528 Russian Chemical Bulletin, International Edition, Vol. 59, No. 3, pp. 528—532, March, 2010

Isothiocyanates as derivatization reagents in the determination of 1,1-dimethylhydrazine by gas chromatography coupled with mass spectrometry

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Alkyl isothiocyanates were proposed for the determination of 1,1-dimethylhydrazine (DMH) in the form of 4-alkyl-1,1-dimethylthiosemicarbazides by gas chromatography coupled with mass spectrometry (GC-MS). 4-Alkyl-1,1-dimethylthiosemicarbazides are selectively formed under mild conditions in the absence of catalysts. During the chromatography, these thiosemicarbazides are efficiently resolved from excess of alkyl isothiocyanates. A possibility of identification of DMH derivatives on the basis of the chromatographic retention parameters and fragmentation data under electron ionization conditions was demonstrated.

Key words: gas chromatography, mass spectrometry, 1,1-dimethylhydrazine, isothiocyanates, thiosemicarbazides.

1,1-Dimethylhydrazine (DMH) is a highly reactive compound widely used as a component of rocket propellant and in fine organic synthesis and semiconductor production. The reliable determination of DMH in the production and use, the evaluation of purity, and the determination of the impurity content are important tasks.

The existing chromatographic[1—3] and GC-MS methods[4—8] of analysis are based on the transformation of DMH into a more convenient analytical form using derivatization reagents and have several drawbacks: derivatization is carried out at elevated temperature; considerable excess of the reagent is used; acid-base catalysts capable of accelerating DMH decomposition are used; inefficient chromatographic resolution of a reagent—product pair; low informative content of mass spectra that do not allow DMH to be reliably identified.

Compounds with isocyanate and isothiocyanate groups are widely used in chromatographic analysis of amino compounds.[9] It is known that phenyl isocyanate (PIC) vigorously reacts with DMH to form a series of products, whose composition depends on the reactant ratio. For instance, to obtain the equimolar addition product capable of acting as an analytical form, it is necessary to use a threefold excess of DMH.[10] Because of this fact and formation of oligoureas, PIC cannot be used in the determination of DMH. Another substantial disadvantage of PIC is its non-selectivity to N- and O-nucleophiles, such as secondary amines, alcohols, thiols, carboxylic acids, hydroxylamines, and water, which impedes the determination. Phenyl isothiocyanate was used in the determination of ammonia and aliphatic amines by HPLC with UV detection.[11] Allyl isothiocyanate was used for the determination by pyrolytic GC-MS of the content of aromatic amines in the form of the corresponding aryl isothiocyanates obtained by the pyrolysis of *N*-allyl-*N*´-arylthioureas in the injector of the chromatograph.[12] Nevertheless, no isothiocyanates were proposed for DMH determination by gas chromatography or GC-MS.

The purposes of the present work are the study of the reactivity of DMH in reactions with alkyl isothiocyanates, selectivity of derivatization, formation of by-products. chromatographic behavior of derivatization products, regularities of their fragmentation in the electron ionization (EI) mode, and evaluation of a possibility of DMH identification from chromatographic and GC-MS data.

Experimental

1,1-Dimethylhydrazine (GOST V 17803-72) was additionally distilled from sodium hydroxide. Ethyl isothiocyanate and allyl isothiocyanate (Aldrich), dichloromethane (special purity grade, Kriokhrom, Russia), graphitized thermal carbon black (GTC, Sterling MT) with a specific surface of 7.6 $m^2 g^{-1}$, and sodium hydroxide (analytical purity grade, KhIMMED, Russia) were used.

Analysis was carried out on a JEOL JMS-D300 GC-MS instrument coupled with an HP-5890 chromatograph. A quartz capillary column 30 m × 0.53 mm with the DB-5 (J&W) stationary phase was used for chromatographic resolution; the chromatographic resolution conditions were as follows: injector temperature 300 °C, gas carrier (helium) rate 5 mL min^{-1}, flow ratio

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 517—520, March, 2010.

1 : 10. The parameters of the temperature-programmed regime of the column were the following: the 30 °C isotherm for 4 min and then programming to 300 °C (5 °C $\min^{-1}$) followed by the isothermal regime for 15 min. Chromatograms were detected by the total ionic current (TIC) with the energy of ionizing electrons 70 eV in the mass number range from 15 to 450 m/z. Identification was carried out by the library search program or on the basis of decoded mass spectra using the main regularities of electron ionization fragmentation of organic compounds.[13]

Mass spectrometric experiments with the surface-assisted laser desorption/ionization from the GTC surface were carried out on a Bruker Ultraflex II TOF mass spectrometer with a nitrogen laser (λ = 337 nm). The accelerating voltage was 25 kV. The spectra were obtained in the positive ion mode.

Derivatization of 1,1-dimethylhydrazine by isothiocyanates. Freshly distilled 1,1-dimethylhydrazine (75 μL) was added to a solution of isothiocyanate (150 μL) in dichloromethane (10 mL). The mixture was stored for 1 h at ~20 °C without air to the completion of the reaction. The reaction mixture (1 μL) was introduced into the chromatograph injector.

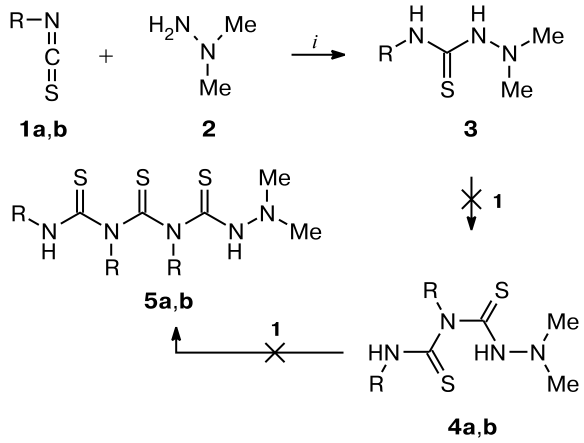
Preparation of samples to mass spectrometry with surface-assisted laser desorption/ionization. A suspension (10 μL) prepared from GTC (100 mg) in CH_2Cl_2 (1 mL) was deposited on the target surface for stainless steel samples. After DMH derivatization, an isothiocyanate excess was removed by the evaporation to dryness of the reaction mixture (0.5 mL), the residue was dissolved in CH_2Cl_2 (1 mL), and the resulting mixture (1 μL) was deposited on the GTC surface.

Results and Discussion

Alkyl isothiocyanates were chosen, because their alkyl substituents provide higher volatility compared to the aromatic analogs.[14] In addition, their reaction with DMH does not produce water or hydrogen halides, which are the unavoidable secondary reaction products of DMH with carbonyl compounds or carboxylic acid chlorides impeding the analysis.

It was found that the reaction of an excess of alkyl isothiocyanates **1** with DMH **2** occurred at ~20 °C in the absence of catalysts and afforded 4-alkyl-1,1-dimethylthiosemicarbazides **3** (Scheme 1).

Scheme 1



R = Et (**a**), All (**b**)

i. 20 °C, 1 h.

It was established by surface-assisted laser desorption/ionization that the reaction proceeded without the subsequent formation of by-products of the addition of thiosemicarbazides to an excess of alkyl isothiocyanates **4** and **5** characteristic of phenyl isocyanate.[10] The mass spectra of the obtained DMH derivatives contain peaks of ions with m/z = 148 $[M + H]^+$ of 4-ethyl-1,1-dimethylthiosemicarbazide (**3a**), as well as m/z = 160 $[M + H]^+$ and 182 $[M + Na]^+$ of 4-allyl-1,1-dimethylthiosemicarbazide (**3b**).

The chromatographic behavior is characterized by the efficient resolution of thiosemicarbazides and an excess of the derivatization reagents, which improves the quantitative determination of DMH due to the increased measurement accuracy of the peak areas of the DMH derivative, which is not overlapped with the chromatographic peak of the derivatization reagent (Fig. 1).

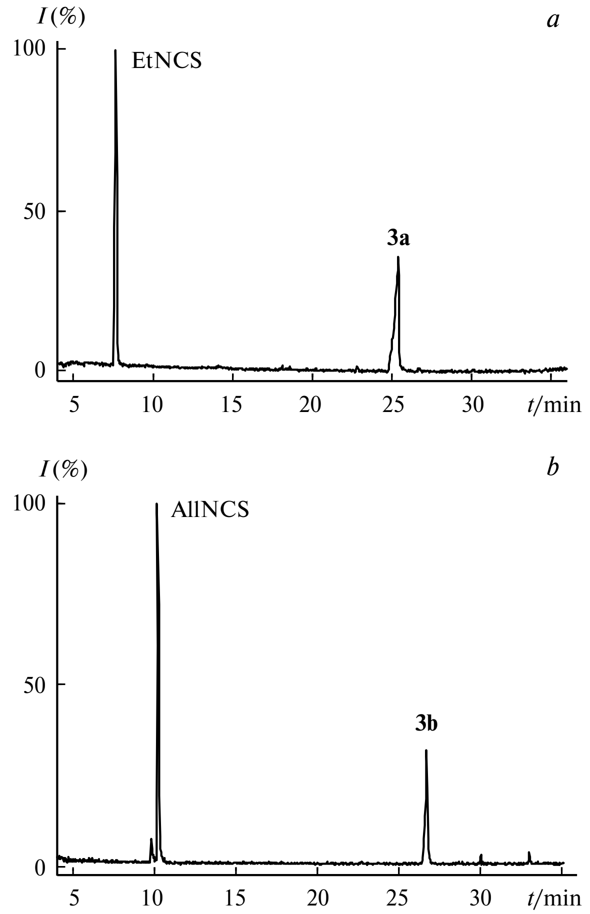


Fig. 1. The TIC chromatogram of mixtures of DMH with ethyl isothiocyanate (*a*) and allyl isothiocyanate (*b*).

The mass spectrum of derivative **3a** exhibits the high-intensity peak of the molecular ion with $m/z = 147$ and the pair of peaks of the characteristic ions with $m/z = 59$ and 60 presumably formed by the elimination of the DMH ion with $m/z = 60$ and its fragment with $m/z = 59$ (Fig. 2).

It is seen from the mass spectrum (see Fig. 2) that the molecular ion has the mass to charge ratio and isotopic pattern similar to those observed in the mass spectra of the organosilicon compounds.[15] Such compounds are widely used for the preparation of stationary phases for capillary columns. The coincidence of ion mass in the analyzed compound and in the background of the chromatographic column should be taken into account for analyses performed in the mass fragmentation mode by characteristic ions. For the DMH derivative under study, the molecular ion with the ions with $m/z = 59$ or 60 should be used. The retention time and the shape of the chromatographic peak should serve as additional criteria of identification (see Fig. 1).

In addition to the molecular ion peak with $m/z = 159$, the mass spectrum of derivative **3b** contains an additional pair of peaks of characteristic ions with $m/z = 115$ and 116 (Fig. 3).

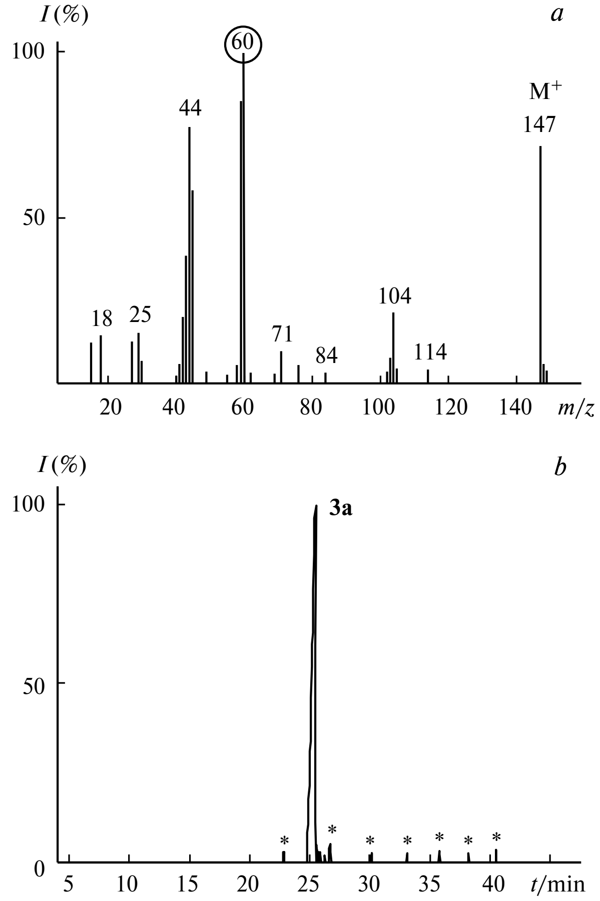
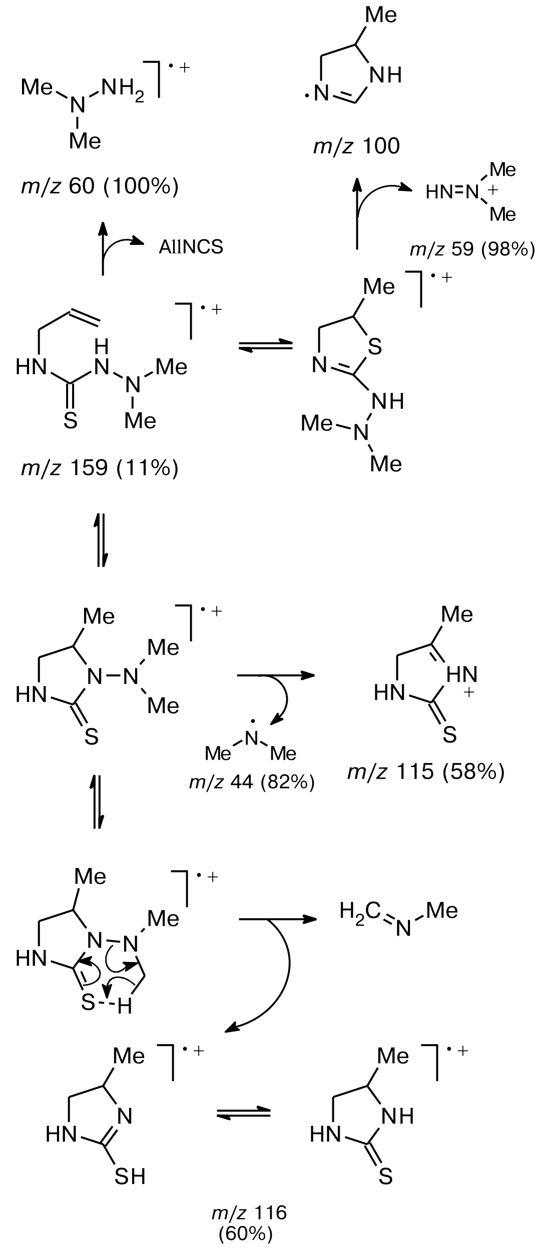


Fig. 2. (*a*) The EI mass spectrum of DMH derivative **3a** and (*b*) the mass chromatogram of **3a** by the ion with $m/z = 147$.

It is most likely that the formation of the additional pair of peaks of characteristic ions is due to the cyclization of molecular ion **3b** to the 2-imidazolidinethione ring followed by the elimination of the dimethylamino group and formaldehyde methylimine from the molecular ion. The proposed scheme of molecular ion fragmentation is presented in Scheme 2.

Scheme 2



The mass spectrum (see Fig. 3) shows that the molecular ion of **3b** is lowly intense. When working with microamounts, the determination sensitivity can be increased by the detection of the mass fragmentation pattern of this

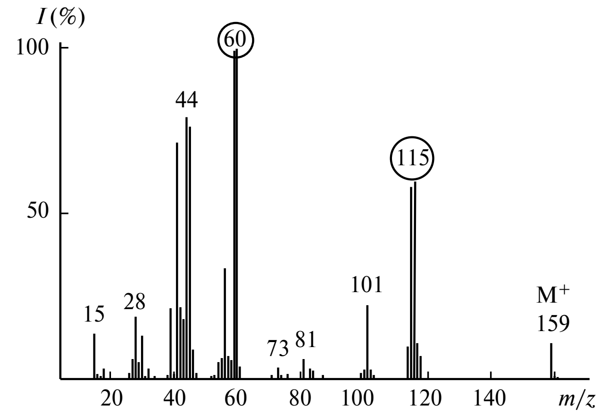


Fig. 3. The EI mass spectrum of DMH derivative **3b**.

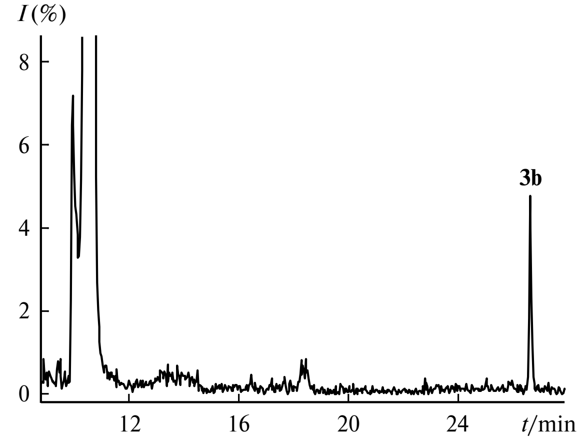


Fig. 4. The TIC chromatogram of the reaction mixture of DMH with allyl isothiocyanate.

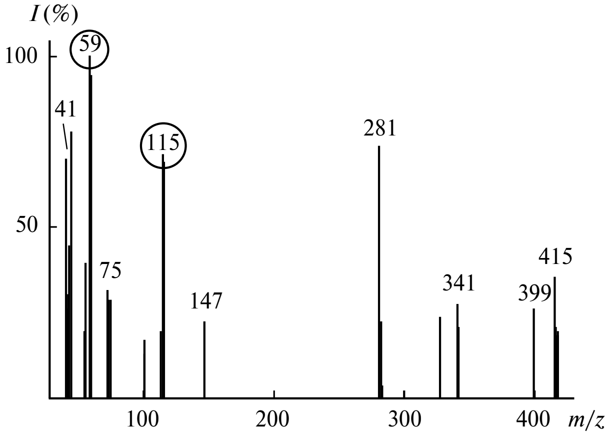


Fig. 5. The mass spectrum of the chromatographic peak of **3b**. The peaks of ions with m/z = 147, 281, 327, 399, and 415 correspond to the stationary liquid phase. The pairs of peaks of ions with m/z = 59, 60, and 115, 116 correspond to 4-allyl-1,1-dimethylthiosemicarbazide, while the peak of the molecular ion with m/z = 159 is absent.

Table 1. Ratio of peak areas (S) of the characteristic ions of compound **3b**

Entry	Ratio of peak areas (%)					
	S_{159}/S_{116}	S_{159}/S_{115}	S_{159}/S_{60}	S_{159}/S_{59}	S_{116}/S_{60}	S_{115}/S_{59}
1	15.2	15.4	10	9.7	64.1	62.7
2	19	19.2	11.1	11.4	58.2	59.7
3	16.1	15.1	9.1	10.2	56.4	67.6
R^a	16.8	16.6	10.1	10.4	59.6	63.3
RSD^b	11.8	13.8	10.0	8.4	6.8	6.3

[a] Average value.

[b] Relative standard deviation.

DMH derivative using other characteristic ions with m/z = 59 and/or 60 and 115 and/or 116 with a higher intensity. The retention time or retention indices should serve as an additional criterion of identification for this variant of determination.

The ratios of the peak areas of the characteristic ions recommended for DMH identification were obtained on the basis of the mass spectra of **3b** of different intensity (Table 1).

The presence in the mass spectra of two pairs of highly intensive characteristic ions of compound **3b** makes it possible to identify the DMH derivative even when the molecular ion peak is absent and the peaks of ions of the stationary phase are present (Figs 4 and 5).

To conclude, the reaction of an excess of alkyl isothiocyanates with DMH selectively affords 4-alkyl-1,1-dimethylthiosemicarbazides. The use of alkyl isothiocyanates as derivatization reagents makes it possible to achieve high yields of the products, allows the derivatization to be performed under mild conditions, and provides considerable efficiency of the chromatographic resolution of the pair derivatization reagent—product. The reliability of DMH identification is enhanced by the use of allyl(ethyl) isothiocyanate as a derivatization reagent having the characteristic EI fragmentation.

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Received June 25, 2009;
in revised form November 24, 2009