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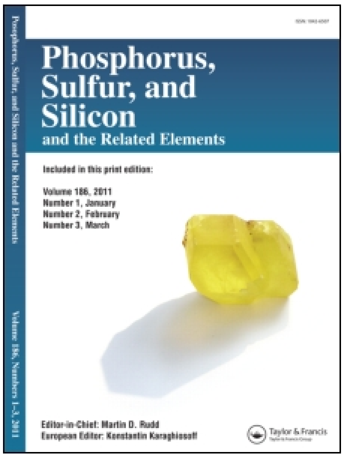

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Reaction of Lewisite-1 with Alcohols, Diols, and Thiols in Water—A Simple Method of Derivatization of Thiodiglycol

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Reaction of 2-chlorovinyldichloroarsine (Lewisite-1) with alcohols, thiols, diols, and hydroxy thiols in water at 40°C has been examined. The expected derivatization products, dialkyl 2-chlorovinylarsonites or corresponding arsonodithiolites, were obtained with alcohols and thiols, whereas reactions with bifunctional diols and hydroxythiols produced analogous cyclic esters. All derivatives may be easily detected using gas chromatography. This reaction was found useful to easily transform bis(2-hydroxyethyl) sulfide (thiodiglycol), a sulfur mustard decomposition product, to a stable eight-membered cyclic arsonite derivative. After extraction with dichloromethane, the derivative may be easily and selectively detected using GC/MS at a 100 ppb level thiodiglycol content in water matrices, eliminating tedious evaporation of water and then silylation. This method may be applied to analyze Chemical Weapons Convention related environmental water samples.

Keywords Alcohols; derivatization; diols; gas chromatography; lewisite; thiodiglycol

INTRODUCTION

2-Chlorovinyldichloroarsine (Lewisite-1 or L1, **1**), usually containing varying amounts of its analogs: bis(2-chlorovinyl)chloroarsine (Lewisite-2, **2**) and tris(2-chlorovinyl)arsine (Lewisite-3, **3**), is a compound listed in Schedule 1 of toxic chemicals in the Annex on Chemicals of the Chemical Weapon Convention (CWC).[1] Despite of its relatively low polarity, L1 is not easily separated using gas chromatography except at a very high concentration level. However, Lewisite-1 easily reacts with alcohols[2] and thiols[3] in organic solvents, as acetone, producing appropriate esters or thioesters of 2-chlorovinylarsonic acid.

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Only the reaction of L1 with one of the thiols, methyl thioglycolate (HS-CH_2COOMe, **4**) has been reported to proceed in water at 60–70°C.[4] To our best knowledge, no reaction of Lewisites with alcohols in water has been described in the literature as yet.

Reactions with dithiols could be performed in both organic solvents and water. Thus, 1,2-ethanedithiol **5**,[5–10] 1,3-propanedithiol **6**[5,6,10,11] and their homologues up to 1,8-octanedithiol[6] in water, ethanol, 2-propanol or acetone, as well as 3,4-dimercaptotoluene (DMT **7**)[10,12] in hexane transform L1 into appropriate 5- to 11-membered cyclic thioesters, which are stable derivatives and easy to identify on GC/MS. Also 1,2-propanedithiol (British anti-Lewisite, BAL **8**) reacts with Lewisite-1 in water to form a stable and non-toxic 5-membered arsonodithiolite, preventing the toxic Lewisite effects.[10,13] However, to our knowledge, no reaction of Lewisites with diols and hydroxy thiols in water has been described in the literature as yet.

Analyzing water samples containing low concentrations of compound **1** and some C_6-C_{10} alcohols, we unexpectedly found the reaction products of L1 and alcohols.[14] That is why we decided to investigate this reaction.

Bis(2-hydroxyethyl) sulfide (thiodiglycol, TDG, **9**) is the most important sulfur mustard decomposition product, as well as a starting material for its production, a compound listed in Schedule 2 of toxic chemicals in the Annex on Chemicals of the CWC.[1] Due to its high polarity and the absorptive nature, TDG is not extractable from water or soil using an organic solvent, except at a very high concentration, for the same reason it is also not easy to analyze it directly using GC.[15] As described in the literature procedures,[14,16] the water solution has to be evaporated to dryness using for example rotating vacuum evaporator,[17] following by silylation with *N*,*O*-bis(trimethylsilyl) trifluoroacetamide (BSTFA) in tetrahydrofuran and identification on GC/MS as a bis(trimethylsilyl) derivative.[15] This arduous and time consuming procedure often did not give a satisfactory recovery and was basically developed to confirm presence of TDG in an aqueous sample at the 10 ppm (μg/g) level. However, a solid phase micro extraction (SPME) method allowed the GC/MS detection of TDG in water at a 200 ppb level as *tert*-butyldimethylsilyl derivative, obtained from *N*-methyl−*N*-(*tert*-butyldimethylsilyl) trifluoroacetamide (MTBSTFA).[18] Other developed methods of TDG derivatization were pentafluorobenzoylation[14] or acylation with heptafluorobutyric anhydride.[19]

In this article, reaction of Lewisite-1 **1** with different primary alcohols, thiols, diols (including TDG) and hydroxy thiols in water has been examined, and the resulting products were analysed using GC/MS and GC/FID/FPD.

TABLE I Derivatives of 2-Chlorovinylarsonous Acid and Alcohols or Thiols

	Chemical name	M.w. (*m*/*z*)	RI
10	*O*,*O*-dimethyl 2-chlorovinylarsonite	198	1018
11	*O*,*O*-diethyl 2-chlorovinylarsonite	226	1136
12	*O*-methyl *O*-isopropyl 2-chlorovinylarsonite	226	1198
13	*O*-ethyl *O*-isopropyl 2-chlorovinylarsonite	240	1167
14	*O*-ethyl *O*-propyl 2-chlorovinylarsonite	240	1221
15	*O*,*O*-diisopropyl 2-chlorovinylarsonite	254	1271
16	*O*,*O*-dipropyl 2-chlorovinylarsonite	254	1309
17	*O*,*O*-dibutyl 2-chlorovinylarsonite	282	1491
18	*S*,*S*–dibutyl 2-chlorovinylarsonodithiolite	314	1933

RESULTS AND DISCUSSION

The derivatives **10–24** of Lewisite-1 with alcohols, thiols and glycols, obtained according to procedures described in the experimental section, are presented in Tables I and II. In water solution, Lewisite-1 undergoes complex transformations, depending on pH. Only if pH is lower than 2 and in presence of hydrochloric acid, Lewisite-1 is expected to exist mainly in its form **1** in water solution.

In weakly acidic and neutral water solutions, Lewisite-1 has tendency to hydrolyze affording 2-chlorovinylarsonous acid $L1(OH)_2$**25**.[10,20] This acid is in equilibrium with its anhydride, called Lewisite-1 oxide, with a formal structure Cl—CH=CH—As=O **26**. At higher concentration levels, this anhydride exists, however, mainly in different polymeric or oligomeric forms,[10] the most common is the trimeric form, 2,4,6-tris(2-chlorovinyl)-1,3,5-trioxa-2,4,6-triarsane $(L1\text{-}O)_3$, (**26a**). This form is non polar (easy to extract from water solutions with dichloromethane), volatile and can be identified by gas chromatograph with a reasonable retention time under standard

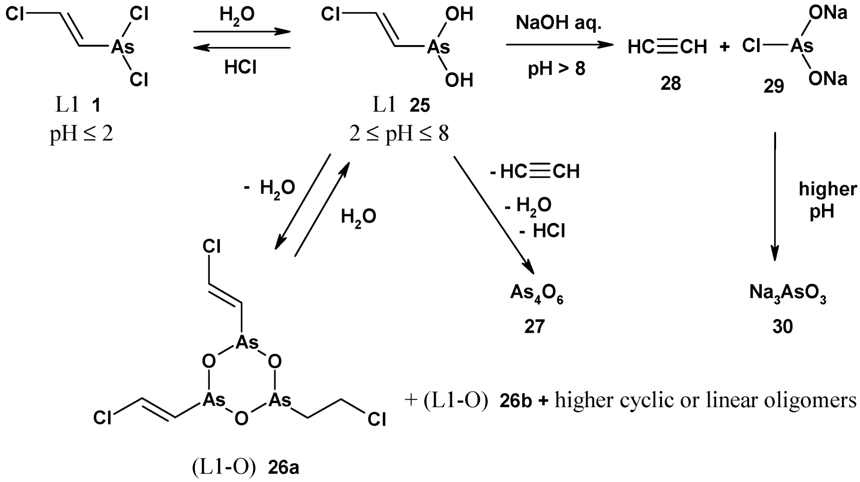
TABLE II Cyclic Derivatives of 2-Chlorovinylarsonous Acid

	Chemical name, acronym	M.w. (*m*/*z*)	RI
19	2-(2-chlorovinyl)-1,3,2-dioxarsole, L1=EG	196	1129
20	2-(2-chlorovinyl)-1,3,2-oxathiarsole, L1=2-ME	212	1345
21	2-(2-chlorovinyl)-1,3,6,2-dioxathiarsocane, L1=TDG	256	1656
22	2-(2-chlorovinyl)-1,3,9-trioxa-6,12-dithia-2-arsacyclotetradecane, L1=$(TDG)_2$	360	2455
23	2-(2-chlorovinyl)-1,3,6,7,2-dioxadithiarsonane, L1=SS	288	1910
24	2-(2-chlorovinyl)-1,3,6,2-trioxarsocane L1=DEG	240	1438

conditions (RI = 2177). The homologous tetrameric form – $(L1\text{-}O)_4$ **26b** may be only observed on LC, and possibly some other in water and organic solvents insoluble[10] higher cyclic or linear polymers may also form; they were not examined in this work however. Moreover, an acetylene elimination in a *retro*-Michael reaction may be also observed.[21,22] The resulting chloroarsenous acid derivative dehydrates and eliminates HCl affording arsenic(III) oxide As_4O_6 (**27**). This relatively volatile—even though polar—inorganic compound is always present in all gas chromatograms as a broad peak (RI = 1427) and produces a characteristic mass spectrum in GC/MS ($M^{+\cdot}$ at m/z 396); the decomposition may also occur in the GC injector.

In alkaline solution, the *retro*-Michael elimination occurs already quantitatively, 2-chlorovinylarsonic acid loses an acetylene HC≡CH **28** molecule,[21,22] and due to alkaline conditions, the resulting chloroarsenous acid is at the same time transformed into its disodium salt affording disodium chloroarsenite **29**. At higher pH, the remaining chlorine atom hydrolyses and finally only trisodium arsenite (Na_3AsO_3, **30**) is present in the water solution (Scheme 1).

Reactions of Lewisite-1 with C_1-C_4 aliphatic alcohols were first examined. The reactions were carried out at 40°C during 2 to 3 h with diluted solution of the appropriate alcohol (50 ppm, m/m) and Lewisite-1 (250 ppm) in water. The reactions with mixtures of alcohols were also carried out in such a way as to maintain fivefold excess of L1 with respect to every alcohol, present at 50 ppm level. The examined alcohols methanol **31**, ethanol **32**, propanol **33**, isopropanol **34**, and butanol **35**



SCHEME 1 The transformations of Lewisite-1 in water.

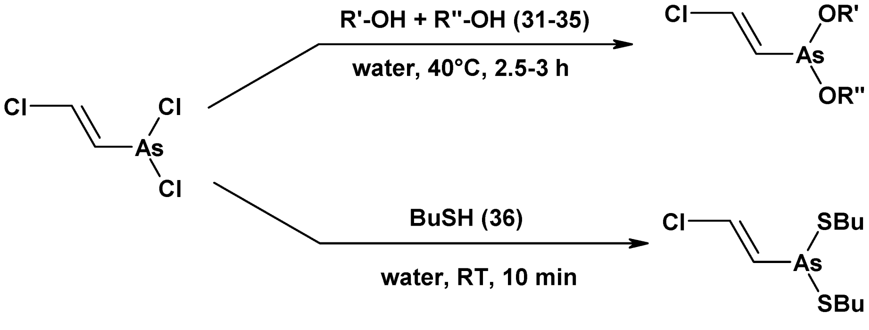
afforded the appropriate *O*,*O*-dialkyl 2-chlorovinylarsonites **10–17**, detected on GC/MS (Scheme 2). The extension of the reaction time decreased the yield of the derivative and after 17 h (overnight) there was no derivatisation product detected on GC/MS. Thus the dialkyl 2-chlorovinylarsonites and especially the esters of lower alcohols, were not stable.

Since arsenic shows a high affinity to sulfur, it may be expected that derivatization of Lewisite-1 in water with a thiol proceeds faster, even if there is neither dichloroarsine form **1** nor Lewisite-1 oxides (such as $(L1\text{-}O)_3$, **26a**) present in the water solution. Thus, both forms **1** and **26a** were carefully removed from the Lewisite-1 water solution by washing with dichloromethane, and only 2-chlorovinylarsonous acid $L1(OH)_2$ **25** (250 ppm) was practically present in water. Reaction with 1-butanethiol **36** (250 ppm) in water at room temperature during 10 min smoothly transformed the arsonous acid form of Lewisite-1 **25** into *S*, *S*–dibutyl 2-chlorovinylarsonodithiolite **18**.

However, the same reaction of $L1(OH)_2$ **25** with propanol **33** carried out at 40°C did not produce *O*,*O*-dipropyl 2-chlorovinylarsonite **16** even after 17 h. Thus, Lewisite-1 reacts with alcohols in water only in its anhydride form $(L1\text{-}O)_3$ **26a**, and—of course—in dichloroarsine form **1**, whereas reaction with thiols occurs easily with all forms existing in water, including 2-chlorovinylarsonous acid **25**.

The retention indices (RIs) of the 2-chlorovinylarsonous acid esters obtained are presented in Table I.

EI MS spectra of the dialkyl 2-chlorovinylarsonites **10–17** contain occasionally a very weak peak for the molecular ion, but usually no peak for this ion at all. In most cases, the $[M\text{-}^{\cdot}OR]^+$ is the base ion, except for *O*,*O*-dimethyl 2-chlorovinylarsonite **10**, where the characteristic



SCHEME 2 Reactions of Lewisite-1 with alcohols and 1-butanethiol.

Cl—CH=CHAsH(OMe)$^{+\cdot}$ ion at *m/z* 168 and the [M-CH$_2$O]$^{+\cdot}$ ion are observed instead. The ions As(OMe$_2$)$^+$ at *m/z* 137 and HAs=O$^+$Me at *m/z* 107 give the most intense signals present in the spectrum. In the case of the isopropyl esters, also the [M-$^\cdot$CH$_3$]$^+$ ion is found. Characteristic As(OR$_2$)$^+$ ions also are found in all spectra. Ions Cl—CH=CH—As=O$^+$R, Cl—As=O$^+$R (acetylene elimination), HO—As=O$^+$H at *m/z* 109, AsC$_2$H$_2^+$ at *m/z* 101, As≡O$^+$ at *m/z* 91 and characteristic As$^+$ (no isotope ions) at *m/z* 75 are observed in all spectra and additionally confirm the structure.

As an example, the EI MS spectrum of *O*,*O*-dibutyl 2-chlorovinylarsonite **17** is presented in Figure 1. The spectrum shows only a very weak peak of the M$^{+\cdot}$ ion at *m/z* 282 (1%) as well as a peak for the As(OBu)$_2^+$ ion at *m/z* 221 and the intense signal of ClCH=CH—As=O$^+$Bu ion at *m/z* 209 (base ion). The ions As(OH)OBu$^+$ at *m/z* 165, ClCH=CH—As=O$^+$H at *m/z* 153, ClCH=CHAsH$^+$ at *m/z* 137, ClCH=CHAs$^{+\cdot}$ at *m/z* 136, ClAs=O$^+$H at *m/z* 127, HO—As(OH)$_2^+$ at *m/z* 109, AsC$_2$H$_2^+$ at *m/z* 101, as well as *m/z* 57 and 41 (*n*—butyl group in the esters) confirm the structure. An intense signal at *m/z* 71 (no chlorine atom) may correspond to a dihydrofuranylium ion C$_4$H$_7$O$^+$ resulting from a rearrangement of the *n*—butoxy group.

The mass spectrum of the sulfur analogue is different. In the EI MS spectrum of *S*, *S*—dibutyl 2-chlorovinylarsonodithiolite **18**, the relatively intense M$^{+\cdot}$ ion at *m/z* 314 (12%) as well as [M-$^\cdot$Bu]$^+$ at *m/z* 257 and [M-$^\cdot$SBu]$^+$ at *m/z* 225 are present, together with the ions Cl—As=S$^+$Bu at *m/z* 199, ClCH=CH—As=S$^+$H at *m/z* 169, As=S$^+$Bu at *m/z* 164, AsCl$^+$ at *m/z* 110, As≡S$^+$ at *m/z* 107, SBu$^+$ at *m/z* 89, and As$^+$ at

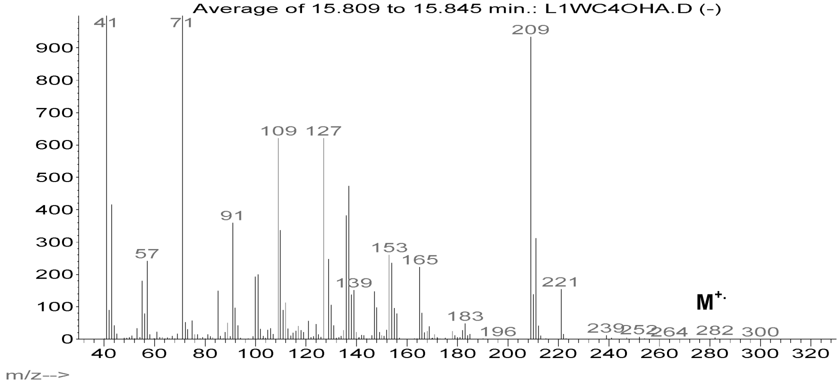


FIGURE 1 MS spectrum of *O*,*O*-dibutyl 2-chlorovinylarsodithiolite **17**.

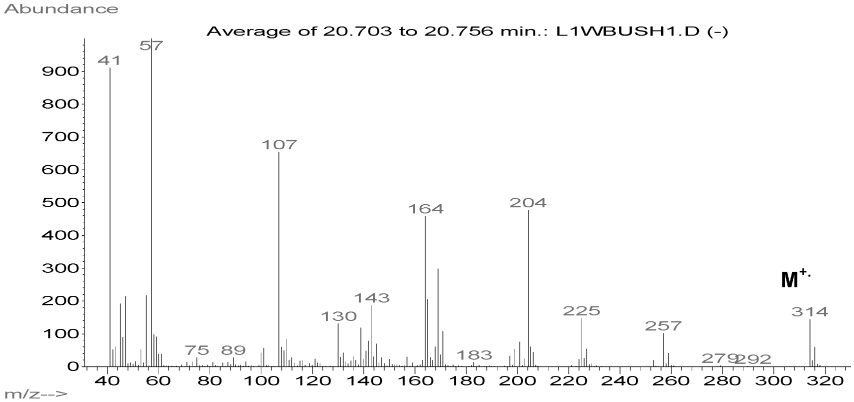
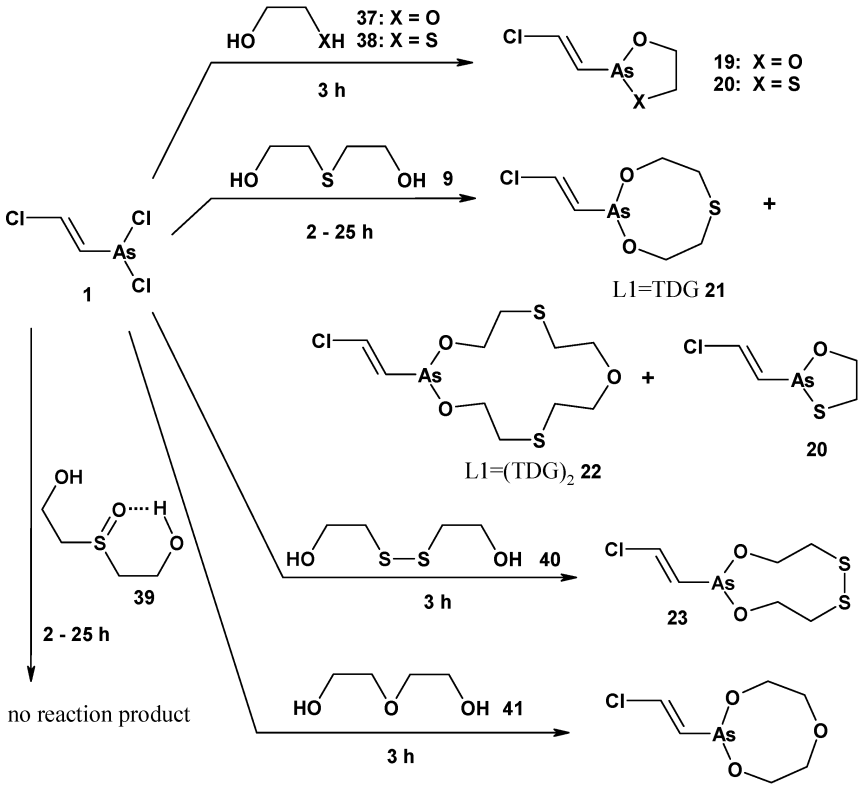


FIGURE 2 MS spectrum of *S*, *S*-dibutyl 2-chlorovinylarsodithiolite **18**.

m/*z* 75. The intense ions Bu^+ at *m*/*z* 57 and [*n*-Bu - $CH_4]^+$ at *m*/*z*41, typical for the *n*—butyl group, additionally confirm the structure. The prominent ion at *m*/*z* 204 (no chlorine, 2 sulfur atoms) corresponds to $BuSCH{=}CHSBu^{+\cdot}$, resulting from a rearrangement (Figure 2).

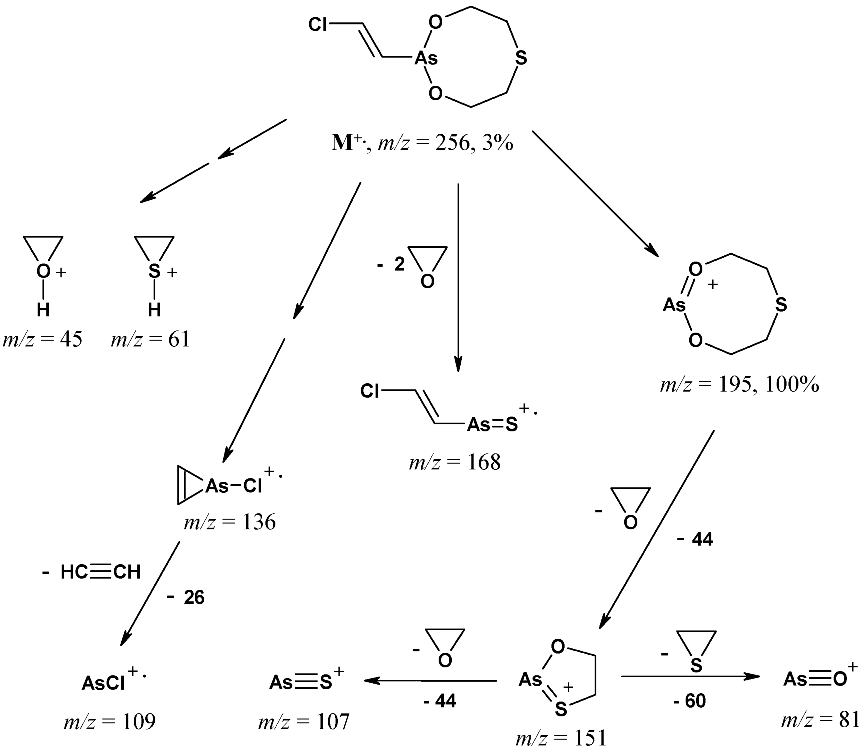
The reactions of L1 with bifunctional alcohols and thiols were also carried out. Since 5-membered cyclic arsonodithiolite derivatives of Lewisite-1 with 1,2-ethanetiol **5** and 3,4-dimercaptotoluene**7** are easy to prepare,[5,9–11] the analogous compounds were expected to form from ethylene glycol (EG, **37**) and 2-mercaptoethanol (2-ME, **38**). Derivatizations were performed in water at 40°C for 3 h at 10 ppm concentrations of compounds **37** and **38** and a large excess (200 ppm) of L-1 **1**. Cyclic derivatization products, appropriately 2-(2-chlorovinyl)-1,3,2-dioxarsolane (L1=EG, **19**) and 2-(2-chlorovinyl)-1,3,2-oxathiarsolane (L1=2-ME, **20**), have been smoothly obtained (Scheme 3).

The EI mass spectra of compounds **19** and **20** show distinguishable to strong molecular ions at *m*/*z* 196 (8%) and 212 (43%), respectively. The base peaks in the mass spectra, the dioxarsolylium ion at *m*/*z* 135 for L1=EG and the oxathiarsolylium ion at *m*/*z* 151 for L1=2-ME, in SIM mode showed high abundance and excellent signal-to-noise (*S*/*N*) ratio, thus derivatization with L1 is a method to easily detect diols **37** and **38** in water at least at a ppm level. Other ions present in the spectrum of **19**, $[M - H_2C{=}O]^{+\cdot}$ at *m*/*z* 166 and $As{\equiv}O^+$ at *m*/*z* 91, and in the spectrum of **20** $[M - HC{\equiv}CH]^{+\cdot}$ at *m*/*z* 186 and $As{\equiv}S^+$ at *m*/*z* 107, as well as present in both spectra $Cl{-}CH{=}CHAs^{+\cdot}$ at *m*/*z* 136, $AsCl^+$ at *m*/*z* 110, $AsC_2H^{+\cdot}$ at *m*/*z* 100 and As^+ (*m*/*z* 75), additionally confirm the structure of compounds **19** and **20**.



SCHEME 3 Reactions of Lewisite-1 with bifunctional alcohols and thiols in water at 40°C.

Nonetheless, derivatization of bifunctional thiodiglycol TDG **9** showed to be much more interesting. Already after 2 h at 40°C, TDG present in water in a large concentration range from 100 ppb to 10000 ppm, in the presence of an excess (3 to 200 times) of Lewisite-1, was unexpectedly easily transformed into an 8-membered cyclic arsonite derivative, 2-(2-chlorovinyl)-1,3,6,2-dioxathiarsocane (L1=TDG, **21**). The derivatization carried out at pH 6 and 2 gave similar results. All forms of Lewisite-1—the dichloroarsine form **1**, the arsonous acid form L1(OH)$_2$, the form **25** as well as the (L1-O)$_3$ form **26a** are suitable to derivatize TDG in water. The reaction may be also performed with the (L1-O)$_3$ form **26a** in dichloromethane. In the SIM mode, the base ion in the MS of L1=TDG at *m*/*z* 195 showed a high selectivity (practically only one ion present in the SIM chromatogram) and an excellent



SCHEME 4 EI MS fragmentation pathways of L1=TDG**21**.

S/*N* ratio, more than 1000 even at 100 ppb concentration range. In the TIC mode, in a concentration of 1–10 ppm the L1=TDG **21** peak was a prominent and easily to distinguish signal, even in very complex water matrices.

The TDG and L1 derivatization product **21** showed to be a very stable compound. When the reaction time was extended up to 25 h, it was still present in the sample in a high concentration. However, some side reactions have been observed. Thus a 14-membered condensation product of two molecules of TDG with L1, L1=(TDG)$_2$ **22** was observed in the TIC at a higher retention time. The formation of macrocyclic rings is favored by the high dilution during derivatization and by the presence of catalytic amounts of aprotic dipolar solvents, like DMSO, or similar to DMSO thiodiglycol sulfoxide (TDGO, **31**). Moreover, a considerable amount of L1=TDG **21** degradation product, identical with 2-(2-chlorovinyl)-1,3,2-oxathiarsolane (L1=2-ME, **20**) has been found in the TIC (Figure 4).

In the EI MS of 2-(2-chlorovinyl)-1,3,6,2-dioxathiarsocane (L1=TDG) **21**, the distinctly visible molecular ion at *m/z* 256 (3%) is present. The fragmentation pathways are shown in the Scheme 4, and the mass spectrum in Figure 3.

The EI MS spectrum of 2-(2-chlorovinyl)-1,3,9-trioxa-6,12-dithia-2-arsacyclotetra-decane, L1=$(\mathrm{TDG})_2$ **22** (Figure 4) contains a weak signal for the molecular ion at *m/z* 360 and a prominent signal of the $[\mathrm{M - ClCH{=}CH^{\cdot}}]^+$ ion at *m/z* 299**.** Other ions present in the spectrum, $[\mathrm{L1{=}TDG\text{-}H}]^+$ at *m/z* 255 ($[299]^+$ - ethylene oxide), *m/z* 239 ($[299]^+$ - ethylene sulfide), dioxathiarsocanylium ion $\mathrm{C_4H_8AsO_2S^+}$ at *m/z* 195, oxathiarsolylium ion $\mathrm{C_2H_4AsOS^+}$ at *m/z* 151, $\mathrm{AsOCH_2^{+\cdot}}$ at *m/z* 105, [ethylene sulfide]$^{+\cdot}$ at *m/z* 60, [ethylene sulfide ± $\mathrm{H^{\cdot}}$]$^+$ at *m/z* 59 and 61, $\mathrm{EtOH^{+\cdot}}$ at *m/z* 46, [ethylene oxide + $\mathrm{H^{\cdot}}$]$^+$ at *m/z* 45, as well as

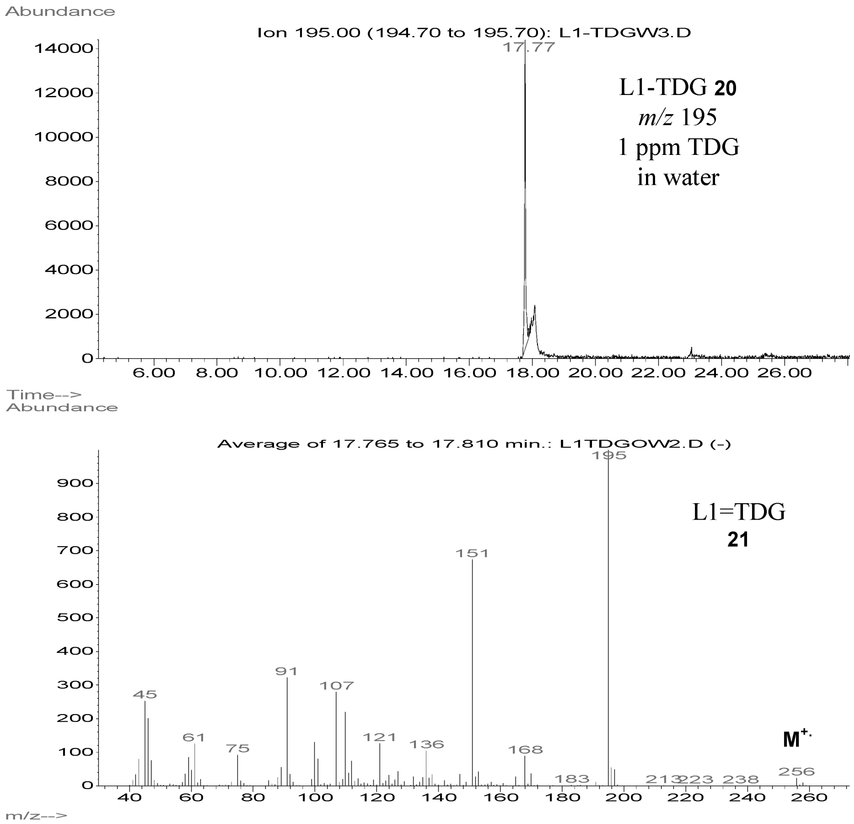


FIGURE 3 SIM chromatogram and MS of L1=TDG **21** (1 ppm TDG in water derivatised with L1).

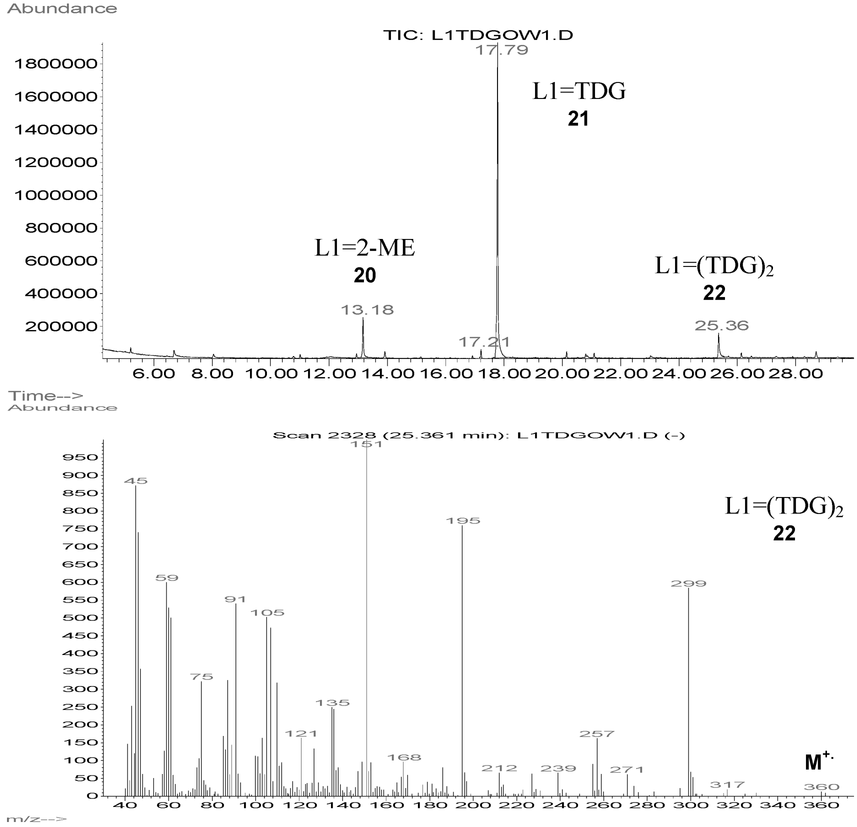


FIGURE 4 TIC chromatogram and MS of L1=(TDG)$_2$ **22**.

the previously discussed ions at *m*/*z* 136, 110, 107, 91, and 75 additionally confirm the structure of 14-membered heterocycle L1=(TDG)$_2$ **22**.

The derivatization reaction may be also performed with equimolar amounts of TDG and L1. However, it failed when TDG was present in a large excess, possibly due to the tendency of this bifunctional alcohol to polymerise. That is why the described method is a very simple and efficient way to detect trace amounts of TDG in water using L1 as a derivatization agent, rather then the opposite. The sample preparation is very simple, and a tedious and time-consuming evaporation of water and then silylation may be eliminated. Moreover, the detection limit and the selectivity of the reaction are very good.

The reaction of L1 with a higher sulfur homologue of TDG, bis(2-hydroxyethyl) disulfide **40**, in water was also examined. After 3 h at 40°C, the disulfide **40** was smoothly transformed into the analogous 9-membered cyclic arsonite derivative, 2-(2-chlorovinyl)-1,3,6,7,2-dioxadithiarsonane **23**.

The EI MS spectrum of the compound **23** contains the molecular ion at *m/z* 288 (9%). The base ion, [M - ClCH=CH$^{\cdot}$]$^+$ at *m/z* 229 corresponds to a dioxadithiarsonylium structure $C_4H_8AsO_2S_2^+$. The 1,3,4,2-oxadithiarsinylium ion $C_2H_4AsOS_2^+$ at *m/z* 183 (base ion—ethylene oxide), and the previously discussed ions at *m/z* 212 and 151 are also observed in the mass spectrum.

This method may be also used to derivatize diethylene glycol (DEG, **41**), a TDG oxygen analogue, in water. 10 ppm DEG in water was easily transformed after 3 h at 40°C into an analogous 8-membered cyclic arsonite derivative, 2-chlorovinyl-1,3,6,2-trioxarsocane (L1=DEG, **24**, Figure 5).

The EI MS spectrum of 2-chlorovinyl-1,3,6,2-trioxarsocane (L1=DEG, **24**, Figure 5) contains the weak molecular ion at *m/z* 240 (2%). The base ion [M - ClCH=CH$^{\cdot}$]$^+$ at *m/z* 179 gave high abundance in both TIC and SIM modes with an excellent S/N ratio in SIM mode. The trioxarsocanylium ion $C_4H_8AsO_3^+$ at *m/z* 135 and the other ions present in the spectrum: the previously mentioned ions at *m/z* 136, 100, 91, and 75, as well as oxiranium ion $C_2H_3O^{+\cdot}$ at *m/z* 43 additionally confirm the structure of compound **24**.

The structures of all 5-, 8-, 9-, and 14-membered cyclic arsonite derivatives discussed in this article were additionally confirmed by chemical ionization mass spectrometry (CI MS, reagent gas: isobutane). The MH$^+$ quasi-molecular ions were found as base peaks (100%) in the CI MS of the following compounds (*m/z*): **19** (197), **20** (213), 21 (257),

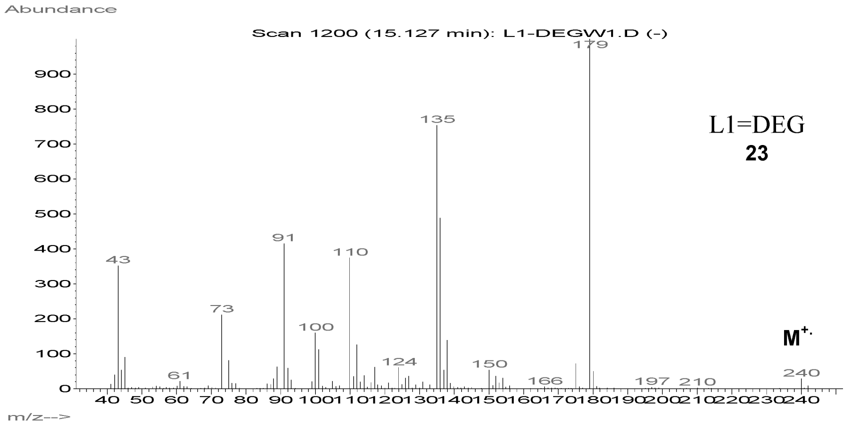


FIGURE 5 Mass spectrum of L1=DEG **23**.

23 (289), and **24** (241). In the CI MS spectrum of the 14-membered cyclic compound **22** the signal for the MH^+ ion at m/z 361 was of lower intensity (15%).

Nevertheless, the attempts to derivatise bis(2-chloroethyl) sulfoxide (thiodiglycol sulfoxide, TDGO **39**), another environmental oxidation product of a sulfur mustard, unexpectedly failed. Even 400–600 ppm water solutions of TDGO did not produce any derivative with L1. This may be due to the different geometry and high polarity[10] of the TDGO molecule (see Scheme 3). The ^1H NMR spectrum shows that the molecule is asymmetrical.[22] Maybe also a redox reaction takes place, and the resulting As(V) analogue of Lewisite-1, 2-chlorovinyldichloroarsine oxide **42** does not form derivatives with TDG also due to a different molecule geometry. Our experience showed as well, that As(V) organic compounds, such as cacodylic acid $Me_2As(O)OH$ **43**, did not form any esters with alcohols and diols in water.[23]

The RIs of the cyclic 2-chlorovinylarsonous acid esters obtained are shown in Table II.

All Lewisite derivatives discussed in this article showed in TIC usually two or sometimes more peaks. This was due to geometrical isomerism of the Lewisite molecule. According to NMR data, the highest peak corresponded to (*E*)-2-chlorovinyl isomer, (*E*)-Cl–CH=CH–$AsCl_2$, (J_{HH} = 15 Hz), whereas the smaller peaks corresponded mainly to (*Z*)-isomer (J_{HH} = 8 Hz). This is in contrast to some literature data, where the (*E*) and *gem* (CH_2 =CHCl–$AsCl_2$, J_{HH} = 1 Hz) isomers are mainly expected in the Lewisite molecules, whereas the (*Z*)-2-chlorovinyl isomer, (*Z*)-ClCH=CH–$AsCl_2$, is practically absent.[24] However, the mass spectra of the isomers of the compounds discussed in this article did not show any significant differences.

CONCLUSIONS

The method described above may be used not only to derivatize Lewisite-1 in water with alcohols (and especially thiols), but also to derivatize some alcohols, particularly diols—such as thiodiglycol **9**—with Lewisite in water matrices at 100 ppb levels, alternatively to time-consuming evaporation and silylation. This simple novel method has been successfully applied to the analysis of CWC related environmental water samples.

The stable derivatives resulting from the reaction of TGD **9** and bis(2-hydroxyethyl) disulfide **40** with Lewisite-1 contain 8-, 9-, and 14-membered rings of arsenic, oxygen and sulfur atoms and are new types of heterocyclic compounds, not described before in the literature.

EXPERIMENTAL

Materials

2-Chlorovinyldichloroarsine **1** (Lewisite-1), 5 mg/mL solution in water, was obtained from Spiez Laboratories, Spiez, Switzerland. Bis(2-hydroxyethyl) sulfide **9** (for chromatography, International Enzymes Ltd.), methanol **31** (spectrometric grade, Aldrich, 99.9%), ethanol**32** (analytical grade, Baker >99.8%), propanol **33** (analytical grade, Baker >99%), isopropanol **34** (analytical grade, Baker >99%), butanol **35** (Aldrich, 99%), 1-butanethiol **36** (Aldrich, >99%), ethylene glycol **37** (Aldrich, >99%), 2-mercaptoethanol **38** (Aldrich, 98%), thiodiglycol sulfoxide **39** (Radian, 99%), bis(2-hydroxyethyl) disulfide **40** (Aldrich, tech. grade), diethylene glycol **41** (Aldrich, 99%), dichloromethane (analytical grade, Baker, 99.9%), acetone (analytical grade, Baker, 99.5%), hydrochloric acid 0.1 M (analytical grade, Boom), and anhydrous sodium sulfate (Fluka, >99%) were used.

Water matrix: demineralized or tap water.

Equipment

GC/MS Conditions

HP 6890 Series gas chromatograph was coupled on-line with a HP 5792A Mass Selective Detector (MSD).

GC/MS analysis was performed on Hewlett-Packard, HP 6890 GC /5972A MSD. The instrument conditions used were as follows:

GC conditions. FSOT capillary column, 30 m × 0.25 mm I.D., phase: 5-HP MS (95% dimethylsiloxane, 5% phenylsiloxane), film 0.25 μm, carrier gas: helium, constant flow 0.9 ml/min; injection: split/splitless (splitless mode with 1 min splitless period), injection volume 1-2 μl (manually), injector temperature: 250°C. Column temperature: 40°C (2 min) then increased to 280°C (10°C/min) and at 280°C (4 min).

Mass spectrometry conditions. Electron ionization (EI) at 70 eV, ion source temperature 180°C, trap current 200 μA, accelerating voltage 1870 V, analyzator: quadrupole. Resolution 0.7 u, mass range 40 to 550 u. The chromatograms were performed in both Total Ion Current (TIC) or Selected Ions Monitoring (SIM) modes. Chemical Ionization (CI): reagent gas: isobutane.

GC/FID/FPD Conditions

HP 6890 Series gas chromatograph equipped with an autosampler and, in parallel, Flame Ionization Detector (FID) and Flame Photometric Detector (FPD), optical filter wavelength for sulfur: 394 nm. CG conditions: the same as for GC/MS.

Sample Preparation

Derivatization and Sample Preparation—General Procedure

To 1 mL of the water solution of an appropriate alcohol, hydroxythiol or diol **31–35**, **37–41** in a 4-mL vial with PTFE-lined screw-cap, the 5 mg/mL water solution of Lewisite-1 **1** was added in such amounts that the content of the alcohol/hydroxy thiol/diol in solution was in the range 100 ppb (ng/g)–10,000 ppm (μg/g), usually 1–10 ppm, and Lewisite was in molar excess of 1 to 200 times (usually 3 to 6 times). Reaction was usually carried out at pH 6; if the reaction was performed at pH 2, the appropriate amount of 0.1 M aqueous hydrochloric acid was added. The cap was then screwed on and derivatization was carried out at 40°C for 2–25 h, usually 3 h. After cooling, the water matrix was washed with dichloromethane (3 × 1 mL), the combined organic layers were dried with anhydrous sodium sulfate for 30 min and filtered. Depending on the concentration of the alcohol, samples were concentrated (fivefold) or not, in a mild nitrogen flow at room temperature (usually, at 1–10 ppm concentration, no evaporation was necessary).

One to two μL of the resulting dichloromethane solution was injected in GC/MS or GC/FID/FPD. Linear (van den Dool) retention indices (RI) were calculated by a linear polygon method[25] with retention times (R_T) of even carbon number hydrocarbons from C_8 (octane) to C_{24} (tetradecane), 10 μg/mL each, injected under the same conditions in the GC/MS.

All discussed spectra fragmentations were confirmed by calculating the intensity of the isotope peaks of the fragment ions.

Derivatization of Thiodiglycol 9 with Lewisite-1 1 in Water

To 1 mL of water containing 10 μg of thiodiglycol **9** (10 ppm) in a 4-mL vial with PTFE-lined screw-cap, 20 μL of water solution of Lewisite-1 **1** (5 mg/mL, molar excess 5.9 times) was added. The cap was then screwed on and derivatization was carried out at 40°C for 2 h. After cooling, the mixture was washed with dichloromethane (3 × 1 mL), the combined organic layers were dried with anhydrous sodium sulfate for 30 min and filtered. one μL of the resulting dichloromethane solution was injected in the GC/MS. In the above described conditions, the R_T of 2-chlorovinyl-1,3,6,2-dioxathiarsocane **21** was 17.77 min.

Derivatization of Thiodiglycol 9

(i) With Water Solution of 2-Chlorovinylarsonous Acid L1(OH)$_2$ **25***.* One mL of Lewisite-1 in water (5 mg/mL) were washed with dichloromethane (3 × 1 mL). To the water phase, containing mainly 2-chlorovinylarsonous acid **25**, was added 1 mL of water containing 2 ppm of thiodiglycol **9** and derivatization was performed in a 4-mL screw-cap

vial at 40°C for 2 h. After cooling, the water matrix was worked out as described in general procedure. Two μL of the organic solution was directly injected in the GC/MS and GC/FID/FPD. R_T of compound **21** was as above.

(ii) With Lewisite-1 Oxide Trimer (L1-O)$_3$ **26a** *in Dichloromethane.* Three hundred μL of the above combined organic layers, containing mainly (L1-O)$_3$ **26a**, was shaken with 1 mL of water solution of TDG (1 ppm, 1 μg) in a 4-mL screw-cap vial. The reaction mixture was kept at 40°C for 2 h, shaking occasionally. After cooling, the reaction mixture was worked out as described in general procedure. Two μL of the organic solution was directly injected in the GC/MS and GC/FID/FPD. R_T of compound **21** was as above.

(iii) Synthesis of Compound **21** *from $(L1 - O)_3$* **26a** *and TDG 9 in Dichloromethane.* Three mL of Lewisite-1 in water (5 mg/mL, containing 15 mg (72 μmol) of Lewisite-1) was washed with dichloromethane (1 × 2 + 3 × 1 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and then added to 5.16 mg (42 μmol) of thiodiglycol **9** in a 4-mL vial equipped with a PTFE-lined screw-cap. The reaction mixture was kept at 40°C for 3 h, cooled, and the unreacted TDG was washed out with water (3 × 2 mL). The organic phase was dried (Na_2SO_4), filtered and evaporated to dryness in a mild stream of nitrogen at room temperature. Uncolored oil, yielded 5.3 mg (49%).

EI and CI GC/MS: see discussion.

^{1}H NMR (500 MHz, $CDCl_3$, δ [ppm]): 2.63 (ddd, 2H, **H**-5, **H**-7); 2.98 (ddd, 2H, **H**-5, **H**-7); 4.02 (ddd, 2H, **H**-4, **H**-8); 4.37 (ddd, 2H, **H**-4, **H**-8); 6.56 (d, J_{HH} = 15 Hz, 1H, **H**-1), 6.65 (d, J_{HH} = 15 Hz, 1H, **H**-2); (configuration *E*−).

^{13}C NMR (DEPT 90°, 125.7 MHz, $CDCl_3$, δ [ppm]): 29.7 (**C**-5, **C**-7), 68.3 (**C**-4, **C**-8).

Derivatization of 2-Chlorovinylarsonous Acid 25 with 1-Butanethiol 36 in Water

1 mL of Lewisite-1 in water (5 mg/mL) was washed with dichloromethane (3 × 1 mL). To the water phase, containing mainly 2-chlorovinylarsonous acid **25**, solution of 1-butanethiol **36** in acetone (5 mg/mL, 100 μL) was added. After 10 min at room temperature, the reaction mixture was worked out as described in the general procedure. One μL of the organic solution was directly injected in the GC/MS and GC/FID/FPD. Under the conditions described above R_T of *S*, *S*–dibutyl 2-chlorovinylarsonodithiolite **18** was 20.74 min.

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