# Application of the Transpiration Method To Determine the Vapor Pressure and Related Physico-Chemical Data of Low Volatile, Thermolabile, and Toxic Organo(thio)phosphates

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**Supporting Information** 

**ABSTRACT:** The present work represents the most recent study on the physico-chemical properties of the organophosphate compound class being directly related to the Chemical Weapons Convention (CWC). This compound class is of great importance in the ongoing conflict in Syria. Here, the vapor pressure of the deadly organo(thio)phosphate Amiton and seven of its derivatives was investigated. These medium to low volatile analytes pose a potential threat toward human life by inhalation or direct contact with the skin at very low doses. Therefore, the vapor pressures in ambient temperature regimes were measured by utilizing the transpiration method to determine the saturation vapor pressure  $p_{sat}$  and the enthalpy of vaporization  $\Delta_{\rm g}^{\rm g} H_{\rm m}^{\rm m}$  at 298.15 K. We also successfully applied the transpiration method for the



examination of thermolabile compounds. In particular, five of the molecules can undergo a thiono-thiolo rearrangement at elevated temperatures within a couple of hours and thus could possibly alter in the course of the experiment. In addition we demonstrate that the concentration under diffusion conditions,  $c_{dif}$  is a useful parameter for the choice of suitable gas phase detection equipment for Amiton and its derivatives, because it can be directly compared with the limit of detection LOD [ng  $L^{-1}$ ] of the device used. Finally, we proved the transpiration method to be applicable for the investigation of toxic and also high boiling and even thermolabile chemicals in general.

## 1. INTRODUCTION

The vapor pressure is the physico-chemical parameter that is linked to the saturation equilibrium concentration of the analytes to be detected from the gas phase. The knowledge of the gas phase concentration of the analyte is essential for the definition of the air volume that needs to be sampled for exceeding the limit of detection (LOD) of the applied detector system. In the case of substances being toxic or harmful by inhalation or direct contact with the skin, early detection is of great importance for obvious reasons. Such substances are primarily those listed as nerve agents or choking agents in the annexes of the Chemical Weapon Convention (CWC).<sup>1</sup> The molecule Amiton (I) belongs to the class of very toxic compounds which cause severe injury and even death.<sup>2,3</sup> Organophosphates themselves are a well-known compound class that is readily available in nature, e.g., in RNA and DNA.<sup>4</sup> Besides this, they have several industrial applications ranging from plasticizers and flame retardants to pesticides and chemical warfare agents.<sup>1,5-7</sup> Especially organo(thio)phosphates, which are less toxic than organophosphates, can undergo a so-called thiono–thiolo rearrangement at elevated temperatures and are thus thermolabile (Figure 1). $^{8-10}$ 

$$\begin{array}{c} \overset{S^{-}}{\underset{R}{\overset{P^{+}}{\longrightarrow}}} - O^{-R^{1}} \xrightarrow{\Delta} & R^{-P^{+}} - S^{-R^{1}} \\ \overset{R}{\underset{R}{\overset{P^{+}}{\longrightarrow}}} & \overset{R^{-}}{\underset{R}{\overset{P^{+}}{\longrightarrow}}} - S^{-R^{1}} \end{array}$$

Figure 1. Minimum structural prerequisites for an organothiophosphate molecule capable of undergoing a thiono-thiolo rearrangement. R can be O-alkyl/O-aryl or O-alkyl/S-aryl;  $R^1$  has to be alkyl.<sup>11,12</sup>

However, this feature of organo(thio)phosphates can have an impact on the determination of the vapor pressure data because the isomers have different vapor pressure values. Thus, measurements with isomer mixtures will result in mixed vapor pressures weighted by the molar ratio of the isomers

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 $\label{eq:relation} R^1: (CH_2)_2 N(Et)_2 \quad R^2: (CH_2)_3 N(Et)_2 \quad R^3: (CH_2)_2 N(Me)_2 \quad R^4: (CH_2)_3 N(Me)_2 \quad R^5: CH(CH_3) CH_2 N(Me_2) = (CH_2)_3 N(Me_2) + (CH_2)_3 N(Me_2)$ 

**Figure 2.** Chemical structures of Amiton (I) and its derivatives II–VIII. They differ from each other by (i) the variation of the configuration of the position of the chalcogens (O, S) attached to the phosphorus atom, (ii) the variation in the amino side chain by altering the spacing between the oxygen and the nitrogen atom, and (iii) the variation of the alkyl substituent of the nitrogen atom.

according to Dalton's Law of partial pressures for a binary mixture.

Today's standard mobile detection instruments of civilian and military action forces are based on, e.g., ion mobility spectroscopy or gas chromatography coupled to mass spectrometry and can thus only detect airborne substances without laborious sampling and sample pretreatment procedures.<sup>13,14</sup> Moreover, if the vapor pressure of a substance is very low, the compound poses only a little threat to living beings by inhalation but is therefore more persistent in the environment and causes a severe threat upon direct contact.

However, the vapor pressure data can also help to estimate a hazardous area and time frame after the release of such substances. Organo(thio)phosphates were chosen in this study because only a small number of values on the vapor pressure of pesticides and especially chemical warfare agents are reported in literature so far<sup>15,16</sup> and their detectability is thus hard to predict. With the ideal gas equation, the saturation concentration  $c_{\rm sat}$  of an analyte can be calculated from its vapor pressure:

$$c_{\rm sat} = \frac{p_{\rm sat} \times M}{R \times T} \tag{1}$$

with  $c_{sat}$  the saturation concentration [mg L<sup>-1</sup>], *R* the ideal gas constant (8.31446 J mol<sup>-1</sup> K<sup>-1</sup>), *T* the temperature [K], and *M* the molecular mass [g mol<sup>-1</sup>]

The vapor pressure is an essential parameter in a multitude of models for the evaporation of droplets.<sup>17–19</sup> To overcome this lack of information on vapor pressure data and other physico-chemical values for Amiton, we synthesized a set of eight different molecules (Figure 2), which are structurally closely related to each other, and determined the (i) vapor pressure,  $p_{sav}$  and (ii) and enthalpy of vaporization  $\Delta_{\rm F}^{\rm F} H_{\rm m}^{\rm o}(298.15 \text{ K})$ .

Therefore, the vapor pressure in ambient temperature regimes of I (298–343 K), II (293–343 K), III (293–343 K), IV (298–343 K), V (293–338 K), VI (279–318 K), VII (293–333 K), and VIII (283–323 K) was measured with the transpiration method, which is a well-established method for the determination of vapor pressures for medium to low volatility analytes.<sup>20–22</sup>

This transpiration experiment has been newly established in the research group of Prof. Klapötke at the University of Munich. The method was adapted from the existing experimental setup of Prof. S. Verevkin from the University of Rostock.<sup>20–22</sup> The basic principle of the transpiration experiment is to saturate a well-defined carrier gas stream at a temperature  $T_{\rm exp}$  and to measure the concentration of the analyte within. Additionally, we wanted to prove the general applicability of this method for the investigation of highly toxic and thermolabile compounds.

## 2. EXPERIMENTAL SECTION

**2.1. Safety Aspects.** Organophosphates are known to be (strong) acetylcholine esterase inhibitors and thus pose a threat toward human health and life. While handling the substances under consideration, proper PPE has to be worn, which is at least butyl rubber gloves, lab coat and safety goggles or preferably a face shield. All work has to be done in a fume cupboard. Moreover, all glassware and equipment in contact with the organo(thio)phosphates was thoroughly decontaminated by cleaning with reactive skin decontamination lotion. During the preparational part of this work an emergency medical assistant was available in the lab and a toxicological trained emergency physician was available on short notice.

**2.2. Synthesis.** The molecules investigated in this study were synthesized on a 40 mmol scale according to literature-known procedures<sup>23,24</sup> at the Chemistry Section of the CBRN Defense, Safety, and Environmental Protection School of the German Army. All reagents were of *purum* grade, and solvents were of analytical grade and were used without further purification prior to use.

The general reaction pathway is shown in Figure 3. The synthesis and isolation of the Amiton analogs follows a one-pot



**Figure 3.** General schema of the one-pot two-step syntheses with R = Me, Et, according to Gupalo et al.<sup>24</sup>

two-step procedure: step I, formation of the (thio)alcoholate anion; step II, coupling with the chloro(thio)phosphate.

The purities and degree of isomerization were determined by either a GC-FID or HPLC-MS measurement. Because the focus of this work is the determination of the physico-chemical properties of the molecules no further details on synthetic aspects are given here. Additional information regarding the synthesis will be published separately soon or can be requested from the corresponding author in the meantime. However, it has to be noted that some of the compounds are regulated under the CWC and restrictions may be applicable.

**2.3. Transpiration Method Setup.** The basic concept of the transpiration method has already been established<sup>20-22</sup> and is realized in this work as follows: From a nitrogen tank 1 (Figure 4) the carrier gas (nitrogen, Air Liquide, Stickstoff HG flüssig,  $\geq$ 99.999 vol %) is conducted through a pressure reduction valve 2 and a phosphorus pentoxide (Sicapent) drying tower. The flow rate of the carrier gas is adjusted and

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**Figure 4.** Transpiration method experimental setup: 1, nitrogen reservoir; 2, pressure reduction valve; 3,  $P_4O_{10}$  drying tower; 4, mass flow controller; 5, saturator; 6, condenser pipe; 7, cooling trap; 8, soap film flowmeter.

kept constant by a mass flow controller 4 (Natec Sensors MC-100 CCM) before it reaches the saturator 5, which is a cylindrical glass vessel (height 25 cm, diameter 10 cm) containing a U-shaped tube (length 50 cm, diameter 0.8 cm) filled with glass beads (diameter 1 mm). The glass beads are coated with the analyte (0.6 g) of choice by mixing of the liquid and beads in a beaker. The saturator is thermostated by a circulation thermostat (Huber Ministat 230) pumping a thermofluid (ethylene glycol (50% aqueous)) through it. At the end of the saturator the carrier gas stream reaches its saturation equilibrium with the analyte and then passes a cooling trap with the temperature  $T_{CT}$  (-30 °C). The flow rate of the carrier gas stream is measured under ambient conditions  $(T_{amb}, p_{amb})$  with a soap film flowmeter (HP #0101-0113). The experimental time to generate one data point ranges from 15 min to 24 h. This time is needed to collect a sufficient amount of analyte (Table S5-S12) in the cooling trap to meet the requirements of the analytical instruments used for quantification.

At the end of the experiment the condenser pipe is separated from the saturator and tert-butyl methyl ether solvent is added together with a solution of the internal standard (n-alkanes C-12, C-14, or C-16) of known concentration ( $\approx 1 \text{ mg/mL}$ ). The solution of analyte and standard is then used for internal standard quantification using either a Thermo Fisher Scientific GC/FID system equipped with a TriPlus RSH autosampler or a Shimadzu VO-GC/MS<sup>25</sup> system equipped with an AOC-20i autosampler. The exact chromatographic setup and operational modes can be found in Supporting Information Tables S2 and S3, respectively. For an initial validation of the experimental setup the following reference compounds were chosen: naphthalene, anthracene, isoamyl acetate, n-hexanol, and noctanol. The obtained results were compared to a large number of literature values. Detailed information on the results of this study can be found in the Supporting Information.

The transpiration method setup is suitable for the purification of the analytes during the experiment. Prior to the experiment, the analyte is conditioned by subjection to the carrier gas stream at elevated temperatures for the removal of impurities. The weight of the substance sample for the internal standard calibration was corrected by the purities stated in Table 1.

#### 3. RESULTS AND DISCUSSION

**3.1. Synthesis.** All but one (VII) of the synthesized compounds have been reported in the literature before by different authors.<sup>15,26–29</sup> Compound V was synthesized and recently published by us for the first time among other molecules (I–IV) of this study with the basic IR, GC–MS, HPLC–MS, and <sup>31</sup>P NMR data of compounds I–V.<sup>10</sup> Thus, a detailed discussion can be omitted at this point. Additional

Table 1. Calculation of Molar Heat Capacity Differences  $c_{dif}$ at T = 298.15 K

compd	$C^{\circ}_{p,m}(\mathrm{l})^{a}$ [J mol <sup>-1</sup> K <sup>-1</sup> ]	$\Delta_l^g C_{p,m}^{\circ b}$ [J mol <sup>-1</sup> K <sup>-1</sup> ]	purity <sup>c</sup>	$T_{\rm boil}^{d}$	$\rho^e$ [g cm <sup>-3</sup> ]
Ι	488.03	137.47	97.38	364	1.044
II	488.03	137.47	98.54	338	1.010
III	504.08	141.64	97.42	363	1.035
IV	471.98	133.29	95.07	326	1.061 <sup>33</sup>
V	519.51	145.65	99.07	405	1.015
VI	425.07	121.10	97.88	301	1.059
VII	456.55	129.28	99.71	312 <sup>f</sup>	1.021
VIII	456.55	129.28	96.28	387	1.034

<sup>*a*</sup>Calculated with elemental increments by Hurst et al.<sup>34</sup> <sup>*b*</sup>Calculated by  $\Delta_{1}^{8}C_{p,m}^{\circ} = 10.58 + C_{p,m}^{\circ}(1) \times 0.26$ .<sup>32</sup> <sup>*c*</sup>Purity according to GC-FID analysis. <sup>*d*</sup>Boiling point at 101325 Pa = 1 atm. <sup>*e*</sup>Density at 293.15 K (gravimetric determination with calibrated Eppendorf pipet (100  $\mu$ L)). <sup>*f*</sup>Linear estimation with  $\Delta_{1}^{8}C_{p,m}^{\circ} = 0$  due to nonconvergence of iteration process.

information on spectroscopic and spectrometric properties of the molecules will be published soon. The purities, which are important for the vapor pressure experiment, are given in Table 1 and range from 95.07 to 99.71%. Because compounds II, III, and V–VIII have the structural prerequisites to undergo the described thiono-thiolo rearrangement at elevated temperatures (Figure 1), the degree of isomerization was checked at the beginning and end of the transpiration experiment by means of HPLC–MS (Supporting Information Table S4). In all cases the observed conversion was less than 0.5% and thus no correction of the obtained data necessary.

**3.2. Determination of Vapor Pressure and Enthalpy of Vaporization.** The vapor pressure of the analyte  $p_{sat}(T_{exp})$  can be calculated using the Ideal Gas Law and Dalton's Law of partial pressures under the assumption that the volume of the carrier gas stream is significantly higher than that of the gaseous analyte.<sup>20,22</sup>

$$p_{\rm sat}(T_{\rm exp}) = \frac{m_{\rm a} R T_{\rm amb}}{M V_{\rm amb}}$$
(2)

with  $p_{sat}$  the vapor pressure of the analyte [Pa],  $T_{exp}$  the temperature of the saturator [K],  $m_a$  the mass of analyte [kg],  $T_{amb}$  the ambient temperature [K],  $V_{amb}$  the volume of carrier gas at ambient conditions [m<sup>3</sup>], M the molecular weight of the analyte [kg mol<sup>-1</sup>], and R the universal gas constant: 8.31446 [J mol<sup>-1</sup> K<sup>-1</sup>].

The  $p_{\text{sat}}-T_{\text{exp}}$  values obtained for each analyte are analyzed with a fitting function based on the Clarke–Glew equation:<sup>30</sup>

$$\ln p_{\rm sat} / p^{\circ} - \frac{\Delta_{\rm l}^{\rm g} C_{p,m}^{\circ}}{R} \ln \frac{T}{T_0} = A - \frac{B}{T}$$
(3)

with  $p^{\circ}$  the reference pressure being 1 [Pa],  $\Delta_{\Gamma}^{e}C_{p,m}^{\circ}$  the molar heat capacity difference from liquid to gaseous state [J K<sup>-1</sup> mol<sup>-1</sup>], *T* the temperature [K], *T*<sub>0</sub> the reference temperature [K], and *A* and *B* fitting coefficients (*A* [-], *B* [K]).

The enthalpy of vaporization at temperature T can be calculated by

$$\Delta_{l}^{g}H_{m}^{\circ}(T) = RB + \Delta_{l}^{g}C_{p,m}^{\circ}T$$
(4)

with  $\Delta_{I}^{g}H_{m}^{o}(T)$  the molar enthalpy of vaporization [J mol<sup>-1</sup>].

The heat capacities  $C_{p,m}^{\circ}$  at 298.15 K of the analytes I–VIII in liquid state are calculated according to the empirical element-increment approach by Hurst et al.<sup>34</sup> (cf. Table 1). The

Table 2. Compilation of	Obtained Data or	Enthalpies of	Vaporization,	$\Delta_{\rm I}^{\rm g} H_{\rm m}^{\rm o}$ , and	d Saturation V	Vapor 1	Pressures, p	sat,"	for
Compounds I–VIII									

compd <sup>a</sup>	method <sup>b</sup>	T range [K]	$T_{\rm avg}$ [K]	$\Delta_l^g H_m^o(T_{avg}) [kJ mol^{-1}]$	$\Delta_{\mathrm{f}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(298.15 \mathrm{~K})^{c} \mathrm{~[kJ~mol^{-1}]}$	$p_{\rm sat}(298.15 \ { m K})^d \ [{ m Pa}]$	$M [g mol^{-1}]$
Ι	Т	298.2-342.9	318.6	$80.9 \pm 0.2$	$83.6 \pm 0.3$	0.070	269.34
$I^{31}$	na	293.2-323.2	304.3	$77.0 \pm 0.5$	$78.4 \pm 0.6$	0.073	269.34
$I^{16}$	na, O	358.0-407.0	382.3	94.5	106.0	0.005	269.34
II	Т	293.3-343.0	314.2	$76.2 \pm 0.4$	$78.5 \pm 0.5$	0.278	269.34
III	Т	293.2-342.9	315.7	$83.8 \pm 0.2$	$86.3 \pm 0.3$	0.045	285.40
IV	Т	298.2-342.9	318.4	$76.5 \pm 0.2$	$79.0 \pm 0.3$	0.258	253.28
V	Т	293.3-338.1	318.0	$78.9 \pm 0.2$	$81.4 \pm 0.3$	0.100	283.37
VI	Т	278.5-318.1	297.7	$72.7 \pm 0.2$	$72.7 \pm 0.3$	0.988	241.29
VII	Т	293.3-333.1	310.9	$75.2 \pm 0.2$	$76.9 \pm 0.3$	0.035	255.31
VIII	Т	283.4-323.1	302.5	$70.9 \pm 0.2$	$71.5 \pm 0.3$	0.636	255.31
acres	· C 1·c	1 by				1. ( 1 1.	

<sup>*a*</sup>Citation given for literature values. <sup>*b*</sup>Methods: T, transpiration; O, equation only. <sup>*c*</sup>Enthalpies of sublimation were adjusted according to Chickos et al.<sup>32</sup> with  $\Delta_{\rm F}^{\rm s}C_{\rm p,m}^{\rm o}$  and  $C_{\rm p,m}^{\rm o}({\rm liq})$  according to Table 1. <sup>*d*</sup>Vapor pressure at 298.15 K, calculated according to eq 3. na: not available.

corresponding heat capacity differences with the gaseous state are calculated according to the procedures by Chickos et al., which were also used for the adjustment of the obtained enthalpies of vaporization to 298.15 K for the reason for comparability. The detailed error estimation and error calculation, which is valid for this work and its experiments was elucidated before<sup>21</sup> for a nearly identical experimental setup that was adapted in this work. Table 2 is a compilation of the results obtained in this work in comparison with the few available literature values of Amiton (I) concerning the vaporization enthalpies investigated at the average temperature of the measurement and the reference temperature 298.15 K.<sup>15,16</sup> Additionally, the vapor pressure at 298.15 K is stated. For all analytes the results obtained by the transpiration method for the absolute vapor pressures  $p_{sat}$  and thermodynamic properties of vaporization are available in Supporting Information Tables S5-S12. A condensation of the data can be achieved by a Clausius-Clapeyron plot (Figure 5) for each



**Figure 5.** Clausius-Clapeyron plot of p-T data of compounds I–VIII:  $(\diamondsuit)$  I + I\*;  $(\bigcirc)$  II;  $(\Box)$  III + IV;  $(\bigtriangleup)$  V;  $(\bullet)$  VI × VII × VIII. \*Literature data were provided by Baldit.<sup>31</sup>

analyte and also allows a visual comparison of the results with literature data. Actually, the authors did not always derive vaporization enthalpies from their determined vapor pressures or they performed that calculation in a different manner. The literature vapor pressures were thus treated using eqs 3 and 4 and the calculated enthalpies of vaporization adjusted<sup>32</sup> to 298.15 K for the sake of comparison with our results (Table 2).

In terms of vapor pressure, the following observations can be made for Amiton (I) (P=O, P-S), II (P=S, P-O), III (P=S, P-S), and IV (P=O, P-O), which have different chalcogen coordinations at the phosphorus atom but the same carbon backbone. I and II only differ in the position of the sulfur atom, which is located in the P-S single bond in one and in the formal P=S double bond in II.

With respect to the octet rule, the formal P=S and P=O double bonds should be regarded as more polar P<sup>+</sup>--S<sup>-</sup> and  $P^+-O^-$  single bonds. II ( $p_{sat}(298.15 \text{ K})$ , 0.278 Pa;  $\Delta_{\rm f}^{\rm g} H_{\rm m}^{\circ}(298.15 \text{ K})$ , 78.5 ± 0.5 kJ mol<sup>-1</sup>) is more volatile than I ( $p_{sat}(298.15 \text{ K})$ , 0.070 Pa;  $\Delta_1^g H_m^o(298.15 \text{ K})$ , 83.6  $\pm$  0.3 kJ  $mol^{-1}$ ). This can be justified by the increased polarity of the  $P^+-0^-$  bond in I compared to that of the  $P^+-S^-$  bond in II. Increased bond polarity generally results in stronger intermolecular dipole-dipole interactions. Interestingly, compound IV ( $p_{sat}(298.15 \text{ K})$ , 0.258 Pa;  $\Delta_{p}^{g}H_{m}^{o}(298.15 \text{ K})$ , 79.0 ±  $0.3 \text{ kJ mol}^{-1}$ ) has a vaporization behavior very similar to that of the more toxic<sup>35</sup> compound II. Therefore, II might be used as a precise simulant for compound IV in terms of gas phase detectability. Compound III ( $p_{sat}$ (298.15 K), 0.045 Pa;  $\Delta_{\rm f}^{\rm g} H_{\rm m}^{\circ}(298.15 \text{ K})$ , 86.3 ± 0.3 kJ mol<sup>-1</sup>) has the highest molecular weight and is therefore the least volatile compound among Amiton (I) and its derivatives II-IV.

Compounds V–VIII are derivatives of compound II with identical chalcogen coordinations of the phosphorus atom (P=S, P–O). In compound V ( $p_{sat}(298.15 \text{ K})$ , 0.100 Pa;  $\Delta_{\rm I}^{\rm g}H_{\rm m}^{\rm o}(298.15 \text{ K})$ , 81.4 ± 0.3 kJ mol<sup>-1</sup>) the alkyl bridge between the thiophosphate unit and amine functionality is extended by a CH<sub>2</sub> unit, which results in a lower vapor pressure and a higher (+2.9 ± 0.6 kJ mol<sup>-1</sup>) enthalpy of vaporization. In compound VI ( $p_{sat}(298.15 \text{ K})$ , 0.988 Pa;  $\Delta_{\rm I}^{\rm g}H_{\rm m}^{\rm o}(298.15 \text{ K})$ , 72.7 ± 0.3 kJ mol<sup>-1</sup>) the terminal *N*-ethyl chains are substituted with *N*-methyl substituents, which results in a higher vapor pressure and lower (-5.8 ± 0.6 kJ mol<sup>-1</sup>) enthalpy of vaporization.

The difference of compound VII ( $p_{sat}(298.15 \text{ K})$ , 0.035;  $\Delta_{\rm F}^{\rm g} H_{\rm m}^{\rm o}(298.15 \text{ K})$ , 76.9  $\pm$  0.3 kJ mol<sup>-1</sup>) and compound VI is the length of the alkyl chain between thiophosphate and amine functionality. In compound VII it is extended by a CH<sub>2</sub> unit. With respect to this, the vapor pressure and enthalpy of vaporization of VII are increased (+4.2  $\pm$  0.4 kJ mol<sup>-1</sup>) in comparison to that of VI. Compound VIII ( $p_{sat}(298.15 \text{ K})$ , 0.636 Pa;  $\Delta_{\rm F}^{\rm g} H_{\rm m}^{\rm o}(298.15 \text{ K})$ , 71.5  $\pm$  0.3 kJ mol<sup>-1</sup>) is a branched constitutional isomer of compound VII. With respect to the reduced contact surface for van der Waals interactions of the alkyl functionalities, the vapor pressure of VIII is increased and

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the enthalpy of vaporization is decreased  $(-5.4 \pm 0.4 \text{ kJ mol}^{-1})$  in comparison to that of VII.

For Amiton (I) one p-T data set (20, 25, and 50 °C) published by Baldit<sup>31</sup> and one p-T equation published by Stephenson et al.<sup>16</sup> (358–407 K) are available. In both publications the purity of the sample and the method of measurement are not stated. The data derived from the p-Tdata published by Baldit<sup>31</sup> ( $p_{sat}$ (298.15 K), 0.073 Pa;  $\Delta_{\rm f}^{\rm g} H_{\rm m}^{\circ}$  (298.15 K), 78.4 ± 0.6 kJ mol<sup>-1</sup>) are in fair agreement with the values obtained in this work. Especially the literature value reported by Baldit<sup>31</sup> at 298.2 K (0.072 Pa) is in good agreement with the two values obtained in this work (0.071  $\pm$ 0.007 and 0.069  $\pm$  0.007 Pa; cf. Supporting Information Table S5). The vapor pressure of I at 323.2 K (0.800 Pa) reported by Baldit<sup>31</sup> does not match the three values obtained in this work at 323.0 K (0.90  $\pm$  0.03, 0.90  $\pm$  0.03, 0.87  $\pm$  0.03 Pa; cf. Supporting Information Table S5). Therefore, the value reported by Baldit<sup>31</sup> at 323.2 K is considered to be imperfect, which explains the discrepancy regarding the enthalpies of vaporization. The data derived from the p-T equation published by Stephenson et al.<sup>16</sup> ( $p_{sat}(298.15 \text{ K})$ , 0.005 Pa;  $\Delta_{\rm f}^{\rm g} H_{\rm m}^{\circ}(298.15 \text{ K})$ , 106.0 kJ mol<sup>-1</sup>) do not agree with the data obtained in this work and those published by Baldit.<sup>31</sup>

**3.3. Calculation of Concentration**  $c_{dif}$  **under Diffusion Conditions of Amiton Derivatives in Air.** Vapor pressures are measured under ideal saturation conditions. In a real case scenario the saturation equilibrium of the analyte will not be reached and diffusion processes will dictate the air concentration of the analyte. Dravnieks et al.<sup>36</sup> have stated a mathematical model for the estimation of the nonequilibrium air concentration of an explosive, which is applied to compounds I–VIII in the following using the equations and values provided by Bird et al.<sup>37</sup>

Fick's Law of Diffusion provides a suitable approximation for the rate of molecular vapor emission *J*:

$$J = A \times D_{AB} \times \frac{n_{\rm c} - n_{\rm a}}{d} \tag{5}$$

with *J* the emission flux [molecules  $s^{-1}$ ], *A* the area of analyte exposed to air [cm<sup>2</sup>],  $D_{AB}$  the diffusivity of analyte vapor in air [cm<sup>2</sup>  $s^{-1}$ ],  $n_c$  the concentration of analyte under saturation conditions [molecules cm<sup>-3</sup>],  $n_a$  the concentration of the analyte in air [molecules cm<sup>-3</sup>], and *d* the thickness of nonturbulent layer air [cm].

The concentration of the analyte in the air is considered to be negligibly small  $(n_c - n_a \sim n_c)$ , and the thickness of the nonturbulent layer of air surrounding the analyte is considered to be 0.2 cm.<sup>36</sup>

The diffusivity  $D_{AB}$  can be calculated by the following formula:<sup>39-41</sup>

$$D_{\rm AB} = 0.0018583 \frac{1}{p \sigma_{\rm AB}^{2} \Omega_{\rm D,AB}} \sqrt{T^{3} \left(\frac{1}{M_{\rm A}} + \frac{1}{M_{\rm B}}\right)}$$
(6)

with *T* the temperature [K] (298.15 K),  $M_{\rm A}$  the molecular mass of the analyte [g mol<sup>-1</sup>],  $M_{\rm B}$  the molecular mass of air [g mol<sup>-1</sup>] (28.97 g mol<sup>-1</sup>), *p* the total pressure [atm] (1 atm),  $\sigma_{\rm AB}$  the combined collision diameter [Å], and  $\Omega_{\rm D,AB}$  the collision integral for diffusion.

$$\sigma_{\rm AB} = (\sigma_{\rm A} + \sigma_{\rm B})/2 \tag{7}$$

with  $\sigma_A$  the collision diameter of analyte [Å] and  $\sigma_B$  the collision diameter of air [Å] (3.617 Å).<sup>37</sup>

$$\varepsilon_{\rm AB} = \sqrt{\varepsilon_{\rm A} \varepsilon_{\rm B}} \tag{8}$$

with  $\varepsilon_A$  the characteristic energy of analyte [J] and  $\varepsilon_B$  the characteristic energy of air [J].

Though the collision diameter  $\sigma_{\rm B}$  (3.617 Å)<sup>37</sup> and the characteristic energy  $\varepsilon_{\rm B}$  ( $\varepsilon_{\rm B}/\kappa = 97.0$  K)<sup>37</sup> of air are known, the collision diameter of the analyte  $\sigma_{\rm A}$  and its characteristic energy  $\varepsilon_{\rm A}$  have to be estimated. These values may be estimated from the liquid at the boiling point (b):

$$\varepsilon/\kappa = 1.15T_{\rm b}$$
  $\sigma = 1.166\sqrt[3]{V_{\rm b}}$  (9)

with  $T_{\rm b}$  the boiling point [K],  $V_{\rm b}$  the molar volume of the liquid at the boiling point [cm<sup>3</sup> mol<sup>-1</sup>], and  $\kappa$  the Boltzmann constant (1.38065 × 10<sup>-23</sup> J K<sup>-1</sup>).

With  $\varepsilon_{\rm AB}$  the collision integral for diffusion  $\Omega_{\rm D,AB}$  can be calculated according to

$$\Omega_{\rm D,AB} = \frac{1.16145}{T^{*0.15610}} + \frac{0.19300}{\exp(0.47635T^*)} \\ + \frac{1.03587}{\exp(1.52996T^*)} + \frac{1.76474}{\exp(3.89411T^*)}$$
(10)

where

$$T^* = \kappa T / \varepsilon_{AB}$$

with T the temperature [K].

In the case of compounds I–VIII the diffusion coefficient can be calculated from their boiling point, which is calculated by extrapolation of the p-T data obtained in this work with eq 3 to the atmospheric pressure (101 325 Pa) (cf. Table 1). The molar volume  $V_{\rm b}$  at the boiling point can be approximated from the density at 20 °C (cf. Table 1) using an equation that was derived from the thermal expansion of the model compound triethylphosphate<sup>38</sup> by linear regression of the temperaturedependent density data provided:

$$\rho_b = \rho_{20^{\circ}\text{C}} - 0.0009943(T_b - 293.15) \tag{11}$$

with  $\rho_{\rm b}$  the density at boiling point [g cm<sup>-3</sup>] and  $\rho_{20^{\circ}\rm C}$  the density at 20 °C.

The molar volume at the boiling point can be calculated by  $V_{\rm b} = M/\rho_{\rm b}$  (12)

With eqs 5–12 the diffusion coefficient of a liquid analyte in air can be approximated when solely its melting point and a density are known and eq 5 can be used to calculate the mass flux of material from the analyte to the air. With 
$$A = 1 \text{ cm}^2$$
,  $n_a \sim 0$ , and  $d = 0.2 \text{ cm}$  it can be written

$$J = \frac{D_{\rm AB}}{0.2 \text{ cm}} \times n_{\rm c} \tag{13}$$

If the concentration  $n_c$  is converted to partial pressure  $(n_c = 2.47520 \times 10^{14} p, p$  is the vapor pressure [Pa]) and the emission flux is converted into a mass flux (unit conversion factor:  $M/N_A$ ), the mass flux can be calculated:

$$Q = 2.47520 \times 10^{14} \times D_{AB} \times p \times (M/N_A)$$
<sup>(14)</sup>

with Q the emission flux of analyte [g s<sup>-1</sup> cm<sup>-2</sup>] and  $N_{\rm A}$  the Avogadro constant (6.022 × 10<sup>23</sup> mol<sup>-1</sup>).

An example of this calculation for Amiton (I) can be found in Supporing Information Table S1. With the emission flux Q in hand, the concentration of the analyte in air can be calculated:

$$c_{\rm dif} = S \times Q \times r \tag{15}$$

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Table 3. Condensed Summary of the Calculated Saturation Concentration  $c_{sat}$  and Concentration under Diffusion Conditions  $c_{dif}$  for the Molecules of This Study

	compound <sup>a</sup>							
	I	II	III	IV	V	VI	VII	VIII
M [g mol <sup>-1</sup> ] <sup>b</sup>	269.34	269.34	285.40	253.28	283.37	241.29	255.31	255.31
$\rho [g \text{ cm}^{-3}]^c$	1.044	1.011	1.035	1.061	1.015	1.059	1.021	1.034
$p_{\rm sat}  [{ m Pa}]^d$	0.070	0.278	0.045	0.258	0.100	0.988	0.035	0.636
$c_{\rm sat}  \left[ {\rm ng}  {\rm L}^{-1} \right]^e$	7606	30205	5181	26360	11431	96166	3605	65503
$c_{\rm dif} [\rm ng \ L^{-1}]^f$	1.5	5.8	1.0	5.5	2.0	20.9	0.7	12.5
$c_{\rm sat}/c_{ m dif}$	5232	5208	5424	4828	5730	4597	4899	5255
	1	l						

<sup>*a*</sup>Compound according to Figure 2. <sup>*b*</sup>Molar weight. <sup>*c*</sup>Density at 20 °C. <sup>*d*</sup>Vapor pressure at 25 °C. <sup>*e*</sup>Saturation concentration at 25 °C calculated according to eq 1. <sup>*f*</sup>Concentration under diffusion conditions at 25 °C calculated according to eq 15 for an exposed surface of 1 m<sup>2</sup>.

with  $c_{\rm dif}$  the concentration of analyte in air  $[g L^{-1}]$ , S the surface of analyte exposed to air  $[cm^2]$ , and r the attenuation factor  $(10^{-4}) [s^{-1}]$ . The attenuation factor r has been established in the study by Dravnieks et al.<sup>36</sup>

For a surface area of 1 m<sup>2</sup> the values for  $c_{dif}$  stated in Table 3 were obtained. These values can serve as a kind of standardized surface density if 1 m<sup>2</sup> is used as a reference area for the analyte under investigation. However, this value must be regarded as the maximum concentrations of analyte that can be present for detection in air in an open-exposure scenario under the given environmental conditions, e.g., temperature.

From the calculated values for the concentration under diffusion conditions, it is possible to estimate the sampling volume necessary to meet the analytical requirements of the detection instrument used. Moreover, it is possible to predict under which environmental conditions (e.g., operating temperature) it is possible to detect the analyte in the gas phase or not. Knowing this is crucial for first responders who are threatened by evaporating toxic gases. On the contrary, if the detection device is not giving an alert, one could easily be lulled into a false sense of security because the molecules investigated in this study still pose a threat to human life by being also active as a contact poison.

#### 4. CONCLUSIONS

As a main finding of this work, the transpiration method approach was successfully applied for the determination of the vapor pressure of Amiton (I) and seven derivatives (II–VIII). Furthermore, this approach proved viable for both thermolabile and highly toxic compounds. Additionally, the concentration  $c_{\rm dif}$  of freshly synthesized compounds I–VIII, of which compound VII has not yet been reported in the literature, was calculated on the basis of a diffusion model stated by Dravnieks et al.<sup>36</sup> With equations and values published by Bird et al.<sup>37</sup> it was possible to determine values for the concentrations  $c_{\rm sat}$  and  $c_{\rm dif}$ . They range from 3605 (VII) to 96 166 ng L<sup>-1</sup> (VI) for  $c_{\rm sat}$  and from 0.7 (VII) to 20.9 ng L<sup>-1</sup> (VI) for  $c_{\rm dif}$  respectively. The ratio of  $c_{\rm sat}/c_{\rm dif}$  is in the range 4597–5730. A condensed summary of the values obtained is given in Table 3.

For a quick conservative estimation of  $c_{\text{dif}}$  for Amiton derivatives it is recommended to divide  $c_{\text{sat}}$  by 6000.

The concentration  $c_{dif}$  is a useful parameter for the choice of suitable gas phase detection equipment for Amiton and its derivatives because it can be directly compared with the limit of detection LOD [ng L<sup>-1</sup>] of the device used.

Our results, for example, allow us now to easily estimate the necessary sampling volume, in the case of analyte enrichment from the gas phase, by dividing the limit of detection by the concentration under diffusion conditions.

## ASSOCIATED CONTENT

### **Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpca.7b01177.

Calculation of the emission flux of Amiton, compilation of VO-GC/MS, GC-FID, and HPCL-ESI-MS parameters, detailed measurement results of the transpiration method for compounds I–VIII, reference compound measurements with the transpiration method (PDF)

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The manuscript was written through contributions of all authors.

#### Notes

The authors declare no competing financial interest.

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