f -value of the nitration product is almost twice as great as that of the starting compound phenacetine. Although nitration has occurred, the molecules exhibit less dipolar character that indicates intramolecular hydrogen bridges. This is only possible if the acetylamino and nitro groups are located in 1.2-positions.

In accordance with the +M-effect of the acetyl amino group one should expect that the nitro group would be favoured in a (free) ortho-position because of the lowered activation energy. On the other hand, one would not expect multiple nitration because of the "mild reaction conditions" (see below) and also because of the electron withdrawing mesomeric effect (-M-effect) and the inductive electron withdrawal (-I-effect) of the nitro group that has entered the molecule.

Nitration product: 4-Ethoxy-2-nitroacetanilide
The melting point confirms this observation.

1.2 The nitration reaction is carried out relatively rapidly, at relatively low temperature in dilute solution and without using fuming nitric acid or "nitration acid".
Instead of sulphuric acid concentrated acetic acid is used. The molecules of the latter compound neither protonate the HNO_3 sufficiently nor do they do solvate the

NO_2^+ ions. As a result, the equilibrium reactions

$$HONO_2 + HONO_2 \rightleftharpoons H_2O^+\text{-}NO_2 + {}^-O\text{-}NO_2$$

and

$$H_2O^+\text{-}NO_2 \rightleftharpoons {}^+NO_2 + H_2O$$

are shifted far to the left. This effect is counterbalanced by the high reactivity (+M-effect) of phenacetine.

1.3 Phenacetine is oxidized by iron(III) ions and a molecule of p-quinone type and iron(II) ions are formed. The iron(II) ions react immediately with the hexacyanoferrate(III) ions to give Turnbull's Blue.

1.4 Neutralization with sodium or potassium hydroxide solution, use of calcium hydroxide solution and argumentation:

NO_3^--ions, CH_3COO^- ions and 4-ethoxy-2-nitroacetanilide are removed by biological metabolism.

PROBLEM 2 (practical)

Determination of the content of phosphoric acid in a cola drink

Apparatus:

500 ml round-bottom flask with stirrer, reflux condenser, heating mantle, magnetic stirrer, water bath.

Preparation of the sample:

The content of a cola drink bottle is stirred for two or three minutes in a round-bottom flask. Afterwards, 6.0 g powdered active charcoal are added. The entire suspension is carefully heated to reflux and is maintained there for ten minutes. The glass joint of the reflux condenser must not be greased!

The heating mantle is then exchanged with an ice water bath. After the sample has been cooled to 20 ^{o}C, it is filtered through a double fluted filter paper. The initial filtrate should be recycled several times.

Adjustment of the pH-meter:

The pH-meter is adjusted to the working electrode by using two buffer solutions.

Titration:

150 ml of the unknown solution are titrated using pH indication with a standardized sodium hydroxide solution (c(NaOH) = 0.0500 mol dm^{-3}).

The first equivalence point of the phosphoric acid is reached after about 6 ml of the NaOH solution have been consumed. The titration is to be continued until more than about 12 ml of sodium hydroxide solution have been added.

Results of the experiment:

a) Draw the titration curve and determine the first equivalence point.
b) Determine the pH value of the heated cola drink and the pH value at the first equivalence point.
c) Calculate the concentration of phosphoric acid in the cola drink. Write the calculation and the result in your report.

Interpretation of the experiment:

1. Describe and explain your observations during the titration.
2. Is it possible that the active charcoal could have influenced your titration result? Give reasons for your presumption.

Chemicals:

Powdered active charcoal

Sodium hydroxide solution; c(NaOH) = 0.0500 mol dm^{-3}

Buffer solutions