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Purity assay of sodium mercaptododecaborate by high-performance liquid chromatography

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ABSTRACT

A simple high-performance liquid chromatographic (HPLC) method for purity monitoring and determination of $[B_{12}H_{11}SH]^{2-}$ (**I**) and its oxidation impurities $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ (**II**) and $[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$ (**III**) is presented. The method is based on the use of the hydroxyethylmethacrylate sorbent Separon HEMA-BIO 300 and 100 m*M* sodium perchlorate in 0.01 *M* phosphate buffer as mobile phase. Common HPLC equipment with direct spectrophotometric detection in the range 200–210 nm was used throughout. The minimal detectable amounts of the sodium salts of anions **I**, **II** and **III** at 204 nm were $8.6 \cdot 10^{-8}$, $8.8 \cdot 10^{-9}$ and $6.4 \cdot 10^{-8}$ g, respectively. The application of the method to the study of the stability of the sodium salt of **I** in solution revealed a strong positive effect of trace amounts of Cu^{+} in enhancing the $Na_2B_{12}H_{11}SH$ oxidation rate.

INTRODUCTION

The disodium salt of the *closo*-undecahydro-1-mercaptododecaborate anion, $[B_{12}H_{11}SH]^{2-}$ (**I**) (Fig. 1), is the most widely used agent in boron neutron capture therapy (BNCT) of brain tumours [1].

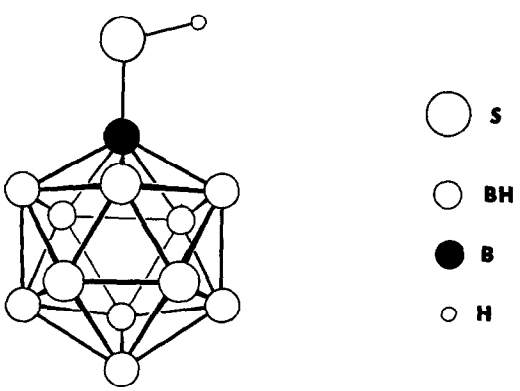

Fig. 1. Framework of the *closo*-$[B_{12}H_{11}SH]^{2-}$ anion.

BNCT is based on the selective accumulation of a boron compound in the malignant tissue, followed by subsequent destruction of the tumour cells by α-particles produced from the nuclear reaction of the ^{10}B nuclei contained in the isotopically enriched $[^{10}B_{12}H_{11}SH]^{2-}$ anion with thermal neutrons.

The known syntheses of the sodium salt of anion **I** proceed via several steps [2,3] and the final product can contain a wide range of impurities, as do the most important precursors $[(C_2H_5)_3NH]_2B_{12}H_{12}$ and $[(CH_3)_4N]_2B_{12}H_{11}SH$ [2]. The crystallinity of the final and intermediate products does not seem to be a valid indications of purity, as seemingly pure crystals have often been found to be mixtures [4]. When the intermediate product, *closo*-$[(C_2H_5)_3NH]_2B_{12}H_{12}$, is not sufficiently pure, some smaller cage *closo*-borate impurities and $[B_{12}H_{12}]^{2-}$ anion derivatives may be transferred to the final product.

The mercapto group of the sodium salt of **I** is sensitive to oxidation, yielding compounds of higher toxicity, sodium salts of anions **II** and **III** being

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the main oxidation products [4–8]. Efficient quantitative monitoring of the oxidation products during both the transformation of mercaptododecaborate to the drug form and its storage is therefore necessary.

The physical and chemical properties of the anion **I** and other *closo*-hydroborate impurities are very similar. The sodium salts are hygroscopic and highly soluble in water. The main factors governing the solution behaviour of this class of compounds are derived from the properties of relatively highly charged symmetrical boron cages. Consequently, these salts behave as very strong inorganic electrolytes, simultaneously exhibiting hydrophobic properties comparable to those of organic aromatic molecules, which causes the mixtures of such compounds to be difficult to separate.

Thin-layer chromatography [4] and capillary isotachophoretic methods [6,7] have been developed to determine the purity of the sodium salt of anion **I**, but the resolution of both methods is insufficient for all contaminants.

Recently, a paper dealing with the preparation of some oxidation products of the caesium salt of **I** was published [8] that included a short description of an HPLC method based on ion-pair chromatography on octadecyl silica using UV detection at 254 nm for determining both the oxidation impurities and the parent compound. We have recently reported the influence of separation conditions on the separation of some *closo*-$[B_{12}H_{12}]^{2-}$ derivatives on differently surface-modified Separon HEMA hydroxyethylmethacrylate sorbents [9], and in this study we have tried to extend the scope of the method to the separation of the anion **I** and its oxidation impurities, anions **II** and **III**.

EXPERIMENTAL

Columns

A broad range of cartridge glass columns (150 × 3.3 mm I.D.) packed with Separon HEMA hydroxyethylmethacrylate supports were provided by Tessek (Prague, Czechoslovakia). The columns were packed with low-capacity (0.03–0.1 mequiv./g) sorbents for ion-exchange chromatography or ion-exclusion chromatography [Separon HEMA-S 1000 Q-L (quarternary ammonium groups, 10 and 12 μm), Separon HEMA-S 1000 DEAE (diethylaminoethyl groups, 12 μm) and Separon HEMA-BIO 1000 CM (carboxy groups, 7 μm)], and with supports for hydrophobic interaction chromatography or the separation of biomolecules (Separon HEMA-S 1000, 10 and 12 μm; Separon HEMA-BIO 300, lot 3401, 12 and 15 μM, lot 1311, 10 μm; and Separon HEMA-BIO 1000, 10 μm).

Eluents

Deionized water produced with a Milli-Q apparatus (Millipore) was used throughout. All chemicals were of analytical-reagent grade [Lachema (Brno, Czechoslovakia) and Laborchemie (Apolda, Germany)]. The eluents were prepared by dissolving the calculated amount of electrolyte either in water or in 0.01 *M* phosphate buffer with the pH adjusted with sodium hydroxide solution. The eluents were filtered before use through a 0.45-μm filter and degassed under vacuum.

Apparatus

A simple isocratic HPLC system was used, consisting of a pulseless dual-piston high-pressure VCR 40 pump and a six-port sampling valve K 1 with 20- or 50-μl loops (Development Workshops of the Czechoslovak Academy of Sciences, Prague, Czechoslovakia), an LCD 2040 variable-wavelength (190–360 nm) UV spectrophotometric detector (Laboratory Instruments, Prague, Czechoslovakia), a PKS-1 column holder (Tessek) equipped with a heating glass jacket with circulating water from a thermostated bath, a Servogor 2s line recorder (Brown Boveri, Germany) and a CI 100 integrator (Laboratory Instruments).

A Pye Unicam system consisting of a PU 4010 pulseless dual-piston pump, PU 4031 oven, PU 4700 autoinjector with a 20-μl sample loop, a PU 4021 diode-array UV detector and a PU 4850 computer with PU Chromascan software routines was used for optimization of the spectrophotometric detection mode.

Sample preparation

The free acid and sodium and tetramethylammonium salts of anion **I** were prepared in the Institute of Inorganic Chemistry, Czechoslovak Academy of Sciences, by a modified published procedure [2,3].

The tetramethylammonium salts of anion **II** was prepared by the oxidation of an aqueous solution of

the free acid of **I** by oxygen. The oxidation course was monitored by the HPLC method under discussion and stopped at the moment when the peak of **I** had disappeared and the solution contained the maximum amount of anion **II** together with a smaller amount of anion **III**. The pure tetramethylammonium salt was obtained by adding 10% tetramethylammonium hydroxide at pH 8.5–9 and a five recrystallization from a weakly basic aqueous solution. The tetramethylammonium salt of **III** was prepared by oxidation of the free acid of **I** by hydrogen peroxide and threefold recrystallization of product resulting from the precipitation with 10% aqueous tetramethylammonium hydroxide from a weakly basic aqueous solution. The purity of the products was monitored by HPLC. Individual products were identified *via* ^{1}H and ^{11}B NMR spectroscopy by comparing their NMR chemical shifts with published data [2].

Solid substances used in the preparation of standard solutions were dried *in vacuo* over P_2O_5 at 50°C.

Free acids or sufficiently water-soluble salts of the *closo*-$[B_{12}H_{12}]^{2-}$ derivatives, *e.g.*, salts with Li^+, Na^+, K^+, Rb^+, Cs^+, NH^+_4, $N(CH_3)^+_4$ counter cations, were directly injected as aqueous 0.05–10 μmol/ml solutions. Sparingly soluble compounds, *e.g.*, salts with bulky cations, were converted into sufficiently soluble forms before injection using standard ion-exchange techniques or suitable metathetical methods [10]. Before injection all samples were filtered through a 0.45-μm nylon microfilter (Tessek).

Data evaluation

ADSTAT statistical software (TriloByte, Prague, Czechoslovakia) was used for data evaluation and regression analysis.

RESULTS

As in the previous study [9], we employed a wide range of both types of hydroxyethylmethacrylate sorbents modified for ion-exchange chromatography and unmodified for hydrophobic interaction chromatography to try to effect a reasonable separation of anion **I** and its oxidation impurities. On all types of materials, the dependence of the capacity factor (k') on the mobile phase (aqueous $NaClO_4$) ionic strength, pH and acetonitrile content and on the separation temperature in the range 20–60°C was studied. As a result, the behaviour of anion **I** was established as being analogous to that of other monosubstituted *closo*-$[B_{12}H_{12}]^{2-}$ derivatives. On all materials used, the k' values for anion **I** follow well the order of monosubstituted derivatives (see Fig. 2, for example), lying between those of *closo*-$[B_{12}H_{12}]^{2-}$ and *closo*-$[B_{12}H_{12}Cl]^{2-}$. The retention on unmodified materials increases with increasing concentration of $NaClO_4$ in the mobile phase up to 0.1 *M* following a slight decrease at higher concentrations. Therefore, such chromatographic behaviour can be attributed to the hydrophobic interaction of *closo*-hydroborate anions with hydrophobic sites of the hydroxyethylmethacrylate polymer [9]. With materials for ion-exchange chromatography, ion-exchange interaction

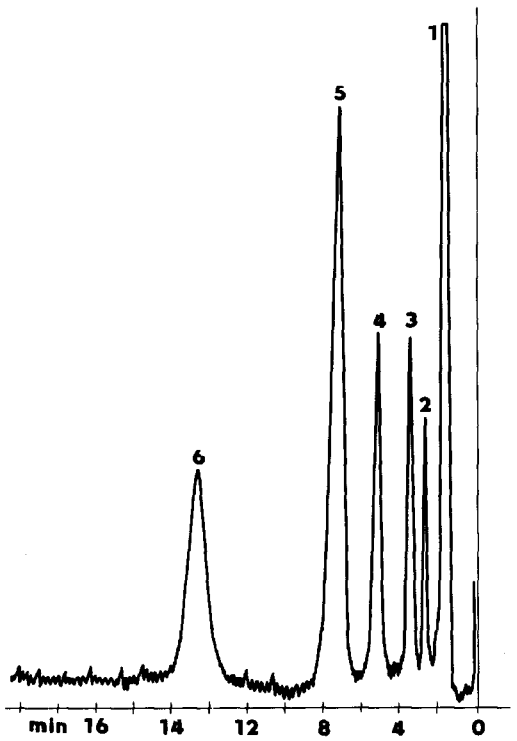

Fig. 2. Example of the separation of the unsubstituted *closo*-$[B_{12}H_{12}]^{2-}$ anion and some of its monosubstituted derivatives, including the *closo*-$[B_{12}H_{11}SH]^{2-}$ anion. Column, Separon HEMA-BIO 300 (12 μm); eluent, 0.1 *M* $NaClO_4$ in 0.01 *M* phosphate buffer (pH 8.5); flow-rate, 0.5 ml/min; detection, UV at 205 nm; temperature of separation, 40°C. Peaks: 1 = $[B_{12}H_{11}OH]^{2-}$; 2 = $[B_{12}H_{12}]^{2-}$; 3 = $[B_{12}H_{11}SH]^{2-}$; 4 = $[B_{12}H_{11}Cl]^{2-}$; 5 = $[B_{12}H_{11}Br]^{2-}$; 6 = $[B_{12}H_{11}I]^{2-}$.

makes the separation mechnism more complex, causing some trailing of the peaks of anion **I**.

Unfortunately, the oxidation products **II** and **III** with molecular structures based on two *closo*-$[B_{12}H_{12}]^{2-}$ moieties linked by sulphur bridges [3,5] did not follow the typical chromatographic behaviour of the uncoupled *closo*-hydroborate anion derivatives mentioned above. As a result, substantial changes in the selectivity of anions **II** and **III** on individual materials were observed, the most significant being those in the elution order of both oxidation impurities and anion **I**. On most of the materials used, the k' values of the anions **II** and **III** were smaller than that of the anion **I**, causing a poor resolution. Such chromatographic behaviour of impurities cannot be explained on the basis of a simple hydrophobic interaction model as for the corresponding parent compounds. Owing to these difficulties we considered only the practical aspects of the separation study. Of all the materials used, only Separon HEMA-BIO 300, lot 3401, 12 and 15 μm sorbents allowed a reasonable separation of anion **I** and the two well known oxidation impurities **II** and **III** along with at least three other unknown contaminants which were undoubtedly formed by subsequent oxidation reactions of anions **II** and **III**. One of two such additional peaks (compounds **IV** and **V**) in Fig. 3, can be probably ascribed to the recently reported [8] sulphinylsulphone $[B_{12}H_{11}SO\text{-}SO_2B_{12}H_{11}]^{4-}$.

The best separation conditions for a routine purity assay of anion **I** arising from optimization proce-

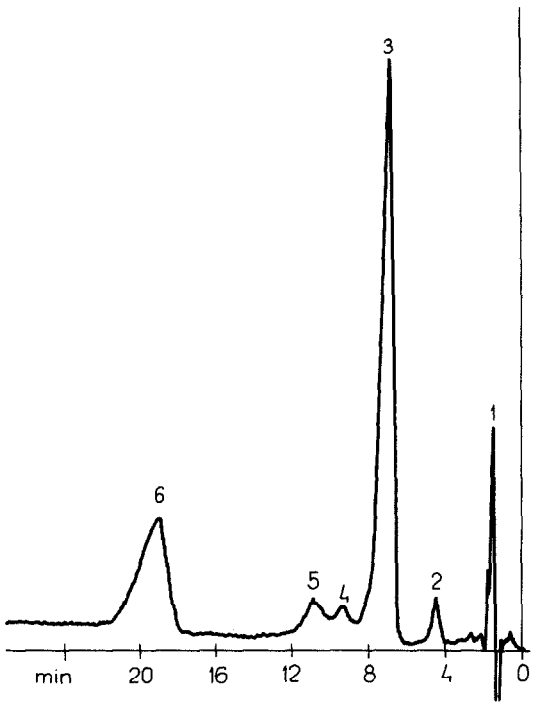

Fig. 3. Separation of highly oxidized sample of $Na_2B_{12}H_{11}SH$ in distilled water after an 8-day air exposure. Initial concentration, 5.7 μmol/ml. Column, Separon HEMA-BIO 300 (12 μm); eluent, 0.1 *M* $NaClO_4$ in 0.01 *M* phosphate buffer (pH 8.5); flow-rate, 0.5 ml/min; detection, UV at 204 nm; temperature of separation, 25°C; injection volume, 50 μl. Peaks: 1 = unknown; 2 = $[B_{12}H_{11}SH]^{2-}$ (**I**); 3 = $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ (**II**); 4,5 = unknown hydroborate impurities (**IV** and **V**); 6 = $[B_{12}H_{11}S(O)\text{-}SB_{12}H_{11}]^{4-}$ (**III**).

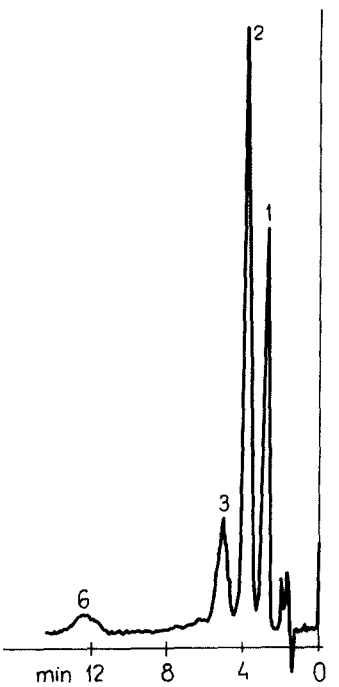

Fig. 4. Separation of a sample of an aqueous solution of the drug form (containing 8% of sodium salt of anion **II**) of $Na_2B_{12}H_{11}SH$ (concentration 1.14 μmol/ml, diluted for analysis) in Milli-Q-purified water after 8 days of air exposure. Temperature, 40 °C; other separation conditions as in Fig. 3. Peaks: 1 = $[B_{12}H_{12}]^{2-}$ (internal standard); 2 = $[B_{12}H_{11}SH]^{2-}$ (**I**); 3 = $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ (**II**); 6 = $[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$ (**III**).

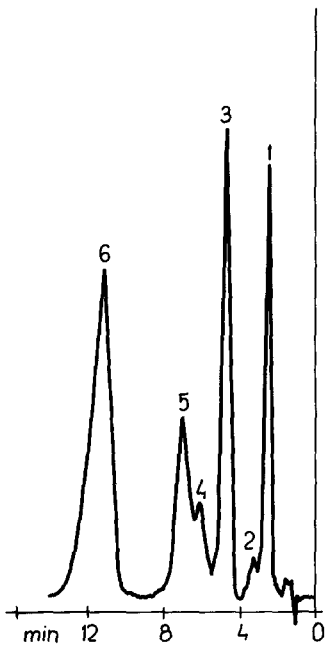

Fig. 5. Separation of a sample of an aqueous solution of the drug form (containing 8% of the sodium salt of anion II) of $Na_2B_{12}H_{11}SH$ (concentration 1.14 μmol/ml) in Milli-Q-purified water after 5 days of air exposure in the presence of a trace amount of Cu^+ (130 μg/l). Chromatographic conditions as in Fig. 4. Peaks: 1 = $[B_{12}H_{12}]^{2-}$ (internal standard); 2 = unknown impurity; 3 = $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ (**II**); 4,5 = unknown hydroborate impurities (**IV** and **V**); 6 = $[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$ (**III**).

dures are shown in Figs. 3–5. Separation at ambient temperature 25°C (Fig. 3) can be recommended for samples with a high degree of oxidation of anion **I**, giving a better resolution of anions **II, IV** and **V** (compare with the separation of another highly oxidized sample in Fig. 5 at 40°C). The procedure at 25°C can also be employed for the purity assay of $[(C_2H_5)_3NH]_2B_{12}H_{12}$, which is a significant intermediate product in the synthesis (Fig. 6). It is strongly recommended that the analysis of this compound, prepared as described [11], is performed before the sulphydrylation step of *closo*-$[B_{12}H_{12}]^{2-}$ [2,3] in order to avoid either transfer of *closo*-hydroborate impurities to the final product or a decrease in the yield of **I**.

Additional desirable analyses can be performed by applying the above-mentioned type of sorbent using different eluent compositions and a separation temperature of 40°C (Fig. 7). Thus the $[B_{12}H_{11}SCSC_6H_4NCH_3]^-$ anion, an intermediate adduct of N-methylbenzothiazole-2-thione with the *closo*-$[B_{12}H_{12}]^{2-}$ anion formed in the sulphydrylation step [2] of the synthesis of **I** can be determined. However, this compound has never been found as an impurity in the usual samples of *closo*-$[B_{12}H_{11}SH]^{2-}$ used for biomedical applications.

The calculated k' values of all the compounds under discussion are summarized in Table I.

Detection and detection limits

The UV spectra of compounds **I, II** and **III** recorded during the chromatographic experiment at the peak maxima using a PU 4021 diode-array spectrometric detector are shown in Fig. 8. The spectra indicate that *closo*-$[B_{12}H_{11}SH]^{2-}$ exhibits a maximum at 204 nm and its oxidation impurities, **II** and **III**, at 204 and 207 nm, respectively. In the shorter (down 200 nm) and longer (up to 210) wavelength regions, a relatively large decrease in the absorbance can be observed, and the use of wavelengths outside the 200–210 nm range thus leads to a marked decrease in the direct UV detection sensitivity.

With the use of the LCD 2040 UV spectrophotometric detector at 204 nm the minimum detectable amounts (defined as the amount of solute that caus-

TABLE I

CAPACITY FACTORS k' OF THE *closo*-HYDROBORATE ANION UNDER DISCUSSION

Chromatographic conditions: column, cartridge glass column, Separon HEMA-BIO 300 (12 μm); eluent, 0.1 *M* $NaClO_4$ in 0.01 *M* phosphate buffer (pH 8.5); detection, UV at 204 nm; flow-rate, 0.5 ml/min; temperature, 25 or 40°C.

Anion	k'	
	25°C	40°C
$[B_{10}H_{10}]^{2-}$	0.33	
$[B_{12}H_{12}]^{2-}$	1.66	1.25
$[B_{12}H_{11}SH]^{2-}$	2.75	2.08
$[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$	4.6	3.2
IV	6.7	3.9
V	8.2	4.6
$[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$	15.2	8.7
$[B_{12}H_{11}SCSC_6H_4NCH_3]^-$		8.9[a]

[a] Eluent: 0.1 *M* $NaClO_4$ in acetonitrile–water (25:75).

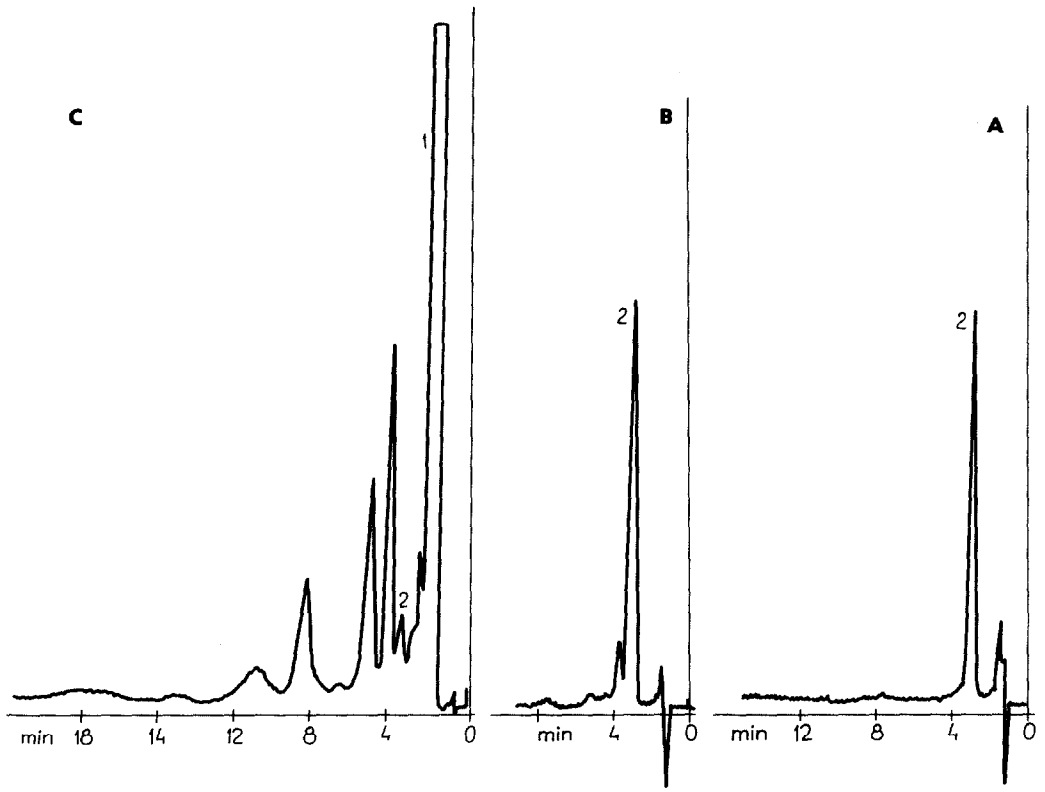

Fig. 6. Determination of impurities in samples of $[B_{12}H_{12}]^{2-}$ anion prepared as described [10]. (A) Pure anion $[B_{12}H_{12}]^{2-}$ after purification process; (B) crude product before purification) (C) mixture of hydroborate impurities isolated from the crude product. Chromatographic conditions as in Fig. 3. Peaks: 1 = $[B_{10}H_{10}]^{2-}$; 2 = $[B_{12}H_{12}]^{2-}$; other peaks, unknown hydroborate impurities.

es a detector signal of twice the noise intensity) were $8.6 \cdot 10^{-8}$, $8.8 \cdot 10^{-9}$ and $6.4 \cdot 10^{-8}$ g for the sodium salt of anion **I** and anions **II** and **III**, respectively.

Calibration

The calibration graphs for the anions **I–III** were measured using standard solutions of non-hygroscopic tetramethylammonium salts instead of highly hygroscopic sodium salts with variable water contents. The calibration graphs are shown in Fig. 9. The relationships between peak area and amount of the tetramethylammonium salts of anions **I, II** and **III** was linear up to concentrations of 50, 26 and 50 mg/ml, respectively. As no other peaks or baseline drift were observed, it was concluded that no oxidation of the compounds actually occurred.

Stability of anion I in aqueous solutions

Recent papers dealing with the isotachophoretic determination of anion **I** [7] and the preparation of its oxidation products [8] initiated studies of the oxidation processes involving $Cs_2B_{12}H_{11}SH$ in aqueous solutions exposed to air. Nevertheless, comparison of the experimentally determined estimates of the oxidation rates thus obtained indicates some discrepancies.

As we have found, dissolution of real analytical samples of the sodium salt of the anion **I** in different lots of distilled water in the course of analyses and the use of chemicals of different quality in the syntheses cause considerable fluctuations in the oxidation rates during the storage of aqueous samples (*e.g.*, compare Figs. 3 and 4). Therefore, a study of the influence of several factors, including metal impurities, on the stability of aqueous solutions of **I** was performed.

Additions of Fe^{2+}, Co^{2+}, Ni^{2+} and Cr^{3+} salts to the Milli-Q-purified water solutions of the sodium

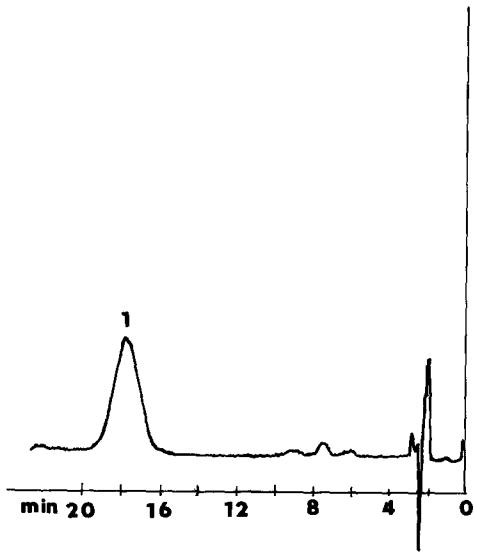

Fig. 7. determination of the $[B_{12}H_{11}SCSC_6H_4NCH_3]^-$ anion (peak 1), an intermediate adduct of N-methylbenzothiazole-2-thione with the *closo*-$[B_{12}H_{12}]^{2-}$ anion formed in the sulphydrylation step [2] of the synthesis of **I**. Temperature, 45°C; eluent, 0.1 *M* solution of $NaClO_4$ in acetonitrile–water (25:75).

salt of anion **I** (drug form containing 8% of sodium salt of **II**; Léčiva Měcholupy, Czechoslovakia) in amounts corresponding to ten times smaller molar concentrations than that of **I** caused a decrease in the concentration of anion **I** only at the beginning of a 10-day study, owing to the formation of a weakly dissociated salt. On the other hand, addition of Cu^+ ions at a comparatively low concentration affected the oxidation rate very strongly. This effect is exemplified in Figs. 5 and 10, showing that the presence of a trace amount of Cu^+ caused complete oxidation of anion **I** within a few days. Moreover, the replacement of Cu^+ with Cu^{2+} increased the oxidation rate within the initial 3 h of oxidation, which resulted in an increased content of anion **II** in the sample. However, the composition of the products after an 8-day period was identical with that in the presence of Cu^+, which seems to be consistent with the involvement of a Cu^+–Cu^{2+} equilibrium in the oxidation mechanism. Another experiment indicated that the addition of Fe^{3+} causes an equivalent part of anion **I** to be oxidized to generate a mixture of compound **III** with an unknown oxidation product **IV**. In agreement with earlier findings [4], the oxidation of $Na_2B_{12}H_{11}SH$ with hydrogen peroxide gave anion **III** directly, but we also identified two other peaks of unknown oxidation impurities (**IV** and **V**), in small amounts, in the corresponding reaction mixture.

The above-mentioned observations indicate that the oxidation rate can be affected by the presence of trace amounts of some transition metal ions and probably also by other substances present in the water used. Indeed, in samples of compounds of anion **I** dissolved in the commonly used distilled water (single distillation step), the disappearance of anion **I** was observed after 8–20 days (an example is shown in Fig. 3), depending on the initial concen-

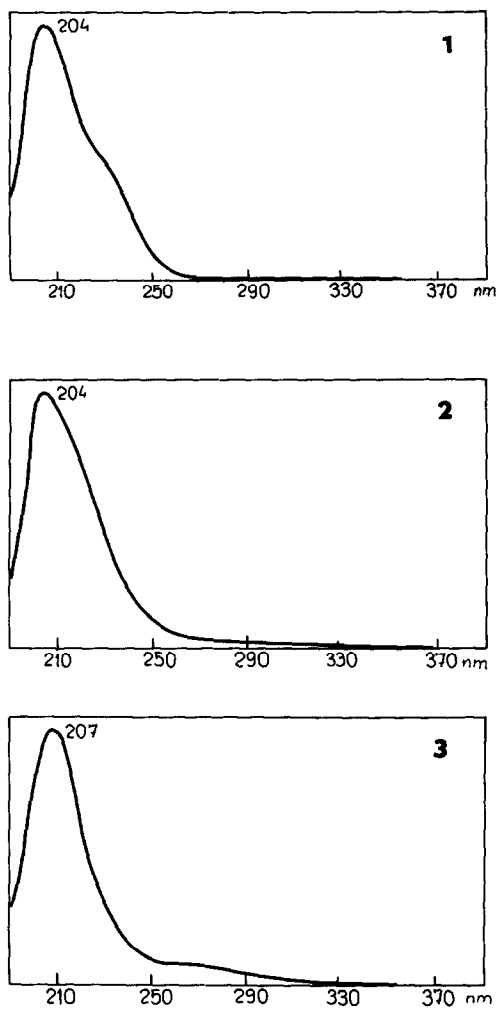

Fig. 8. Plots of UV spectra of anions **I**–**III**. 1 = $[B_{12}H_{11}SH]^{2-}$ **I**; 2 = $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ **II**; 3 = $[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$ **III**.

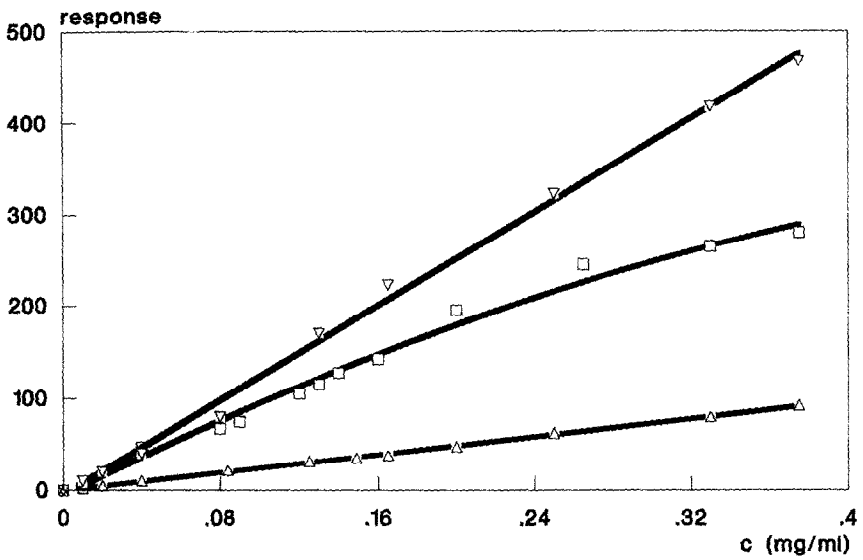

Fig. 9. Calibration graphs for tetramethylammonium salts of anions **I–III**. Chromatographic conditions as in Fig. 4; detection, UV at 204 nm; sensitivity, 0.16 a.u.f.s. Curves: △, $[B_{12}H_{11}SH]^{2-}$ **I**; □, $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ **II**; ▽, $[B_{12}H_{11}S(O)SB_{12}H_{11}]^{4-}$ **III**.

tration of **I** (0.1–5.46 μmol/ml). It was also found that the free acid of anion **I** exhibited lower and the tetramethylammonium salt higher stability than the sodium salt under comparable conditions.

In contrast, the stability of solutions of the sodium salt of **I** in Milli-Q-purified water was appreciably higher. Three standard solutions (0.65, 1.14 and 2.20 μmol/ml) of the drug form of $Na_2B_{12}H_{11}SH$ (containing 8% of the sodium salt of **II**) were used in this study. The samples were analysed at 24 h intervals over a period of 10 days. The first and third sample were also analysed after a 123-day exposure to air. At the end of the 10-day period, the concentration of anion **I** was found to be almost unchanged (Fig. 4), with only 2% (w/w) of the sodium salt of **III** being generated from the oxidation of the anion **II** present. After 123 days, a 28% and 31% decrease in the content of anion **I** and corresponding increases of 14 and 17% of **II** and 11 and 12% of the sodium salt ion **III** in the samples of initial concentrations 2.2 and 0.65 μmol/ml, respectively were found. At least three additional but unidentified oxidation impurities with k' values lower than that of anion **I**, which were not found in the most concentrated sample, could be detected in the most diluted sample.

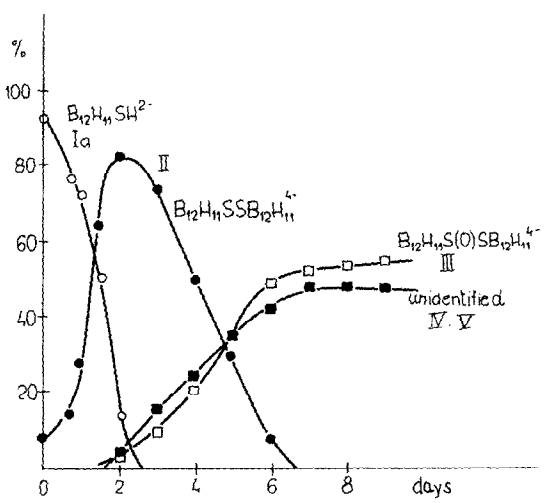

Fig. 10. Time course of the oxidation of the drug form of the sodium salt of anion **I** (1.14 μmol/ml) in aqueous solution (Milli-Q-purified water) in the presence of a trace amount of Cu^+ (130 μg/l). The curve represents the percentage of sodium salts of anions **I–III** and unknown hydroborate impurities **IV** and **V**.

CONCLUSIONS

A simple, rapid and quantitative method, based on HPLC on the hydroxyethylmethacrylate Separon HEMA-BIO 300 (12 μm) sorbent, was devel-

oped for purity assay and determination of $Na_2B_{12}H_{11}SH$. Optimum separation was obtained using 0.1 *M* aqueous $NaClO_4$ in 0.01 *M* phosphate buffer (pH 8.5) as the mobile phase and direct UV detection at 204 nm. The method can also be used for sensitive detection and determination of both of the most significant oxidation impurities, $Na_4B_{12}H_{11}SSB_{12}H_{11}$ and $Na_4B_{12}H_{11}S(O)SB_{12}H_{11}$.

The oxidation study also revealed an unexpectedly high resistance of aqueous $Na_2B_{12}H_{11}SH$ solutions oxidation when sufficiently pure water is used for sample preparation. An appreciable effect of trace amounts of Cu^+ on the increase in the oxidation rate was demonstrated.

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