Chem. Anal. (Warsaw), **50**, 47 (2005)

Coulometric Titration of Disulfides with Electrogenerated Chlorine

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Key words: coulometric titration, disulfides, electrogenerated chlorine

The coulometric titration of some disulfides with anodically generated chlorine using the biamperometric end-point detection is presented. Chlorine breakes the disulfide bond and a sulfonic acid is formed. The range of determination is 0.50–3.75 μmol for 2,2-dithiodiglycolic acid, 0.375–1.50 μmol for 3,3'-dithiodipropionic acid, 1.00–2.50 μmol for cystamine dihydrochloride and 0.50–2.75 μmol for L-cystine. The titrations were performed in solutions containing 0.5 mol L^{-1} H_2SO_4 and various amounts of NaCl. The error for all determinations is below 1%.

Przedstawiono kulometryczne miareczkowanie disiarczków anodowo generowanym chlorem z zastosowaniem biamperometrycznej detekcji punktu końcowego. W reakcji z chlorem następuje rozerwanie wiązania disiarczkowego i powstaje kwas sulfonowy. Zakres oznaczalności wynosi 0.50–3.75 μmoli dla kwasu 2,2'-ditiodiglikolowego, 0.375–1.50 μmola dla kwasu 3,3'-ditiodipropionowego, 1.00–2.50 μmoli dla dichlorowodorku cystaminy i 0.50–2.75 μmoli dla L-cystyny. Miareczkowania były prowadzone w roztworach zawierających 0.5 mol L^{-1} H_2SO_4 i różne ilości NaCl. Opracowana metoda umożliwia oznaczanie disiarczków z błędem poniżej 1%.

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Coulometric titration with anodically generated chlorine has been known for about 50 years [1].

This method was previously applied for determination of thiols and thiones (*e.g.* N-acetylcysteine [2], 2-amino-6-mercaptopurine, 2-thiouracil [3]), thiophosforus compounds (*e.g.* methamidophos, iso-malation [4]) and many other organic compounds (*e.g.* nizatidine [5], folic acid [6], hydrocortisone [6]).

In this paper application of titration with electrogenerated chlorine using the biamperometric end-point detection for determination of 2,2-dithiodiglycolic acid, 3,3'-dithiodipropionic acid, cystamine dihydrochloride and L-cystine is presented.

The possibility of determination of disulfides in this way was previously not described in literature.

Disulfides have found applications in various fields of technology. They are used as corrosion inhibitors, components of photographic emulsions, ink-jet recording and lithographic plate materials. 2,2'-Dithiodiglycolic acid is also used as a component of hair wave-setting preparations. L-cystine is an important compound of human skin and hair. It functions as an antioxidant, aids in protein synthesis and presents cellular change.

2,2-Dithiodiglycolic acid was determined iodometrically after its reduction to thioglycolic acid [8,9,10] with visual end-point detection. This compound was also titrated using mixture composed of potassium perborate and potassium bromide [11]. Potentiometric titration with potassium hydroxide using glass and silver–silver chloride electrodes was also developed [12].

3,3'-Dithiodipropionic acid was previously determined potentiometrically after its reduction to the corresponding thiol using silver nitrate as titrant and a sulfide-selective indicator electrode [13,14].

Cystamine dihydrochloride was determined coulometrically with electrogenerated bromine [15]. Potentiometric titration of this compound after its reduction using silver nitrate as titrant and sulfide-selective indicator electrode was also elaborated [14].

L-cystine was determined by coulometric titration with electrogenerated bromine [16,17,18] and with silver(I) after its reduction to cysteine [18]. Coulometric titration with the use of the iodine-azide reaction was also applied [19]. Several volumetric methods for determination of L-cystine were developed. The investigated compound was titrated using N-bromosuccinimide [20], bromine chloride [21] chloramine-T [22], perchloric acid [23].

The titrimetric procedure based on reaction L-cystine with alkaline potassium permanganate [24] in the presence of barium chloride was described. In all titrations visual end-point detection was applied. Determination of L-cystine using silver nitrate after its reduction to the L-cysteine was also presented [25]. This compound was titrated amperometrically using potassium periodide [26,27].

EXPERIMENTAL

Apparatus

Measurements were performed using an universal coulometric analyser of type OH–404 „Radelkis" (Hungary). An electrolysis cell with two platinum electrodes of 5 cm^2 area, working in a generating circuit and a double electrode OH–9381 working in a biamperometric indicator circuit were used. The cathode and anode compartments of the electrolysis cell were separated by a sintered glass G–4 disk.

Reagents and solutions

Doubly distilled water in glass apparatus and the following reagents were used: sulfuric acid, sodium chloride, acetonitrile (POCH Gliwice).

The following compounds were used: 2,2-dithiodiglycolic acid (99% – Sigma), 3,3'-dithiodipropionic acid (99% – Aldrich), cystamine dihydrochloride (98% – Aldrich) L-cystine (99% – Fluka).

Solutions of determined compounds in a concentration of 5×10^{-3} mol L^{-1} were freshly prepared by dissolving weighed amounts of reagents in acetonitrile solution.

The supporting electrolyte was an aqueous solution composed of 0.5 mol L^{-1} sulfuric acid and sodium chloride of concentration 0.1 mol L^{-1} for 2,2-dithiodiglycolic acid and 3,3'-dithiodipropionic acid, 0.2 mol L^{-1} for cystamine dihydrochloride or 2.0 mol L^{-1} for L-cystine.

Procedures

A sample solution containing the tested compound was added to the supporting electrolyte (25 mL) placed in the anodic compartment of the electrolysis cell. The polarization voltage 150 mV was applied to the indicator system of electrodes. After switching on the mechanical stirrer, a stabilized current was passed through the solution. The current in the generating circuit was adjusted according to the amount of the determined compound so as to maintain the titration time at several min. The charge (Q) was registered after completing the titration of a compound up to an indicator current of 0.04 μA. The excess of chlorine that appeared in the solution after the reaction was finished, was responsible for the end-point detection. In the same way the solution was titrated in the absence of the tested compound (blank experiment) and a charge Q_o (7.0–10.0 mC) was noted.

The contents n [μmol] of a compound in the tested sample was calculated according to the Faraday's law.

$$n = \frac{\Delta Q}{zF} \cdot 10^3$$

where:

$$\Delta Q = Q - Q_o \text{ [mC]};$$

Q_o is the charge corresponding to a blank titration; z is the number of electrons transferred per mole of an oxidized substance, z = 10; F is the Faraday constant (96 485 C mol^{-1}).

RESULTS AND DISCUSSIONS

In solutions containing hydrogen and chloride ions at high concentrations, oxidation of platinum (material of electrode) may occcur. If concentration of hydrogen and chloride ions is too low then water may be oxidized. In both cases current efficiency is lower than 100% and the results are not correct. Concentration of hydrogen and chlorine ions in reaction solution depends on rate of reaction between chlorine and investigated compound and should be chosen experimentally [28].

Based on a survey of the literature we performed measurements in various reaction solutions containing hydrochloride acid or sulfuric acid and sodium chloride at different concentrations (Tab. 1).

Table 1. The results of the determination of disulfides at different supporting electrolytes

Compound	Supporting electrolyte	z*
2,2'-Dithiodiglycolic acid	1 mol L^{-1} HCl	9.08
	0.25 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	9.75
	0.5 mol L^{-1} H_2SO_4 0.1 mol L^{-1} NaCl	9.84
	0.5 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	9.94
	0.5 mol L^{-1} H_2SO_4 0.4 mol L^{-1} NaCl	9.76
3,3'-Dithiodipropionic acid	1 mol L^{-1} HCl	9.74
	0.25 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	10.15
	0.5 mol L^{-1} H_2SO_4 0.1 mol L^{-1} NaCl	10.04
	0.5 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	10.15
	0.5 mol L^{-1} H_2SO_4 0.4 mol L^{-1} NaCl	10.11
Cystamine dihydrochloride	1 mol L^{-1} HCl	10.17
	0.25 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	9.75
	0.5 mol L^{-1} H_2SO_4 0.1 mol L^{-1} NaCl	10.19
	0.5 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	10.06
	0.5 mol L^{-1} H_2SO_4 0.4 mol L^{-1} NaCl	9.80

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Table 1 (Continuation)

L-Cystine	1 mol L^{-1} HCl	10.11
	0.25 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	9.81
	0.5 mol L^{-1} H_2SO_4 0.1 mol L^{-1} NaCl	10.22
	0.5 mol L^{-1} H_2SO_4 0.2 mol L^{-1} NaCl	10.17
	0.5 mol L^{-1} H_2SO_4 0.4 mol L^{-1} NaCl	10.11
	0.5 mol L^{-1} H_2SO_4 2 mol L^{-1} NaCl	10.02

* Number of electrons transferred per mole of determined compound.

The results of the measurements given in Table 1 show that optimum determination conditions are: 0.5 mol L^{-1} H_2SO_4 and 0.1 mol L^{-1} NaCl for 2,2-dithiodiglycolic acid and 3,3'-dithiodipropionic acid, 0.5 mol L^{-1} H_2SO_4 and 0.2 mol L^{-1} NaCl for cystamine dihydrochloride and 0.5 mol L^{-1} H_2SO_4 and 2.0 mol L^{-1} NaCl for L-cystine. These conditions guaranteed the accurate and reproducible results, constancy of z value and small RSD values.

The use of the biamperometric end-point detection gave correct and reproducible results of determination in the range of 0.50–3.75 μmol for 2,2-dithiodiglycolic acid, 0.375–1.50 μmol for 3,3'-dithiodipropionic acid, 1.00–2.50 μmol for cystamine dihydrochloride and 0.50–2.75 μmol for L-cystine (Tab. 2). In titration of larger or smaller amounts of the studied compounds than these given in Table 2, the error increased above 1%.

Table 2. The results of the determination of disulfides; n = 6

Compound	Taken μmol	Found $\bar{x} \pm t_{0.95} \cdot \frac{s}{\sqrt{n}}$ μmol	RSD %	Current mA
2,2'-Ditiodiglycolic acid	0.5000	0.4963 ± 0.0003	0.05	2
	1.000	0.9923 ± 0.0002	0.02	5
	2.500	2.497 ± 0.0005	0.05	5
	3.750	3.786 ± 0.0004	0.04	7.5
3,3'-Dithiodipropionic acid	0.3750	0.3718 ± 0.0002	0.05	2
	0.5000	0.5014 ± 0.0002	0.04	2
	1.000	1.004 ± 0.0003	0.03	5
	1.500	1.512 ± 0.0003	0.03	5

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Table 2 (Continuation)

Cystamine dihydrochloride	1.000	1.006 ± 0.0005	0.05	5
	2.500	2.477 ± 0.0003	0.01	5
L-cystine	0.1250	0.1243 ± 0.0002	0.18	1
	0.2500	0.2509 ± 0.0003	0.12	2
	0.5000	0.5014 ± 0.0004	0.08	2
	1.000	1.008 ± 0.0004	0.04	5
	2.500	2.497 ± 0.0004	0.01	5

In the case of coulometric titrations described previously in literature [2,3] in which a visual end-point detection was used the error and RSD amounted to several percent.

Reaction between determined dislufide and chlorine can be presented schematically by the equation:

$$RS{-}SR + 5Cl_2 + 6H_2O \rightarrow 2RSO_3H + 10HCl$$

where:

R = $-CH_2COOH$ for dithiodiglycolic acid
$-CH_2CH_2COOH$ for dithiodipropionic acid
$-CH_2CH_2NH_2\cdot HCl$ for cystamine dihydrochloride
$-CH_2CH(NH_2)COOH$ for L-cystine

The presented coulometric titration is the only coulometric method available for determination of 2,2-dithiodiglycolic acid and 3,3’-dithiodipropionic acid.

The new method of coulometric determination of disulfides is characterised by a short analysis time, high precision and accuracy, simplicity and the use of commonly available reagents. The coulometric method is partly automated and as an absolute method requires no standard solutions.

We have tried to apply coulometric titration with electrogenerated chlorine for determination of lipoic acid, which contains a disulfide bond in the pentacyclic ring, the reaction between lipoic acid and chlorine proceeds slowly and incompletely.

Since the rate of the reaction was relatively low, in order to titrate the entire amount of lipoic acid we applied the delay time 30 s. That made it possible to switch on the current in the generating circuit again, when in 30 s, as a result of the reaction, the indicator-current decreased below the assumed value of 0.04 µA, at which the current in the generating circuit was stopped automatically. Based on the results obtained for these measurements, despite the delay time, the error was about 10%. In conclusion, we did not find conditions in which reaction of lipoic acid with chlorine could proceed fast and stoichiometrically.

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Received September 2004
Accepted December 2005