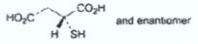
B. (*E*)-butenedioic acid (fumaric acid),



and enantiomer

C. (2*RS*)-2-sulfanylbutanedioic acid (thiomalic acid).

01/2008:0123
corrected 6.0

SODIUM BENZOATE

Natrii benzoas

$C_7H_5NaO_2$ M_r 144.1
[532-32-1]

DEFINITION

Sodium benzenecarboxylate.

Content: 99.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline or granular powder or flakes, slightly hygroscopic.

Solubility: freely soluble in water, sparingly soluble in ethanol (90 per cent *V/V*).

IDENTIFICATION

A. It gives reactions (b) and (c) of benzoates (*2.3.1*).

B. It gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 10 mL of *carbon dioxide-free water R* and 0.2 mL of *phenolphthalein solution R*. Not more than 0.2 mL of *0.1 M sodium hydroxide* or *0.1 M hydrochloric acid* is required to change the colour of the indicator.

Halogenated compounds: maximum 200 ppm for ionised chlorine and maximum 300 ppm for total chlorine.

All glassware used must be chloride-free and may be prepared by soaking overnight in a 500 g/L solution of nitric acid R, rinsed with water R and stored full of water R. It is recommended that glassware be reserved exclusively for this test.

Test solution. To 20.0 mL of solution S add 5 mL of *water R* and dilute to 50.0 mL with *ethanol (96 per cent) R*.

Determination of ionised chlorine

In three 25 mL volumetric flasks, prepare the following solutions.

Solution (a). To 4.0 mL of the test solution add 3 mL of *dilute sodium hydroxide solution R* and 3 mL of *ethanol (96 per cent) R*. This solution is used to prepare solution A.

Solution (b). To 3 mL of *dilute sodium hydroxide solution R* add 2 mL of *water R* and 5 mL of *ethanol (96 per cent) R*. This solution is used to prepare solution B.

Solution (c). To 4.0 mL of *chloride standard solution (8 ppm Cl) R* add 6.0 mL of *water R*. This solution is used to prepare solution C.

In a fourth 25 mL volumetric flask, place 10 mL of *water R*. To each flask add 5 mL of *ferric ammonium sulfate solution R5*, mix and add dropwise and with swirling 2 mL of *nitric acid R* and 5 mL of *mercuric thiocyanate solution R*. Shake. Dilute the contents of each flask to 25.0 mL with *water R* and allow the solutions to stand in a water-bath at 20 °C for 15 min. Measure at 460 nm in a 2 cm cell the absorbance (*2.2.25*) of solution A using solution B as the compensation liquid, and the absorbance of solution C using the solution obtained with 10 mL of *water R* as the compensation liquid. The absorbance of solution A is not greater than that of solution C.

Determination of total chlorine

Solution (a). To 10.0 mL of the test solution add 7.5 mL of *dilute sodium hydroxide solution R* and 0.125 g of *nickel-aluminium alloy R* and heat on a water-bath for 10 min. Allow to cool to room temperature, filter into a 25 mL volumetric flask and wash the filter with 3 quantities, each of 2 mL, of *ethanol (96 per cent) R* (a slight precipitate may form that disappears on acidification). Dilute the filtrate and washings to 25.0 mL with *water R*. This solution is used to prepare solution A.

Solution (b). In the same manner, prepare a similar solution replacing the test solution by a mixture of 5 mL of *ethanol (96 per cent) R* and 5 mL of *water R*. This solution is used to prepare solution B.

Solution (c). To 6.0 mL of *chloride standard solution (8 ppm Cl) R* add 4.0 mL of *water R*. This solution is used to prepare solution C.

In four 25 mL volumetric flasks, place separately 10 mL of solution (a), 10 mL of solution (b), 10 mL of solution (c) and 10 mL of *water R*. To each flask add 5 mL of *ferric ammonium sulfate solution R5*, mix and add dropwise and with swirling 2 mL of *nitric acid R* and 5 mL of *mercuric thiocyanate solution R*. Shake. Dilute the contents of each flask to 25.0 mL with *water R* and allow the solutions to stand in a water-bath at 20 °C for 15 min. Measure at 460 nm in a 2 cm cell the absorbance (*2.2.25*) of solution A using solution B as the compensation liquid, and the absorbance of solution C using the solution obtained with 10 mL of *water R* as the compensation liquid. The absorbance of solution A is not greater than that of solution C.

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with test C. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 2.0 per cent, determined on 1.00 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.250 g in 20 mL of *anhydrous acetic acid R*, heating to 50 °C if necessary. Cool. Using 0.05 mL of *naphtholbenzein solution R* as indicator, titrate with *0.1 M perchloric acid* until a green colour is obtained.

1 mL of *0.1 M perchloric acid* is equivalent to 14.41 mg of $C_7H_5NaO_2$.

01/2008:0190
corrected 6.0

SODIUM BROMIDE

Natrii bromidum

NaBr M_r 102.9
[7647-15-6]

DEFINITION

Content: 98.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, granular powder or small, colourless, transparent or opaque crystals, slightly hygroscopic.

Solubility: freely soluble in water, soluble in alcohol.

IDENTIFICATION

A. It gives reaction (a) of bromides (*2.3.1*).

B. Solution S (see Tests) gives the reactions of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *bromothymol blue solution R1*. Not more than 0.5 mL of *0.01 M hydrochloric acid* or *0.01 M sodium hydroxide* is required to change the colour of the indicator.

Bromates. To 10 mL of solution S add 1 mL of *starch solution R*, 0.1 mL of a 100 g/L solution of *potassium iodide R* and 0.25 mL of *0.5 M sulfuric acid* and allow to stand protected from light for 5 min. No blue or violet colour develops.

Chlorides: maximum 0.6 per cent.

In a conical flask, dissolve 1.000 g in 20 mL of *dilute nitric acid R*. Add 5 mL of *strong hydrogen peroxide solution R* and heat on a water-bath until the solution is completely decolourised. Wash down the sides of the flask with a little *water R* and heat on a water-bath for 15 min. Allow to cool, dilute to 50 mL with *water R* and add 5.0 mL of *0.1 M silver nitrate* and 1 mL of *dibutyl phthalate R*. Shake and titrate with *0.1 M ammonium thiocyanate*, using 5 mL of *ferric ammonium sulfate solution R2* as indicator. Not more than 1.7 mL of *0.1 M silver nitrate* is used. Note the volume of *0.1 M silver nitrate* used (see Assay). Carry out a blank test.

Iodides. To 5 mL of solution S add 0.15 mL of *ferric chloride solution R1* and 2 mL of *methylene chloride R*. Shake and allow to separate. The lower layer is colourless (*2.2.2, Method I*).

Sulfates (*2.4.13*): maximum 100 ppm.

15 mL of solution S complies with the limit test for sulfates.

Iron (*2.4.9*): maximum 20 ppm.

5 mL of solution S diluted to 10 mL with *water R* complies with the limit test for iron.

Magnesium and alkaline-earth metals (*2.4.7*): maximum 200 ppm, calculated as Ca.

10.0 g complies with the limit test for magnesium and alkaline-earth metals. The volume of *0.01 M sodium edetate* used does not exceed 5.0 mL.

Heavy metals (*2.4.8*): maximum 10 ppm.

12 mL of solution S complies with limit test A. Prepare the standard using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 3.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

ASSAY

Dissolve 2.000 g in *water R* and dilute to 100.0 mL with the same solvent. To 10.0 mL of the solution add 50 mL of *water R*, 5 mL of *dilute nitric acid R*, 25.0 mL of *0.1 M silver nitrate* and 2 mL of *dibutyl phthalate R*. Shake. Titrate with *0.1 M ammonium thiocyanate*, using 2 mL of *ferric ammonium sulfate solution R2* as indicator and shaking vigorously towards the end-point.

1 mL of *0.1 M silver nitrate* is equivalent to 10.29 mg of NaBr.

Calculate the percentage content of NaBr from the expression:

$$a - 2.902\,b$$

a = percentage content of NaBr and NaCl obtained in the assay and calculated as NaBr,

b = percentage content of Cl in the test for chlorides.

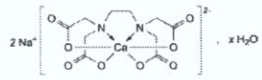
STORAGE

In an airtight container.

01/2008:0231

SODIUM CALCIUM EDETATE

Natrii calcii edetas



$C_{10}H_{12}CaN_2Na_2O_8{\cdot}xH_2O$ M_r 374.3 (anhydrous substance)
[62-33-9]

DEFINITION

Disodium [(ethylenedinitrilo)tetraacetato]calciate(2−).

Content: 98.0 per cent to 102.0 per cent (anhydrous substance).

It contains a variable amount of water of crystallisation.

CHARACTERS

Appearance: white or almost white, hygroscopic powder.

Solubility: freely soluble in water, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, C, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *sodium calcium edetate CRS*.

B. Dissolve 2 g in 10 mL of *water R*, add 6 mL of *lead nitrate solution R*, shake and add 3 mL of *potassium iodide solution R*. No yellow precipitate is formed. Make alkaline to *red litmus paper R* by the addition of *dilute ammonia R2* and add 3 mL of *ammonium oxalate solution R*. A white precipitate is formed.

C. Ignite. The residue gives reaction (b) of calcium (*2.3.1*).

D. Dissolve 0.5 g in 10 mL of *water R* and add 10 mL of *potassium pyroantimonate solution R*. A white, crystalline precipitate is formed. The formation of the precipitate is accelerated by rubbing the wall of the tube with a glass rod.

TESTS

Solution S. Dissolve 5.0 g in *water R* and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

pH (*2.2.3*): 6.5 to 8.0.

Dissolve 5.0 g in *carbon dioxide-free water R* and dilute to 25 mL with the same solvent.

Impurity A. Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*

Solvent mixture. Dissolve 10.0 g of *ferric sulfate pentahydrate R* in 20 mL of *0.5 M sulfuric acid* and add 780 mL of *water R*. Adjust to pH 2.0 with *1 M sodium hydroxide* and dilute to 1000 mL with *water R*.

Test solution. Dissolve 0.100 g of the substance to be examined in the solvent mixture and dilute to 25.0 mL with the solvent mixture.

Reference solution. Dissolve 40.0 mg of *nitrilotriacetic acid R* (impurity A) in the solvent mixture and dilute to 100.0 mL with the solvent mixture. To 1.0 mL of this solution add 0.1 mL of the test solution and dilute to 100.0 mL with the solvent mixture.

Column:

– *size*: *l* = 0.10 m, Ø = 4.6 mm;