UNIVERSIDADE ESTADUAL DE CAMPINAS
FACULDADE DE ENGENHARIA QUÍMICA

LUCIANA APARECIDA ANDRADE PREVIATO FONSECA

CONTRIBUIÇÃO AO ESTUDO DE PROPRIEDADES TERMODINÂMICAS DE TERPENOS OXIGENADOS DE PLANTAS NATIVAS DO BRASIL

CONTRIBUTION TO THE STUDY OF THE THERMODYNAMIC PROPERTIES OF OXYGENATED TERPENES OF BRAZILIAN NATIVE PLANTS

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Tese apresentada à Faculdade de Engenharia Química da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Doutora em Engenharia Química.

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Orientador: Prof. Dr. Marco Aurélio Cremasco

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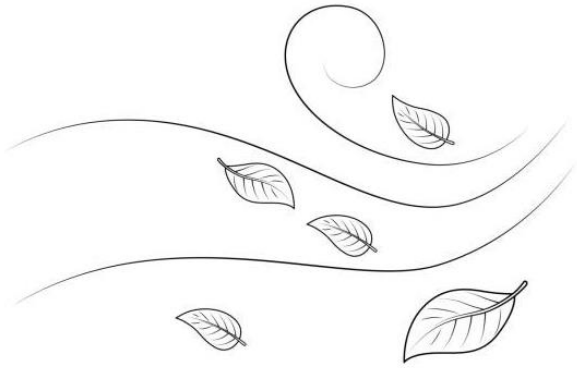

Na concepção dos povos indígenas, tudo na terra tem um propósito, cada doença uma erva para curar, cada pessoa uma missão a cumprir... e o tempo... é apenas um marcador das estações.

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RESUMO

Este estudo oferece uma análise abrangente dos terpenoides, também designados por terpenos oxigenados, sobretudo os compostos encontrados nos biomas brasileiros. Estes compostos estão entre os constituintes majoritários dos óleos essenciais sendo amplamente utilizados nas indústrias farmacêutica, de alimentos, cosméticos e na agricultura. Esta tese de doutorado traz uma contribuição à obtenção de parâmetros termodinâmicos utilizando a correlação por cromatografia gasosa, ao estender a técnica aos terpenos oxigenados, uma abordagem incomum neste campo de estudo. Por meio dessa técnica foram conduzidas determinações experimentais da entalpia de vaporização (ΔH^{vap}), temperatura normal de ebulição (T_{nb}), e pressão de vapor de $\left(P_{vap}\right)$ de terpenóides de plantas nativas do Brasil. Além disso, as estruturas moleculares estudadas foram avaliadas para outro parâmetro termodinâmico, a entropia de vaporização (ΔS^{vap}). Métodos preditivos de contribuição de grupos foram utilizados para prever propriedades termodinâmicas como alternativas às medições experimentais. O estudo também compara diversos modelos preditivos e consolida um modelo de contribuição de grupos especificamente desenvolvido para compostos terpênicos encontrados em óleos essenciais. Esta pesquisa aprimora a compreensão do comportamento dos terpenoides ao apresentar dados termodinâmicos inéditos na literatura e ao avaliar a predição de propriedades termodinâmicas, viabilizando assim a utilização desses compostos em diversas aplicações industriais e difundindo o conhecimento sobre os terpenoides derivados de plantas nativas do Brasil.

Palavras-chave: Terpenoides, Óleos essenciais, Plantas nativas do Brasil, Correlação por Cromatografia gasosa, Parâmetros termodinâmicos, Contribuição de grupos.

ABSTRACT

This study offers an analysis of terpenoids, also known as oxygenated terpenes, especially the compounds found in Brazilian biomes. These compounds are among the major constituents of essential oils and are widely used in the pharmaceutical, food, cosmetics industries, and agriculture. This doctoral Thesis makes a contribution to obtaining thermodynamic parameters through gas chromatography correlation, by extending the technique to oxygenated terpenes, an unusual approach in this field of study. Through gas chromatography correlation, experimental determination of the enthalpy of vaporization (ΔH^{vap}), normal boiling temperature (T_{nb}), and vapor pressure (P_{vap}) of terpenoids from native Brazilian plants were conducted. Additionally, the molecular structures studied were evaluated for another thermodynamic parameter, the vaporization entropy (ΔS^{vap}). Moreover, predictive group contribution methods were utilized to provide thermodynamic properties as alternatives to experimental measurements. The study also compares various predictive models and consolidates a group contribution model specifically developed for terpene compounds found in essential oils. This research enhances the understanding of terpenoid behavior by presenting previously unreported thermodynamic data in the literature and by evaluating the prediction of thermodynamic properties, thereby enabling the utilization of these compounds in various industrial applications, disseminating knowledge about terpenoids derived from native plants in Brazil.

Keywords: Terpenoids, Essential oils, Brazilian Native Plants, Gas Chromatography Correlation, Thermodynamic Parameters, Group Contribution.

Nomenclature

Abbreviation	Description
exp	Experimental
est	Estimated
GC	Gas chromatography
G	Gibbs energy [J]
H	Enthalpy [kJ.mol^{-1}]
I_X	Kováts retention index
lit	Literature
MRD	Mean relative deviation
P_{vap}	Vapor pressure [Pa]
RD	Relative deviation
r^2	Correlation coefficient
R	Universal gas constant [J mol^{-1} K^{-1}]
S	Entropy [J K^{-1} mol^{-1}]
T	Temperature [K]
T_0	Reference temperature [K]
T_{nb}	Normal boiling temperature [K]
T_R	Retention time [s]
U	Internal energy [J]
X	Solute, analyzed compound
γ^{∞}	Infinite dilution activity coefficient
z	Carbon number
ΔH^{vap}	Enthalpy of vaporization [kJ mol^{-1}]
ΔS^{vap}	Vaporization entropy [J K^{-1} mol^{-1}]

SUMMARY

CHAPTER I

1. Introduction

In the past, thorough knowledge and utilization of plants were often associated with mystical beliefs and folklore (GRAHAM-BROWN; HEALSMITH, 2018; LLANES et al., 2022), frequently linked to the realm of witchcraft. Across different countries, legends and stories depict witches using specific plants in their spells and potions. In Brazil, indigenous groups have developed a comprehensive understanding of native flora (FONSECA; CREMASCO, 2022), recognizing their healing properties and incorporating them into traditional medicinal practices (BRAGA, 2021). These cultures have long possessed wide-ranging knowledge of the medicinal properties of local plants, utilizing them to treat illnesses and maintain overall well-being. Brazil, the most biologically diverse country globally, holds the top position among the world's 17 megadiverse countries and is surpassed only by Indonesia in terms of species endemism. Brazil encompasses six terrestrial biomes: Amazon Forest, Atlantic Forest, Cerrado, Caatinga, Pantanal, and Pampa. Currently, at least 103,870 animal species and 43,020 plant species are known, constituting 70% of the world's cataloged animal and plant species. Based on the Convention on Biological Diversity (2023), Brazil is estimated to host between 15% and 20% of the world's biological diversity, boasting the highest number of endemic species globally.

Given Brazil's biological richness, its native plants offer a wide variety of essential oils. According to the International Organization for Standardization (ISO) in their ISO 9235 standard, an essential oil is derived from natural plant materials through methods such as steam distillation, mechanical processes from citrus fruit epicarps, or dry distillation, with the aqueous phase separated by physical processes if present, primarily consisting of terpenes and terpenoids. These compounds, commonly found in plant extracts, are associated with essential oil properties and potential applications. Terpenes are characterized as molecules with isoprene units in their hydrocarbon structures, while terpenoids are defined as a modified class of terpenes, featuring various oxygenated functional groups, including alcohols, ketones, carboxylic acids, and esters.

Terpenoids, also known as oxygenated terpenes, constitute a highly diverse group of natural compounds. With over 80,000 known representatives boasting a wide spectrum of biological activities, including antiallergic, antibiotic, anticancer, anti-inflammatory, antimicrobial, antioxidant, antiviral, and insect resistance properties (BONCAN et al., 2020; FONSECA; CREMASCO, 2022; POWDER-GEORGE, 2024), they find extensive applications

across various industries such as pharmaceuticals, food, cosmetics, chemicals, and agriculture.

The technological application of terpenoids is intricately linked to the understanding of thermodynamic properties, including enthalpy of vaporization (ΔH^{vap}), vapor pressure (P_{vap}), normal boiling temperature (T_{nb}), and vaporization entropy (ΔS^{vap}). These parameters are essential from extraction to industrial production. In extraction, the normal boiling temperature provides a fundamental reference for determining optimal vaporization conditions during methods such as distillation. Additionally, enthalpy of vaporization is crucial for calculating the amount of heat required to vaporize these compounds, directly affecting the efficiency and cost of extraction processes. Vaporization entropy represents the measure of molecular disorder during the liquid-to-vapor transition, influencing the volatility and stability of compounds. In turn, vapor pressure determines the tendency of terpenoids to evaporate at different temperatures and pressures, directly affecting the volatility of these compounds and consequently their applicability in various industrial products. While techniques for identifying terpenes and terpenoids in essential oils are well-established (CHAMORRO et al., 2012), there are gaps in the literature regarding experimental data on thermodynamic properties of oxygenated terpenes.

This study contributes to the analysis of terpenoids from Brazilian native plants using gas chromatography correlation techniques in the experimental determination of thermodynamic parameters, extending it to terpenoids. Supplying the literature with unpublished experimental data, as well as evaluating the performance of predictive models for obtaining thermodynamic properties.

1.1 Objectives

Overall objective

The technological application of terpenoids hinges on comprehending their thermodynamic properties to enhance extraction processes and their utilization across the chemical, pharmaceutical, and food industries.

The overarching goal of this study is to experimentally determine thermodynamic data, including vapor pressure, enthalpies of vaporization, and normal boiling temperature, for terpenoids present in essential oils using the gas chromatography correlation technique.

Specific objectives

I. Determine the suitable temperature range for analyzing the studied compounds.

II. Acquire chromatographic retention data for each analyzed compound within the identified temperature range.

III. Calculate Kováts retention indices for each analyzed compound at various temperature intervals using the chromatographic retention data.

IV. Apply Kirchhoff-Rankin-type equations to determine the evaluated thermodynamic quantities.

V. Extend the well-established gas chromatographic correlation methodology for terpene compounds to terpenoids, particularly oxygenated terpenes, to consolidate an unusual approach through experimental data.

VI. Validate the proposed chromatographic methodology by comparing it with literature data.

VII. Test group contribution models regarding their specificity to the structure of terpene and terpenoid compounds and compare them with the experimental enthalpy of vaporization data obtained in this study.

1.2 Document structure

This document is organized as follows, after a brief introduction and summarizing of objectives:

Chapter II presents a literature review addressing the chemistry of terpenoids and a thermodynamic foundation, including the thermodynamic parameters discussed throughout this work.

In chapters III and IV, publications in collaboration with Nova Science Publishers are highlighted, addressing the potential of Brazilian biodiversity, the ancestral knowledge of indigenous groups about plants, and the role of science in preserving this biodiversity and traditional knowledge to promote sustainable development.

Chapter III provides an overview of the distribution of terpenes and terpenoids in the six Brazilian biomes, focusing on their therapeutic properties.

Chapter IV discusses the thermodynamic properties of terpene compounds present in the essential oil of *Lippia gracilis* Schum, a species native to the Caatinga, including a study on vaporization entropy to correct vapor pressure.

Chapters V and VI explore the methodology of experimental determination of thermodynamic properties through correlation via gas chromatography, now expanded to include terpenoids, with the presentation of unpublished data. These studies identified the ideal temperature range and Kováts retention indices for the compounds studied, validating the

applicability of gas chromatography correlation approach in the experimental determination of thermodynamic properties such as vapor pressure, enthalpy of vaporization, and normal boiling temperature for oxygenated terpenes. Additionally, methods of group contribution are discussed as complementary tools for estimating thermodynamic properties.

Chapter VII presents an article discussing the relationship between the molecular structure of terpenes and terpenoids and the calculation of vaporization entropy for these compounds.

Chapter VIII describes a specific group contribution model to estimate vapor pressure and enthalpy of vaporization of terpenes and terpenoids found in essential oils.

Chapter IX presents the final considerations, conclusions, and recommendations for future research.

CHAPTER II

2. Literature Review

2.1 Therapeutic and industrial potential of Brazil's native plants

The Brazilian native plants are significant resources, not only for the environmental services but also for the opportunities presented for development and sustainable use. Represented by more than 200 indigenous groups and 170 languages, Brazil is megadiverse from a cultural perspective as well. The substantial knowledge on flora species, including traditional management systems, possessed by the large number of local communities, is fundamental for the conservation and sustainable use of the country’s genetic and biological reserves.

Each ethnic group has its own pharmacopoeia, consisting of specific plants used to treat various conditions. For example, Andiroba (*Carapa guianensis*) whose name derives from the Tupi term ãdi'roba, meaning "bitter oil," found in the Amazon region, is used by indigenous communities as an anti-inflammatory and wound healer (NOVELLO; SCAPINELLO; MAGRO, 2015). Jaborandi (*Pilocarpus microphyllus*), whose name means "plant that makes you sweat and salivate," native to the Brazilian Cerrado with distribution in the states of Maranhão and Piauí, is used to treat eye problems and stimulate sweating (COSTA, 2012). Different plant parts, such as leaves, bark, roots, and seeds, are utilized to prepare infusions, decoctions, ointments, and poultices (GAUDÊNCIO; RODRIGUES; MARTINS, 2020). The preparation and administration of traditional remedies often involve rituals and prayers, as healing is considered a holistic process encompassing not only the physical body but also spiritual and emotional aspects (ALMEIDA, 2011).

From ancestral usage to the present day, it's important to highlight that knowledge concerning bioactive molecules has significantly increased in recent years, generating interest and recognition within the scientific community. Studies have been conducted to identify phytochemicals isolated from plants (LEITE; CAMARGO; CASTILHO, 2021), revealing various applications in the food (FALLEH et al., 2020; PANDEY et al., 2017), cosmetics (KAURA; KAUR; SALUJA 2023), agricultural (CHAUBEY, 2019), and pharmaceutical industries (EL HACHLAFI et al., 2021; SILVA et al., 2021; WANG et al., 2021; GAO et al., 2020; GUIMARÃES et al., 2019).

Beyond the evident biological richness, Brazil's native plants possess a remarkable characteristic: the abundant presence of terpenes and terpenoids. These volatile organic compounds are associated with essential oils properties.

Essential oils exhibit a high variability in their composition of terpenes and terpenoids, both qualitatively and quantitatively. This variability is influenced by factors that can be divided into two categories: intrinsic factors associated with the plant and its interaction with the environment, such as soil type, climate, and the plant's degree of maturity (FONSECA; CREMASCO, 2022); and extrinsic factors related to the extraction method, where parameters such as temperature and pressure are particularly relevant. Table 2.1 presents some Brazilian native plants, their occurrences, and the terpene or terpenoid evaluated in this study.

Table 2.1 Occurrence of terpenes and terpenoids in plant species of Brazilian biomes.

Scientific name	Popular name	Occurrence in Brazilian Biomes	Terpene/Terpenoid
Aniba rosaeodora	pau-rosa	Amazon Rain Forest	linalool [1]
Eremanthus erythropappus	candeia	Pantanal	terpinene-4-ol [2]
Eugenia uniflora L.	pitanga	Atlantic Forest	β-damascenone [3]
Lantana camara L.	camará	Amazon Rain Forest	limonene [4]
Hyptis suaveolens L.	hortelã do campo	Cerrado	camphor, menthone [5]
Lippia gracilis Schum	erva-baleeira	Caatinga	p-cymene [6]
Passiflora edulis	maracujá	Atlantic forest	4-(4-hydroxyphenyl)-2-butanone [7]
Poiretia latifolia Vogel	erva de touro	Pampa	(R)-(-)-carvone [8]
Solidago chilensis Meyen	arnica brasileira	Atlantic Forest and Cerrado	acetophenone [9]

[1] Teles et al., 2021; [2] Lima et al., 2013; [3] Bicas et al., 2011; [4] Silva et al., 1999; [5] Martins, Santos, Polo, 2006; [6] Oliveira, 2012; [7] Monteiro et al., 2016; [8] Porto et al., 2010; [9] Liz et al., 2008.

The advancement of chromatographic techniques represents significant progress in the study of the chemical composition of essential oil. Gas Chromatography (GC) stands out

owing to its simplicity, rapidity, and efficiency, for both the identification and quantification of essential oil components and composition variations (CHAMORRO et al., 2012).

Gas chromatography is the primary step in essential oil analysis because the mixture is separated into individual components. This technique uses a ‘column’ to achieve this separation. A small amount of the essential oil is injected at the start of the column and a gas pushes the mixture through the column to the other side where each of the separated components meet a detector, usually a flame ionization detector (FID) or a mass detector (MS).

As relevant as the chemical composition of essential oils, thermodynamic parameters including vapor pressure, normal boiling temperature, enthalpy of vaporization, and vaporization entropy are necessary for studying the stability, solubility, and reactivity of these compounds in biological and industrial environments. These parameters contribute to optimizing extraction processes, enhancing efficacy in applications for the pharmaceutical, food, and cosmetic industries.

2.2 Terpenoids in essential oils chemistry

Essential oils are responsible for the fragrance of plants due to their volatile and lipophilic nature, resulting from secondary metabolism and found in nearly two thousand plant species distributed across sixty families (SILVA et al., 2005). They can be stored in flowers, leaves, bark, wood, roots, fruits, and seeds, with composition varying even within the same species (SOUZA et al., 2010).

Volatile oils are obtained from plant parts through steam distillation or by expression of citrus fruit pericarps. Other extraction methods include hydro-distillation, enfleurage, extraction by supercritical CO_2, and by nonpolar organic solvents (MODASSAR et al., 2023). These oils are generally liquid, aromatic, and composed of a complex mixture of various classes of substances, mainly terpenes and terpenoids.

Terpenoids, also known as oxygenated terpenes or isoprenoids, constitute the largest and most diverse family of natural products, with over 80,000 known compounds. They find wide-ranging applications across industries such as food, cosmetics, and pharmaceuticals. Initially, the term "terpene" was coined to describe hydrocarbons extracted from turpentine, with the suffix "ene" indicating the presence of carbon-carbon double bonds (SELL, 2003). While terpenoids share chemical similarities with terpenes, they incorporate atoms beyond carbon and hydrogen, often including oxygen. Terpenoids are classified based on the number and structural arrangement of carbons resulting from the linear concatenation of C_5 isoprene units, followed by cyclization and rearrangement of the carbon skeleton according to the

isoprene rule. Isoprene, the basic unit of terpenoids, is 2-methylbuta-1,3-diene (C_5H_8) (Figure 2.1). Thus, the individual isoprene unit represents the simplest terpenoid class, termed hemiterpenoids (SELL, 2003; CHRISTIANSON, 2017; LI et al., 2021). Additional terpenoid groups are delineated in Table 2.2.

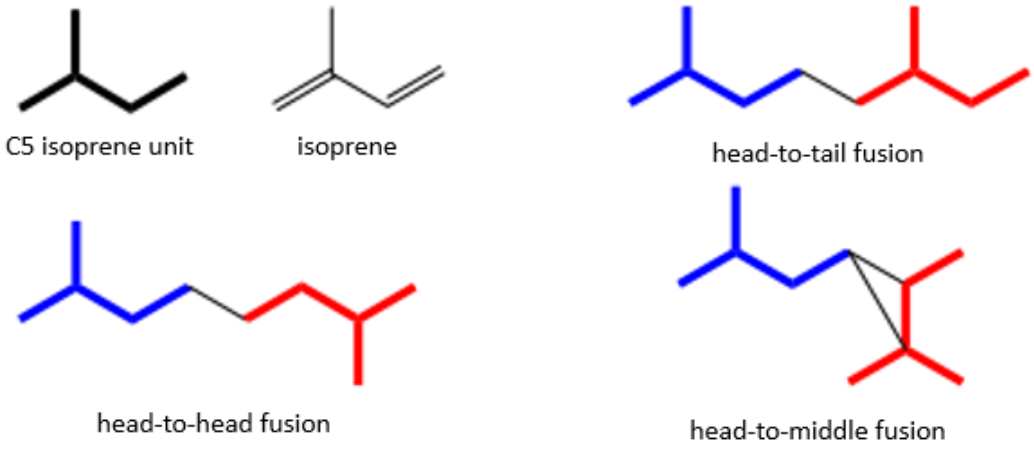


Figure 2.1 Coupling of Isoprene Units in Terpenoid Backbone Formation.

Table 2.2 Classification of terpenoids.

Class	Number of monomeric isoprene units	Number of carbon atoms	General formula
Hemiterpenoids	1	5	C_5H_8
Monoterpenoids	2	10	$C_{10}H_{16}$
Sesquiterpenoids	3	15	$C_{15}H_{24}$
Diterpenoids	4	20	$C_{20}H_{32}$
Sesterterpenoids	5	25	$C_{25}H_{40}$
Triterpenoids	6	30	$C_{30}H_{48}$
Tetraterpenoids	8	30	$C_{40}H_{64}$
Polyterpenoids	>8	>40	$(C_5H_8)_n$

The isoprene rule, established by Otto Wallach in 1887 and further refined by Robinson and Ruzicka, states that all terpenoids arise from the systematic joining of isoprene units, typically in a head-to-tail manner. However, non-head-to-tail condensation of isoprene units also occurs. Head-to-head fusions are common among triterpenoids and carotenoids, while certain compounds are formed through head-to-middle fusions (CONNOLLY; HILL,

1991; ALVAREZ, 2014). Figure 2.1 illustrates the prevalent fusions of isoprene units and how they relate to the original backbone.

Terpenoids originate from either the mevalonate (mevalonic acid; MVA) pathway, active in the cytosol, or the plastidial 2-C-methyl-D-erythritol 4-phosphate (MEP) pathway. Hemi-, mono-, di-, sester-, and tetraterpenoids are primarily synthesized via the MEP pathway, while sesqui-, tri-, and polyterpenoids are products of the MVA pathway, although exceptions and crosstalk between the pathways exist (DEWICK, 2009; GASTALDO et al., 2019).

Terpenoids are commonly recognized as major constituents of essential oils, responsible for the characteristic aroma of numerous plants chemically, terpene essential oils can be divided into two classes: mono and sesquiterpenoids, distinguished by their boiling point range (monoterpenoids boiling point 140°C–180°C, sesquiterpenoids boiling point >200°C) (HÜSNÜ CAN BASER; BUCHBAUER, 2015).

2.3 Thermodynamic of vaporization

In the realm of science and engineering, vaporization thermodynamics involves determining parameters as enthalpy of vaporization, vaporization entropy, vapor pressure, and normal boiling temperature. These parameters are indispensable for optimizing processes, including distillation, evaporation, crystallization, and the development of cutting-edge equipment.

Vapor pressure (P_{vap}) is a fundamental thermodynamic property that describes the tendency of a liquid substance to evaporate and turn into vapor at room temperature. As a liquid substance is heated, its molecules gain kinetic energy and become more agitated. Some of these molecules gain enough energy to escape from the liquid's surface and enter the vapor phase. Vapor pressure is directly proportional to temperature; as temperature increases, vapor pressure also increases. The vapor pressure of a substance is an indicator of its volatility and directly influences the rate of vaporization.

The normal boiling temperature (T_{nb}) is the temperature at which the vapor pressure of a substance reaches a standard atmospheric pressure of 1 atm (101.3 kPa). Each substance has its own normal boiling temperature, which is an intrinsic characteristic determined by the strength of molecular interactions in the liquid. Boiling temperature varies with pressure and is lower at high altitudes where atmospheric pressure is lower.

The enthalpy of vaporization (ΔH^{vap}) is the amount of energy required to vaporize a specific quantity of a substance at constant temperature and pressure. This process involves

breaking the intermolecular forces in the liquid and converting the molecules into vapor. The enthalpy of vaporization is a property that directly influences the boiling temperature of a substance.

The vaporization entropy (ΔS^{vap}) is a measure of the change in entropy during the vaporization process. Entropy is a measure of disorder in a system. Vaporization increases the disorder of the system as liquid molecules are dispersed into the vapor phase. Therefore, the vaporization entropy is generally positive, indicating an increase in disorder. The relationship between enthalpy of vaporization and vaporization entropy is fundamental in determining the spontaneity of a vaporization process, as predicted by the Gibbs-Helmholtz equation.

Thermodynamics of vaporization is fundamental to understanding processes that involve phase changes. It is not confined to the laboratory; it permeates practical applications that impact various aspects of our daily lives. In oil refining, crude oil is distilled into different fractions such as gasoline, diesel, and jet fuel based on their distinct boiling points. This separation process relies heavily on vaporization principle. In the realm of chemical manufacturing, it helps control reaction conditions and optimize the separation of products. For instance, the production of ethanol involves distillation, where vaporization is key in achieving the desired product purity. In pharmaceutical production they are applied to purify and separate active ingredients from reaction mixtures or to produce high-purity solvents essential for drug formulation. Even in the food processing industry, vaporization is utilized. Concentration processes, where water is evaporated from substances like fruit juices and dairy products to extend their shelf life, depend on vaporization. Perfume manufacturing is yet another example where vaporization principles come into play. Perfume makers employ these principles to extract and purify aromatic compounds from natural sources such as flowers and herbs. In summary, an understanding of the thermodynamics of vaporization is fundamental for comprehending the thermodynamic properties of the substances involved, optimizing efficiency, and enhancing selectivity in chemical processes like distillation. This knowledge enables the separation of components based on their unique vaporization behaviors.

2.4 Classical thermodynamic theory

In the context of a single-component system with two phases in equilibrium, it's important to note that this system possesses only one degree of freedom. This means that there is a sole independent variable characterizing it, which is typically the temperature (MAJER; SVOBODA; PICK, 1989).

The thermodynamic relationship in Eq. (2.1) is a fundamental equation that relates the Gibbs free energy (G) to the enthalpy (H), temperature (T), and entropy (S).

$$G = H - TS \tag{2.1}$$

Applying the total differential rule to the sum of two functions yields Eq. (2.2) and Eq. (2.3).

$$dG = dH - d(TS) \tag{2.2}$$

$$dG = dH - SdT - TdS \tag{2.3}$$

To express dH in terms of infinitesimal changes in dT and dP, the definition of enthalpy is used, which includes the internal energy (U) and the product of pressure (P) ad volume (V). When differentiating Eq. (2.4), Eq. (2.5) is obtained.

$$H = U + PV \tag{2.4}$$

$$dH = dU + PdV + VdP \tag{2.5}$$

substituting dH into Eq. (2.3), yields Eq. (2.6).

$$dG = dU + PdV + VdP - TdS - SdT \tag{2.6}$$

By resorting to the first law of thermodynamics, the differentiation of the internal energy can be expressed as Eq. (2.7).

$$dU = TdS - PdV \tag{2.7}$$

substituting dU into Eq. (2.6), yields Eq. (2.8).

$$dG = TdS - PdV + PdV + VdP - TdS - SdT \tag{2.8}$$

algebraically rearranging Eq. (2.8) yields Eq. (2.9).

$$dG = VdP - SdT \tag{2.9}$$

Applying Eq. (2.9) to the vapor and liquid phases in equilibrium results in Eq. (2.10).

$$V_s^L\, dP - S_s^L\, dT = V_s^V\, dP - S_s^V\, dT \tag{2.10}$$

where the subscript s indicates a change in equilibrium, the superscripts V and L correspond to the vapor and liquid phases, respectively. Rearranging Eq. (2.10) yields the Clapeyron equation as shown in Eq. (2.11).

$$\frac{\Delta S}{\Delta V} = \frac{\Delta H}{T\,\Delta V} = \left(\frac{dP}{dT}\right)_s \tag{2.11}$$

Variations in both enthalpy and volume are always positive. Thus, vapor pressure always increases with temperature. In regions of moderate temperature, typically below the boiling point, deviations from the ideality of the Clapeyron equation ($\Delta V = \Delta ZRT/p_s$) are minimized, and it becomes the Clausius-Clapeyron equation, as shown in Eq. (2.12)

$$\Delta H = RT^2 \left(\frac{d \ln P}{d\, T}\right)_s \tag{2.12}$$

where the volume of the liquid phase is completely negligible compared to that of the vapor phase.

The integration of the Clausius-Clapeyron equation, as shown in Eq. (2.13), allows for the determination of the enthalpy of vaporization using the natural logarithm of vapor pressure and the reciprocal of temperature.

$$\ln P = -\frac{\Delta H}{RT} + \text{constant} \tag{2.13}$$

2.5 Obtaining thermodynamic properties

Static and dynamic methods are the most classical ways of experimentally determining thermodynamic properties such as P_{vap}, ΔH^{vap}, and T_{nb}. Static methods directly

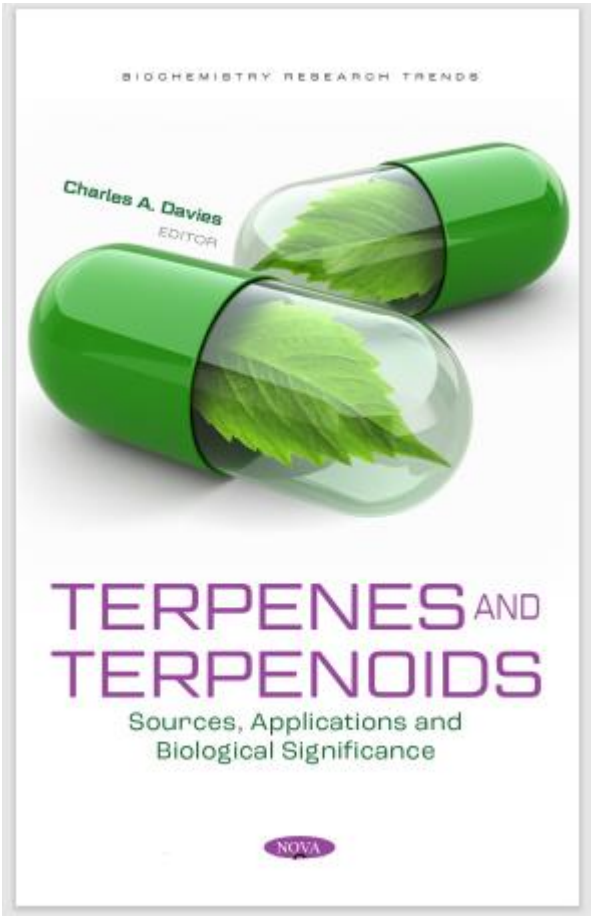
measure the pressure exerted by vapor in equilibrium with its liquid (or solid). In contrast, dynamic methods involve collecting a sample of saturated vapor, followed by the determination of vapor concentration. With the emergence of new techniques, methods have been classified into direct experimental determination, indirect experimental determination, and prediction methods (SITE, 1997).

Regarding vapor pressure, the most well-known experimental techniques for direct determination are gas saturation and the Knudsen cell. For direct experimental determination of ΔH^{vap} and T_{nb}, calorimetric methods are often employed (MAJER; SVOBODA; PICK, 1989). Direct measurement techniques are generally considered more accurate. However, they have limited applicability to low molar mass compounds or highly volatile substances. Therefore, indirect experimental methods have been adopted.

Among the indirect methods, we can mention the thermogravimetric analysis, where the vapor pressure of a substance is determined by the rate of sample mass loss as a function of temperature (OLIVEIRA; CREMASCO, 2014) and the gas chromatography correlation method, in which thermodynamic parameters are obtained from chromatographic retention data (CHICKOS; HOSSEINI; HESSE, 1995; SVOBODA; KOUTEK, 2002; HOSKOVEC et al., 2005; RUŽIČKA et al., 2012; FONSECA; SARTORATTO; CREMASCO, 2021).

CHAPTER III

Published Chapter



FONSECA, L. A. A. P; CREMASCO, M A. **Characteristics and Applications of Terpenes and Terpenoids from Brazilian Flora**. In: Charles A. Davies. (Org.). Terpenes and Terpenoids: Sources, Applications and Biological Significance. 1ed.New York: Nova Science Publishers, 2022, v. 1, p. 197-213.

This chapter provides a comprehensive overview of the distribution of terpenes and terpenoids in the six Brazilian biomes. This publication is a fundamental part of this Thesis as it establishes the basis for understanding essential oils, the molecular structures of oxygenated terpenes, and the potential applications of these bioactive compounds, highlighting the biodiversity and indigenous knowledge of native plants in Brazil.

Chapter 7

Characteristics and Applications of Terpenes and Terpenoids from Brazilian Flora

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Abstract

This chapter presents a discussion about the importance of Brazilian flora for herbal medicine. Ethnomedical knowledge was possessed by different Brazilian native groups and consisted of complex practices, especially with the use of native herbs. Terpene and terpenoid compounds are natural products isolated from different natural sources. It consists of five-carbon isoprene units, which are assembled from many isoprene units. Terpenes are simple hydrocarbons, while terpenoids are modified terpenes with different functional groups (ketones, alcohols, esters, carboxylic acids, aldehydes) and oxidized methyl groups moved or removed at various structural positions. Terpenes and terpenoids are key components of essential oils. Brazil is considered the country with the greatest biodiversity in the world. According to the Brazilian Ministry of Environment, at least 103,870 animal species and 43,020 plant species are known. These species are distributed in six biomes with different characteristics and vegetation: Amazon Rainforest, Cerrado, Atlantic Forest, Caatinga, Pantanal, and Pampa. The wisdom of Brazilian natives

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transcends historical time and extermination to offer hope, especially in times of pandemics.

Keywords: Brazilian flora, essential oil, terpene, terpenoid

Introduction

When the Spaniards arrived in the Americas in the 16th century, the South American countries as we know them today did not exist; however, parts of Uruguay, Paraguay, Argentina, and Brazil were identified as the territory of Guayrá, currently located in the state of Paraná, Brazil. The Guarani people inhabited the jungles, and their culture was considered uncivilized by Europeans in that century as well as today [1]. When Guayrá natives are referred to as crude, rude or uncultured, this elicits reflection on Western civilization's ethnocentric assumption that a society is strengthened insofar as it accumulates and spreads knowledge. This occurs, among other means, through the recording of history, offering the impression that writing and the progress of society are part of a linear and irreversible process. The written or great works are evidence of this process, constituting a tradition. In this tradition, nonliterate societies were considered savages who lacked history. The Guarani are a typical example as their exclusion was decreed in different ways. Initially, for an idea already acquired: they contributed nothing remarkable, no durable product before the arrival of so-called civilization, mainly from Europe.

For this reason, it is essential to emphasize the vast knowledge of the Brazilian natives, originating mainly from manifestations of nature. One of these is Kaa'pora or the forest spirit, which manifested itself in several ways, including in medicinal herbs against snake venom [2] or stomach ailments [3].

The genesis of herbal medicine in Brazil is directly correlated with the cultural identity of the country. Before arrival of the colonizers, there were around 200,000 native nations in Brazil [4]. This cultural richness is still evident in the variety of native languages found among native Brazilians, totaling 188 languages, including Guarani, Arawake-Maipure, Yanomami, and Tupi in addition to dialects such as Xavante and Tapaiúna [5].

The Brazilian natives had a vast knowledge of plants; for example, the Guarani had a more profound comprehension of plants than the Europeans of the 16th century [6, 7]. In the Guarani culture, the domain of medicinal properties associated with botanical species that permeated their daily life was one of the most solid accounts of their botanical and therapeutic knowledge, highly adapted to the contexts in which they lived. Medicinal plants, among which those found mainly in the *Myrtaceae, Fabaceae, Asteraceae, Lauraceae, Poaceae* families [8] are highlighted.

It should be noted that the Kaiowá of the Guarani linguistic trunk and originating from the Kaa'gua, which mean "those of the forest," are traditionally farming people having a strong territorial identity. Guarani-Kaiowá cosmology and knowledge have a sacred dimension of the earth and its inhabitants. Myth reflects their way of being [9]. When someone does not acknowledge the wisdom of natives, they ignore ancient knowledge as of medicinal herbs [10, 11] found in Brazil. In times of pandemic where drugs are sought to combat Covid-19, plants with therapeutic uses related to the respiratory system cannot be overlooked.

Forest peoples, whose wisdom comes from the heart of the jungle, know applications for a variety of medicinal species. In addition to the Fabaceae family (species *Cedrela fissilis* and *Pterodon emarginatu*), the Amaranthaceae (species Moquiniastrum polymorphum and Achyrocline satureioides) and Bignociaceae families (species Ananas ananassoides) can be mentioned [12]. When a people or nation is said to come from the jungle, this is far from an insult. It implies recovery of an immense cultural wealth, the so-called traditional community's worldvie with cultural and symbolic practices.

The Kayapó methods and techniques for handling species in Amazon are considered the path for discovering new foods, medicines, dyes, and essential oils [13]. It is worth emphasizing the importance of native knowledge for Brazilian culture, including for herbal medicine, especially in times when we are experiencing a new genocide of indigenous peoples in Brazil [14]. Approximately five hundred years later, herbal medicine's promising applications increase the interest in studying essential oil compounds such as terpenes and terpenoids for creating an effective and culturally appropriate option [15].

Essential oils are obtained from plant material, including flowers, roots, bark, leaves, seeds, and fruits [16]. Terpenes and terpenoids are key components of essential oils, usually composed of mono- and sesquiterpenes, which may be hydrocarbons or oxygenated compounds. However, these compounds can also be aliphatic or alicyclic derivatives, and some may have aromatic structures.

Terpene compounds are natural products isolated from different natural sources. These are known as secondary metabolites since they are formed by enzymatic reactions of primary metabolites (amino acids, sugars, vitamins), and they consist of five-carbon isoprene units, which are assembled from many isoprene units. Terpenes are simple hydrocarbons, while terpenoids are modified terpenes with different functional groups (ketones, alcohols, esters, carboxylic acids, aldehydes) and oxidized methyl groups moved or removed at various structural positions.

Brazil is considered the country with the greatest biodiversity in the world. According to the Brazilian Ministry of Environment [17], at least 103,870 animal species and 43,020 plant species are known in the country. These species are distributed in six biomes with different characteristics: Amazon Rainforest, Cerrado, Atlantic Forest, Caatinga, Pantanal, and Pampa. Due to its incredible natural wealth, Brazil stands out as one of the leading exporters of essential oils and derivatives.

Brazilian Production of Essential Oils and Derivates

The industrialization of essential oils in Brazil began in the 20th century based on extraction of native essences, basically rosewood. In 1940, due to the great demand by Western industries, deprived of their traditional sources of supply due to the World War II, production of essential oils began in a more organized way with the introduction of other crops to obtain oils from mint, orange, sassafras cinnamon, eucalyptus, lemongrass, patchouli, and others, with a focus on foreign markets [18]. The country enjoys a prominent place in the production of essential oils and is considered one of the four major producers alongside India, China, and Indonesia. The Brazilian position is due to citrus essential oils, obtained as by-products of the juice industry, with limonene being the principal terpene obtained from processing essential oils [19].

Brazilian biodiversity offers excellent potential for producing terpene and terpenoid compounds from essential oils of native flora. Effective coordination between the government, research institutions, and the private sector are needed to obtain quality products and prices capable of competing in the market. ABRAPOE (Brazilian Association of Essential Oils Producers) was founded in 2008 for this purpose. Its objective is to bring together producers and research centers to improve essential oils through research and standardization studies, provide market data and represent the class in government programs [19].

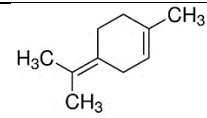
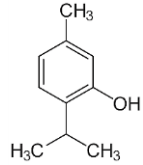
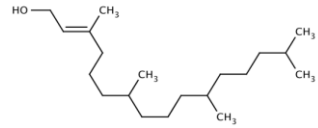
Even though Brazil has the most extraordinary biodiversity, predatory exploitation of natural resources has led to a scarcity of raw materials, including terpenes and terpenoids. A representative case is the collection of the essential oil rich in safrole from cinnamon sassafras. The sources - large trees - have already been sold out in Brazil [20]. Deforestation also offers risks to the production of terpenes and terpenoids from native flora. Recently, it was reported that the destruction of Brazilian biomes increased by 14% in 2020 [21].

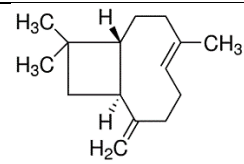
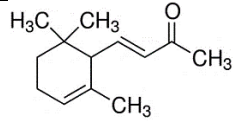
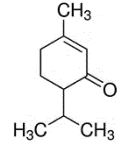
Biodiversity, Distribution of Flora, and Distribution of Terpenes and Terpenoids in Biomes

Brazilian flora and fauna are distributed in six terrestrial biomes. Brazil hosting 15-20% of the world's biological diversity, is the most biologically diverse country [17]. The native vegetation covering a region is directly linked to its edaphoclimatic conditions. Brazil has a great diversity of plant species with unique characteristics in each biome.

Table 1 presents Brazilian biome characteristics [17], some native plants and their distribution in the biomes, and some terpenes and terpenoids in essential oils and their pharmacological activities.

Table 1. Brazilian Biomes: Characteristics, Terpenes and Terpenoids from Native Flora

Biome	**Flora**	**Native species**	**Terpene/ Terpenoid**	**Molecular structure**	**Application**
1.Amazon Rainforest	It is the largest forest formation on the planet, conditioned by the humid equatorial climate. Most of Brazil is covered by the forest of Amazon within which there are about 55,000 different species of plants.	*Piper hispidinervum*	α-terpinolene		antitumor
2. Cerrado	The Cerrado is made up of grasslands, savannahs, and dry forests. It is the second-largest biome behind the Amazon in South America.	*Lippia gracilis*	thymol		anti-inflammatory
3. Caatinga	The Caatinga has dry soils, and its vegetation is composed of palm trees. This biome is at high risk of desertification.	*Spondias sp*	phytol		antinociceptive

Biome	Flora	Native species	Terpene/ Terpenoid	Molecular structure	Application
4.Atlantic Forest	The Atlantic Forest has different structures and compositions of flowers due to the climatic characteristics of the region where it occurs, having as a common element the exposure to the humid winds that blow from the ocean.	*Baccharis dracunculifolia*	β-caryophyllene		antioxidant
5. Pampa	Herbaceous species characterize this biome. The plains, plateaus, and reliefs have specie of savannah vegetation.	*Bougainvilla glabra*	β-ionone		antimicrobial
6. Pantanal	This biome is an alluvial plain influenced by rivers, where fauna and flora of rare beauty and abundance are found. This ecosystem is formed of predominantly sandy terrains, covered by different physiognomies due to variety of microregions and flood regimes.	*Mentha arvensis*	piperitone		vermifuge

Phytotherapic Uses of Essential Oils and Derivates

The uses of essential oils and their terpenes and terpenoids are highly diverse, depending on source, quality, and extraction procedure. They are widely used in the food, cosmetics, perfumery, cleaning, and pharmaceutical industries. An interesting aspect of these oils is their potential as therapeutic agents. The most common pharmaceutical applications of essential oils are in diluted forms and inhaled in steaming water [22] and as ointments, creams, and compresses [23].

Brazilian flora offers a great diversity of native plants with pharmacological activities associated with essential oils and their derivatives. An example is *Aloysia gratissima*, which has antibacterial, antifebrile, and digestive activities. It is recommended to treat stomach problems, headaches, fevers, bronchitis, pneumonia, flu, and bladder ailments. The essential oil presents sesquiterpenes (α-bisabolol, β-elemene, viridiflorol, and β-caryophyllene), diterpenes (kaurane), and triterpenes (α-amyrin, betulinic acid, and ursolic acid) [24]. The essential oils extracted from Brazilian native plants are still used as an expectorant for treating coughs and bronchitis (*Mikania laevigata*), a regulator of blood pressure (*Psidium cattleianum* Sabine), and a healing agent (*Polygonum punctatum* Elliott), among other uses [24].

Figure 1 presents some Brazilian native plants, their distribution through the biomes, and a terpene or terpenoid compound present in their essential oil. The native plant species represented by numbers 1-6 are linked to Table 1.

Essential Oils Extraction Processes

Traditionally, essential oils are obtained by steam distillation or water distillation from different plant parts [16]. When water and plant material are kept in different recipients, and the water vapor passes through the plant material, contact is brief. The oil can be collected just a few minutes after the process starts [25]. One of the disadvantages of these methods is that essential oils undergo chemical alteration, and the heat-sensitive compounds can easily be destroyed. Therefore, the quality of the essential oil extracts is significantly impaired [26].

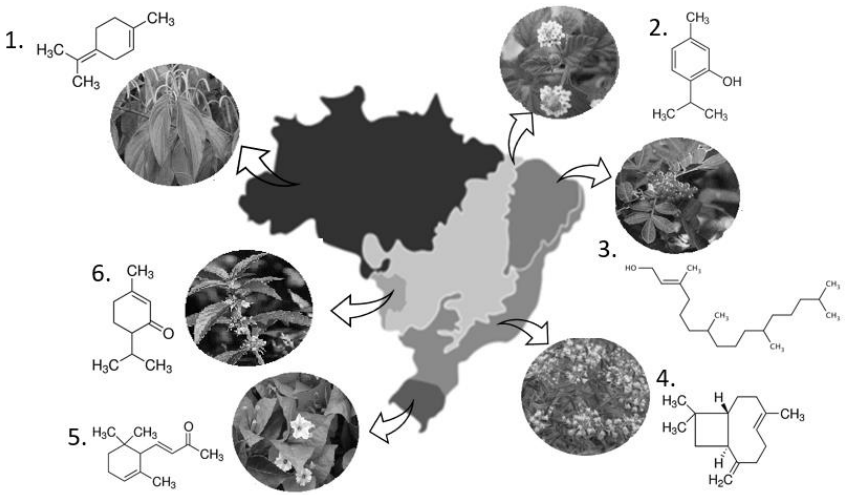


Figure 1. Brazilian native flora: terpenes and terpenoids (authors).

Other processes for obtaining essential oils include maceration, enfleurage, solvent extraction, and use of supercritical fluids. Maceration can be used when the yield from distillation is poor, while enfleurage and solvent extraction are suitable for expensive, delicate, and thermally unstable materials [25].

The extraction of essential oils using supercritical carbon dioxide is more attractive than to conventional processes in terms of product quality [27-29]. Knowledge of the mass-transfer mechanism, the kinetics parameters, and the thermodynamics restrictions of the extraction conducted in a bed of plant material can be used in an economic evaluation of the extraction process [30].

Identification of Terpenes and Terpenoids by Gas Chromatography

The development of chromatographic techniques has contributed considerably to the study of the chemical composition of essential oils. Gas chromatography (GC) is the best method due to its simplicity, rapidity, and efficiency in identifying and quantifying essential oil components and composition variations [25].

Gas Chromatography combined with a flame ionization detector (FID) and mass spectrometry (MS) represents a robust quantitative and qualitative

analysis tool. It is also used in quality control, authentication, and detection of adulteration [31]. Additionally, GC is the method of choice for analyzing essential oil compounds [25].

Gas Chromatography coupled with MS makes it possible to carry out in a single operation a qualitative analysis together with an indication of the amount of the components for samples of 1 μL. Kováts indices are standards for comparing substances that are being identified. They have generally been used for GC analyses [32, 33]. In GC, the Kováts indices indicate the compound's retention behavior compared to a mixture of saturated n-alkanes of different numbers of carbon atoms. This parameter provides information about the elution sequence of the compound and varies as a function of stationary phase and temperature, independently of experimental conditions [34]. The retention times are used as references to identify terpene and terpenoid compounds present in essential oils using the Kováts retention indices.

Conclusion

The uses of essential oils are highly diverse, depending on the source, quality, and extraction procedure. An interesting aspect of these oils is their potential as therapeutic agents. These oils have antitumor (*Piper hispidinervum*), anti-inflammatory (*Lippia gracilis*), antinociceptive (*Spondias sp*), antioxidant (*Baccharis dracunculifolia*), antimicrobial (*Bougainvillea glabra*), vermifuge (*Mentha arvensis*) uses, among others.

Brazil has a prominent place in the production of essential oils and their derivatives as terpenes and terpenoids. This is basically due to citrus essential oil with limonene, obtained as a by-product of the juice industry, being the most exported terpene. Brazilian production of essential oils and their derivatives can conquer markets. However, strategic actions such as sustainable extraction, investment in research, and knowledge transfer to producers in cooperatives are needed.

In Brazil, natives have knowledge of the application of essential oils for therapeutical purposes. Thus, it is worth emphasizing the importance of this knowledge to Brazilian culture. With the extinction of these native peoples, their cultures and languages, knowledge about some native plants is also threatened.

European ships brought the measles, smallpox, and flu viruses to Americas. These diseases spread among the natives, invading the coast, and

advancing inland. Smallpox decimated the Aztecs and the flu virus, unknown to the natives, caused devastating epidemics, especially among the Guarani. It is estimated that more than 90% of the indigenous population died from the diseases brought by the Europeans [12]. The Brazilian indigenous population witnessed the extermination of several of its people's following encounters with the Europeans. This process, driven by ambition and greed, reduced a population was between two and four million inhabitants in 1500 to around 750,000, spread across Brazil today. In addition to the occupation of its cultural territory, this decline is due to epidemics such as smallpox, measles, whooping cough, chickenpox, typhus, diphtheria, influenza, bubonic plague, among others [35]. However, the wisdom of peoples from the jungles transcends historical time to offer hope to those who claiming to be civilized, especially in times of pandemics.

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Complementary Discussion

The history of Brazil is marked by a rich exchange between cultures and an exuberant biodiversity. In addition to the native plants, long employed by indigenous nation in their traditional customs, many plants brought from other parts of the world also found fertile soil and favorable climate in Brazilian territory, adapting surprisingly, and contributing to the country's economy and identity.

Brazil holds prominence in the production and commercialization chain of essential oils (EOs), offering this type of input to the international market for almost 100 years (BIZZO et al., 2009). Different EOs have been produced over this century of history, from both native species like rosewood (*Aniba rosaeodora*) to non-native ones like orange (*Citrus sinensis*), eucalyptus (*Eucalyptus*), cinnamon (*Cinnamomum verum*), and lemongrass (*Cymbopogon citratus*) (BIZZO; HOVELL; REZENDE, 2009), with citrus plants standing out among them. Citrus fruits were brought from Asia to Brazil in the second half of the 16th century by Jesuits, but it was only in 1930 that the first extraction of orange essential oil was recorded, carried out by Italian immigrants in São Paulo (BRAGA, 1971). Fluctuations in North American and European exports of oranges and their derivative products in the post-World War II period favored Brazil's entry as a promising alternative hub in the export of concentrated orange juice (SILVA SANTOS, 2002). In the following decades, international companies producing cosmetics, perfumes, pharmaceuticals, and food products saw a great opportunity to establish themselves in Brazil, thus contributing to the consolidation and development of the domestic market (SEBRAE, 2019).

Currently, Brazil is the world's largest producer and exporter of orange juice and, consequently, the largest producer and exporter of orange essential oil (mainly *Citrus sinensis*, among other species) (ITC, 2024). It is worth noting that orange essential oil is a raw material to produce limonene and various terpene by-products resulting from the de-terpenation of essential oils. According to Brazilian Institute of Geography and Statistics (IBGE), in 2018 (the last year available for consultation), 154.6 thousand tons of orange EOs were produced (Figure 3.1), equivalent to R$ 1.5 billion or US$ 418 million (IBGE, 2024). These data include both oils obtained by cold pressing the fruit, called orange EO, and that obtained by distillation of the leaves and branches, called petitgrain EO.

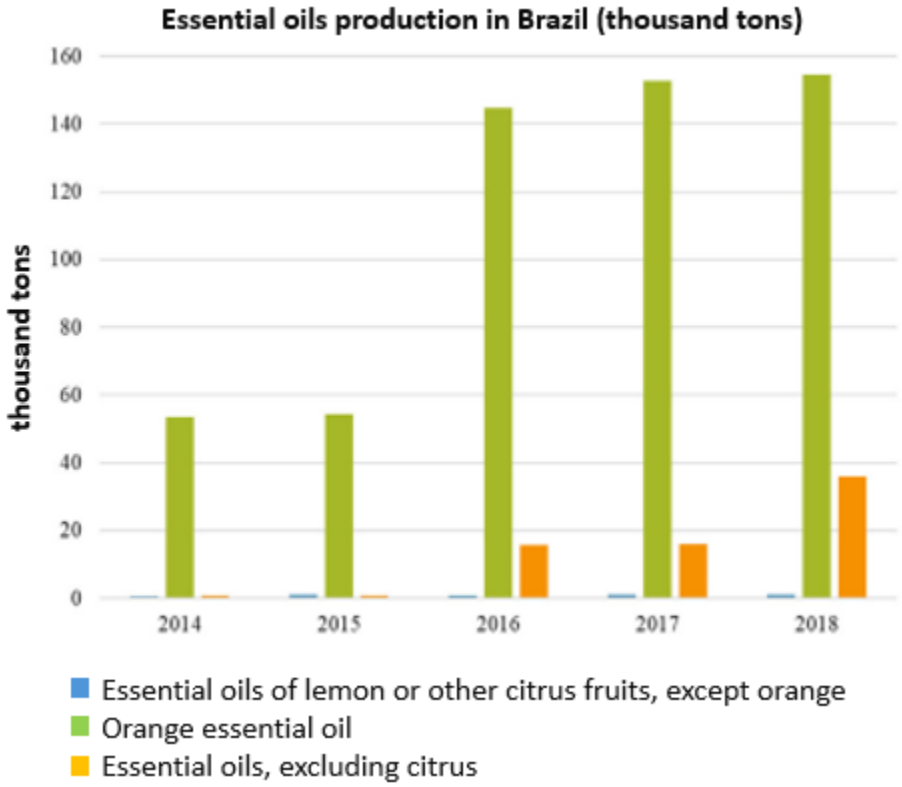


Figure 3.1 Production data of essential oils in Brazil (IBGE, 2024).

According to data from the Ministry of Industry, Foreign Trade, and Services (MDIC, 2024), eucalyptus essential oil, another species well adapted to Brazilian soil, although native to Australia, is the second largest in volume produced in Brazil, with half of the national production destined for export.

The global essential oils market was valued at USD 11.41 billion in 2023 and is projected to grow from USD 12.47 billion in 2024 to USD 27.82 billion by 2032, exhibiting a compound annual growth rate (CAGR) of 10.55% during the forecast period. The global market is primarily driven by the robust trend of green consumerism amid the increasing popularity of natural inputs for sensory-related aspects and food preservation (FORTUNE BUSINESS INSIGHTS, 2024). The United States, China, India, France, and Brazil are the main global players (BIZZO; REZENDE, 2022) in this cenario. The Covid-19 pandemic has impacted the global essential oils market, with increased demand for EOs claiming to enhance health and immunity. According to industry experts, amid the chaotic pandemic situation, people should incorporate essential oils into their daily lives to improve their immune system and achieve a healthy and calm mind. Numerous EOs, such as eucalyptus oil, which have the potential for aromatherapy and antibacterial and antiviral qualities, have increased demand for the products during this pandemic (FORTUNE BUSINESS INSIGHTS, 2024).

Brazil, a megadiverse country with a favorable climate for the development of different agricultural cultures, has a comfortable and prosperous position in the essential oils market. There is an expectation of stable growth in the EO market throughout the 2020s (MARKETS AND MARKETS, 2024).

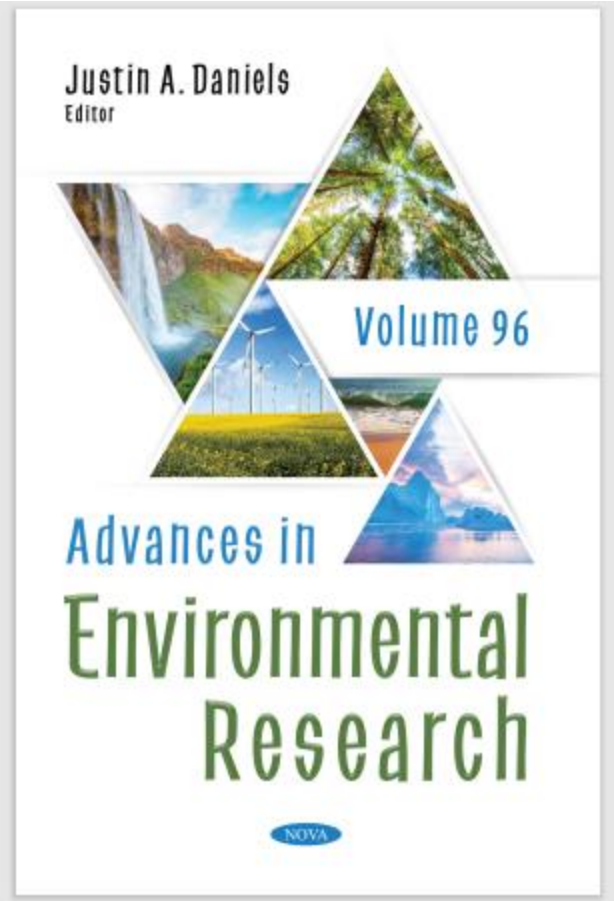
It is important to emphasize Brazil's great potential in the production of essential oils, whose substances are rich in terpene compounds, with applications in the chemical, pharmaceutical, and food industries, especially due to the demand for natural additives as replacements for synthetic ones by these industrial sectors. The substitution of synthetic materials by natural products has been a constant trend, directly influenced by consumers, mainly in Northern Hemisphere countries. This preference for natural products has led to a gradual change in the ingredients of foods and beverages, reflecting positively on the essential oils market (FORTUNE BUSINESS INSIGHTS, 2024).

Obtaining the thermodynamic properties of compounds present in essential oils becomes highly relevant, as they are associated with their industrial applications. Vapor pressure $\left(P_{vap}\right)$, enthalpy of vaporization (ΔH^{vap}), and normal boiling temperature (T_{nb}) of terpenes and terpenoids found in EOs are data that can guide from equipment optimization and extraction techniques to sustainable raw material production, consequently generating income for local populations.

Errata. In the text of Chapter III *Characteristics and Applications of Terpenes and Terpenoids from Brazilian Flora*, where it reads "When the Spaniards arrived in the Americas in the 16th century", read "15th century".

CHAPTER IV

Published Chapter



FONSECA, L.A.A.P.; BERTAN, A. S. CREMASCO, M.A. **The Soul of Brazil's White Forest**. In: Justin A. Daniels. (Org.). Advances in Environmental Research. 1ed.New York: Nova Science Publishers, 2023, v. 96, p. 217-230.

Focusing on the essential oil of *Lippia gracilis* Schum, a native species of the Caatinga biome, this chapter explores the thermodynamic properties of terpene and terpenoid compounds. By investigating vaporization entropy and its effects on vapor pressure correction, it seeks to bridge the gap between ecological context and scientific analysis. This study enhances the understanding of how the molecular structures influence the thermodynamic properties of terpenes and terpenoids.

Chapter 10

The Soul of Brazil's White Forest

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Abstract

Essential oils (EOs), also referred to as volatile odoriferous oils, are natural, volatile, and complex liquids characterized by an intense aroma and flavor that varies depending on the constituents present in the oil. They are secondary metabolites produced by aromatic plants, particularly those found in warm regions like Brazilian biomes, where they have a significant role in traditional medicine. The Caatinga, one of the Brazilian biomes, is renowned for its vegetation resistance and unique beauty, with *Lippia gracilis* Schum being one of its most characteristic species. Terpenes derived from this plant, including thymol and carvacrol, find applications in herbal medicine. To design separation equipment for essential oil processing, reliable thermodynamic properties, which encompass vapor pressure and vaporization entropy, are crucial. This chapter aims to present the characterization of essential oil from *Lippia gracilis* Schum and provide a description of the thermodynamic properties of its primary terpenes.

Keywords: *Lippia grata*, *Lippia gracilis* Schum, *Lippia grata* Schauer, vapor pressure, vaporization entropy, essential oils, terpenes

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Essential Oils as the Plant's Soul

The concept of quintessence as the soul of a plant was first introduced and named by the Swiss physician Theophrastus von Hohenheim, also known as Paracelsus, in the 16th century. Today, this term still refers to essential oils - complex compounds containing volatile and lipophilic substances that are typically liquid and have a strong odor [1]. These oils are produced through the secondary metabolism of plants [2] and can be extracted from various parts of the plant, including flowers, buds, leaves, and branches [3]. They contain volatile aromatic compounds that have a variety of activities, such as antimicrobial, anticancer, antinociceptive, and anti-inflammatory effects [4].

The use of plants for their therapeutic properties, based on their bioactive molecules, has been traced back to ancient times [2]. The World Health Organization (WHO) defines medicinal plants as those used for medicinal purposes, which may not necessarily be available for sale, but are used in the production of herbal medicine [4]. According to Silva (2018), 11% of the 252 basic and essential drugs identified by WHO are obtained from plants, and a significant number of drugs are synthetic compounds derived from natural precursors. Additionally, essential oils are not only used in the pharmaceutical industry but also serve as raw materials for other sectors, such as food, perfumery, and cosmetics [1]. Essential oils are crucial, serving as the soul of the plant as envisioned by Paracelsus and symbolizing vitality, cultural significance, and health. In this context, *Lippia gracilis* Schum, a Brazilian native plant, deserves attention for its remarkable therapeutic properties. It is used in herbal medicine to treat common ailments such as skin, mouth, and throat diseases [5].

Natural Occurrence: Geographic Distribution

Brazil has the highest biodiversity in the world, comprising more than 45,000 species of higher plants, which account for about one-fifth of the existing flora on the planet [4]. This biodiversity is distributed across six biomes or ecoregions: the Amazon Rainforest, Atlantic Forest, Cerrado, Caatinga, Pampa, and Pantanal. The Caatinga, which is one of the largest and most distinct of the Brazilian biomes [6], covers an area of approximately 800,000 km2 [7] and represents 70% of Brazil's northeastern territory, including parts of the states of Piauí, Ceará, Rio Grande do Norte, Paraíba, Pernambuco,

Alagoas, Sergipe, Bahia, and Minas Gerais. The term "Caatinga" originated in the indigenous Tupi language, combining the word "ka'a" (meaning scrubland, shrub, herb, or grass) with "tinga" (white) to signify "White Forest." The name alludes to the whitish landscape that the vegetation exhibits during the dry season. When looking at the horizon of the Caatinga (Figure 1), it is necessary to dispel some prejudices, especially those related to the perceived poverty of the landscape by those who are unaware of the richness and importance of the "White Forest." Although the diversity of plants and animals in arid and semi-arid environments is less than in lush tropical forests, deserts have plants and animals adapted to their extreme conditions [6]. To appreciate its wealth, a closer look is needed, revealing its great biodiversity, biological protection, and unique beauty.

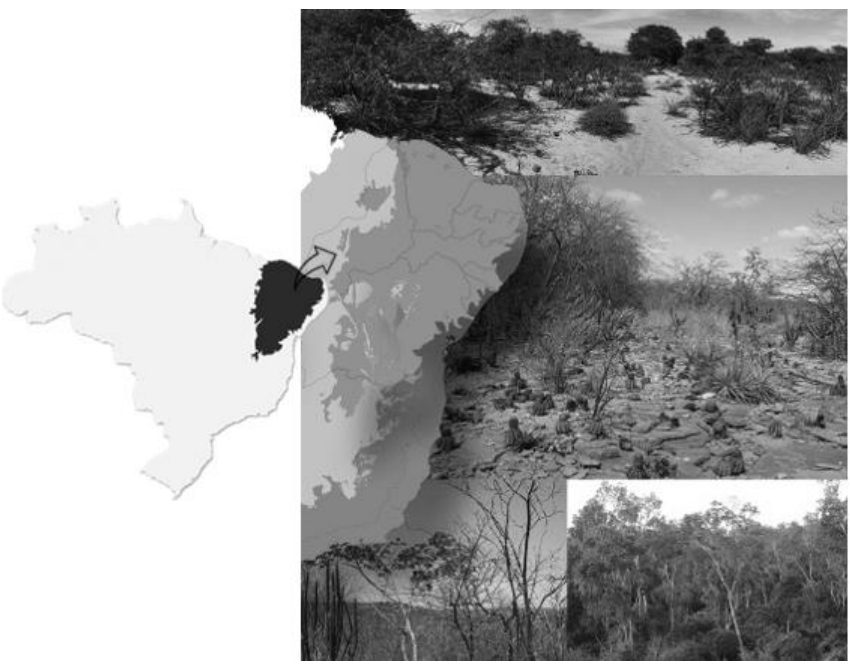


Figure 1. The diversity of vegetation in the Caatinga varies between the dry and rainy seasons [8, 9].

The Caatinga biome has an exceptional species richness and endemism. It encompasses a wide range of structural types that occur under diverse environmental conditions, including elevation, climate, soil types, and topography. Seasonally dry forests and woodlands dominate the biome, with

profusely ramified deciduous trees and shrubs that are frequently spinescent and microphyllous [9]. These are intermixed with succulent plants, such as cacti and aphyllous euphorbs, as well as terrestrial bromeliads [7].

The Caatinga flora comprises a total of 3347 species [9] and represents approximately 10% of the total plant diversity recorded in Brazil [10]. The anatomy of the plants in this biome is naturally adapted to defend against long droughts and regrow after the rains. One of the species that best characterizes the Caatinga vegetation is the *Lippia* genus, particularly *Lippia gracilis* Schum (Figure 2). *Lippia gracilis*, commonly known as "alecrim-da-chapada" or "alecrim-de-tabuleiro," is a deciduous shrub with brittle, branched stems that can grow up to 2 meters tall. The genus's name, "Lippia", is a reference to the French naturalist Augustin Lippi or Linnaeus (1678-170), while "gracilis" refers to the Latin term for "slender," possibly because of the plant's leaves. *L. gracilis* is also known as *Lippia grata*, which means "graceful" in Latin. This plant, as well as its essential oil, is considered to be blessed.

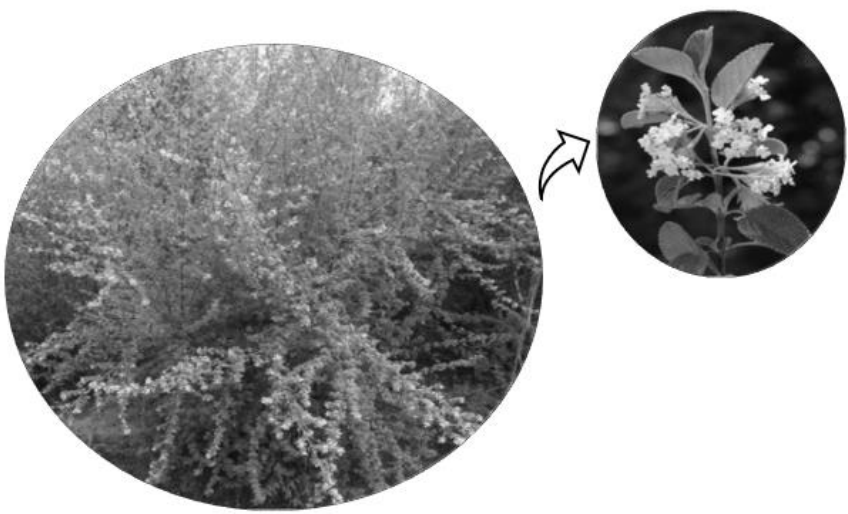


Figure 2. *Lippia gracilis* is a *native* species of the *Caatinga [authors].*

Lippia species are commonly used in folk medicine for treating various ailments such as colds, bronchitis, coughs, stomach and liver disorders, and muscle relaxation in the Brazilian northeast region [1, 4]. The traditional communities, native and rural people, prepare this plant in the form of teas, syrups and infusions [4]. Essential oil obtained from *Lippia gracilis* has

demonstrated antibacterial activity against gingivitis and dental plaque caused by *Staphylococcus aureus*, *Bacillus subtilis*, and *Mycobacterium smegmatis* [3, 11]. It also exhibits antifungal activity against resistant strains of *Candida sp* [1]. The therapeutic effects of *Lippia gracilis* essential oil, such as antimicrobial and antiseptic properties, are mainly attributed to the presence of thymol and carvacrol [12, 13]. Table 1 presents the chemical composition of *Lippia gracilis* Schum essential oil, which shows that the levels of thymol and carvacrol vary as the major compounds for each author, and the constituent terpenes differ, possibly due to differences in the edaphoclimatic conditions where the plants were collected [14].

Table 1. Chemical composition of *Lippia gracilis* Schum

Compound	**Silva et al., (2008) [15] (%)**	**Neves et al., (2008) [16] (%)**	**Oliveira (2012) [17] (%)**
Thymol	3.83	38.3	81.73
Carvacrol	44.43	0.70	0.48
γ-Terpinene	9.16	0.28	-
α-Terpinene	-	-	0.12
p-Cymene	-	-	2.46
β-Ocymene	-	3.40	-
o-Cymene	9.42	-	-
β-Caryophyllene	8.83	-	-
Thymol methyl ether	5.85	-	3.92
Eucalyptol	-	-	0.52
Myrcene	-	0.70	-
β- Myrcene	1.67	-	0.49
α-Copaene	-	3.80	0.36
Bicyclogermacrene	2.88	-	-

Thermodynamic Properties

Designing separation equipment for essential oil processing requires accurate thermodynamic properties, such as vapor pressure (P^{vap}), which are essential for various technological processes like evaporation and distillation [18].

Effusion, gas saturation, and gas chromatography are the most common methods used for measuring the thermodynamic properties of pure compounds [19,20,21]. The first two methods require special care for obtaining accurate results, as measurements of low-volatility compounds may vary significantly by up to one order of magnitude or more [22, 23]. In contrast, gas chromatography provides simplicity, speed, purity, small sample size, and reproducibility [24]. This method employs Kováts retention indices (I_X) to obtain thermodynamic properties, which are defined as:

$$I_X = 100z + 100\left(\frac{\ln t_{R,X} - \ln t_{R,z}}{\ln t_{R,z+1} - \ln t_{R,z}}\right) \quad (1)$$

The retention time of solute X in the stationary phase is represented by $t_{R,X}$ where subscripts z and z+1 identify the reference n-alkanes with z and z+1 carbon atoms whose retention times encompass that of solute X. Equation 1 can be rewritten as Equation 2, which is a function of the vapor pressure $\left(P_X^{vap}\right)$ and infinite dilution activity coefficient (γ_X^{∞}) of solute X.

$$I_X = 100z + 100\frac{\ln(\gamma_z^{\infty} P_z / \gamma_X^{\infty} P_X)}{\ln(\gamma_z^{\infty} P_z / \gamma_{z+1}^{\infty} P_{z+1})} \quad (2)$$

Table 2 presents the Kováts retention indices to Thymol and Carvacrol and other terpene compounds in *Lippia gracilis* essential oil.

Expressing $\left(P_X^{vap}\right)$ from Equation 2, considering $\gamma_x^{\infty} = \gamma_z^{\infty} = \gamma_{z+1}^{\infty}$, it is possible to write Equation 3.

$$\ln P_X^{vap} = \ln P_z^{vap} + \frac{(100z - I_X)\ln(P_z^{vap}/P_{z+1}^{vap})}{100} \quad (3)$$

Considering 298.15 K a reference in many applications, Equation 3 is extrapolated to obtain the vapor pressure at this temperature using non-linear regression techniques. So, Equation 3 has been rewritten as Equation 4.

$$\ln P_X^{vap\,(298.15\,K)} = \ln P_z^{vap} + \frac{\left(100z - I_X^{298.15\,K}\right)\ln(P_z^{vap}/P_{z+1}^{vap})}{100} \quad (4)$$

Table 2. Kováts retention indices of some terpene compounds in *Lippia gracilis* essential oil from literature [24]

Compounds	**Kováts Retention Indices**									
	Temperature (K)									
	363.15	**373.15**	**383.15**	**393.15**	**403.15**	**413.15**	**423.15**	**433.15**	**443.15**	**453.15**
Thymol*	1230.54	1233.65	1233.11	1234.87	1238.14	1239.03	1241.75	1243.69	1245.59	1247.27
Carvacrol	1297.62	1298.35	1297.86	1298.39	1299.68	1301.39	1302.58	1305.37	1307.63	1308.32
Thymol	1288.52	1289.02	1286.94	1287.13	1288.90	1289.04	1290.88	1292.25	1293.90	1295.08
γ-Terpinene	1061.21	1066.12	1065.39	1068.03	1072.73	1073.89	1076.29	1080.62	1082.16	-
p-Cymene	1027.72	1033.00	1032.39	1035.39	1040.90	1042.26	1045.11	1050.28	1052.53	-

*Thymol methyl ether.

The retention index at 298.15 K for each substance was calculated as $I_X^{298.15\ K}$. Table 3 presents the vapor pressure data for some terpene compounds in *Lippia gracilis* essential oil, obtained by extrapolating Equation 3 using non-linear regression techniques. The n-alkanes vapor pressures used in the extrapolation were obtained from Majer et al., (1989) [20]. To validate the results, they were compared with the data available in the literature.

Table 3. Vapor pressure for some terpene compounds at 298.15 k: literature $\left(\mathbf{P_{lit}^{vap}}\right)$ and obtained in this work through Equation 4 $\left(\mathbf{P_{Eq.4}^{vap}}\right)$

Compounds	$I_X^{298.15\ K}$	P_{lit}^{vap} *(kPa)*	$P_{Eq.4}^{vap}$ *(kPa)*	*RD(%)*
Thymol methyl ether	1212.26	-	0.01560	-
Carvacrol	1311.62	0.0035[(a)]	0.00497	42.00
Thymol	1314.30	0.004[(b)]	0.00482	20.50
γ-Terpinene	1037.38	0.137[(b)]	0.11784	13.99
p-Cymene	999.96	0.193[(b)]	0.18208	5.66

[(a)] [26].
[(b)] [24].

The accuracy of the results was based on the absolute relative deviation (RD) value, defined as Equation 5.

$$\mathrm{RD}\ (\%) = 100.\,\mathrm{abs}\left[\left(\mathrm{P_{lit}^{vap}} - \mathrm{P_{exp}^{vap}}\right)/\mathrm{P_{lit}^{vap}}\right] \tag{5}$$

Equation 4 allows for the calculation of vapor pressures at 298.15 K based on accurate values of the solute's Kováts' indices and the vapor pressures of n-alkane references, known at this temperature [27, 28]. However, the relative deviations in Table 3 demonstrate that Equation 4 was not adequate for obtaining vapor pressure data at 298.15 K for the studied compounds. The same pattern was observed by Hoskovek et al., (2005) [24], and these authors proposed a readjustment to improve the estimates based on the molecular structure. The difference in the logarithms of activity coefficients of two substances (i,j) was approximated by the corresponding difference in ideal gas solubility, $\mathrm{X^g}$, derived from the van't Hoff equation, considering

$$\ln\gamma_i^{\infty} - \ln\gamma_j^{\infty} \approx \ln X_i^{\infty} - \ln X_i^{\infty} \cong \frac{\Delta S_{vap}^{b,i}\left(T_{nb}^{i} - T\right)}{RT} - \frac{\Delta S_{vap}^{b,j}\left(T_{nb}^{j} - T\right)}{RT} \tag{6}$$

In Equation 6, R is the universal gas constant; T is the absolute temperature and ΔS_{vap}^{b} is the vaporization entropy at the normal boiling point (T_{nb}). Equation 7 presents the vapor pressure calculation at 298.15 K corrected using the vaporization entropy as proposed by Hoskovek et al., (2005) [24].

$$\ln P_X^{vap\,(298.15\ K)} = \ln P_z^{vap} + \frac{\Delta S_{vap}^{b,i}\left(T_{nb}^{i} - T\right)}{RT} - \frac{\Delta S_{vap}^{b,j}\left(T_{nb}^{j} - T\right)}{RT} + \frac{\left(100z - I_X^{298.15\ K}\right)\left[\ln\left(P_z^{vap}/P_{z+1}^{vap}\right) + \Delta S_{vap}^{b,i}\left(T_{nb}^{i} - T\right)/RT - \Delta S_{vap}^{b,j}\left(T_{nb}^{j} - T\right)/RT\right)]}{100} \quad (7)$$

The vaporization entropy was calculated for selected terpene compounds in *Lippia gracilis* essential oil. This entropy is proportional to the ratio of the degree of randomness in the vapor and liquid phases. The values for a pure substance are related to the molecular structure and can be estimated from the effective number of torsional bonds (τ) and the polar group number capable of hydrogen bonding (HBN). The value of ΔS_{vap}^{b} can be calculated using specific routines proposed by Myrdal and Yalkowsky (1997) [29].

The vaporization entropy, ΔS_{vap}^{b} in Equation 8, is influenced by the presence of hydrogen bond (HBN) that facilitates the phase change and the molecule conformation (τ), as described by (Myrdal and Yalkowsky, 1997) [29].

$$\Delta S_{vap}^{b} = 86 + 0.4\,\tau + 1421\ HBN \quad (8)$$

The effective number of torsional bonds (τ), which measures the overall molecular flexibility, was determined from Myrdal and Yalkowsky (1997) [29].

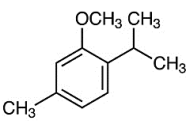
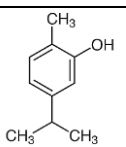
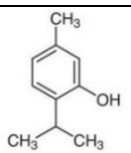
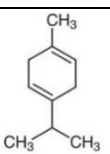
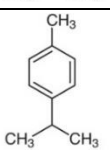
$$\tau = \sum(SP3 + 0.5\ SP2 + 0.5\ Ring) - 1 \quad (9)$$

SP3 and SP2 refer to non-ring and non-terminal sp3 and sp2 atoms, respectively. The variable 'Ring' denotes the number of independent ring systems present in the compound. The empirical measure of the effective number of torsional bonds is represented by τ. Upon analyzing Equation 8, it can be inferred that a higher number of non-terminal sp3 and sp2 atoms result in greater molecular flexibility, ultimately leading to a higher value of vaporization entropy. The vaporization entropy also requires the polar group number capable of hydrogen bonding (HBN). This effect is calculated by Equation 10.

$$HBN = \sqrt{\frac{OH+COOH}{M}} \quad (10)$$

The variables OH and COOH represent the number of alcohols and carboxylic acids, respectively, while M stands for the molecular weight of the compound. Table 4 displays the molecular structure of the chosen terpenes, along with their corresponding values for τ and HBN parameters, and the entropy of vaporization at the normal boiling point.

Table 4. Effective number of torsional bonds (**τ**), polar group number capable of hydrogen bonding (**HBN**), and vaporization entropy at the normal boiling point (ΔS^{b}_{vap}) of terpenes analyzed in this study

Compound	**Molecular structure**	**τ**	**HBN**	$\Delta S^{vap}_{b,X}$ **(J K^{-1}mol^{-1})**
Thymol methyl ether		1.5	0.000	86.60
Carvacrol		0.5	0.007	95.66
Thymol		0.5	0.007	95.66
γ-Terpinene		0.5	0.000	86.20
p-Cimene		0.5	0.000	86.20

Upon analyzing the molecular structures of the selected terpenes, it is apparent that some molecules have less flexibility due to the number of unsaturation and rings. Additionally, one can evaluate the propensity for phase change given the presence of hydrogen bonds, which renders Equation 8 physically consistent. The parameters τ and HBN are related to the molecular structure. The presence of hydrogen-bonding groups (OH and COOH) inhibits rotational freedom and increases the disorder magnitude that occurs during vaporization. Consequently, compounds that contain hydrogen-bonding groups, such as thymol and carvacrol, have higher vaporization entropy.

Table 5 shows a comparison between literature vapor pressures, and the vapor pressures corrected using vaporization entropy presented in Equation 7. Table 5 demonstrates that the vapor pressure calculated by Equation 7 and the literature data exhibit better agreement. It is also observed that the correction term using the vaporization entropy decreased the relative deviation (RD) for all the studied compounds, which suggests that the vaporization entropy should be considered in the vapor pressure calculations.

Table 5. Comparison between vapor pressures provided by literature $\left(\mathbf{P}_{\mathbf{lit}}^{\mathbf{vap}}\right)$ and by Equation 7 $\left(\mathbf{P}_{\mathbf{Eq.7}}^{\mathbf{vap}}\right)$

Compounds	$\mathbf{P}_{\mathbf{lit}}^{\mathbf{vap}}$ **(kPa)**	$\mathbf{P}_{\mathbf{Eq.7}}^{\mathbf{vap}}$ **(kPa)**	**RD (%)**
Thymol methyl ether	-	0.0137	-
Carvacrol	0.0035[(a)]	0.0030	14.29
Thymol	0.004[(b)]	0.0035	12.50
γ-Terpinene	0.137[(b)]	0.1345	1.80
p-Cymene	0.193[(b)]	0.1921	0.47

[(a)] [26].
[(b)] [24].

Conclusion

The Black Forest in Europe has inspired legends and fairy tales, much like the stories written by the Grimm Brothers. In Brazil, there is a semi-arid tropical vegetation called the White Forest, or Caatinga, with unique characteristics found exclusively in Brazil. This means that a significant portion of its biological heritage cannot be found anywhere else on the planet. One of the

plants that represents this biome is *Lippia grata*. Due to its therapeutic applications and cultural importance in Brazilian folk medicine, the essential oil extracted from *Lippia gracilis* Schum has become a source of scientific research, particularly for obtaining its major components thymol and carvacrol.

Reliable vapor pressure data for essential oils are crucial for the design of equipment used in distillation to concentrate major components and for a better understanding of the separation process [30]. This chapter focuses on presenting the vaporization entropy at 298.15 K to improve the accuracy of vapor pressure calculations. We suggest the direct use of this parameter, associated with gas chromatography, to obtain thermodynamic properties. The vaporization entropy $\left(\Delta S_{vap}^{b}\right)$ values are influenced by the presence of hydrogen bonds (HBN) that facilitate phase change and molecular conformation (τ), which translates molecular flexibility. This is a necessary increment in the calculated vapor pressures.

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Complementary Discussion

The composition of essential oils can be a true symphony of volatile compounds that confer distinct aromas, fragrances, and biological activities. This composition is not static and varies significantly depending on edaphoclimatic conditions and other environmental factors.

The term "edaphoclimatic" refers to the interaction between soil (edaphic) and climate (climatic) in each environment. The soil and climate of a specific region can determine the growth and development of plants, directly affecting the composition of the essential oils they produce. For example, a plant of the same species grown in soil rich in certain minerals may produce an essential oil with different characteristics from the same plant grown in soil with distinct mineral properties.

On the other hand, the term "chemovariability" refers to the chemical variability of compounds present in essential oils. A single plant species can produce essential oils with different chemical compositions depending on the environmental conditions in which it was cultivated. For instance, lavender essential oil (*Lavandula dentata* L.) may contain different proportions of compounds such as linalool, cyneol, camphor, and others, depending on factors such as altitude, temperature, humidity, and nutrient availability in the soil (MASETTO et al., 2011).

This interaction between edaphoclimatic factors and chemovariability can be observed in various plant species. For example, lavender cultivated in drier climates may produce essential oil with high concentrations of linalool, while in areas with higher humidity, the same plant may produce essential oil with a higher content of cyneol (MASETTO et al., 2011).

Another example is peppermint (*Mentha piperita*), which in nutrient-rich soils may produce essential oil with a high content of menthol, known for its analgesic and refreshing properties, while in less fertile soils, the same plant may prioritize the production of other compounds such as menthone and pulegone, conferring different biological activities to the essential oil (PEGORARO et al., 2010).

A study conducted to evaluate the influence of climate (rainfall, humidity, and mean temperature) and foliar nutrition on the chemovariability of essential oil from the leaves of eucalyptus (*Eucalyptus microcorys*) (OLIVEIRA et al., 2014) identified significant variability in the composition of the essential oil over twelve months, the data are presented in Table 4.1.

Table 4.1 Percentages of essential oil constituents of *E. microcorys* leaf oil samples collected during twelve months (Oliveira et al, 2014).

Compound	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUNE	JULY	AUG
α-Thujene	4.8	9.9	9.9	5.4	4.6	24.9	10.2	17.6	21.2	20.7	12.4	9.4
Camphene	1.6	0.7	0.5	0.4	0.7	1.4	1.5	0.1	0.3	0.4	1.4	1.5
p-Cymene	2.9	3.1	5.3	5.1	3.6	4.2	4.2	5.6	3.9	4.7	2.3	2.4
Limonene	0.1	2.6	1.9	1.6	0.8	6.2	-	4.0	4.3	4.1	4.6	3.8
1,8-Cyneol	78.3	71.4	70.6	73.8	74.9	37.2	69.3	62.3	62.1	61.5	68.5	71.5
γ-Terpinene	-	-	-	-	-	0.5	0.1	1.1	2.1	1.1	0.1	0.1
Isopentyl Isovalerate	0.5	-	0.6	0.5	0.6	0.1	0.5	0.4	0.3	0.4	0.4	0.3
endo-Fenchol	1.9	1.4	1.2	1.4	1.6	2.0	1.9	0.7	0.5	0.6	1.5	1.4
α-Campho*	-	-	-	-	-	5.3	-	-	-	-	-	-
trans-Pino**	1.1	2.3	2.5	2.9	4.1	0.1	0.6	0.9	-	0.6	0.4	0.7
Pinocarvone	1.6	2.7	2.8	3.2	4.5	0.1	0.7	1.1	0.1	0.8	0.3	0.8
Borneol	3.5	2.7	2.2	2.9	3.2	4.7	4.3	1.6	1.0	1.2	3.0	3.1
α-Terpineol	3.4	3.1	2.3	2.4	1.2	7.6	6.2	4.5	3.7	3.7	5.1	4.7
Monoterpene hydrocarbons	9.3	16.3	17.6	12.5	9.7	37.2	15.8	28.3	31.9	31.1	20.8	17.1
Oxygenated monoterpenes	89.8	83.6	81.7	86.7	89.6	56.8	83.1	71.2	67.2	68.5	78.7	82.3
Others	0.5	-	0.6	0.5	0.6	0.01	0.5	0.4	0.3	0.4	0.4	0.3
Total (%)	99.7	100	100	99.7	100	94.1	99.5	100	99.5	100	100	99.8

* α-Campholenal;** trans-Pinocarveol.

Upon examining the data presented in Table 4.1, an interplay of fluctuations in constituent percentages over the course of the year is observed. From α-Thujene to α-Terpineol, each compound exhibits its unique pattern of variation, reflecting the plant's response to changing environmental conditions. For instance, α-Thujene shows peaks in February and June, indicating potential seasonal preferences or metabolic shifts during these months. Conversely, constituents like Camphene and Isopentyl isovalerate appear sporadically, suggesting a less consistent presence influenced by specific environmental triggers.

Notably, certain compounds such as 1,8-Cyneol display significant variability, with pronounced peaks in September, November, and February. This variability underscores the intricate interplay between environmental cues and biochemical processes governing essential oil production.

Furthermore, the presence of Monoterpene hydrocarbons and Oxygenated monoterpenes shows consistent peaks in November, February, and June, indicating potential seasonal trends in overall oil composition.

These variations reflect the plant's ability to adapt and respond to environmental stimuli, including temperature, humidity, soil conditions, and light intensity. Factors such as soil mineral composition and climatic fluctuations can profoundly influence plant metabolism, ultimately shaping the composition of essential oils.

Understanding these variations is crucial not only for elucidating the complex interactions between plants and their environment but also for optimizing essential oil production and quality. By harnessing insights into seasonal variations, researchers and growers can refine cultivation practices to maximize oil yield and enhance desired aromatic and therapeutic properties.

These examples shed light on the intricate dynamics underlying the variation in essential oil compositions among plants of the same species, driven by environmental conditions. They underscore the complexity of factors at play and highlight the direct impact of the environment on the chemical variability of these compounds.

Errata. In the text of Chapter IV *"The Soul of Brazil's White Forest"* where it reads " (1678-170)", read "(1678-1704)".

CHAPTER V

Published Article

FONSECA, L.A.A.P.; SARTORATTO, A.; CREMASCO, M.A. **Experimental determination of thermodynamic properties of terpene and aromatic ketones by gas chromatography**. Journal of Molecular Liquids JCR, v. 322, p. 114531, 2021.

This chapter represents the essence of this doctoral Thesis. Within this publication, an extension of the gas chromatography correlation technique was introduced to obtain thermodynamic properties of oxygenated terpenes, an unusual approach in this field of study, presenting unpublished data, and discussing the validation of the methodology. A comparison was made between experimental data and predictions from group contribution models. This approach not only complements the theoretical discourse but also provides insights into the behavior of terpenoids.

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Experimental determination of thermodynamic properties of terpene and aromatic ketones by gas chromatography

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ABSTRACT

The terpene and aromatic ketones are among oxygenated compounds present in essential oils (Eos). They are substances of great importance to the chemical, pharmaceutical, and the food industries. Because of their applications in these industries, it is extremely necessary to know their thermodynamic properties and to obtain reliable data of these properties. This work aims to determinate experimentally the enthalpy of vaporization (ΔH^{vap}) and normal boiling temperature (T_{nb}) of some terpene and aromatic ketones and other oxygenated compounds present in essential oils by the gas chromatography technique (GC). The additional goal is to evaluate three group contribution models developed to estimate enthalpies of vaporization. The experimental determination of thermodynamic data using GC involves the use of the chromatographic retention index in combination with Kirchhoff-Rankin type equations. Gas chromatography experiments were carried out within a defined temperature range consistent with the nature of the compounds studied. In all, 11 compounds were evaluated. The ΔH^{vap} data were determined at 298.15 K. The results obtained agreed with those found in the literature, showing small relative deviations (RD), demonstrating that the CG technique can be a good tool for obtaining the thermodynamic properties studied. In addition, unpublished data of ΔH^{vap} at 298.15 K and T_{nb} for the compounds bicyclo [2,2,2]octan-2,5-dione, methyl-jasmonate and 4-(4-hydroxyphenyl)-2-butanone are reported.

1. Introduction

Essential oils (Eos) are complex mixtures of compounds from different organic classes. Among the compounds present in the Eos, are terpene and aromatic ketones to which antioxidant, anti-inflammatory, anti-microbial, anti-tumor, gastroprotective and neuroprotective activities have been attributed [1].

The interest in the study of essential oils can be attributed to the promising applications of herbal medicines for configuring an effective and culturally appropriate option. Herbal medicine has attracted great attention in the past few years, and it is increasingly used as alternatives to currently prescribed drugs. Several lines of evidence support the positive impact of medicinal plants in the prevention and cure of a wide range of diseases [1]. In Brazil, between 2013 and 2015, growth in the search for herbal medicines and herbal treatments by the Unified Health System (SUS) was 161% [2].

The industrial application of the compounds present in Eos requires important thermodynamic properties, such as the enthalpy of vaporization (ΔH^{vap}), vapor pressure (P_{vap}) and normal boiling point (T_{nb}) necessary for many technological processes associated with evaporation [3].

The most commonly used methods for measuring thermodynamic properties of pure compounds are effusion, gas saturation, and gas chromatography [4,5]. The first two methods require great care for accurate results, and it is not unusual for measurements made by different methods and/or laboratories to differ by as much as one order of magnitude or more, especially for compounds of low volatility [6,7]. The gas chromatographic (GC) method offers great advantages in terms of simplicity, speed, purity, small sample size and reproducibility. In the correlation gas chromatography method, the thermodynamic properties are obtained through retention data [8–11].

Since, it is not practical to measure the thermodynamic properties as the need arises, estimation methods are generally employed [12]. The accomplishments of all these experiments are too expensive and time-consuming, so the calculation or estimation methods are good way to solve this problem. The group contribution methods are suitable tools for estimation of many physicochemical properties of pure compounds and mixtures too as has been shown and confirmed below for some cases. The biggest advantage of these methods is they need knowledge only of the chemical structure of the compounds without any other input information [13].

This aim of this study was to determine experimental thermodynamic properties (enthalpy of vaporization ΔH^{vap} and normal boiling point T_{nb}) of terpene and aromatic ketones by the gas chromatography

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technique. The ΔH^{vap} data was determined at 298.15 K. Three group contribution methods to estimate the enthalpy of vaporization of terpene and aromatic ketones were also evaluated. In addition, unpublished data of ΔH^{vap} at 298.15 K and T_{nb} for the compounds bicyclo [2,2,2]octan-2,5-dione, methyl-jasmonate and 4-(4-hydroxyphenyl)-2-butanone are presented.

2. Theory

2.1. Kováts retention indices

Isothermal Kováts retention indices (I_X) are defined as:

$$I_X = 100z + 100\left(\frac{\ln t_{R,X} - \ln t_{R,z}}{\ln t_{R,z+1} - \ln t_{R,z}}\right) = 100z + 100\frac{\ln\left(\gamma_z^\infty P_z/\gamma_X^\infty P_X\right)}{\ln\left(\gamma_z^\infty P_z/\gamma_{z+1}^\infty P_{z+1}\right)} \quad (1)$$

In Eq. (1) $t_{R,X}$, P_X, and γ_X^∞ represent the retention time, vapor pressure and infinite dilution activity coefficient, respectively, of a solute X in the stationary phase, and subscripts z and z + 1 identify the reference n-alkanes with z and z + 1 carbon atoms whose retention times encompass that of solute X.

Expressing P_X from Eq. (1), we obtain Eq. (2):

$$\ln P_X = \ln\left(\frac{P_z\gamma_z^\infty}{\gamma_X^\infty}\right) + \frac{(100z - I_X)\ln\left(P_z\gamma_z^\infty/P_{z+1}\gamma_{z+1}^\infty\right)}{100} \quad (2)$$

which under assumption $\gamma_x^\infty = \gamma_z^\infty = \gamma_{z+1}^\infty$ gives Eq. (3):

$$\ln P_X = \ln P_z + \frac{(100z - I_X)\ln\left(P_z/P_{z+1}\right)}{100} \quad (3)$$

Eq. (3), directly allow computation of vapor pressures at 298.15 K provided that accurate values of the Kováts indices of the solute and vapor pressures of n-alkane references at this temperature are known [14,15].

The temperature dependence of the partition coefficient K relevant to the gas phase–stationary phase partitioning in GC was based on the original assumption of Clarke and Glew [16] that the enthalpy changes of a given process can be expressed as a perturbation of the standard enthalpy value at some reference temperature by means of Taylor's series expansion, led to a general equation:

$$\ln K = a + \frac{b}{T} + c\ln T + dT + \ldots \quad (4)$$

Several types of $I_X = f(T)$ relationships have been employed, depending on the number of terms on the right side of Eq. (4) taken into consideration. A three-parameter Kirchhoff–Rankin-type Eq. (5) became popular to describe $I = f(T)$ dependence, particularly for polar compounds [17–21].

$$I(T) = C_0 + \frac{C_1}{T} + C_2\ln T \quad (5)$$

In Eq. (5), C_0, C_1, and C_2 are empirically determined constants and T is the thermodynamic temperature in Kelvin. The constants are determined using non-linear regression techniques.

It should be noted that several other empirical forms of $I = f(T)$ function have also been utilized to date including linear [22,23], simple quadratic [24,25], polynomial [26] and hyperbolic [27] equations.

2.2. Group contribution methods

In these methods, the property of a compound is a function of structurally-dependent parameters, which are determined by summing the frequency of each group occurring in the molecule times its contribution. These methods provide the advantage of quick estimates without requiring substantial computational resources [12].

For the estimation of enthalpy of vaporization (ΔH^{vap}) of terpenes and aromatic ketones, the group-contribution methods given by Joback and Reid [28], Kolská et al. [13] and Oliveira [11] were used in this work. These methods were chosen for their simplicity of application and the diversity of the molecules covered.

2.2.1. Joback and Reid [28]

The Joback and Reid [28] method predicts eleven important and commonly thermodynamic properties of pure components from molecular structure only. This method assumes that there are no interactions between the groups and therefore only uses additive contributions.

$$\Delta H^{vap} = 15.30 + \sum_i N_i h_{v,i} \quad (6)$$

In Eq. (6) N_i is the occurrence of each group in the structure and $h_{v,i}$ is the contribution to the enthalpy of vaporization from each group. The application of this method is in Table 1.

2.2.2. Kolská et al. [13]

In this method [13], the estimation of the properties is done in three procedures, which covers the levels of first order, second order and third order. Basically, the first-order groups allow the description of a wide variety of organic compounds and should describe the entire molecule without any fragment being represented. Still, a fragment cannot be part of other fragments. In molecules containing aromatic rings, the aromatic carbon (aC) must have preference in the choice of first order groups, as shown in Fig. 1.

$$\Delta H^{vap} = 9.67 + \sum_i N_i C_i + \sum_j M_j D_j + \sum_j O_k E_k \quad (7)$$

In Eq. (7) N_i, M_j, O_k are the occurrence of first, second and third order groups that appear in the structure of the molecule and, C_i, D_j, E_k represent their corresponding contributions to the enthalpy of vaporization. The data are obtained for the reference temperature of 298.15 K. The application of this method is illustrated in Table 2.

2.2.3. Oliveira [11]

This method [11] presents group contribution to compounds with *cis-trans* isomerism and contribution to bicyclic compounds. It is important to highlight that the proposed method is specific to substances present in essential oils and only includes compounds containing oxygen in their structure, while the other literature methods analyzed are general methods.

$$\Delta H^{vap} = 19.55 + \sum_i N_i C_i \quad (8)$$

Table 1
Enthalpy of vaporization of Carvone by Joback and Reid (1987) method.[a]

Group	Occurrences	Contribution
=C<	1	2.139
=CH−(ring)	1	2.546
$=CH_2$	1	1.725
=C<(ring)	1	3.061
CH_3	2	2.374
>C = O(ring)	1	8.972
>CH−(ring)	1	1.943
$-CH_2-_{(ring)}$	2	2.399
	ΔH_{vap}^{est}	45.23 kJ mol^{-1}
	$\Delta H_{vap}^{exp(a)}$	58.20 kJ mol^{-1}

[a] [29].

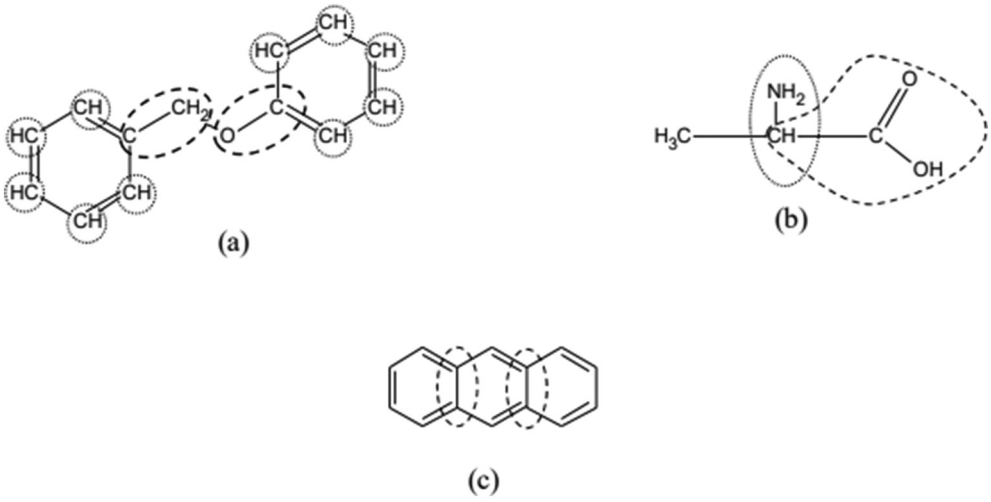

Fig. 1. Correct description of the Kolská et al. [13] method for: (a) first-order groups; (b) second-order groups; (c) third-order groups.

In Eq. (8) N_i is the occurrence of each group in the structure and C_i is the contribution to the enthalpy of vaporization from each group. The application of this method is in Table 3.

3. Experimental

3.1. Gas chromatography

The retention times of the examined compounds were determined using a Thermo Scientific (Trace GC Ultra) gas chromatograph/flame ionization detector equipped with a HP5-MS, capillary column (30 m × 0.25 mm i.d. × 0.25 μm film thickness) under isothermal conditions of column (80 °C to 200 °C), injector temperature of 220 °C, detector at 250 °C and injection volume of 1.0 μL. The carrier gas (He) flow rate was 1.0 mL min^{-1}. The compounds were dissolved in methanol at concentration of 20 mg mL^{-1} and the peaks were identified by calculating their retention indices and using co-injection of a standard hydrocarbon mixture (C_8 to C_{17}). The analyzes were performed in triplicate. Table 4 provides a list of the 11 compounds used in this study with their Kováts retention indices at 8 or 13 temperatures.

3.2. Chemicals

The compounds examined were acetophenone (99.0% purity), bicyclo[2,2,2]octan-2,5-dione (95.0% purity), 4-(4-hydroxyphenyl)-2-butanone (99.0% purity), carvone (96.0% purity), camphor (95.0% purity), menthone (90.0% purity), damascenone (99.0% purity), methyljasmonate (99.0% purity), p-cymene (99.0% purity), linalool (99.0% purity), terpinen-4-ol (99.0% purity), and the n-alkanes standards (C_8–C_{16}) were purchased from Sigma Aldrich (Holzminden, Germany).

The compounds linalool, p-cymene, terpinen-4-ol were included by molecular structure similarity to the terpene and aromatic ketones analyzed in this work.

3.3. Database

The vapor pressures of reference C_8 to C_{17} n-alkanes at different temperatures used in this work were calculated using Eq. (9).

$$\ln\left(\frac{P}{P_0}\right) = \left(1-\frac{T_0}{T}\right)\exp\left(A_0 + A_1 T + A_2 T^2\right) \quad (9)$$

In Eq. (9) the coefficients derived for temperatures between the triple and boiling points were taken from a critical compilation of n-alkanes data [30].

Published P values of the compounds studied at 298.15 K were obtained from web-available databases [8]. The same sources along with the commercial Sigma Aldrich catalogue served as a literature source for normal boiling point (T_{nb}) data.

3.4. Data treatment

The nonlinear regression routines and graphic outputs were performed by Origin 8.1 (Origin Lab, Northampton, Massachusetts, USA).

Table 2
Enthalpy of vaporization of Carvone by Kolská et al. (2005) method.[a]

Group	Occurrences	Contribution
First order		
CH_3	2	2.266
$C = CH_2$	1	7.741
$CH_{(ring)}$	1	4.075
$CH_{2\ (ring)}$	2	4.013
$C = O$	1	14.837
Second order		
$CH = C_{(ring)} - CH_3$	1	3.216
$CH_{(ring)} - C$	1	1.565
	ΔH_{vap}^{est}	53.66 kJ mol^{-1}
	$\Delta H_{vap}^{exp(a)}$	58.20 kJ mol^{-1}

[a] [29].

Table 3
Enthalpy of vaporization of Carvone by Oliveira's (2017) method.[a]

Group	Occurrences	Contribution
CH_3	2	0.475
$=CH_2$	1	-1.196
$=C<$	1	5.008
$>CH-_{(ring)}$	1	3.197
$=CH-_{(ring)}$	1	3.048
$=C<_{(ring)}$	1	4.862
$>C = O_{(ring)}$	1	10.589
$-CH_2-_{(ring)}$	2	2.793
	ΔH_{vap}^{est}	51.59 kJ mol^{-1}
	$\Delta H_{vap}^{exp(a)}$	58.20 kJ mol^{-1}

[a] [29].

Table 4
Kováts retention indices of studied compounds.

Compound	Kováts retention indices												
	Temperature (K)												
	353.15	363.15	373.15	383.15	393.15	403.15	413.15	423.15	433.15	443.15	453.15	463.15	473.15
p-Cymene	1022.82	1025.68	1028.11	1030.37	1034.39	1038.11	1041.26	1044.39	1048.36	1049.69	1050.11	1060.42	1070.79
Acetophenone	1067.92	1070.42	1067.52	1074.80	1079.56	1087.60	1091.38	1093.22	1107.14	1108.00	1113.68	1117.89	1154.41
Linalool	1101.21	1101.50	1102.54	1102.66	1102.85	1104.35	1105.20	1104.63	1108.33	1106.40	1109.57	1110.47	1113.38
Camphor	1139.99	1146.31	1152.42	1158.97	1165.11	1172.76	1178.58	1186.49	1194.01	1197.42	1216.89	1221.32	1230.56
Menthone	1147.93	1152.64	1157.93	1162.24	1166.97	1173.17	1177.79	1184.07	1187.87	1188.34	1206.13	1204.65	1216.41
Terpinen-4-ol	1176.41	1181.63	1184.83	1192.62	1199.29	1204.00	1208.96	1214.56	1221.60	1225.10	1234.09	1250.00	1248.54
Carvone	1232.65	1236.80	1240.93	1245.51	1250.07	1255.93	1260.50	1265.32	1271.56	1276.72	1282.85	1289.85	1294.48
Bicyclo[2,2,2][a]	1266.42	1271.97	1277.15	1282.93	1289.97	1296.35	1304.87	1312.48	1319.63	1328.57	1335.77	1348.22	1356.55
Damascenone			1369.62	1374.60	1379.14	1384.66	1390.99	1396.69	1401.95	1408.61	1414.04	1421.31	1428.10
4-(4-Hydroxy[b]						1548.98	1552.01	1556.15	1559.03	1564.15	1569.46	1576.60	1581.26
Methyl-jasmonate						1634.46	1637.98	1641.34	1646.10	1650.07	1654.33	1658.63	1664.13

[a] Bicyclo[2,2,2]octan-2,5-dione.
[b] 4-(4-Hydroxyphenyl)-2-butanone.

4. Results

4.1. Experimental thermodynamic data

A brief inspection of the data in Table 4 reveals that, occasionally, the numerical values of I_X do not change regularly with increasing temperatures. Consequently, we applied Eq. (5) to evaluate the I_X versus T relationship for each of the compounds. A routine for the nonlinear regression (Levenberg–Marquardt algorithm) was used to determine the coefficients C_0, C_1, and C_2.

Based on the r-squared statistics, the $I = f(T)$ model represented by Eq. (5) explains more than 99.0% of the variance in the data for all compounds, implying it provides a highly significant description of the retention data. For the compounds investigated in this work and the temperature ranges used, the model seems to show a high flexibility resulting. Figs. 2 and 3 are characterized by linear dependence of I on T for carvone and damascenone, respectively.

With the requisite collection of Kováts indices assembled by Eq. (5) the vapor pressures were determined from Eq. (3). The vapor pressure curves for the analyzed compounds are present in Figs. 4 and 5. The Antoine Equation, Eq. (10), parameters A, B, C were determined using non-linear regression techniques and are presented in Table 5.

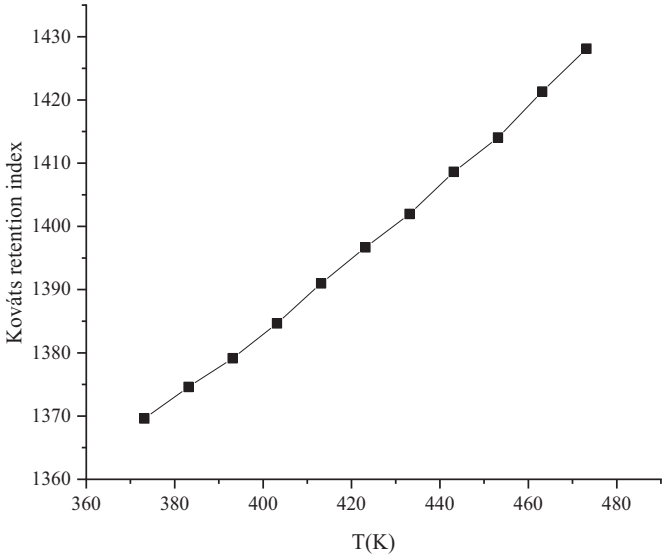

Fig. 3. Dependence of Kováts retention index on temperature for damascenone.

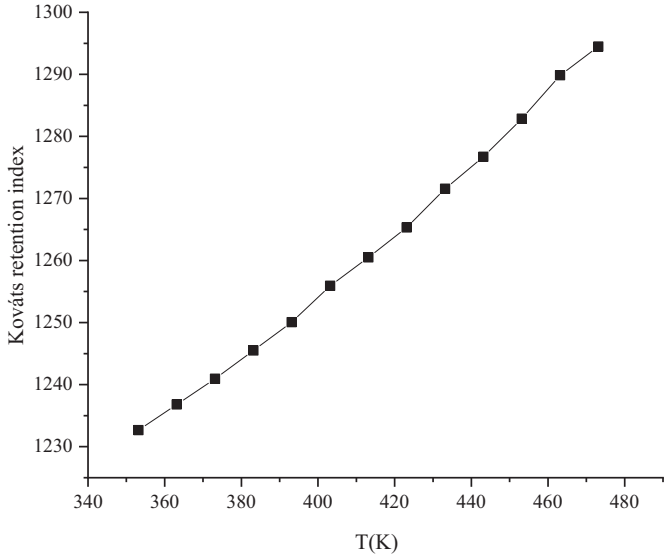

Fig. 2. Dependence of Kováts retention index on temperature for carvone.

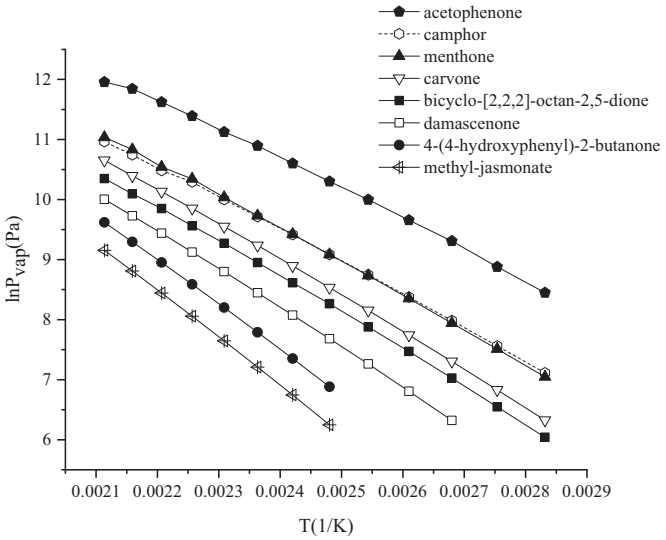

Fig. 4. Vapor pressure (P_{vap}) curves for aromatic and terpene ketones studied in this work.

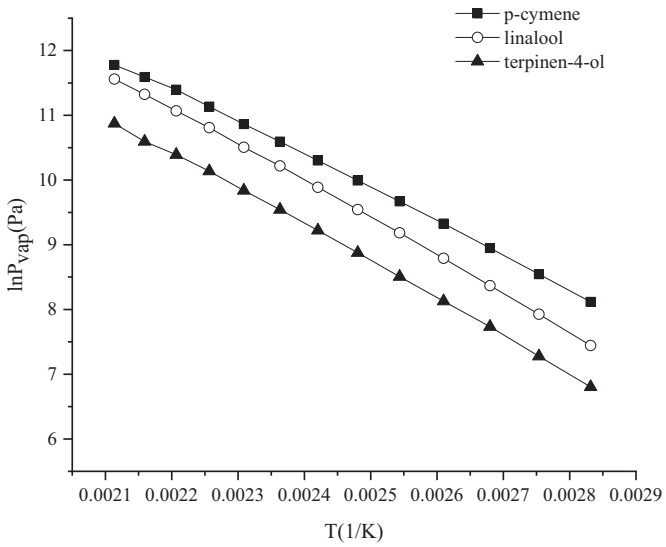

Fig. 5. Vapor pressure (P_{vap}) curves for hydrocarbon and other oxygenated compounds included in this study.

$$\ln P_{vap}(Pa) = A - \frac{B}{T(K) + C} \tag{10}$$

For processing the (P_{vap}) versus T data, the Kirchhoff–Rankin-type Eq. (11) was used again [10].

$$\ln P_{vap} = \frac{1}{R} b_0 + \frac{1}{RT} b_1 + \frac{1}{R} b_2 \ln (T/T_0) \tag{11}$$

Parameters of Eq. (11) are presented in Table 6.

In Eq. (11), T_0 is arbitrary equalled to 298.15 K and R = 8.3145 J K^{-1} mol^{-1}. The enthalpy of vaporization at temperature T may be calculated from Eq. (12).

$$\Delta H^{vap} = -b_1 + b_2 T \tag{12}$$

Eqs. (11) and (12) were thus implemented to predict ΔH^{vap} values at 298.15 K for all 11 compounds as shown in Table 7. Additionally, since it is known that the normal boiling temperature T_{nb} of a substance in the liquid phase is one whose vapor pressure equals atmospheric pressure (atm), is possible to define P in Eq. (11) as 101.325 kPa to obtain the T_{nb} data of the compounds analyzed.

The experimental results for the enthalpy of vaporization in this work agreed with others obtained by gas chromatography as reported in the literature with small relative deviations, as presented in Table 7. A comparison of our boiling point temperatures calculated from Eq. (11) by extrapolating our data to 101.325 kPa (using an iteration procedure in the standard Excel program) with literature, results in a low relative deviation in predicting T_{nb}^{exp} (Table 7), demonstrating that the CG technique using alkanes as standards can be a good tool to obtain these thermodynamic properties.

The relative deviation (RD) is defined as Eq. (13).

$$RD\% = \left(\frac{\left| \Delta H_{est}^{vap} - \Delta H_{exp}^{vap} \right|}{\Delta H_{exp}^{vap}} \right) x100 \tag{13}$$

In Eq. (13), ΔH_{est}^{vap} and ΔH_{exp}^{vap} are estimated and experimental enthalpy of vaporization, respectively.

4.2. Estimated enthalpy of vaporization by group contribution

Analyzing Table 8 by comparison with experimental data of ΔH_{exp}^{vap}, it is verified that the Oliveira [11] model presented, on average, the best estimates for selected compounds with relative deviations under 15% for all compounds studied in this work. This method contemplates only compounds containing oxygen in their structure and provides group contribution to bicyclic compounds.

Kolská's et al. [13] model presented good estimates for terpene, and aromatic ketones studied. The mean relative deviation for all analyzed compounds was 12.82%. However, this behavior did not occur for three oxygenated compounds selected and presented the most considerable relative deviations for linalool, terpinen-4-ol, and 4-(4-hydroxyphenyl)-2-butanone, 29.01%, 34.56%, and 34.74%, respectively. This method

Table 5
Vapor pressure: Antoine Equation parameters.

Compound	A	B	C	r^{2a}
p-Cymene	19.73 ± 0.34	2993.09 ± 209.40	−95.57 ± 10.78	0.99980
Acetophenone	18.40 ± 0.39	2148.98 ± 209.23	−137.34 ± 12.91	0.99958
Linalool	20.51 ± 0.12	3404.84 ± 79.02	−92.66 ± 3.61	0.99998
Camphor	18.99 ± 0.30	2962.56 ± 184.35	−103.93 ± 9.32	0.99986
Menthone	19.74 ± 0.38	3299.84 ± 236.39	−93.31 ± 11.12	0.99983
Terpinen-4-ol	19.54 ± 0.34	3265.34 ± 213.32	−97.01 ± 10.02	0.99986
Carvone	20.00 ± 0.06	3543.19 ± 37.49	−94.02 ± 1.67	0.99999
Bicyclo-[2,2,2]-octane-2,5-dione	19.13 ± 0.10	3197.52 ± 52.92	−108.91 ± 2.67	0.99999
Damascenone	20.08 ± 0.09	3760.90 ± 55.86	−99.7296 ± 2.36	0.99999
4-(4-Hydroxyphenyl)-2-butanone	21.11 ± 0.04	4178.49 ± 26.15	−109.39 ± 1.02	0.99999
Methyl-jasmonate	21.46 ± 0.03	4513.80 ± 22.44	−106.50 ± 0.82	0.99999

[a] Correlation coefficients (r^2, %).

Table 6
Parameters of Eq. (11).

Compound	b_0	b_1	b_2	r^{2a}
p-Cymene	275.12 ± 11.58	−69,417.71 ± 3587.25	−65.71 ± 8.79	0.99990
Acetophenone	324.58 ± 18.41	−83,573.27 ± 5700.01	−104.49 ± 13.97	0.99962
Linalool	288.28 ± 4.16	−75,849.49 ± 1286.94	−69.32 ± 3.15	0.99999
Camphor	286.38 ± 4.16	−75,706.35 ± 3442.28	−76.35 ± 8.44	0.99988
Menthone	280. 75 ± 13.18	−74,362.93 ± 4080.29	−68.80 ± 10.00	0.99985
Terpinen-4-ol	286.25 ± 12.37	−76,749.58 ± 3829.59	−73.11 ± 9.38	0.99984
Carvone	291.73 ± 2.79	−80,040.27 ± 864.16	−73.79 ± 2.13	0.99999
Bicyclo-[2,2,2]-octane-2,5-dione	309.71 ± 4.09	−86,285.33 ± 1265.50	−89.61 ± 3.10	0.99999
Damascenone	305.79 ± 3.64	−87,749.66 ± 1136.22	−80.56 ± 2.71	0.99999
4-(4-Hydroxyphenyl)-2-butanone	342.58 ± 2.36	−103,473.29 ± 746.43	−95.17 ± 1.71	0.99999
Methyl-jasmonate	349.95 ± 1.61	−108,285.51 ± 507.84	−97.50 ± 1.16	0.99999

[a] Correlation coefficients (r^2, %).

Table 7
T_{nb} and ΔH^{vap}: Properties calculated at 298.15 K and 101.325 kPa.

Compound	T_{nb}^{lit} K	T_{nb}^{exp}[a] K	RD %	ΔH_{lit}^{vap} kJ mol^{-1}	ΔH_{exp}^{vap}[b] kJ mol^{-1}	Method	RD %
p-Cymene	457.50[c]	460.33[a]	0.62	48.32[c]	49.83[b]	GC	3.11
Acetophenone	440.00[d]	449.61[a]	2.18	53.44[e]	52.42[b]	GC	1.91
Linalool	471.15[f]	471.67[a]	0.11	55.25[c]	55.18[b]	GC	0.12
Camphor	480.57[g]	501.90[a]	4.44	55.30[h]	52.94[b]	GC	4.27
Menthone	480.15[g]	495.82[a]	3.26	–	53.85[b]	GC	–
Terpinen-4-ol	495.50[c]	505.24[a]	1.97	55.52[c]	54.95[b]	GC	1.03
Carvone	504.00[i]	513.70[a]	1.93	58.20[h]	58.04[b]	GC	0.28
Bicyclo-[2,2,2]-octan-2,5-dione	–	533.06[a]	–	–	59.57[b]	GC	–
Damascenone	547.15[j]	542.22[a]	0.90	–	63.73[b]	GC	–
4-(4-Hydroxyphenyl)-2-butanone	–	547.68[a]	–	–	75.10[b]	GC	–
Methyl-jasmonate	–	563.83[a]	–	–	79.22[b]	GC	–

(T_{nb}^{lit} literature normal boiling temperature; ΔH_{lit}^{vap} literature enthalpy of vaporization at 298.15 K; relative deviation (RD); gas chromatography (GC)).
[a] T_{nb}^{exp} denotes experimental normal boiling point temperature (this work).
[b] ΔH_{exp}^{vap} denotes experimental enthalpy of vaporization at 298.15 K (this work).
[c] [10].
[d] [30].
[e] [8].
[f] [31].
[g] [32].
[h] [29].
[i] [33].
[j] [34].

Table 8
Enthalpy of vaporization to studied compounds at 298.15 K: experimental ($\Delta H_{exp}^{vap.}$) and estimated (ΔH_{est}^{vap}) by group contribution methods selected.

Compound	Formula	Enthalpy of vaporization ΔH^{vap}, kJ mol^{-1}						
		ΔH_{exp}^{vap}	Joback and Reid [28]		Kolská et al. [13]		Oliveira [11]	
			ΔH_{est}^{vap}	RD%[e]	ΔH_{est}^{vap}	RD%[e]	ΔH_{est}^{vap}	RD%[e]
Terpene ketones								
Bicyclo[2,2,2][*]	$C_8H_{10}O_2$	59.57[a]	46.73	21.55	63.55	6.68	56.24	5.59
Carvone	$C_{10}H_{14}O$	58.20[b]	45.23	22.29	59.66	2.51	51.59	11.36
Camphor	$C_{10}H_{16}O$	55.30[b]	39.49	28.59	52.12	5.75	50.16	9.29
Menthone	$C_{10}H_{18}O$	53.85[a]	41.83	22.32	56.26	4.48	50.51	6.20
Damascenone	$C_{13}H_{20}O$	63.73[a]	52.42	17.75	66.79	4.80	64.96	1.93
Methyl-jasmonate	$C_{13}H_{20}O$	79.22[a]	57.84	26.99	69.46	12.32	75.98	4.09
Aromatic ketones								
Acetophenone	C_8H_8O	55.30[c]	42.44	23.25	58.24	5.32	47.98	13.24
4-(4-Hydroxy-[**]	$C_{10}H_{12}O$	75.10[a]	59.89	20.25	101.19	34.74	67.16	10.57
Other compounds								
p-Cymene	$C_{10}H_{14}$	48.32[d]	40.42	16.35	48.71	0.81	50.4	4.30
Linalool	$C_{10}H_{18}O$	55.25[d]	52.62	4.76	71.28	29.01	63.44	14.82
Terpinen-4-ol	$C_{10}H_{18}O$	55.52[d]	54.4	2.02	74.71	34.56	63.39	14.18
MRD %[f]				18.74		12.82		8.69

[*] Bicyclo[2,2,2]-2,5-dione.
[**] 4-(4-Hydroxyphenyl)-2-butanone.
[a] Experimental enthalpy of vaporization at 298.15 K (this work).
[b] [29].
[c] [8].
[d] [10].
[e] Relative deviation (RD).
[f] Mean relative deviation (MRD).

describes a wide variety of organic and inorganic compounds being a general model and presents molecular descriptors for interaction between groups.

The mean relative deviation (MRD) is defined as Eq. (14).

$$MRD\% = \frac{1}{n}\sum_{i=1}^{n} RD\% \quad (14)$$

In Eq. (14), n is the number of analyzed compounds.

Joback and Reid's model [28], although, applicable to many chemical species, did not present good accuracy for the terpene and aromatic ketones studied, with a mean relative deviation of 18.74%.

5. Conclusion

The ΔH^{vap} data for selected aromatic and terpene ketones were determined at 298.15 K. The results obtained agreed with the literature showing small relative deviations demonstrating that the GC technique using alkanes as standards can be a good tool to obtain this thermodynamic property. Also, unpublished data of ΔH^{vap} at 298.15 K and T_{nb} for the compounds bicyclo[2,2,2]octan-2,5-dione, methyl-jasmonate, and 4-(4-hydroxyphenyl)-2-butanone were presented.

Prediction performance for enthalpy of vaporization was compared to three models: Joback and Reid [28], Kolská et al. [13], and Oliveira [11]. Oliveira's [11] model is specific to substances present in essential oils and only includes compounds containing oxygen in their structure and provides group contributions for bicyclic compounds, obtained, on average, the best results for the analyzed compounds, with a mean relative deviation of 8.69%.

CRediT authorship contribution statement

Luciana A. A. P. Fonseca: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data Curation, Writing - original draft, Visualization. **Adilson Sartoratto:** Methodology, Formal analysis, Writing - review & editing. **Marco A. Cremasco:** Methodology, Writing - review & editing, Project administration.

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Declaration of competing interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoria; educational grants; participation in speckers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Complementary Discussion

In this section, the discussion on experimental techniques to determine thermodynamic properties is revisited. The availability of high-quality experimental data provides a solid foundation for theoretical development and model validation, essential for ensuring the reliability and replicability of analytical techniques. One of the most effective ways to contribute to the literature with experimental data is by publishing results obtained in carefully conducted studies.

Conventional methods for determining thermodynamic properties are divided into direct methods, which generally rely on calorimetric measurements, and indirect methods where thermodynamic properties are derived from other data sources. Table 5.1 presents the main analytical techniques for the experimental determination of thermodynamic properties.

Table 5.1 Conventional methods for obtaining thermodynamic data.

Method	Advantages	Disadvantages
Static	Suitable for moderate pressures with precise results.	Volume variations during measurement can impact vapor pressure.
Dynamic	Can be coupled with another ebulliometer to eliminate errors related to superheated vapor. Provides precise boiling and condensation temperatures.	Small differences between boiling and condensation temperatures may occur.
Effusion	Comprehensive apparatus minimizes measurement errors.	Requires large sample quantities. Analysis time is relatively long.
Thermogravimetry	Requires minimal sample quantities. Short experimental time. Exhibits good reproducibility. Comparability with conventional methods.	Requires reference substance with similarity. Substances with low thermal stability may affect reproducibility. Atmosphere may affect data.
Chromatography	Capable of analyzing substances in mixtures. Does not demand completely pure samples. Requires minimal sample quantity. Yields rapid results. Applicable to complex substances.	Dependency on reference substances with known pressure data.

In the literature, direct methods for determining thermodynamic properties include calorimetric (condensation and vaporization), manometric and isentropic (static method), ebulliometric (dynamic method), and Knudsen cells (effusion method), as listed in Table 5.1.

Among the indirect methods, gas chromatography and thermogravimetry determinations can be mentioned (MAJER; SVOBODA; PICK, 1989). Table 5.2 provides values for the enthalpy of vaporization of key compounds identified in *Lippia gracilis* Schum essential oil, obtained using gas chromatography and thermogravimetry.

Table 5.2 Enthalpy of vaporization (ΔH^{vap}) of compounds in *Lippia gracilis* essential oil.

Compound	Thermogravimetry[1]		Gas Chromatography[2]	
	ΔH^{vap} (kJ/mol)	Temperature Range (K)	ΔH^{vap} (kJ/mol)	Temperature (K)
Thymol	56.98	371.48 – 480.55	66.43	298.15
Carvacrol	42.23	378.28 – 479.05	67.12	298.15
3-BHA	49.87	430.55 – 513.38	84.88	298.15
Terpinen-4-ol	35.56	366.65 – 451.82	55.80	298.15
Trans-caryophyllene	39.93	364.36 – 478.62	54.01	298.15

[1] (OLIVEIRA, 2012); [2] (OLIVEIRA, 2017).

The data presented in Table 5.2 were collected over different temperature ranges for each technique, posing challenges for direct comparison of the results. However, gas chromatography and thermogravimetry can be used complementarily. In thermogravimetry, it is possible to assess the thermal stability of a substance, including changes in mass concerning temperature. This is particularly useful for determining phase transition points, such as the melting, sublimation, or decomposition temperature of a substance. On the other hand, in gas chromatography, a complex mixture such as essential oils can be separated into its individual components, enabling their identification. Furthermore, gas chromatography provides qualitative and quantitative data on the components present in the sample, which is crucial for calculating thermodynamic properties such as enthalpy of vaporization. Therefore, by combining these techniques, it is possible to obtain a more comprehensive understanding of the thermodynamic properties of a substance, especially in complex systems or when sample purity cannot be guaranteed.

In this doctoral Thesis, gas chromatography correlation was chosen for obtaining the thermodynamic parameters under investigation. Gas chromatography (GC) separation processes involve equilibrium between two phases. Classical GC analyses entail comparing retention data of an unknown sample with that of a known sample (GROB, 1977).

A chromatographic peak provides crucial information such as residence time or the difference in elution between two peaks, shape, and size. Generally, adjusted retention time or

adjusted retention volume are used in qualitative analyses. Since the retention times of an unknown and known component might be the same, chromatographic separations utilize the Kováts retention index (KAISER, 1977).

$$I_R = 100.z + 100\left[\frac{\ln t_{R,X} - \ln t_{R,z}}{\ln t_{R,z+1} - \ln t_{R,z}}\right] \tag{5.1}$$

where $t_{R,X}$ is the retention time of the compound of interest, z, and z+1 are the n-alkanes that encompass the compound X. Or in terms of retention volume,

$$I_R = 100.z + 100\left[\frac{\ln V_{R,X} - \ln V_{R,z}}{\ln V_{R,z} - \ln V_{R,z+1}}\right] \tag{5.2}$$

Analyzing Eq. (5.2), the retention volume can be related to the ideal gas equation,

$$PV = RT \tag{5.3}$$

The partial pressure of each component can be obtained by applying Raoult's law (SMITH; VAN NESS; ABBOTT, 2007),

$$y_i P = x_i P_i^{sat} \tag{5.4}$$

where x_i is the molar fraction of the liquid phase, y_i is the molar fraction of the vapor phase, and P_i^{sat} is the vapor pressure of pure species i at the working temperature. The left side of Eq. (5.4) , $y_i P$, refers to the partial pressure of species i.

By summing the molar fractions in the vapor phase to 1, $\sum_i y_i = 1$, and substituting Eq. (5.3) into Eq. (5.4) results

$$\frac{RT}{V} = \sum_i x_i P_i^{sat} \tag{5.5}$$

Since few applications have ideal conditions, it is necessary to consider deviations from ideality, γ_i^{∞}, in Eq. (5.5). Solving such equation for V leads to

$$V = \frac{RT}{\gamma_i^{\infty} P_i^{sat}} \tag{5.6}$$

where γ_i^{∞} is the activity coefficient at infinite dilution of species i.

Applying Eq. (5.6) to the relative retention volume (or time) between a reference substance (n-alkane with z carbon atoms) and a substance of interest X, i.e., $V_{R,z}/V_{R,X}$ (HINCKLEY; BIDLEMAN; FOREMAN, 1990)

$$\frac{V_{R,z}}{V_{R,X}} = \frac{RT}{P_z^{sat}\gamma_z^{\infty}} \cdot \frac{P_X^{sat}\gamma_X^{\infty}}{RT} = \frac{P_X^{sat}\gamma_X^{\infty}}{P_z^{sat}\gamma_z^{\infty}} \tag{5.7}$$

Substituting Eq. (5.7) into Eq. (5.1) or Eq. (5.2) and performing the same mathematical treatment for a reference substance with $z + 1$ carbon atoms result in

$$I_R = 100.z + 100\left[\frac{\ln(\gamma_z^{\infty}P_z^{sat}/\gamma_X^{\infty}P_X^{sat})}{\ln(\gamma_z^{\infty}P_z^{sat}/\gamma_{z+1}^{\infty}P_{z+1}^{sat})}\right] \tag{5.8}$$

In the gas chromatography correlation method, it is assumed that $\gamma_X^{\infty} = \gamma_z^{\infty} = \gamma_{z+1}^{\infty}$. Inserting this assumption into Eq. (5.8) and expressing it in terms of P_X^{sat} , results in the equation proposed by Hoskovec et al., 2005.

$$\ln P_X^{sat} = \ln P_z^{sat} + 100\left[\frac{(100.z - I_R)\cdot \ln(P_z^{sat}/P_X^{sat})}{\ln(P_z^{sat}/P_{z+1}^{sat})}\right] \tag{5.9}$$

where the vapor pressure of a substance of interest is related to the Kováts retention index I_R and the vapor pressures of two reference substances. Eq (5.9) serves as the starting point for the calculation of vapor pressure vapor pressure (P_{vap}),enthalpy of vaporization (ΔH^{vap}) and normal boiling temperature (T_{nb}) for a large number of organic compounds (HOSKOVEK et al., 2005).

For the experimental data produced in this doctoral Thesis, the chosen chromatographic column was the HP5-MS (30 m × 0.25 mm i.d. × 0.25 μm). This capillary column is characterized by a low-polarity stationary phase composed of (5%-phenyl)-methylpolysiloxane, which is ideal for efficiently separating compounds such as terpenes and terpenoids, which are generally non-polar or slightly polar. The analyses were conducted under isothermal conditions of the column, ranging from 80°C to 200°C, with an injector temperature of 220°C, a detector at 250°C, and an injection volume of 1.0 μL. The carrier gas (He) flow rate was 1.0 mL min^{-1}. The compounds were dissolved in methanol at a concentration of 20 mg mL^{-1}, and the peaks were identified by calculating their retention indices and using co-injection

of a standard hydrocarbon mixture (C_8 to C_{17}). Another highly relevant aspect of the experimental data is the experimental uncertainties. In the experiments conducted in this study, analyses were performed in triplicate. The accuracy and reliability of the results obtained were assessed by calculating the standard deviation of retention times, as per Equation (5.10).

$$\sigma = \sqrt{\frac{1}{n}\sum_{i=1}^{n}\left(\delta_i - \bar{\delta}\right)^2} \tag{5.10}$$

where σ corresponds to one standard deviation, n is the number of observations in the data set, δ_i is each individual value in the data set, and $\bar{\delta}$ is the mean of values in the dataset.

The standard deviation is a statistical measure that indicates the dispersion of data around the mean of a distribution. It provides an estimate of the variability or spread of values around the mean. A larger standard deviation indicates that the data is more spread out from the mean, while a smaller standard deviation suggests that the data is more clustered around the mean. Thus, the standard deviation is an essential tool for assessing the consistency and reliability of data, allowing researchers to better understand the distribution of values and identify potential patterns or discrepancies in the data.

Tables 5.3 and 5.4 correspond to the triplicates of the experiments conducted and published in the article “Experimental Determination of Thermodynamic Properties of Terpene and Aromatic Ketones by Gas Chromatography.” The analyzed compounds were p-Cymene, Acetophenone, Linalool, Camphor, Menthone, Bicyclo[2,2,2]octan-2,5-dione, Damascenone, 4-(4-Hydroxyphenyl)-2-butanone, and Methyl jasmonate. Table 5.5 presents the average retention time values, and Table 5.6 shows the standard deviation values calculated by Equation (5.10).

Table 5.3 Triplicate Retention Times (Runs 1 to 3) for p-Cymene, Acetophenone, Linalool, Camphor, and Menthone obtained on a 30 m HP5-MS capillary column.

		Retention times (min)				
Compounds		**p-Cymene**	**Acetophenone**	**Linalool**	**Camphor**	**Menthone**
Run 1						
Temperature (K)	353.15	10.523	13.517	16.440	22.347	23.608
	363.15	7.588	9.517	11.013	15.010	15.562
	373.15	5.737	7.018	7.875	10.515	10.833
	383.15	4.580	5.438	5.888	7 753	7.848
	393.15	3.815	4.392	4.642	5.960	6.007
	403.15	3.267	3.670	3.815	4.765	4.772
	413.15	2.898	3.190	3.272	3.938	3.927
	423.15	2.627	2.838	2.867	3.392	3.370
	433.15	2.425	2.595	2.602	2.987	2.967
	443.15	2.272	2.397	2.403	2.702	2.667
	453.15	2.148	2.252	2.245	2.485	2.458
	463.15	2.060	2.138	2.117	2.313	2.288
	473.15	1.997	2.058	2.040	2.195	2.180
Run 2						
Temperature (K)	353.15	10.523	13.517	16.343	22.363	23.608
	363.15	7.592	9.475	11.013	15.027	15.563
	373.15	5.742	7.020	7.878	10.545	10.838
	383.15	4.578	5.415	5.892	7.753	7.850
	393.15	3.818	4.392	4.643	5.960	5.982
	403.15	3.268	3.683	3.815	4.765	4.748
	413.15	2.898	3.180	3.277	3.960	3.940
	423.15	2.625	2.843	2.865	3.375	3.370
	433.15	2.425	2.575	2.598	2.988	2.953
	443.15	2.277	2.398	2.402	2.690	2.667
	453.15	2.148	2.250	2.238	2.483	2.460
	463.15	2.062	2.137	2.125	2.315	2.285
	473.15	1.980	2.052	2.047	2.193	2.170
Run 3						
Temperature (K)	353.15	10.523	13.512	16.433	22.343	23.607
	363.15	7.552	9.468	11.008	15.027	15.563
	373.15	5.743	7.022	7.880	10.543	10.855
	383.15	4.578	5.417	5.890	7.752	7.885
	393.15	3.812	4.393	4.642	5.963	6.012
	403.15	3.267	3.683	3.815	4.743	4.770
	413.15	2.900	3.182	3.255	3.938	3.947
	423.15	2.623	2.825	2.870	3.392	3.373
	433.15	2.427	2.593	2.600	2.997	2.968
	443.15	2.277	2.393	2.403	2.698	2.668
	453.15	2.147	2.243	2.247	2.480	2.458
	463.15	2.060	2.128	2.127	2.313	2.282
	473.15	2.000	2.053	2.035	2.198	2.180

Table 5.4 Triplicate Retention Times (Runs 1 to 3) for Bicyclo[2,2,2]octan-2,5-dione, Damascenone, 4-(4-Hydroxyphenyl)-2-butanone, and Methyl jasmonate obtained on a 30 m HP5-MS capillary column.

		Retention times (min)			
Compounds		Bicyclo[2,2,2]*	Damascenone	4-(4-Hydroxy)**	Methyl jasmonate
Run 1					
Temperature (K)	353.15	53.270	-	-	-
	363.15	32.617	-	-	-
	373.15	21.147	37.197	-	-
	383.15	14.273	23.785	-	-
	393.15	10.140	15.898	-	-
	403.15	7.488	11.137	24.952	38.960
	413.15	5.782	8.117	16.605	24.962
	423.15	4.650	6.178	11.467	16.798
	433.15	3.870	4.893	8.360	11.673
	443.15	3.335	4.032	6.355	8.520
	453.15	2.940	3.428	5.008	6.450
	463.15	2.642	2.993	4.097	5.060
	473.15	2.442	2.687	3.465	4.152
Run 2					
Temperature (K)	353.15	53.230	-	-	-
	363.15	32.590	-	-	-
	373.15	21.082	37.193	-	-
	383.15	14.258	23.890	-	-
	393.15	10.130	15.907	-	-
	403.15	7.490	11.138	24.833	38.982
	413.15	5.782	8.088	16.588	24.935
	423.15	4.628	6.153	11.517	16.783
	433.15	3.870	4.873	8.360	11.717
	443.15	3.335	4.015	6.352	8.523
	453.15	2.940	3.430	5.008	6.447
	463.15	2.652	2.985	4.082	5.058
	473.15	2.443	2.692	3.477	4.152
Run 3					
Temperature (K)	353.15	53.315	-	-	-
	363.15	32.587	-	-	-
	373.15	21.163	37.397	-	-
	383.15	14.262	23.770	-	-
	393.15	10.137	15.960	-	-
	403.15	7.493	11.090	24.978	38.960
	413.15	5.782	8.117	16.572	25.037
	423.15	4.628	6.177	11.548	16.770
	433.15	3.872	4.875	8.335	11.702
	443.15	3.337	4.017	6.353	8.523
	453.15	2.940	3.423	5.017	6.450
	463.15	2.652	2.993	4.097	5.058
	473.15	2.448	2.690	3.478	4.145

*Bicyclo[2,2,2]octan-2,5-dione; **4-(4-Hydroxyphenyl)-2-butanone.

Table 5.5 Retention times: average values.

	Average retention times (min)				
Compounds	**p-Cymene**	**Acetophenone**	**Linalool**	**Camphor**	**Menthone**
Temperature (K) 353.15	10.523	13.515	16.439	22.351	23.608
363.15	7.577	9.487	11.011	15.021	15.563
373.15	5.741	7.020	7.878	10.534	10.837
383.15	4.579	5.423	5.890	7.753	7.851
393.15	3.815	4.392	4.642	5.961	6.000
403.15	3.267	3.679	3.815	4.758	4.763
413.15	2.899	3.184	3.268	3.945	3.938
423.15	2.625	2.835	2.867	3.386	3.371
433.15	2.426	2.588	2.600	2.991	2.963
443.15	2.275	2.396	2.403	2.697	2.667
453.15	2.148	2.248	2.243	2.483	2.459
463.15	2.061	2.134	2.123	2.314	2.285
473.15	1.992	2.054	2.041	2.195	2.177

	Average retention times (min)			
Compounds	**Bicyclo[2,2,2]***	**Damascenone**	**4-(4-Hydroxy)****	**Methyl jasmonate**
Temperature (K) 353.15	53.272	-	-	-
363.15	32.598	-	-	-
373.15	21.131	37.262	-	-
383.15	14.264	23.815	-	-
393.15	10.136	15.922	-	-
403.15	7.490	11.122	24.921	38.967
413.15	5.782	8.107	16.588	24.978
423.15	4.635	6.169	11.511	16.784
433.15	3.871	4.880	8.352	11.697
443.15	3.336	4.021	6.353	8.522
453.15	2.940	3.427	5.011	6.449
463.15	2.649	2.990	4.092	5.059
473.15	2.444	2.690	3.473	4.150

*Bicyclo[2,2,2]octan-2,5-dione; **4-(4-Hydroxyphenyl)-2-butanone.

Table 5.6 Standard deviations calculated by Eq. (5.10).

	Standard deviation of retention times				
Compounds	**p-Cymene**	**Acetophenone**	**Linalool**	**Camphor**	**Menthone**
Temperature (K) 353.15	0.000	0.003	0.005	0.011	0.001
363.15	0.022	0.027	0.003	0.010	0.001
373.15	0.003	0.002	0.003	0.017	0.004
383.15	0.001	0.013	0.002	0.001	0.004
393.15	0.003	0.001	0.001	0.002	0.016
403.15	0.001	0.008	0.000	0.013	0.013
413.15	0.001	0.005	0.012	0.013	0.010
423.15	0.002	0.009	0.003	0.010	0.002
433.15	0.001	0.011	0.002	0.006	0.008
443.15	0.003	0.003	0.001	0.006	0.001
453.15	0.001	0.005	0.005	0.003	0.001
463.15	0.001	0.006	0.005	0.001	0.003
473.15	0.011	0.003	0.006	0.003	0.006
Compounds	**Bicyclo[2,2,2]***	**Damascenone**	**4-(4-Hydroxy)****	**Methyl jasmonate**	
Temperature (K) 353.15	0.043	-	-	-	
363.15	0.017	-	-	-	
373.15	0.043	0.117	-	-	
383.15	0.008	0.065	-	-	
393.15	0.005	0.034	-	-	
403.15	0.003	0.027	0.077	0.013	
413.15	0.000	0.017	0.017	0.053	
423.15	0.013	0.014	0.041	0.014	
433.15	0.001	0.011	0.014	0.022	
443.15	0.001	0.009	0.002	0.002	
453.15	0.000	0.004	0.005	0.002	
463.15	0.006	0.005	0.009	0.001	
473.15	0.003	0.003	0.007	0.004	

*Bicyclo[2,2,2]octan-2,5-dione; **4-(4-Hydroxyphenyl)-2-butanone.

Upon examining the data presented in Table 5.6, it is observed that, overall, the analyzed compounds exhibit low standard deviations at different temperatures, indicating good stability in retention times throughout the experiment. However, Damascenone shows greater variability in standard deviations, especially in the lower temperature range of the experiment, suggesting that the optimal temperatures for analysis would be from 403.15 K onwards.

The Kovats retention indices were calculated using the average retention time values, and the other thermodynamic properties studied were derived from these indices. The quality of the fits and the robustness of the obtained results were evaluated based on correlation coefficients.

CHAPTER VI

Published Article

FONSECA, LUCIANA A.A.P.; CREMASCO, MARCO A. **Group contribution methods to predict enthalpy of vaporization of aromatic and terpene ketones at 298.15 K**. Fluid Phase Equilibria JCR, v. 538, p. 113009, 2021.

This chapter, which builds upon the preceding article, demonstrates the continued effort to produce reliable experimental data to corroborate the technique of obtaining thermodynamic parameters of oxygenated terpenes by gas chromatography correlation. In this article, the consolidation of the theory that a consistent database and knowledge of molecular structures, correctly providing a fragmentation scheme between groups, are essential for developing more accurate group contribution models is presented.

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Group contribution methods to predict enthalpy of vaporization of aromatic and terpene ketones at 298.15 K

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ABSTRACT

The physical properties of pure compounds are fundamental to chemical, biochemical, and environmental industries. One of these properties is the enthalpy of vaporization (Δ_{vap}H). Although the experimental values of this property in literature are quite limited, and measurements to derive it are expensive and time-consuming. For this reason, group contribution methods are essential tools. The present work aimed to compare two classes of group contribution methods to predict enthalpies of vaporization of terpene and aromatic ketones, calculated at a constant temperature from Kolská et al. (2005) and Oliveira (2017) methods, and as a function of reduced temperature from Benkouider et al. (2014) method. Both classes of methods configure an alternative to experimental determination. In addition, the performance Oliveiraś (2017) method is verified against a specific class of oxygenated compounds: terpene and aromatic ketones. The experimental Δ_{vap}H at 298.15 K of (−)-Menthone and 4-Methyl-3-penten-2-one was performed by gas chromatography (GC) technique and compared with values estimated by the selected group contribution methods.

1. Introduction

Essential oils (Eos) are a complex mixture of compounds from different organic classes. Its great structural diversity is a potential source of bioactive molecules [1,2]. Among the oxygenated compounds present are terpene and aromatic ketones attributed to antioxidant, anti-inflammatory, anti-microbial, anti-tumor, gastroprotective, and neuroprotective activities [3].

The herbal medicine promising applications increase the interest in the study of essential oil compounds for configuring an effective and culturally appropriate option [4]. The industrial application of these compounds requires important thermodynamic properties, such as the enthalpy of vaporization (Δ_{vap}H) [5]. Among the techniques available for experimental determination of thermodynamic properties such as enthalpy of vaporization, the gas chromatographic (GC) method offers great advantages of simplicity, speed, purity, small sample size and reproducibility [6]. However, it is not always possible to measure or find reliable experimental values of enthalpy of vaporization in the literature. For this reason, the group contribution estimation method is used, and it needs mainly tabulated groups (molecular fragments). It is assumed that the property value is a function of all groups. The property value of any group has the same contribution in all molecules. A group contribution method advantage is its simplicity and applicability to many compounds [7].

In general, group contribution methods can be classified into two classes based on the prediction, at constant temperatures, or as a function of temperature. The first class includes methods for estimating enthalpies of vaporization at a constant temperature (e.g., T= 298.15 K) in which only molecular structure can be used as an input parameter [7–9]. The second-class concerns methods for estimating enthalpies of vaporization as a function of reduced temperature where the critical temperature is used as an input parameter and provides enthalpy of vaporization at different temperatures [10–12].

This work aims to compare both classes of group contribution methods to predict enthalpy of vaporization of terpene and aromatic ketones, at constant temperature and as a function of reduced temperature. The selected methods apply to a wide variety of organic compounds. The most significant advantage is the efficient prediction of the thermodynamic properties of compounds whose data are not available in the literature. Also, the performance of Oliveira's method [13], applicable to oxygenated compounds, especially alcohols, is verified against a specific class of compounds: terpene and aromatic ketones. Experimental Δ_{vap}H of (−)-Menthone and 4-Methyl-3-penten-2-one at 298.15 K were determined by the gas chromatography (GC) technique and compared with values estimated by the selected group contribution methods.

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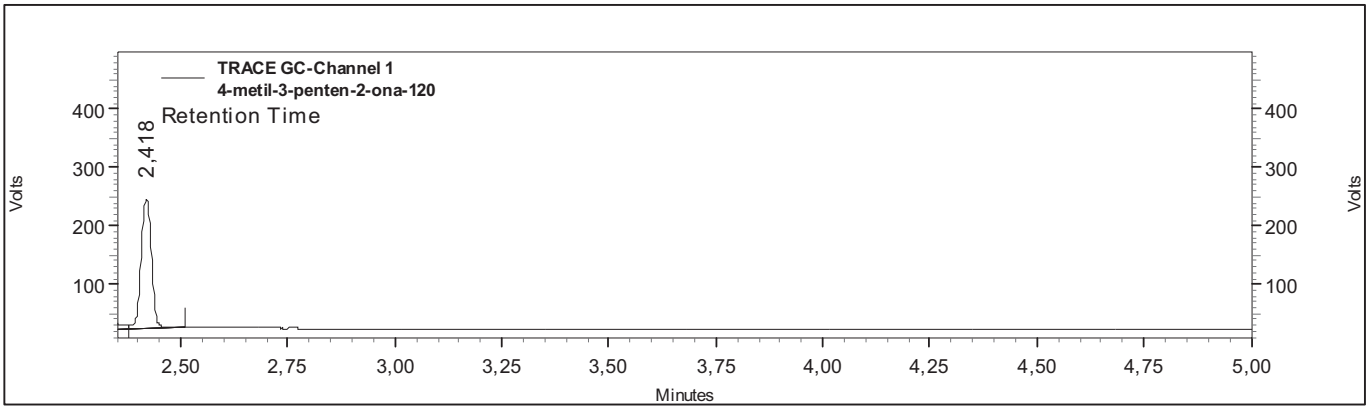


Fig. 1. GC Chromatogram of 4-Methyl-3-penten-2-one at 403.15 K.

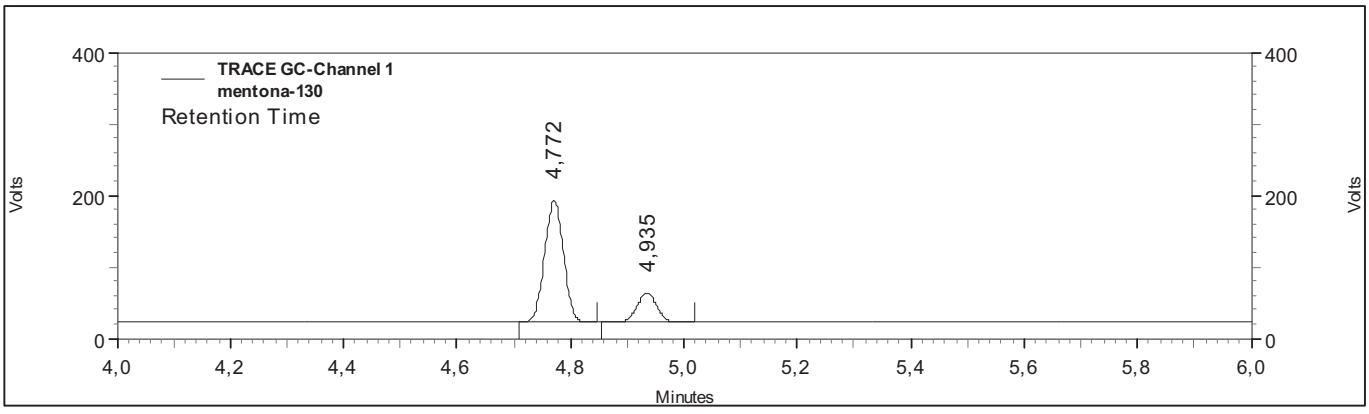


Fig. 2. GC Chromatogram of (−)-Menthone at 403.15 K (expanded from 4 to 6 minutes).

2. Experimental

2.1. Chemicals

All chemicals were purchased from Sigma Aldrich (Holzminden, Germany): (−)-Menthone and 4-Methyl-3-penten-2-one. The descriptions of the samples used in this work are given in Table 1. The purity of the compounds analyzed by gas chromatography was sufficient to determine their retention times. In this regard, the chromatograms obtained are clear enough to obtain retention times as can be seen in Figs. 1 and 2.

2.2. Gas chromatography

The examined compounds retention times were determined using a Thermo Scientific (Trace GC Ultra) gas chromatography/flame ionization detector equipped with an HP5-MS, capillary column (30 m x 0.25 mm i.d. x 0.25 μm film thickness) under isothermal conditions of column (80 °C to 200 °C), injector temperature of 220°C, a detector at 250°C and injection volume of 1.0 μL. The carrier gas (He) flow rate was 1.0 mL.min^{-1}. The compounds were dissolved in methanol at a concentration of 20 mg.mL^{-1} and the peaks were identified by calculating their retention index and using co-injection of a standard hydrocarbon mixture (C_8 to C_{12}). The analyte solutions and the standard mixture of *n*-alkanes were injected under the same chromatography conditions. The analyzes were performed in triplicate. Table 2 provides the Kováts retention indices (I_X) for (−)-Menthone and 4-Methyl-3-penten-2-one at 13 temperatures.

Table 1
Sample descriptions.

Chemical name	CAS RN	M ($g.mol^{-1}$)	Source	Purity
4-Methyl-3-penten-2-one	141-79-7	98.14	Sigma	≥ 99.0 %
(−)-Menthone	14073-97-3	154.25	Sigma	90.0 %

2.3. Kováts retention indices

Isothermal Kováts retention indices (I_X) are defined as:

$$I_X = 100z + 100\left(\frac{lnt_{R,X} - lnt_{R,z}}{lnt_{R,z+1} - lnt_{R,z}}\right) = 100z + 100\frac{ln\left(\gamma_z^{\infty}P_z/\gamma_X^{\infty}P_X\right)}{ln\left(\gamma_z^{\infty}P_z/\gamma_{z+1}^{\infty}P_{z+1}\right)} \quad (1)$$

In Eq. (1) $t_{R,X}$, P_X, and γ_X^{∞} represent the retention time, vapor pressure and infinite dilution activity coefficient, respectively, of a solute X in the stationary phase, and subscripts z and z + 1 identifies the reference n-alkanes with z and z + 1 carbon atoms whose retention times encompass that of solute X.

2.4. Thermodynamic properties

With the requisite collection of the Kováts retention index assembled by Eq. (1), the vapor pressures were determined from Eq. (2).

$$\ln P_x = \ln P_z + \frac{(100z - I_X)\ln\left(P_z/P_{z+1}\right)}{100} \quad (2)$$

The Antoine Equation Eq. (3) parameters A, B, C, were determined using non-linear regression techniques and are presented

Table 2
Kováts retention index of (−)-Menthone and 4-Methyl-3-penten-2-one.

	Kováts Retention Indices												
	Temperature (K)												
Compound	353.15	363.15	373.15	383.15	393.15	403.15	413.15	423.15	433.15	443.15	453.15	463.15	473.15
4-Methyl-3-penten-2-one	801.19	801.31	802.44	803.45	801.62	804.76	802.34	803.66	804.80	809.32	805.56	803.21	830.95
(−)-Menthone	1147.45	1151.76	1155.52	1160.64	1166.21	1173.14	1177.17	1182.23	1190.24	1193.72	1202.27	1207.69	1231.07

Table 3
Vapor pressure: antoine equation parameters.

Compound	A	B	C	$r^{2(a)}$
4-Methyl-3-penten-2-one	20.97 ± 0.06	3209.04 ± 42.33	-59.10 ± 2.28	0.99999
(−)-Menthone	18.86 ± 0.41	2802.60 ± 240.58	116.00 ± 12.33	0.99972

[a] correlation coefficients (r^2, %).

Table 4
Parameters of Eq. (4).

Compound	b_0	b_1	b_2	$r^{2(a)}$
4-Methyl-3-penten-2-one	227.45 ± 1.92	-48981.06 ± 593.42	-30.48 ± 1.45	0.99999
(−)-Menthone	310.55 ± 15.97	-83469.09 ± 494.62	-92.43 ± 12.12	0.99977

[a] correlation coefficients (r^2, %).

Table 5
T_{nb} and $\Delta_{vap}H$: Properties calculated at 298.15 K and 101.325 kPa.

Compound	$T_{nb}^{lit(a)}$K	$T_{nb}^{exp(b)}$K	$D^{(c)}$(K)	$\Delta_{vap}H^{lit(a)}$kJ mol^{-1}	Method[d]	$\Delta_{vap}H^{exp(b)}$kJ mol^{-1}	$D^{(c)}$kJ mol^{-1}
4-Methyl-3-penten-2-one	403.10 ± 0.1[e]	398.88 ± 0.03	4.22	-	GC	39.89 ± 0.15	-
(−)-Menthone	480.15[f]	499.69 ± 0.52	19.54	55.53 ± 0.22[g]	GC	55.91 ± 0.33	0.37

[a] T_{nb}^{lit} and $\Delta_{vap}H^{lit}$: literature normal boiling temperature and enthalpy of vaporization at 298.15 K.
[b] T_{nb}^{exp} and $\Delta_{vap}H^{exp}$: this work experimental normal boiling temperature and enthalpy of vaporization at 298.15 K.
[c] D: the absolute difference between the literature data and experimentally measured value.
[d] Gas Chromatography (GC).
[e] [15].
[f] [16].
[g] [17].

in Table 3.

$$\ln(P_{vap}/Pa) = A - \frac{B}{T(K)+C} \quad (3)$$

For processing the (P_{vap}) versus T data, the Kirchhoff–Rankin-type Eq. (4) was used [6].

$$\ln(P_{vap}/Pa) = \frac{1}{R}b_0 + \frac{1}{RT}b_1 + \frac{1}{R}b_2 ln(T/T_0) \quad (4)$$

Parameters of Eq. (4) are presented in Table 4.

In Eq. (4), T_0 is arbitrary equaled to 298.15 K and R = 8.3145 J. $K^{-1}mol^{-1}$. The enthalpy of vaporization at temperature T may be calculated from Eq. (5).

$$\Delta_{vap}H = -b_1 + b_2 T \quad (5)$$

Eqs. (4) and (5) were thus implemented to predict $\Delta_{vap}H$ values at 298.15 K for (−)-Menthone and 4-Methyl-3-penten-2-one as shown in Table 5. Additionally, since it is known that the normal boiling temperature T_{nb} of a substance in the liquid phase is one whose vapor pressure equals atmospheric pressure (atm), it is possible to define P in Eq. (4) as 1 atm to obtain the T_{nb} data.

3. Theory

Terpene and aromatic ketones with application in herbal medicine and natural defensives, whose enthalpy of vaporization are available in the literature [6, 14, 15], were selected to give consistency to the results. Enthalpies of vaporization were predicted at a constant temperature from Oliveira [13] and Kolská et al. [7] methods and as a function of reduced temperature from Benkouider et al. [10] method. In all methods used, the reference temperature was 298.15 K.

3.1. Group contribution methods

The three group contribution methods addressed in this work are applied to predict the enthalpy of vaporization from molecules of different organic classes. The Benkouider et al. [10] method allows calculating the enthalpy of vaporization as a function of temperature, can provide enthalpy of vaporization at different temperatures, including the reference temperature used in this work, 298.15 K. Kolská et al. [7] and Oliveira [13] methods provide the enthalpy of vaporization at a constant temperature, 298.15 K. These three methods present different group fragmentation schemes and interaction between groups.

Kolská et al. (2005)

In this method [7], the estimation of the properties is done in three procedures, which covers the levels of first order, second order and third order. Basically, the first-order groups allow the description of a wide variety of organic compounds and should describe the entire molecule without any fragment being represented. Still, a fragment cannot be part of other fragments. In molecules containing aromatic rings, the aromatic carbon (aC) must have preference in the choice of first order groups, as shown in Fig. 3.

$$\Delta_{vap}H = 9.67 + \sum_i N_i C_i + \sum_j M_j D_j + \sum_j O_k E_k \quad (6)$$

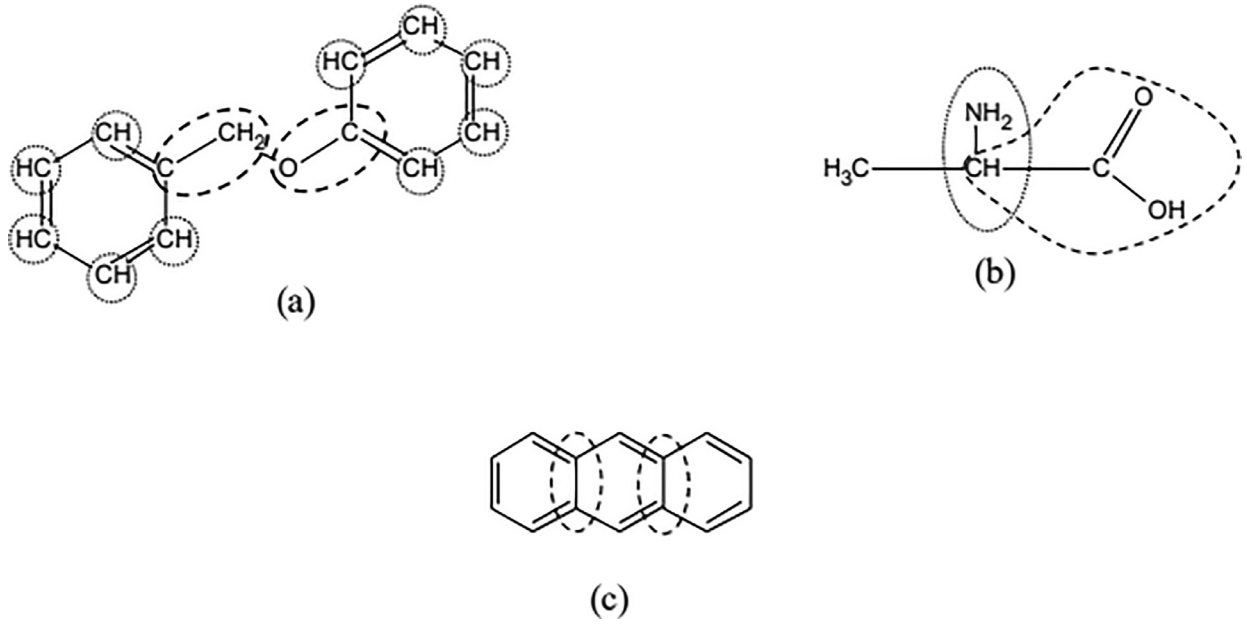
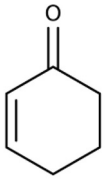


Fig. 3. Correct description of the Kolská et al. (2005) method for: (a) first-order groups; (b) second-order groups; (c) third-order groups.

Table 6
Enthalpy of vaporization ($\Delta_{vap}H^{pred}$) of 2-cyclohexenone predicted at constant temperature (298.15 K). Experimental data [14]: $\Delta_{vap}H^{exp}$ (298.15 K) = 49.5 kJ/mol.

Compound	Kolská et al. [7]		Oliveira [13]	
	Group contribution		Group Contribution	
	h_0	9.672	h_0	19.548
	$CH_{2\,(cyclic)}$	4.013	$CH_{2\,(ring)}$	2.792
	$CH=CH_{(cyclic)}$	9.179	$=CH-_{(ring)}$	3.048
	$>C=O$	14.837	$>C=O_{(ring)}$	10.589
	$\Delta_{vap}H^{pred}$ (kJ.mol^{-1}) 45.72		$\Delta_{vap}H^{pred}$ (kJ.mol^{-1}) 44.61	
2-cyclohexenone				
	$\Delta_{vap}H^{exp}$(kJ.mol^{-1})[(a)] 49.5		$\Delta_{vap}H^{exp}$(kJ.mol^{-1})[(a)] 49.5	
	RD(%)	7.64	RD(%)	9.88

[(a)] [14].

In Eq. (6) N_i, M_j, O_k are the occurrence of first, second and third order groups that appear in the structure of the molecule and, C_i, D_j, E_k represent their corresponding contributions to the enthalpy of vaporization. The data are obtained for the reference temperature of 298.15 K. The application of this method is presented in Table 6.

The relative deviation (RD) for each method is defined in Eq. (7):

$$RD\ (\%) = 100.abs\left[\left(\Delta_{vap}H^{exp} - \Delta_{vap}H^{pred}\right)/\Delta_{vap}H^{exp}\right] \quad (7)$$

In Eq. (7), $\Delta_{vap}H^{exp}$ and $\Delta_{vap}H^{pred}$ are experimental and predicted enthalpies of vaporization, respectively.

Oliveira (2017)

This new group contribution method [13] developed to estimate the enthalpy of vaporization of pure organic compounds at 298.15 K presents a new fragmentation scheme. The group contribution parameters developed from an experimental database of more than 3596 enthalpies of vaporization values.

Fragmentation was based on only one estimation level, distinguishing groups in open-chain, cyclic, aromatic, and bicyclic compounds. They were assigned to different information groups present on rings (aromatic or cyclic) or linked to aromatic or cyclic carbons. This method [12] presents group contribution to compounds with cis-trans isomerism and contribution to bicyclic compounds. It is necessary to highlight that the proposed method is specific to substances present in essential oils and only includes compounds containing oxygen in their structure.

$$\Delta_{vap}H = 15.30 + \sum_i N_i h_{v,i} \quad (8)$$

In Eq. (8), N_i is the occurrence of each group in the structure and, $h_{v,i}$ is the enthalpy of vaporization contribution from each group. The application of this method is presented in Table 6.

Benkouider et al. (2014)

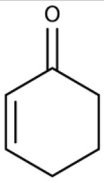
This method [10] presents group contribution as a function of reduced temperature and describes a wide variety of organic compounds with a distinction between isomers. A new fragmentation scheme into four types of groups is presented: first-order groups, second-order groups, ring corrections and group interactions.

$$\Delta_{vap}H(T) = \left(A - AT_r + AT_r^2\right) + [c_1(1-T_r)]^B \quad (9)$$

In Eq. (9), c_1 is an adjustable parameter ($c_1 = 3.261 \times 10^{-3}$). A and B are obtained by summing group contributions: $A = \sum N_i a_i$ and, $B = \sum N_i b_i$; N_i is the number of groups of type i; a_i and b_i are the group contributions of i group and, T_r is the reduced temperature. The application of this method is presented in Table 7.

Benkouider et al. [10] method provides enthalpy of vaporization at different temperatures. However, it needs a critical temperature.

Table 7
Enthalpy of vaporization ($\Delta_{vap}H^{pred}$) of 2-cyclohexenone predicted as function of reduced temperature based on absolute temperature of 298.15 K. Experimental data [14]: $\Delta_{vap}H^{exp}$ (298.15 K) = 49.5 kJ/mol, T_c = 685 K.

Compound	Benkouider et al. [10]		
	Group contribution	a_i (kJ.mol^{-1})	b_i
	$CH_{2\,(ring)}$	434.44	0.03
	$=CH-_{(ring)}$	176.08	-0.002
	C = O	737.43	0.024
	Ring Correction	-1164.32	0.34
	$\Delta_{vap}H^{pred}$ (kJ.mol^{-1})	51.64	
	$\Delta_{vap}H^{exp}$ (kJ.mol^{-1})[a]	49.5	
	RD(%)	4.32	
2-cyclohexenone			

[a] [14].

Table 8
Enthalpy of vaporization at 298.15 K to studied compounds: experimental ($\Delta_{vap}H^{exp}$) (This work; [14]) and predicted ($\Delta_{vap}H^{pred}$)by group contribution methods selected.

Ketones		Enthalpy of vaporization, kJ.mol^{-1}							
			Kolská et al. [7]		Benkouider et at. [10]			Oliveira [13]	
Terpene	Formula	$\Delta_{vap}H^{exp}$	$\Delta_{vap}H^{pred}$	RD%	$\Delta_{vap}H^{pred}$	RD%	T_c	$\Delta_{vap}H^{pred}$	RD%
2-Cyclo hexenone	C_6H_8O	49.5[a]	45.72	7.64	51.64	4.32	685[c]	44.61	9.88
4-Methyl-3-penten-2-one	$C_6H_{10}O$	39.89[b]	41.72	4.59	43.72	9.60	605[c]	36.81	7.72
1-Methyl-2-norbornanone	$C_8H_{12}O$	47.61[c]	49.21	3.36	50.87	6.85	699.54[d]	47.46	0.32
Camphor	$C_{10}H_{16}O$	54.7[a]	52.12	4.72	52.23	4.52	742.75[d]	50.16	8.30
Carvone	$C_{10}H_{14}O$	58.4[a]	59.56	1.99	51.86	11.20	742.52[d]	51.59	11.66
Fenchone	$C_{10}H_{16}O$	51.3[a]	51.88	1.13	48.37	5.71	742.75[d]	50.10	2.34
(−)-Menthone	$C_{10}H_{18}O$	55.91[b]	56.26	0.63	49.21	11.98	728.97[d]	50.51	9.66
Pulegone	$C_{10}H_{16}O$	58.0[a]	55.99	3.47	55.99	3.47	747.18[d]	53.01	8.60
Aromatic									
Acetophenone	C_8H_8O	53.4[a]	58.24	9.06	52.24	2.17	684.79[d]	45.97	13.91
2-Methyl-acetophenone	$C_9H_{10}O$	58.9[a]	62.06	5.37	60.31	2.39	710.50[d]	49.25	16.38
MRD%				4.19		6.22			8.88

[a] [14].
[b] This work.
[c] [15].
[d] Critical temperature (Tc) calculated by Joback and Reid [8] method.

In this work, the reference temperature was 298.15 K, and Eq. (10), provided by Joback and Reid method [8], was used to estimate the critical temperature of a compound when not available in the literature. The critical temperatures are presented in Table 8.

$$T_c(K) = T_b + \left[0.584 + 0.965\sum T_{c,i} - \left(\sum T_{c,i}\right)^2\right]^{-1} \quad (10)$$

In Eq. (10), $T_{c,i}$ is the contribution to the critical temperature from each group (i). This equation needs normal boiling point Tb; if no experimental value is available, it can be calculated by Eq. (11) [8].

$$T_b(K) = 198.2 + \sum T_{b,i} \quad (11)$$

In Eq. (11), $T_{b,i}$ is a contribution corresponding to each group (i).

4. Results and discussion

New experimental data for (−)-Menthone and 4-Methyl-3-penten-2-one at 298.15 K were determined by the gas chromatography (GC) technique. The $\Delta_{vap}\,H$ at 298.15 K of (−)-Menthone was in excellent agreement with the literature [17]. No literature values were found for comparison with results for $\Delta_{vap}\,H$ at 298.15 K of 4-Methyl-3-penten-2-one. A comparison of normal boiling temperatures (T_{nb}) calculated from Eq. (5) (using an iteration procedure in the standard Excel program) with the literature results in deviations of 19.54 K and 4.22 K to (−)-Menthone and 4-Methyl-3-penten-2-one, respectively. It is not known whether this large error in predicting T_{nb} (−)-Menthone is due to a deficiency of the method or due to the inaccuracy of the reported T_{nb} values. Despite this, the T_{nb} of 4-Methyl-3-penten-2-one presented a good agreement with the literature. The results are presented in Table 5.

In the current research, experimental data for enthalpy of vaporization from the literature were compared with data provided from methods to predict enthalpy of vaporization at constant temperature (298.15 K) from Kolská et al. [7] and Oliveira [13] methods, and as a function of reduced temperature based on an absolute temperature of 298.15 K from Benkouider et al. [10] method. The performance of the studied methods was examined and discussed.

In Table 8, the experimental enthalpy of vaporization ($\Delta_{vap}H^{exp}$) of terpene and aromatic ketones studied, obtained in this work and from literature, were compared with predicted values ($\Delta_{vap}H^{pred}$) by the group contribution methods selected. The critical temperature (T_c) applied in the Benkouider et al. [10] method was also shown. As observed, Kolská et al. [7] and Benkouider et al. [10] methods presented better performance. Both models have a complete fragmentation scheme with more than a level of contribution, corrections, and interaction between groups.

The mean relative deviation (MRD) for each method is defined in Equation (12):

$$\text{MRD}\ (\%) = \frac{100}{n}.\text{abs}\left[\left(\Delta_{vap}H^{exp,i} - \Delta_{vap}H^{pred,i}\right)/\Delta_{vap}H^{exp,i}\right] \quad (12)$$

where, n is the number of compounds, and i represents each compound.

Kolská et al. [7] method presented the best performance in the prediction of ketones studied, with mean relative deviation of 4.19%. This method describes a wide variety of organic and inorganic compounds being a general model and presents molecular descriptors for interaction between groups.

Oliveira's (2017) [13] contemplates only oxygenated compounds and presents group contribution to bicyclic nature compounds. In this method, the most significant deviations were for aromatic structures (acetophenone and 2-methyl-acetophenone, 13.91%, and 16.38%), and the smallest deviation was found to a bicyclic compound, 1-methyl-2-norbornanone (0.32%). In this model, there is no correction for the interactions between carbons in aromatic structures.

Benkouider et al. [10] represents a class of methods that consider the reduced temperature dependence to predict the enthalpy of vaporization. The mean relative deviation for terpene and aromatic ketones studied was 6.22%. The enthalpy of vaporization has temperature dependence, decreases with increasing temperature, and becomes more pronounced near the critical point with highly nonlinear behavior. In a detailed study, Yu and Chen [18] reinforce the strong temperature dependence of the enthalpy of vaporization and emphasize the importance of this approach in phase transition studies and calculations. In this work, a prediction method [8] was used besides Benkouider et al. [10] to determine the critical temperature when these data were not available in the literature.

5. Conclusions

In this paper, the enthalpy of vaporization ($\Delta_{vap}H$) at 298.15 K and the normal boiling temperature (T_{nb}) of (−)-Menthone and 4-Methyl-3-penten-2-one were determined by gas chromatography technique using n-alkanes as standards with good results. There are concerns about using the Kováts retention indices of alkanes to evaluate thermodynamic properties of functional groups, as ketones. This work contributes to this regard, revealing that the technique can be extended to functional groups, in addition to hydrocarbons. Others have had varying degrees of success. To ensure activity coefficients tend to cancel, its commonly uses standards that contain the same functionality as targets.

A comparison between group contribution methods to predict enthalpy of vaporization, at a constant temperature, and as a function of reduced temperature, was performed. Both classes of methods configure an alternative to experimental determination.

A reliable database and the fragmentation scheme between groups are essential for an accurate group contribution method. Kolská et al. [7] predict enthalpy of vaporization at 298.15 K, and Benkouider et al. [10] method calculate this property at 298.15 K using the reduced temperature. These two methods present the best performances. Both models have a complete fragmentation scheme with more than a level of contribution, corrections, and interaction between groups.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Complementary discussion

Experimental techniques have a significant advantage as they can yield more accurate and precise results. However, they require analytical time, high-purity inputs, good experimental practice, and theoretical knowledge. Thus, another means of obtaining these properties emerges: predictive models. The use of group contribution methods to predict thermodynamic properties represents a fundamental advancement in chemical research and industrial applications. Despite their potential, these methods are not without challenges and limitations.

A notable aspect when comparing different prediction methods is the temperature dependence in accurately estimating enthalpy of vaporization. While traditional methods, like Joback and Reid (1987), rely solely on additive contributions and neglect temperature effects, more recent approaches, such as Benkouider et al. (2014), explicitly consider temperature dependence. This raises important questions regarding the applicability of traditional methods in accurately predicting physical properties under variable temperature conditions, especially for compounds exhibiting complex behavior near their critical points.

The specificity of prediction methods for certain chemical classes, like oxygenated terpenes, as discussed in Fonseca, Oliveira, and Cremasco (2023), underscores the importance of addressing diverse chemical groups and molecular structures. A method that performs well for a particular class of compounds may not effectively generalize to others, highlighting the challenge of developing universal predictive models. As chemical research continues to explore new applications, there is a growing demand for predictive methods that can accommodate this diversity while ensuring accuracy and reliability.

Discrepancies observed between values predicted by group contribution models and experimental values raise concerns about the quality and consistency of data available in the literature. Inaccuracies in reported normal boiling temperatures and deviations in predicted enthalpies of vaporization indicate potential sources of error in experimental measurements or inconsistencies in data presentation. This highlights the importance of robust validation procedures and the establishment of high-quality databases to ensure the integrity of predictive models and the reliability of research results.

Furthermore, this discussion prompts reflection on the broader implications of accurately predicting properties across various industries and research areas. Reliable predictions of physical properties, such as enthalpy of vaporization, are crucial for optimizing processes and extraction techniques.

While group contribution methods offer valuable tools for predicting physical properties, including enthalpy of vaporization, their effectiveness depends on factors such as temperature, chemical specificity, and data quality. Predictive models provide estimates that enable the application of organic compounds, thus requiring rigorous validation and continuous refinement.

Chapter VII

Published Article

FONSECA, LUCIANA APARECIDA ANDRADE PREVIATO; CREMASCO, MARCO AURÉLIO. **Contribution to Theoretical Study of Vaporization Entropy**. Journal of Engineering Research, v. 2, p. 2-5, 2022.

This chapter delves into the complex relationship between the molecular structure of terpenes and terpenoids and the calculation of vaporization entropy. By elucidating how molecular characteristics influence thermodynamic properties, this study deepens understanding of the fundamental principles governing terpene behavior. This molecular perspective is instrumental in enhancing the accuracy of predictive models.

Journal of
Engineering
Research

CONTRIBUTION TO THEORETICAL STUDY OF VAPORIZATION ENTROPY

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Marco Aurélio Cremasco
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Abstract: There are many techniques to obtain experimental thermodynamic data, including the gas chromatography method. However, to apply this approach it is necessary to consider the molecular structure to improve their thermodynamic parameters predictions. This study aims to present a non-chromatographic parameter, the vaporization entropy calculation of some terpene compounds. The vaporization entropy values are influenced by hydrogen bonding and molecular conformation.

Keywords: Terpene, vaporization entropy, thermodynamic properties, molecular structure.

INTRODUCTION

Reliable thermodynamic experimental data play a key role in the design and chemical processes and product optimization. The most used methods for measuring thermodynamic properties such as vapor pressure, vaporization enthalpy, and normal boiling point are effusion, gas saturation, calorimetric methods, and gas chromatography (Kim et al., 1984; Majer et al., 1989; Delle Site, 1997). The gas chromatography (GC) technique that uses alkanes as standards can be a good approach to obtain thermodynamic properties experimentally (Hoskoveck et al., 2005; Fonseca et al., 2020). In this method, the properties are obtained by CG correlation through the isothermal Kováts' retention indices (I_x), defined as

$$I_X = 100z + 100\left(\frac{\ln t_{R,X} - \ln t_{R,z}}{\ln t_{R,z+1} - \ln t_{R,z}}\right) \quad (1)$$

where $t_{R,X}$ represents the retention time of solute X in the stationary phase; subscripts *z* and z+1 identify the reference n-alkanes with *z* and z+1 carbon atoms whose retention times encompass that of solute X. Equation 1 can be rewritten as a function of vapor pressure (P_X) as well as infinite dilution activity coefficient (γ_x^{∞}) of solute X, according to

$$I_X = 100z + 100\frac{\ln(\gamma_z^{\infty} P_z/\gamma_X^{\infty} P_X)}{\ln(\gamma_z^{\infty} P_z/\gamma_{z+1}^{\infty} P_{z+1})} \quad (2)$$

Expressing P_x from Equation 2, considering $\gamma_x = \gamma_z^{\infty} = \gamma^{\infty}_{z+1}$, it is possible to write

$$\ln P_X = \ln P_z + \frac{(100z - I_X)\ln(P_z/P_{z+1})}{100} \quad (3)$$

Equation 3 allows the calculation of the vapor pressures at 298.15 K from accurate values of the Kováts' indices of the solute and vapor pressures of n-alkane references, once are known at this temperature (Fischer et al., 1992; Fischer and Ballschmiter, 1998). However, Hoskovec et al. (2005) demonstrated that Equation 2 was not adequate to obtain vapor pressure data at 298.15 K for many of the studied compounds, and these authors proposed a readjustment to improve the estimates based on the molecular structure. The difference in the activity coefficients logarithms of two substances (i,j) was approximated by the corresponding difference in ideal gas solubility, X^g, derived from the van't Hoff equation considering

$$\ln\gamma_i^{\infty} - \ln\gamma_j^{\infty} \approx \ln X_i^{\infty} - \ln X_i^{\infty} \cong \frac{\Delta S_{vap}^{b,i}(T_{nb}^i - T)}{RT} - \frac{\Delta S_{vap}^{b,j}(T_{nb}^j - T)}{RT} \quad (4)$$

In Equation 4, R is the universal gas constant; T is the absolute temperature and ΔS^b_{vap} is the vaporization entropy at the normal boiling point (T_{nb}). The vaporization entropy is proportional to the ratio of the degree of randomness in the vapor and the liquid phases. The values for a pure substance are related to molecular structure and can be estimated from the effective number of torsional bounds (τ) and the polar group number capable of

hydrogen bonding (HBN). The ΔS^{b}_{vap} can be calculated from specific routines as proposed by Myrdal and Yalkowsky (1997). Then, the present work aims to estimate the vaporization entropy of some terpene compounds.

MATERIAL AND METHODS

Terpenes are founded in herbal medicine, food, and cosmetics, such as the compounds presented in Figures 1 to 9, which have a variety of molecular structures and functional groups.

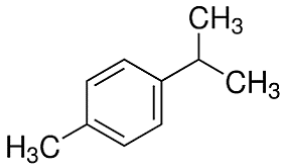

Figure 1- Molecular structure of p-cymene.

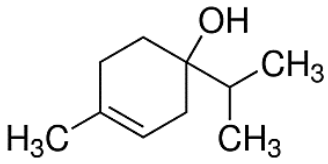

Figure 2 - Molecular structure of terpinen-4-ol.

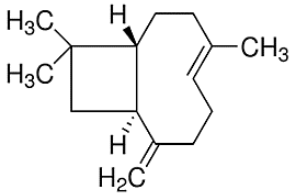

Figure 3 - Molecular structure of trans-caryophyllene.

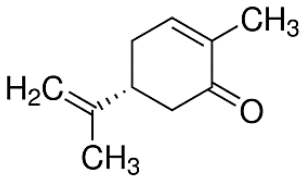

Figure 4 - Molecular structure of carvone.

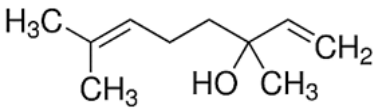

Figure 5 - Molecular structure of linalool

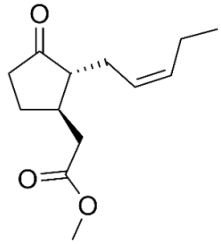

Figure 6 - Molecular structure of methyl-jasmonate.

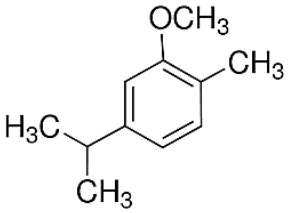

Figure 7 - Molecular structure of thymol-methyl-ether.

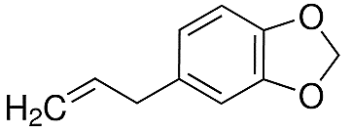

Figure 8 - Molecular structure of safrole.

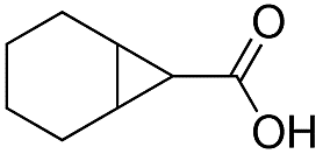

Figure 9 - Molecular structure of bicyclo[4.1.0]heptane-7-carboxylic acid.

The vaporization entropy, ΔS^{b}_{vap}, is influenced by the presence of hydrogen bond (HBN) that facilitates the phase change and the molecule conformation (τ) as described by (Myrdal and Yalkowsky, 1997)

$$\Delta S^{b}_{vap} = 86 + 0.4\,\tau + 1421\,HBN \quad (5)$$

with the effective number of torsional bonds (τ), that measures the overall molecular flexibility, determined from (Myrdal and Yalkowsky, 1997)

$$\tau = \sum(SP3 + 0.5\,SP2 + 0.5\,Ring) - 1 \quad (6)$$

where SP3 and SP2 are non-ring and non-terminal sp^3 and sp^2 atoms; Ring indicates the number of independent ring systems found in the compound. It is important to highlight the vaporization entropy also requires the polar group number capable of hydrogen bonding (HBN). This effect is calculated by

$$HBN = \sqrt{\frac{OH + COOH}{MW}} \quad (7)$$

where OH and COOH are the number of alcohols and carboxylic acids, respectively; MW is the compound molecular weight.

RESULTS AND DISCUSSION

The selected terpene compounds presented in this work have a variety of molecular structures: open chain, cyclic, bicyclic, aromatic, and unsaturated compounds, alcohols, ketones, hydrocarbons, ethers, and carboxylic acids.

Based on the molecular structure of the analyzed compounds, the calculation of the effective number of torsional bounds (τ) and polar group number capable of hydrogen bonding (HBN) were performed, as well as the vaporization entropy at the normal boiling point (ΔS^{b}_{vap}) values was estimated. The results are shown in Table 1.

Analyzing the molecular structures (Figures 1 to 9) it is possible to observe that some molecules have less flexibility due to the number of unsaturation and rings, and even evaluate the propensity to phase change given the presence of hydrogen bonds, which does Equation 5 physically consistent. The parameters τ and HBN are related to molecular structure. The hydrogen bonding inhibits rotational freedom and increases the disorder magnitude that occurs with vaporization. Hence, the vaporization entropy is higher for compounds that hydrogen-bonding groups (OH and COOH) are present, as can

Compounds	τ	HBN	ΔS^{b}_{vap} (J K^{-1} mol^{-1})
p-cymene	0.5	0.000	86.20
terpinen-4-ol	0.5	0.006	95.41
trans-caryophyllene	0.0	0.000	86.00
carvone	0.0	0.000	86.00
linalool	3.5	0.006	96.61
methyl-jasmonate	4.0	0.000	87.60
thymol-methyl-ether	1.5	0.000	86.60
safrole	1.5	0.000	86.60
bicyclo[4.1.0]heptane-7-carboxylic acid	0.0	0.007	96.10

Table 1. Effective number of torsional bounds (τ), polar group number capable of hydrogen bonding (HBN) and vaporization entropy at the normal boiling point (ΔS^{b}_{vap}) of terpene analyzed in this work.

be observed for terpinene-4-ol, linalool, and bicyclo[4.1.0]heptane-7-carboxylic acid. Another significant entropy vaporization parameter is the molecular conformation , which can describe the molecular flexibility. This coefficient confirms that there is a vaporization entropy dependency on molecular conformation, whose results can be observed for linalool and methyl-jasmonate. On the other hand, carvone and trans-caryophyllene, for example, seem less flexible due to unsaturation, and their entropy vaporization values are lower than the other terpenes analyzed in this work.

CONCLUSION

This work presents the values of the effective number of torsional bounds (τ) and the vaporization entropy (ΔS^{b}_{vap}) for some terpene compounds. The molecular structure analysis shows the physical consistency of Myrdal and Yalkowsky's model. The vaporization entropy (ΔS^{b}_{vap}) values are influenced by the presence of a hydrogen bond (HBN), that facilitates the phase change and the molecular conformation (τ) which translates the molecular flexibility.

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Complementary Discussion

The physicochemical properties of molecules are determined by a variety of intrinsic characteristics, such as their molecular structure, types of bonds present, functional groups, and intermolecular forces. The molecular structure defines the properties of a substance, where molecular geometry directly influences its polarity and, consequently, intermolecular interactions.

Different types of bonds, exemplified by molecules like methane, ethene, and ethyne, have distinct impacts on stability and physical properties such as melting and boiling points, due to associated bond energies. Functional groups also confer specific characteristics to molecules, such as the influence of carbonyl groups (C=O) in compounds like carboxylic acids and aldehydes on polarity and intermolecular interactions.

Intermolecular forces also influence substance properties. Dispersion forces, common to all molecules, depend on molecular polarizability, which is related to the number of electrons and molecular mass. Dipole-dipole forces arise in polar molecules due to attraction between partially charged regions, while hydrogen bonds, the strongest among these forces, occur in molecules with hydrogen bonded to highly electronegative atoms. Table 7.1 provides a comparison of molecules with different functional groups, geometries, and polarities, along with their physicochemical properties.

Table 7.1 Physical and chemical properties of different molecules.

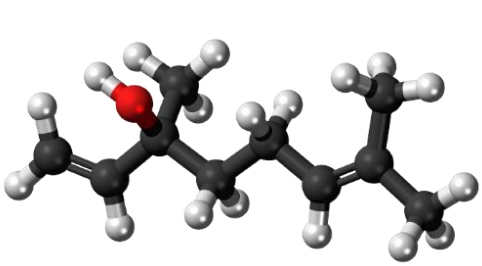
Properties	Acetone (C_3H_6O)	Acetic Acid ($C_2H_4O_2$)	Ethanol (C_2H_6O)
Geometry	Linear	Trigonal Planar	Tetrahedral
Functional Groups	Ketone (C=O)	Carboxylic Acid (COOH)	Alcohol (OH)
Intermolecular Forces	Dipole-dipole, Dispersion Forces	Hydrogen Bonding, Dispersion Forces	Hydrogen Bonding, Dispersion Forces
Melting Point	-10°C	15°C	78°C
Boiling Point	56.05°C	118.1°C	78.37°C
Solubility in Water	Low	High	High
Polarity	Moderately polar	Polar	Polar

Understanding the complex interaction between molecular structure, bond types, functional groups, and intermolecular forces is necessary for predicting and interpreting substance behavior, as these factors collectively determine the physicochemical properties of molecules.

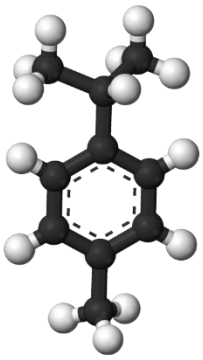
In the context of vaporization entropy, a thermodynamic quantity related to the disorder of a system, the molecular structure of compounds is decisive. Molecular flexibility emerges as a crucial factor, as compounds with more flexible structures generally exhibit higher entropies due to the multiple possible spatial configurations.

The presence of functional groups capable of forming hydrogen bonds also influences the vaporization entropy, as seen in molecules containing hydroxyl (OH) or carboxyl (COOH) groups, which increase disorder due to additional interactions. Additionally, the presence of unsaturation in the carbon chain affects vaporization entropy by increasing molecular flexibility.

Figure 7.1 presents the molecular structures of linalool and p-cymene. Linalool, with its more flexible structure and the presence of functional groups capable of forming hydrogen bonds, tends to have a higher vaporization entropy than p-cymene, which has a less flexible structure and does not contain functional groups that promote greater molecular disorder.



$\Delta S^{vap} = 96.91\ JK^{-1}mol^{-1}$
Linalool



$\Delta S^{vap} = 86.20\ JK^{-1}mol^{-1}$
p-Cymene

Figure 7.1 Molecular representation of linalool and p-cymene.

Linalool is a compound found in essential oils of plants such as lavender and basil. Its molecular structure features a flexible carbon chain with an unsaturation (double bond) and a hydroxyl group (OH). The presence of this unsaturation and the hydroxyl group endows linalool with a molecular structure that promotes greater flexibility and capacity for hydrogen bond formation. Therefore, linalool is expected to have a relatively high vaporization entropy due to its flexible molecular structure and the presence of the OH functional group.

On the other hand, p-cymene is a compound found in citrus oils, such as orange and lemon. Its molecular structure consists of a carbon chain with an unsaturation (double bond) and an aromatic ring. Although p-cymene also contains an unsaturation, its structure is less

flexible compared to linalool, due to the rigidity imposed by the aromatic ring. Additionally, it does not contain functional groups capable of forming hydrogen bonds. Therefore, p-cymene is expected to have a relatively lower vaporization entropy compared to linalool, due to its less flexible molecular structure and the absence of functional groups promoting greater disorder.

CHAPTER VIII

Published Article

FONSECA, LUCIANA A. A. P.; OLIVEIRA, CARLOS E. L.; CREMASCO, MARCO A. **Thermodynamic Properties of Selected Bicyclic Terpenes and Related Substances by Gas Chromatography and Group Contributions**. International Journal of Thermodynamics JCR, v. 26, n.4, p. 48-56, 2023.

The article presented in this chapter validates a group contribution model designed to estimate the vapor pressure and vaporization enthalpy of terpenes and terpenoids found in essential oils. This model represents a practical tool for industry professionals and researchers alike, providing a systematic framework for property estimation. Through this validation, the paper underscores the utility of group contribution methods in addressing complex thermodynamic challenges within the realm of terpenoid chemistry.

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Research Article

Thermodynamic properties of selected bicyclic terpenes and related substances by gas chromatography and group contributions

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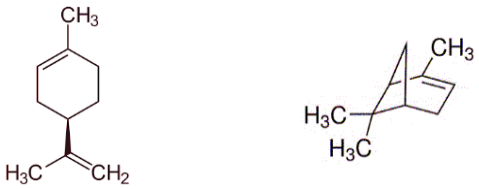
Abstract

Terpene compounds in the lower layer of the atmosphere can contribute to environmental problems through the formation of particulate material known as secondary organic aerosol (SOA). A clear understanding of the formation and composition of these particles hinges on reliable thermodynamic data. Quick estimation of these physical properties is highly desired. While experimental methods require significant resources and time, the prediction of pure-component properties through group contributions is easily applicable and straightforward. The present study compares the experimental enthalpies of vaporization at 298.15 K for bicyclic terpenes and related substances derived from the gas chromatography technique with estimated values provided by three group contribution methods. A new group contribution model specifically designed for terpene compounds is introduced. Furthermore, this study reveals previously unreported values in the literature for the enthalpy of vaporization at 298.15 K and the normal boiling temperature of Thymol methyl ether, Fenchyl alcohol, and Bicyclo [4.1.0] heptane-7-carboxylic acid.

Keywords: *Group contribution; gas chromatography; enthalpy of vaporization; bicyclic compounds.*

1. Introduction

Terpene compounds are naturally produced through secondary metabolism in a wide range of plants. These compounds are simple hydrocarbons that differ in the number of isoprene units. Hemiterpenes are formed by one isoprene unit (C5), monoterpenes by two (C10), sesquiterpenes by three (C15), diterpenes by four (C20), triterpenes by six (C30), and tetraterpenes by eight (C40). Additionally, terpenoids are defined as a modified class of terpenes with different functional groups. Terpenes can be further classified based on the degree of cyclization in the molecule, including acyclic (open chain), monocyclic, or bicyclic structures (see Figure 1) [1]. Compounds from this group have various applications in the chemical, pharmaceutical, and food industries, and they are also emitted into the environment in significant quantities, contributing to the diverse array of organic species found in the atmosphere [2,3].



Monocyclic: (+)-Limonene Bicyclic: α-Pinene

Figure 1. Terpene compounds molecular structures.

The significant presence of terpenes in the lower layer of the atmosphere poses environmental challenges due to their tendency to react with ozone, hydroxyl radicals, and nitrate radicals. These reactions result in the formation of particulate matter known as secondary organic aerosols (SOA) [4]. SOA has the capacity to alter the radiative balance of the atmosphere by either absorbing or scattering solar radiation [5,6,7], thereby impacting air quality [8].

A comprehensive understanding of the formation and composition of these particles depends on reliable thermodynamic data for the compounds responsible for the generation of SOA. For instance, many algorithms used to predict emission rates of terpene compounds are based on physical evaporation and diffusion data [9,10,11].

The lack of such data in the existing literature emphasizes the necessity to explore robust tools capable of determining properties like vapor pressure (P_{vap}), normal boiling temperature (T_{nb}), and enthalpy of vaporization ($\Delta_{vap}H$). Typically, these thermodynamic quantities are obtained through conventional experimental techniques such as isoteniscopy, Knudsen effusion, gas saturation, and gas chromatography [12,13,14], or alternative techniques like thermogravimetry [15]. Gas chromatography, among these methods, provides an accurate means of determining the thermodynamic properties of organic compounds. Its widespread use is attributed to its high purity, small sample size requirement, and reproducibility [14,16,17].

Many experimental techniques require a substantial amount of measured data, chemically pure compounds, and

high-performance equipment, which can be expensive. As the sophistication of chemicals and processes increases, along with greater societal demands for sustainability, health, safety, and economy, there is a growing need to accurately estimate thermodynamic properties and implement property models [18]. Group contribution models are simple and accessible techniques based on molecular structural information. These models are valuable tools when measured data is unavailable and provide a diverse range of property estimates [19]. In recent work, Mann et al. [20] evaluated the prospects of group contribution models and emphasized that combining Artificial Intelligence (AI), data analysis, and models based on fundamental principles, such as classical group contribution models, with the availability of measured data holds promise in this context.

The objective of this study is to determine the enthalpies of vaporization at 298.15 K and normal boiling temperatures for eight terpene compounds using gas chromatography correlation. In addition, unpublished thermodynamic data for thymol methyl ether, alcohol fenchyl and bicyclo [4.1.0] heptane-7-carboxylic acid are provided. Three group contribution methods are employed to estimate the enthalpies of vaporization at 298.15 K for the selected terpene compounds: Chickos et al. [21] present a method that considers the molecular structure of organic compounds and includes intramolecular interactions; Joback and Reid's model [22] is a general approach that incorporates additional contributions; and a new group contribution model specifically designed for terpene compounds is introduced, addressing the gaps left by some models in the literature, with a particular focus on bicyclic terpene compounds.

2. Experimental

2.1 Chemicals

A description of the chemicals used in this work is given in Table 1. The purity of the terpene compounds analyzed by gas chromatography (> 95%) was sufficient to determine their retention times. All chemicals, including the n-alkanes standards (C_5-C_{16}), were provided by Sigma Aldrich (Holzminden, Germany).

Table 1. Sample descriptions.

Chemical name	Formula	Purity, %	M $(g.mol^{-1})$	CAS RN
(+)-Limonene	$C_{10}H_{16}$	97.0	136.23	5989-27-5
Thymol methyl [(1)]	$C_{11}H_{16}O$	≥ 99.0	164.24	1076-56-8
(+)-α-Pinene	$C_{10}H_{16}$	≥ 99.0	136.23	7785-70-8
(+)-β-Pinene	$C_{10}H_{16}$	≥ 99.0	136.23	19902-08-0
5-Vinyl [(2)]	C_9H_{12}	95.0	120.19	3048-64-4
5-Ethylidene [(3)]	C_9H_{12}	99.0	120.19	16219-75-3
Fenchyl alcohol	$C_{10}H_{18}O$	≥96.0	154.25	1632-73-1
Bicyclo [4.1.0] [(4)]	$C_8H_{12}O_2$	95.0	140.18	41894-76-2

[(1)] Thymol methyl ether; [(2)] 5-Vinyl-2-norbornene; [(3)] 5-Ethylidene-2-norbornene; [(4)] Bicyclo [4.1.0] heptane-7-carboxylic acid.

2.2 Gas Chromatography

The compounds' retention times were determined using a Perkin Elmer (Autosystem XL GC) gas chromatograph equipped with a flame ionization detector (FID). A NST 05 capillary column (60 m x 0.25 mm i.d. x 0.25 µm film thickness) was used for compound separation under isothermal conditions of column temperature (40 ºC to 200 ºC), injector temperature of 230 °C, a detector at 250 °C, and an injection volume of 1.0 µL. The carrier gas (He) flow rate was set to 1.0 mL/min. The compounds were dissolved in methanol at a concentration of 20 mg/mL. The n-alkanes (C_5 to C_{16}) were used as reference compounds. Both the studied compounds and the n-alkanes mixture were injected under the same chromatography conditions. The Kováts retention indices (I_x) were calculated using the n-alkanes with retention times encompassing each studied compound. The analyses were performed in triplicate and followed Hoskovec et al. [14] methodology. Table 2 provides the Kováts retention indices for the studied compounds at different temperature ranges.

2.3 Kováts retention indices

Isothermal Kováts retention indices (I_x) defined as Eq (1).

$$I_X = 100z + 100\left(\frac{\ln t_{R,X} - \ln t_{R,z}}{\ln t_{R,z+1} - \ln t_{R,z}}\right) = 100z + 100\frac{\ln(\gamma_z^\infty P_z/\gamma_X^\infty P_X)}{\ln(\gamma_z^\infty P_z/\gamma_{z+1}^\infty P_{z+1})} \quad (1)$$

In Eq. (1), $t_{R,X}$, P_X, and γ_X^∞ represent the retention time, vapor pressure, and infinite dilution activity coefficient, respectively, of solute X in the stationary phase. The subscripts z and z+1 identify the reference n-alkanes with z and z+1 carbon atoms, whose retention times encompass that of solute X.

2.4 Thermodynamic properties

With the requisite collection of the Kováts retention indices assembled by Eq. (1), the vapor pressures were determined from Eq. (2).

$$\ln P_x = \ln P_z + \frac{(100z - I_X)\ln(P_z/P_{z+1})}{100} \quad (2)$$

The vapor pressures of reference C_5 to C_{16} n-alkanes at different temperatures used in this work were calculated using the Cox Equation, Eq. (3).

$$\ln\left(\frac{P}{P_0}\right) = \left(1 - \frac{T_0}{T}\right)\exp(A_0 + A_1T + A_2T^2) \quad (3)$$

In Eq. (3) the coefficients derived for temperatures between the triple and boiling points were taken from a critical compilation of n-alkanes data [23].

Published P values of the compounds studied at 298.15 K were obtained from literature and web- available databases [24, 25]. The same sources along with the commercial Sigma Aldrich catalogue served as a literature source for normal boiling point (T_{nb}) data.

The Antoine Equation Eq. (4) parameters A, B, C, were determined using non-linear regression techniques and are presented in Table 3.

$$\ln(P_{vap}/Pa) = A - \frac{B}{T(K) + C} \quad (4)$$

For processing the P_{vap} versus T data, the Kirchhoff–Rankin-type Eq. (5) was used. The parameters of Eq. (5) are presented in Table 4.

$$\ln(P_{vap}/Pa) = \frac{1}{R}b_0 + \frac{1}{RT}b_1 + \frac{1}{R}b_2\ln(T/T_0) \quad (5)$$

In Eq. (5) T_0 is arbitrary equaled to 298.15 K and R=8.3145 $J.K^{-1}mol^{-1}$. The enthalpy of vaporization at temperature T may be calculated from Eq. (6).

$$\Delta_{vap}H = -b_1 + b_2T \quad (6)$$

Eqs. (5) and (6) were implemented to predict $\Delta_{vap}H$ values at 298.15 K for the studied compounds. In addition, since it is known that the normal boiling temperature T_{nb} of a substance in the liquid phase is the temperature at which its vapor pressure equals atmospheric pressure (1 atm), it is possible to define P in Eq. (5) as 1 atm to obtain the T_{nb} data. Table 5 summarizes the enthalpy of vaporization ($\Delta_{vap}H$) at 298.15 K and the normal boiling temperature (T_{nb}) of studied terpene compounds.

Table 2. Experimental data. Kováts retention indices of studied compounds at different T ranges.

	Kováts Retention Indices (I_x)							
T (K)	Monocyclic Terpenes		Bicyclic Terpenes					
	Limonene	Thymol methyl ether	(+)-α-Pinene	(+)-β-Pinene	5-vinyl [(1)]	5-Ethylidene [(2)]	Fenchyl alcohol	Bicyclo [4.1.0] [(3)]
313.15	-	-	926.35	965.20	-	-	-	-
323.15	1021.19	-	929.58	969.20	-	-	-	-
333.15	1023.72	-	932.52	972.80	878.20	909.84	-	-
343.15	1027.83	1228.54	936.44	978.02	880.76	911.97	-	-
353.15	1030.81	1230.54	939.51	982.15	883.20	913.99	-	-
363.17	1033.93	1233.65	943.49	986.63	885.24	915.47	-	-
373.15	1038.35	1233.11	947.91	992.24	886.95	917.07	1114.62	246.58
383.15	1039.34	1234.87	951.31	994.56	891.24	918.93	1113.78	256.62
393.15	1041.91	1238.14	954.41	998.16	891.70	918.52	1116.50	266.54
403.15	1045.54	1239.03	958.69	1002.91	893.70	920.52	1121.49	276.52
413.15	1049.26	1241.75	963.81	1007.63	894.45	921.01	1126.04	286.63
423.15	1052.04	1243.69	-	-	-	-	1131.15	296.58
433.15	-	1245.59	-	-	-	-	1134.05	246.50
443.15	-	1247.27	-	-	-	-	1136.75	-
453.15	-	-	-	-	-	-	1142.42	-
463.15	-	-	-	-	-	-	1148.00	-
473.15	-	-	-	-	-	-	1155.00	-

[(1)]5-Vinyl-2-norbornene; [(2)] 5-Ethylidene-2-norbornene; [(3)] Bicyclo [4.1.0] heptane-7-carboxylic acid.

Table 3. Vapor Pressure: Antoine Equation Parameters.

Compound	A	B	C	$r^{2(a)}$
(+)-Limonene	20.92 ± 0.14	3741.14 ± 84.79	-62.53 ± 3.44	0.99998
Thymol methyl ether	20.87± 0.16	3866.04 ± 99.65	-86.93 ± 3.99	0.99997
(+)-α-Pinene	20.12 ± 0.10	3185.64 ± 56.06	-70.82 ± 2.51	0.99999
(+)-β-Pinene	20.64 ± 0.14	3597.34 ± 81.82	-57.67 ± 3.39	0.99998
5-Vinyl-2-norbornene	21.19 ± 0.24	3648.92 ± 153.90	-45.65 ± 6.82	0.99996
5-Ethylidene-2-norbornene	21.45 ± 0.19	3667.36 ± 125.39	-34.8 ± 5.71	0.99998
Fenchyl alcohol	19.33 ± 0.27	2869.94 ± 168.46	-113.19 ± 8.91	0.99985
Bicyclo [4.1.0] heptane-7-carboxylic acid	18.80 ± 0.29	2528.18 ± 144.33	-162.43 ± 6.97	0.99997

[(a)]: correlation coefficients (r^2, %).

Table 4. Parameters of Eq. (5).

Compound	b_0	b_1	b_2	$r^{2(a)}$
(+)-Limonene	256.2 ± 3.9	-63822 ± 1168	-50.5 ± 3.2	0.99998
Thymol methyl ether	298.1 ± 5.5	-82189 ± 1705	-73.9 ± 4.3	0.99997
(+)-α-Pinene	257.5 ± 3.1	-61608 ± 922	-56.8 ± 2.6	0.99998
(+)-β-Pinene	244.7 ± 4.0	-58834 ± 1205	-45.4 ± 3.4	0.99997
5-Vinyl-2-norbornene	225.4 ± 6.4	-50452 ± 1954	-29.6 ± 5.3	0.99996
5-Ethylidene-2-norbornene	229.5 ± 4.6	-52642 ± 1398	-30.2 ± 3.8	0.99998
Fenchyl alcohol	295.40 ± 12.0	-77914 ± 3736	-78.6 ± 8.9	0.99984
Bicyclo [4.1.0] heptane-7-carboxylic acid	464.10 ± 17.4	-136073 ± 5412	-190.9 ± 13.3	0.99997

[a]: correlation coefficients (r^2, %).

Table 5. $\Delta_{vap}H$ and T_{nb}: Literature and Experimental data obtained in this work at 298.15 K and 101.325 kPa.

Compound	T_{nb}^{lit} [a] (K)	T_{nb}^{exp} [b] (K)	RD[c] %	$\Delta_{vap}H^{lit}$[a] (kJ mol^{-1})	Method[d]	$\Delta_{vap}H^{exp}$ [b] (kJ mol^{-1})	RD[c] %
(+)-Limonene	451.15[e]	461.44	2.28	49.60[g]	GC	48.77	1.67
Thymol methyl ether	-	501.77	-	-	GC	60.16	-
(+)-α-Pinene	429.35[e]	442.44	3.05	44.84[g]	GC	44.67	0.40
(+)-β-Pinene	439.15[e]	453.01	3.16	46.19[g]	GC	45.30	1.93
5-Vinyl-2-norbornene	414.2[f]	423.12	2.15	42.29[h]		41.64	1.33
5-Ethylidene-2-norbornene	419.2[f]	429.15	2.37	44.30[i]	EB	43.63	1.51
Fenchyl alcohol	-	481.30	-	-	GC	54.47	-
Bicyclo [4.1.0] heptane-7-carboxylic acid	-	516.95	-	-	GC	79.15	-

[a] T_{nb}^{lit} and $\Delta_{vap}H^{lit}$: literature normal boiling temperature and enthalpy of vaporization at 298.15 K.
[b] T_{nb}^{exp} and $\Delta_{vap}H^{exp}$: experimental normal boiling temperature and enthalpy of vaporization at 298.15 K obtained in this work.
[c] RD: absolute relative deviation.
[d] Gas Chromatography (GC), Ebulliometry (EB).
[e][24]. [f][25]. [g][14]. [h][26]. [i][27].

3. Group contribution methods

The group contribution methods are based on the principle that a function of structurally dependent parameters defines the property values. These values are determined by summing the frequency of each group occurring in the molecule multiplied by its contribution. These methods provide quick estimates without requiring substantial computational resources. The representation of molecular structures through functional groups provides these methods with a predictive quality regarding the range of molecular structures that can be handled. Methods based on the group contribution approach have been developed for a wide range of properties and are routinely used when measured data for properties are not available [19].

To ensure consistency in the results, terpene compounds with available enthalpies of vaporization in the literature [14,26,27] were selected. Enthalpies of vaporization at 298.15 K were predicted using the methods proposed by Chickos et al. [21], Joback and Reid [22], and a new group contribution method introduced in this work. Each of these methods employs specific fragmentation schemes and interactions between groups.

3.1 Proposed model

This newly developed group contribution method is designed to estimate the enthalpy of vaporization of pure organic compounds. It introduces a specific fragmentation scheme adapted for essential oil compounds, which primarily consist of monoterpene hydrocarbons, sesquiterpene hydrocarbons, and oxygenated derivatives. The selection of compounds for the database followed specific criteria, including saturated and unsaturated hydrocarbons with open-chain and branched structures ranging from C_7 to C_{15} carbon atoms. It also encompassed bicyclic hydrocarbons and oxygenated derivatives. Due to their low occurrence in essential oils, compounds containing sulfur, nitrogen, and alkynes hydrocarbons were excluded from the database. The proposed method is based on first-order groups. The fragmentation scheme considers molecular characteristics, such as distinguishing between open-chain, cyclic, aromatic groups, and bicyclic structures. A total of 26 groups were defined. Table 6 presents all the groups utilized in the regression and their respective contributions to the prediction of enthalpy of vaporization.

The proposed model comprises a dataset of 1,719 different organic substances, with a total of 3,591 data points for enthalpy of vaporization. Considering that some terpenes in the dataset have multiple values for enthalpy of vaporization, the division was based on the number of compounds. The cross-validation technique was chosen for parameter selection as it enhances the model's generalization capacity [28]. The training and validation phases utilized 80% of the database, while the remaining 20% was allocated for testing. Parameter optimization was performed using gradient descent, which is widely used in training machine learning models, such as linear regression. It provides an efficient way to find optimal parameter values that minimize the cost function, allowing the models to better fit the training data and make accurate predictions on new, unseen data.

Regarding the contribution values, some considerations are necessary. Groups containing carbonyl (C=O) and hydroxyl (-OH) exhibit the highest contributions, which aligns with their polar nature and strong intermolecular dipole-dipole forces. Additionally, groups containing hydroxyl, such as alcohols, phenols, and carboxylic acids, also demonstrate significant contributions due to hydrogen bonding. Descriptors for bicyclic compounds and cis-trans isomerism display negative values, reflecting the stereoisomeric positions in these compound types. Moreover, groups associated with aliphatic compounds or segments of molecules, such as $-CH_3$ and $-CH_2-$, show lower contributions, likely attributed to the branching that diminishes intermolecular attraction and influences thermodynamic properties such as normal boiling temperature and enthalpy of vaporization.

The Eq. 7 performs the prediction by the proposed model.

$$\Delta_{vap}H = 19.55 + \sum_i N_i C_i \quad (7)$$

In Eq. (7), N_i represents the occurrence of each group in the structure, and C_i denotes the contribution to the enthalpy of vaporization from each group. The application of this method is shown in Table 7.

The relative deviation (RD) for each method is defined in Eq. (8).

$$RD\ (\%) = 100.abs\left[\left(\Delta_{vap}H^{exp} - \Delta_{vap}H^{est}\right)/\Delta_{vap}H^{exp}\right] \quad (8)$$

In Eq. (8), $\Delta_{vap}H^{exp}$ and $\Delta_{vap}H^{est}$ represent the experimental and estimated enthalpies of vaporization, respectively.

Table 6. Proposed model group contribution fragments.

Nº	Group	Contribution
0	h_0	19.548
1	$-CH_3$	0.475
2	$-CH_2-$	3.900
3	>CH-	4.172
4	>C<	4.380
5	$=CH_2$	-1.196
6	=CH-	4.525
7	=C<	5.008
8	$-CH_2-$ (cyclic)	2.793
9	>CH- (cyclic)	3.197
10	>C< (cyclic)	4.535
11	=CH- (cyclic)	3.048
12	=C< (cyclic)	4.862
13	=CH (aromatic)	2.808
14	=C< (aromatic)	5.610
15	OH (alcohol)	17.421
16	-O-	2.255
17	O-C=O	12.162
18	C=O	6.301
19	OH (phenol)	7.979
20	-O- (cyclic)	4.307
21	C=O (cyclic)	10.589
22	bicyclic (correction)	-2.053
23	HC=O	8.912
24	OHC=O	30.201
25	*cis* correction	0.983
26	*trans* correction	1.338

Table 7. Estimated enthalpy of vaporization ($\Delta_{vap}H^{est}$) of 5-Vinyl-2-norbornene using this work proposed model at constant temperature (298.15 K). Experimental literature data [26]: $\Delta_{vap}H^{exp}$ (298.15 K) = 42.29 kJ/mol.

Compound	Proposed model	
	Group Contribution	
	h_0	19.548
	$-CH_2-_{(ring)}$	2.792
	$=CH-_{(ring)}$	3.048
	$>CH-_{(ring)}$	3.197
	$=CH-$	4.525
	$=CH_2$	-1.196
5-Vinyl-2-norbornene	Bicyclic correction	-2.053
	$\Delta_{vap}H^{est}$ (kJ.mol^{-1})	42.10
	$\Delta_{vap}H^{exp}$(kJ.mol^{-1}) [(a)]	42.29
	RD (%)	0.45

[(a)][26].

3.2 Chickos et al. (1998)

In this method [21], the evaluation of the nature and location of functional groups is performed. The steric environment of the functional groups is identified using characteristics such as hybridization and substitution.

Estimation is further enhanced by accounting for intramolecular hydrogen bonding.

$$\Delta_{vap}H = 4.69\left(N_C - N_Q\right) + 1.3N_Q + 3.0 + \sum_i n_i F_i b_i + C \quad (9)$$

Eq. (9) defines the parameters N_C and N_Q as the total number of carbons and the total number of quaternary sp³ hybridized carbon atoms, respectively. The product $F_i.b_i$ depends on the nature (b) and location (F) of the functional group, while C represents a correction parameter associated with intramolecular interactions. The application of this method is presented in Table 8.

Table 8. Estimated enthalpy of vaporization ($\Delta_{vap}H^{est}$) of Thymol methyl ether at 298.15 K using the method proposed by Chickos et al. [21]. Experimental data from this study: $\Delta_{vap}H^{exp}$ (298.15 K) = 60.16 kJ/mol.

Compound	Chickos et al.'s [21]	
	Group contribution	
	N_C	11
	N_Q	0
	Functional group class	b_i
	> O	5.0
	Substitution Factor	F_i
	Single substitution on a primary sp³ atom	1.62
	Single substitution on a quaternary sp² atom	0.85
Thymol methyl ether	Correction	C
	Ortho and vicinal alkyl branching cyclic sulfides on sp² and sp³ carbons on 5 and 6 membered rings	-2
	$\Delta_{vap}H^{est}$ (kJ.mol^{-1})	62.69
	$\Delta_{vap}H^{exp}$(kJ.mol^{-1}) [(a)]	60.16
	RD (%)	4.21

[(a)]Experimental enthalpy of vaporization at 298.15 K obtained in this work.

3.3 Joback and Reid (1987)

The method proposed by Joback and Reid [22] predicts eleven important and commonly thermodynamic properties of pure components from molecular structure only. This method assumes that there are no interactions between the groups and therefore only uses additive contributions.

$$\Delta_{vap}H = 15.30 + \sum_i N_i h_{v,i} \quad (10)$$

In Eq. (10), Ni represents the occurrence of each group in the structure, and $h_{v,i}$ denotes the contribution to the enthalpy of vaporization from each group. The application of this method is summarized in Table 9.

Table 9. Estimated enthalpy of vaporization ($\Delta_{vap}H^{est}$) of (+)-Limonene at 298.15 K using the method proposed by Joback and Reid [22]. Experimental literature data [14]: $\Delta_{vap}H^{exp}$ (298.15 K) = 49.60 kJ/mol.

Compound	Joback and Reid's method [22]	
	Group Contribution	
	h_0	15.30
	CH_3	2.373
	$=CH_2$	1.724
	$=C<$	2.138
	$CH_{(ring)}$	1.942
	$=CH_{(ring)}$	2.544
	$=C<_{(ring)}$	3.059
(+)-Limonene	$CH_{2(ring)}$	2.398
	$\Delta_{vap}H^{est}$ (kJ.mol^{-1})	38.55
	$\Delta_{vap}H^{exp}$(kJ.mol^{-1}) [(a)]	49.60
	RD (%)	22.28

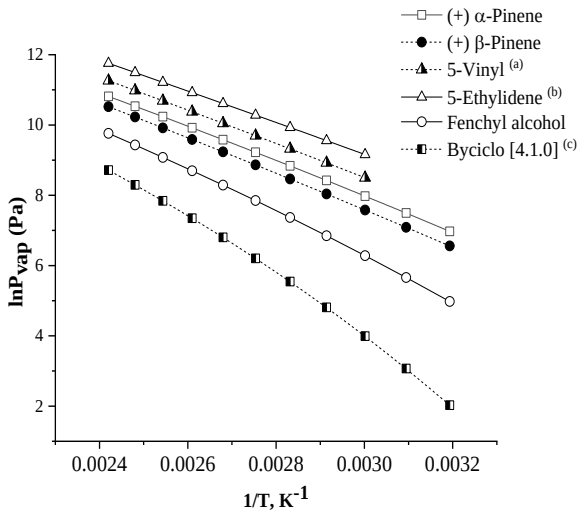
[(a)][14].

4. Results and Discussion

New experimental data were obtained for terpene compounds, including (+)-Limonene, Thymol methyl ether, (+)-α-Pinene, (+)-β-Pinene, 5-Vinyl-2-norbornene, 5-Ethylidene-2-norbornene, Fenchyl alcohol and Bicyclo

[4.1.0] heptane-7-carboxilic acid at 298.15 K using gas chromatography correlation.

Table 2 presents the Kováts retention index values for the monocyclic and bicyclic terpenes evaluated in this study. From the I_x data of each compound within their respective temperature range, the dependence of vapor pressure on temperature was evaluated using Eq. (2). The resulting vapor pressure curves for the analyzed bicyclic and monocyclic terpenes are displayed in Figure 2 and Figure 3, respectively.



(a) 5-Vinyl-2-norbornene; (b) 5-Ethylidene-2-norbornene; (c) Bicyclo [4.1.0] heptane-7-carboxylic acid.

Figure 2. Temperature dependence of the vapor pressure for the bicyclic terpenes studied in this work.

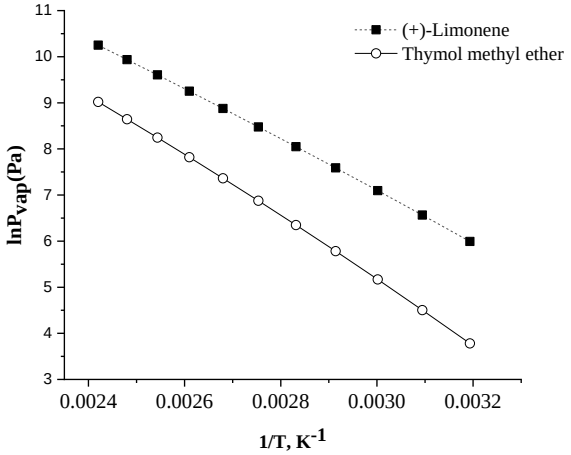


Figure 3. Temperature dependence of the vapor pressure for the monocyclic terpenes studied in this work.

By analyzing the temperature-dependent vapor pressure, the constants of the Antoine equation Eq. (3) were determined. As shown in Table 3, all the compounds exhibited correlation coefficients (r^2) above 0.999, indicating a strong fit to the model.

The enthalpy of vaporization, which is directly related to vapor pressure, was calculated using Eq. (5) based on the obtained vapor pressure curves (Figures 2 and 3). The parameter values for Eq. (5) were obtained through nonlinear regression analysis performed using Origin 8.1 (Origin Lab, Northampton, Massachusetts, USA), and are presented in Table 4. The normal boiling temperature (T_{nb}) was calculated by extrapolating the data to 101.325 kPa using an iteration procedure in Excel. The calculated values for $\Delta_{vap}H$ in this work were compared with literature data, and the absolute relative deviation demonstrated agreement with results reported in the literature, as shown in Table 5. Furthermore, a comparison of our boiling point temperatures with literature values revealed a low relative deviation in predicting T_{nb}^{exp}, indicating that gas chromatography using n-alkanes as standards can be a reliable method for obtaining these thermodynamic properties experimentally.

The absolute relative deviation (RD) is defined as Eq. (11).

$$RD\% = 100.\,abs\left(TP^{lit} - TP^{exp}/TP^{lit}\right) \quad (11)$$

In Eq. (11), TP^{lit} and TP^{exp} referred to the thermodynamic properties of the literature and that obtained experimentally in this work. The TP parameter is substituted by enthalpy of vaporization or normal boiling temperature depending on the analyzed property.

Experimental data for enthalpy of vaporization from the literature and determined in this work were compared with data provided from estimation methods at constant temperature (298.15 K) developed by Chickos et al. [21], Joback and Reid [22] and a new group contribution method proposed in this work. The performance of the studied methods was examined and discussed. The results are presented in Table 10.

The mean relative deviation (MRD) for each method is defined in Equation (12):

$$MRD\ (\%) = \frac{100}{n} abs\left[\frac{\Delta_{vap}H^{exp,i} - \Delta_{vap}H^{est,i}}{\Delta_{vap}H^{exp,i}}\right] \quad (12)$$

In Eq. (12), n is the number of compounds, and i represents each compound.

The method proposed by Chickos et al. [21] demonstrates reasonable estimates for most of the studied monocyclic and bicyclic terpenes, with a mean relative deviation of 9.51%. Although this model incorporates contributions for functional groups, types of carbon bonding and hybridization, as well as correction terms for intramolecular interactions, its database is limited in terms of the number of compounds representing each functional group and molecular structure. Moreover, it does not distinguish the contributions of isomers, as observed in the cases of (+)-α-Pinene and (+)-β-Pinene, as well as 5-Vinyl-2-norbornene and 5-Ethylidene-2-norbornene, respectively.

Joback and Reid [22] proposed a classical group contribution method that utilizes additive contributions and does not consider intramolecular interactions. However, it demonstrated the highest mean relative deviation of 20.00% among the examined models. This method assumes no interactions between groups and relies solely on additive contributions. Additionally, it does not differentiate between aromatic and non-aromatic rings, which significantly impacts the performance of this group contribution method.

The proposed model encompasses terpene compounds and integrates group contribution for bicyclic compounds. In this method, the most significant deviation of 11.69% was observed for (+)-Limonene and Thymol methyl ether, while the smallest deviation was found for bicyclic compounds. This model includes groups that describe the studied molecules, specifically terpene compounds, with the addition of bicyclic structures and isomers. However, it lacks a correction for interactions between carbons in cyclic or

aromatic structures, resulting in a mean relative deviation of 8.00%.

Table 10. The enthalpy of vaporization at 298.15 K: experimental ($\Delta_{vap}H^{exp}$) and estimated ($\Delta_{vap}H^{est}$) data.

Compounds	$\Delta_{vap}H^{exp}$ (kJ.mol^{-1})	Estimated enthalpy of vaporization (kJ.mol^{-1})					
		Chickos et al.'s method [21]		Proposed model		Joback and Reid's method [22]	
		$\Delta_{vap}H^{est}$	RD%	$\Delta_{vap}H^{est}$	RD%	$\Delta_{vap}H^{est}$	RD%
Monocyclic terpene							
(+)-Limonene	49.60 [(a)]	49.90	0.60	43.80	11.69	38.55	22.28
Thymol methyl ether	60.16 [(b)]	62.69	4.21	53.13	11.69	45.72	24.00
Bicyclic terpene							
(+)-α-Pinene	44.84 [(a)]	46.51	3.72	43.35	3.32	37.36	16.68
(+)-β-Pinene	46.19 [(a)]	46.51	0.69	41.42	10.33	36.56	20.85
5-Vinyl-2-norbornene	42.29 [(c)]	45.21	6.90	42.10	0.45	34.95	17.36
5-Ethylidene-2-norbornene	44.30 [(d)]	45.21	2.05	45.43	2.55	36.72	17.11
Fenchyl alcohol	54.47 [(b)]	83.75	53.75	60.18	10.48	51.63	5.21
Bicyclo [4.1.0] [*]	79.15 [(b)]	82.42	4.13	68.46	13.51	50.26	36.50
MRD (%)			9.51		8.00		20.00

[*] Bicyclo [4.1.0] heptane-7-carboxilic acid.
Experimental data from literature: [(a)][14], [(c)] [26], [(d)][27].
[(b)] Experimental data obtained in this work.

Figure 4 illustrates the distribution of the three group contributions to estimated vaporization enthalpies in relation to the experimental data.

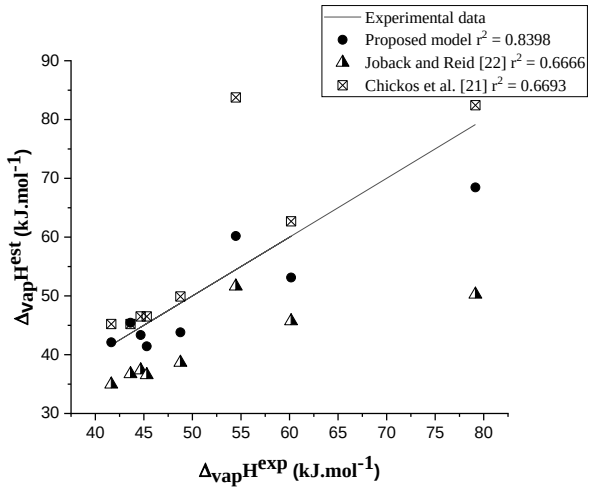


Figure 4. Enthalpies of vaporization distribution: estimated ($\Delta_{vap}H^{est}$) and experimental ($\Delta_{vap}H^{exp}$) data.

Comparing the results obtained by the studied models and analyzing Figure 4, it can be observed that the proposed model achieved a correlation coefficient (r^2) value of 0.8398, indicating a high level of accuracy in fitting the utilized data. In contrast, the Chickos et al. [21] and Joback and Reid [22] proposed models had r^2 values of 0.6693 and 0.6666, respectively, suggesting a comparatively less precise fit. Consequently, the proposed model demonstrated superior performance when compared to the other evaluated models.

5. Conclusion

This paper compares three group contribution methods, including a new model specifically designed for terpene compounds, with different fragmentation schemes. These methods were evaluated against experimental enthalpies of vaporization obtained through gas chromatography correlation. Reliable experimental thermodynamic data are crucial for understanding chemical processes like secondary organic aerosol (SOA) formation and for building the database used in the development of group contribution models. However, experimental techniques often require significant effort. Group contribution methods are valuable in this regard as they only require knowledge of the chemical structure to estimate physical properties.

The enthalpy of vaporization ($\Delta_{vap}H$) at 298.15 K and the normal boiling temperature (T_{nb}) of (+)-Limonene, (+)-α-Pinene, (+)-β-Pinene, 5-Vinyl-2-norbornene, 5-Ethylidene -2-norbornene, Thymol methyl ether, Fenchyl alcohol, and Bicyclo [4.1.0] heptane-7-carboxilic acid were determined by gas chromatography technique using n-alkanes as standards, yielding good results. The referenced thermodynamic parameters of the last three compounds were previously unpublished in literature and are being presented for the first time in this study.

The comparison of the three studied group contributions highlights that a reliable database and the fragmentation scheme are crucial for an accurate group contribution method. Among the studied models, the proposed model demonstrated better performance for the analyzed compounds ($r^2 = 0.8398$). It is a first-order group model. The accuracy of the group contribution-simple (based on first-order groups) is qualitatively acceptable, but a more precise prediction is obtained through the addition of second- and third-order group contributions [29]. The proposed model fills a gap in predictive methods specific to physical properties of terpene compounds and can be further enhanced by incorporating second- and third-order contributions.

Nomenclature

$\Delta_{vap}H$	Enthalpy of vaporization (kJ.mol^{-1})
exp	The superscript symbol "exp" means experimental
est	The superscript symbol "est" means estimated
lit	The superscript symbol "lit" means literature
GC	Gas chromatography
I_X	Kováts retention index
MRD	Mean relative deviation
P_{vap}	Vapor pressure (Pa)
RD	Relative deviation
R	universal gas constant (J.K^{-1}mol^{-1})
r^2	Correlation coefficient
T	Temperature (K)
T_0	Reference temperature (K)
T_{nb}	Normal boiling temperature (K)
TP	Thermodynamic property

t_R	Retention time (s)
X	Solute, analyzed compound
γ^{∞}	Infinite dilution activity coefficient
z	Carbon number

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Complementary Discussion

In this section, a well-established group contribution model in the literature, Kolská et al. (2005), is presented in detail, along with an analysis of the prospects of predictive models.

The Kolská et al. (2005) model is a group contribution method developed to estimate the enthalpy of vaporization at 298.15 K and at the normal boiling temperature. Data from 831 compounds were used for estimations at 298.15 K, and data from 589 compounds were used for estimations at the normal boiling temperature. These data were essential for calculating the group contributions required for the predictions. The models for the estimation of enthalpy of vaporization (ΔH_V) at 298.15 K and at the normal boiling point (T_b) are given by Eq. (8.1) and Eq. (8.2), respectively.

$$\Delta H_V\,(298.15\ \mathrm{K}) = h_0 + \sum_{i=1}^{n_0} N_{h0,i}\,C_{h0,i} + \omega \sum_{j=1}^{m_0} M_{h0,j}\,D_{h0,j} + z \sum_{k=1}^{o_0} O_{h0,k}\,E_{h0,k} \tag{8.1}$$

$$\Delta H_V\,(T_b) = h_b + \sum_{i=1}^{n_b} N_{hb,i}\,C_{hb,i} + \omega \sum_{j=1}^{m_b} M_{hb,j}\,D_{hb,j} + z \sum_{k=1}^{o_b} O_{hb,k}\,E_{hb,k} \tag{8.2}$$

In these equations, $N_{h0,i}$ and $N_{hb,i}$ indicate the number of times the first-level group i appears in the molecular structure and $C_{h0,i}$ and $C_{hb,i}$ respectively represent the corresponding contributions to the property. The terms $M_{h0,j}$ and $M_{hb,j}$ indicate the number of times second-level group j appears in the molecular structure, $D_{h0,j}$ and $D_{hb,j}$ respectively represent their corresponding second-level contributions to the property. The terms $O_{h0,k}$ and $O_{hb,k}$ indicate the number of times third-level group k appears in the molecular structure, and $E_{h0,k}$ and $E_{hb,k}$ respectively represent their corresponding third-level contribution to the property. The subscript "h" indicates the model for enthalpy of vaporization prediction, whereas the subscript "s" indicates the model for vaporization entropy prediction. The subscripts "0" and "b" are used to distinguish between the temperature of estimation: the subscript 0 represents 298.15 K and the subscript b represents the normal boiling temperature. The variables ω and z are weighting factors that are equal to 0 or 1, depending on whether the second-level and third-level contributions, respectively, are used or not. Table 8.1 illustrates the application of the Kolská et al. (2005) model for camphor.

Table 8.1 Estimation of camphor enthalpy of vaporization at 298.15 K and at its normal boiling temperature.

Estimation level	Group	ΔH_V (298.15 K)		ΔH_V (T_b)	
first-level	1	3	2.266	3	2.312
	107	3	4.013	3	2.416
	108	1	4.075	1	2.263
	109	2	3.667	2	3.435
	117	1	14.837	1	19.025
	h_0/h_b	1	9.672	1	14.876
	est		54.76 kJ mol^{-1}		57.22 kJ mol^{-1}
	exp		59.50 kJ mol^{-1}		59.50 kJ mol^{-1}
	RE(%)		8.0		3.8
second-level	55	2	-1.355	2	-0.351
	est		52.05 kJ mol^{-1}		56.52 kJ mol^{-1}
	exp		59.50 kJ mol^{-1}		59.50 kJ mol^{-1}
	RE(%)		12.5		5.0
third-level	8	1	-0.191	1	0.473
	9	1	0.270	1	-0.320
	est		52.12 kJ mol^{-1}		56.77 kJ mol^{-1}
	exp		59.50 kJ mol^{-1}		59.50 kJ mol^{-1}
	RE(%)		12.4		4.6

Table 8.1 presents the enthalpy of vaporization for different estimation levels (first, second, and third levels) for camphor. At the first level of estimation, various groups were considered, each contributing a specific amount to the enthalpy of vaporization. Estimated values ΔH_V at 298.15 K and at normal boiling temperature (T_b) are provided for each group, along with corresponding experimental values and the relative error (RE%). The authors conducted experimental measurements for the enthalpy of vaporization at the normal boiling temperature, determining the value to be 59.50 kJ mol^{-1}.

The model demonstrates improvements over other methods and incorporates new strategies, such as the development of a connectivity index-based method and the inclusion of new second-level groups. However, there are some limitations. The reliance on training data can lead to inaccurate predictions if the data is not sufficiently representative of the diversity of chemical compounds. Additionally, the complexity of molecular structure may limit the model's ability to handle very complex or unusual compounds. Extrapolation to compounds outside the training data range may result in unreliable predictions. Despite these limitations, the Kolská et al. (2005) model remains a valuable tool for estimating thermodynamic properties of organic compounds.

Mann et al. (2023) evaluated the prospects of group contribution models and emphasized that combining Artificial Intelligence (AI), data analysis, and models based on

fundamental principles, such as classical group contribution models, with the availability of measured data holds promise in this context.

The integration of Artificial Intelligence (AI) in the estimation of thermodynamic properties represents a promising field that has garnered increasing interest in the scientific community. The application of machine learning algorithms to predict these properties more accurately has the potential to revolutionize how we understand and utilize chemical compounds in various fields, from industry to medicine.

A practical example of AI usage in estimating thermodynamic properties is the development of regression models to predict the enthalpies of vaporization or boiling points of organic compounds. These models can be trained using datasets containing information about the molecular structure of compounds and their experimentally measured thermodynamic properties (GANI, 2019). With proper training, AI algorithms can learn complex patterns in the data and make accurate predictions for new compounds based on their chemical structure.

Furthermore, AI can also be applied in the development of pattern recognition models to identify correlations between the molecular structure of compounds and their thermodynamic properties. For instance, convolutional neural networks can be used to analyze images of molecular structures and extract relevant features that are related to the thermodynamic properties of the compounds (MANN, 2023).

One of the main challenges of this approach is the availability and quality of training data. Without adequate and representative datasets, AI algorithms may not be able to learn significant patterns or generate accurate predictions. For example, if the training data is limited to compounds from a certain class or chemical family, the model may struggle to make accurate predictions for compounds with different characteristics.

Despite these challenges, the potential of AI in estimating thermodynamic properties is significant and worth exploring. With advancements in technology and the increasing availability of data, we can expect AI algorithms to become increasingly precise and reliable in predicting these properties. This can have a positive impact in various areas, including drug discovery.

CHAPTER IX

9. Final considerations

9.1 Recommendations for future research

Through this doctoral Thesis, a correlation was made between biodiversity, thermodynamics, and molecular structure, providing a comprehensive understanding of terpenes and terpenoids, as well as enabling their numerous applications. The following items can be suggested as developments of this research:

- Determine experimental thermodynamic data such as vapor pressure and enthalpy of vaporization of terpene compounds using two distinct experimental techniques, thermogravimetry, and gas chromatography correlation, studied within the same temperature range.
- Propose the utilization of experimental infinite dilution activity coefficients (γ^{∞}) instead of the presented simplification ($\gamma_X^{\infty} = \gamma_z^{\infty} = \gamma_{z+1}^{\infty}$).
- Examine the effect of different stationary phases (columns) on the calculation of the Kováts retention index.
- Evaluate the relationship between thermodynamic parameters, such as enthalpy of vaporization and vapor pressure, and the biological activity exhibited by terpenes and terpenoids. This analysis could provide insights into the underlying mechanisms of action and reveal correlations with their physicochemical properties.
- Utilize machine learning techniques like artificial neural networks to identify specific molecular descriptors for terpenes and terpenoids. By integrating these descriptors with experimental data, enhance the accuracy and reliability of predictive models.
- Integrate structural information and physicochemical properties of terpenes and terpenoids into machine learning frameworks. This integrated approach can facilitate the prediction of biological activity, therapeutic efficacy, or toxicity, aiding in the identification of promising compounds for drug development or agricultural application

9.2 Overview and discussion

Initially, this doctoral Thesis emphasized the symbiotic relationship between ancestral knowledge about plants and science. The wisdom of indigenous communities, combined with scientific research, can converge to preserve the culture of indigenous groups and biodiversity, thereby paving the way for sustainable development.

This Thesis offers a comprehensive examination of terpenoids, encompassing their distribution, therapeutic properties, thermodynamic behavior, and molecular intricacies. This depth of understanding not only enriches our knowledge of natural compounds but also presents significant opportunities for application across diverse fields. For example, insights into the thermodynamic properties of the terpenoids studied can inform pharmaceutical research, aiding in drug discovery and development. This knowledge is invaluable for sustainable agriculture practices, as terpenoids can be used in plant defense mechanisms and pest control. Such insights can optimize agricultural strategies, promoting environmentally friendly farming practices. Beyond pharmaceuticals and agriculture, terpenoids find applications in various industries, including cosmetics, food additives, and fragrances, highlighting their wide-ranging utility and economic importance.

Terpenoids also find widespread applications in various industries, such as cosmetics, food additives, and fragrances, underscoring their broad utility and economic importance. Moreover, the experimental data generated in these studies are essential for populating databases used to develop group contribution models with enhanced predictive capability. These experimental findings are instrumental in refining and validating predictive models, particularly group contribution models. By utilizing the structural information of terpenoids, these models can estimate vapor pressure, enthalpy of vaporization and normal boiling point with improved accuracy and reliability. Consequently, the integration of experimental data with predictive models enhances our understanding of terpenoid behavior in different environments and applications.

9.3 Conclusions

This doctoral Thesis provides a review of terpenoids sourced from Brazilian native plants, elucidating their diverse therapeutic and cultural significance while also acknowledging the preservation of indigenous knowledge. The studies conducted in Thesis investigate both the practical applications of terpene and terpenoid compounds and technical intricacies involved, including the experimental determination of thermodynamic parameters and the assessment of predictive models for accurate estimation.

The qualitative results of this study have been presented in different articles and refer to experimental data on enthalpy of vaporization and normal boiling temperature calculated at 298.15 K and 101.325 kPa. Thermodynamic properties of terpene and terpenoid compounds were determined, some of which were previously unpublished in the literature under the experimental conditions (Table 9.2).

Table 9.2 T_{nb} and ΔH^{vap} : Properties calculated at 298.15 K and 101.325 kPa.

Compound	T_{nb} (K)	ΔH^{vap} (kJ.mol^{-1})
Bicyclo [2.2.2] -octan-2,5-dione	533.06	59.57
4-(4-Hydroxyphenyl) -2-butanone	547.68	75.10
Methyl jasmonate	563.83	79.22
4-Methyl-3-penten-2-one	403.10	39.89
Thymol methyl ether	501.77	60.16
Fenchyl alcohol	481.30	54.47
Bicyclo [4.1.0] heptane-7-carboxylic acid	516.95	79.45

A major contribution of this Thesis is its extension of gas chromatography correlation to obtain thermodynamic properties to oxygenated terpenes, significantly enhancing the analytical framework's applicability and precision. Furthermore, the meticulous analysis of molecular structures of these compounds offers valuable insights into their physicochemical behavior, enriching the understanding of their complex nature. Moreover, the validation of a specialized group contribution model designed for terpenes and terpenoids found in essential oils represents a significant advancement. This model provides a systematic approach for predicting thermodynamic properties, offering enhanced accuracy and reliability in the evaluation of these natural compounds.

In summary, this doctoral Thesis deepens the understanding of the potentials of Brazilian native plants, emphasizing their importance for human well-being, economic

development, and cultural heritage. By introducing innovative analytical techniques, clarifying molecular structures, and improving predictive models, this Thesis provides a solid basis for future research and practical implementations in diverse fields, including pharmaceuticals and sustainable agriculture.

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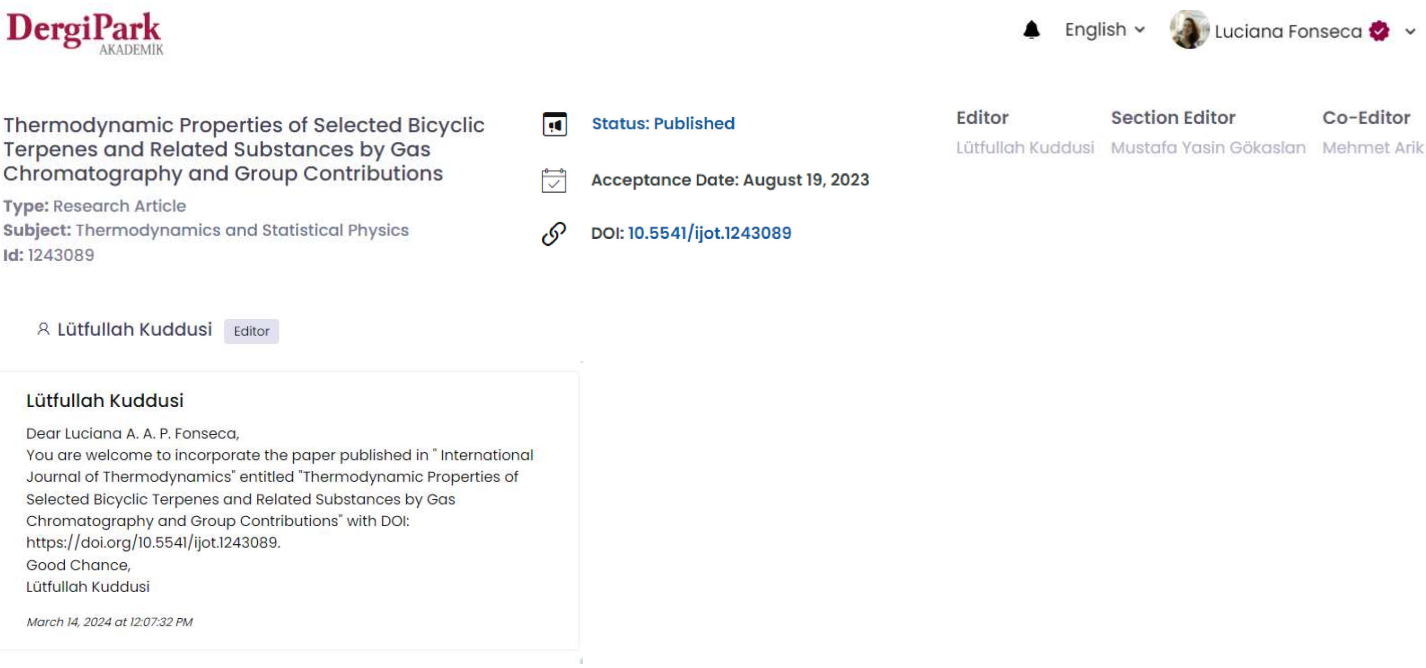
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