



Thermochemistry in the twenty-first century—quo vadis? In silico assisted diagnostics of available thermochemical data

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Abstract

Which comes first, experiment or theory? The answer is obvious—the experiment comes first. But how to be sure that the result of the experiment is reliable? Perhaps the crucial criterion is that the result should be consistent with the network of knowledge already available. In this study, we propose a step-by-step algorithm for quality diagnostics of thermochemical data on enthalpies of formation and enthalpies of phase transitions of organic compounds. The consistency of the data is studied and established using empirical structure–property correlations as well as using quantum chemical calculations. The diagnostic algorithm is exemplarily demonstrated on a series of alkyl-substituted benzophenones for which conflicting thermochemical data were available.

Keywords Enthalpy of formation · Enthalpies of phase transitions · Quantum-chemical calculations · Structure–property relationships, Centerpiece approach

Introduction

According to textbook knowledge, thermochemistry is associated with the enthalpy changes occurring in chemical reactions and/or with the phase transitions of the reactants. The enthalpies of chemical reactions are usually calculated according to Hess's law from the enthalpies of formation of reactants and products. Two common equations relate the thermochemical properties:

$$\Delta_f H_m^o(\text{g}) = \Delta H_m^o(\text{liq}) + \Delta_1^g H_m^o \quad (1)$$

$$\Delta_f H_m^o(\text{g}) = \Delta H_m^o(\text{cr}) + \Delta_{\text{cr}}^g H_m^o \quad (2)$$

Admittedly, the gas-phase enthalpy of formation, $\Delta_f H_m^o(\text{g})$, cannot be measured for the samples in the liquid or crystalline state; however, it is common in physical chemistry to name the result of the summation the condensed state enthalpy of formation, $\Delta_f H_m^o(\text{liq or cr})$, with the corresponding vaporization (or sublimation) enthalpy according to Eqs. (1) or (2) as “experimental” enthalpy of formation. The sublimation enthalpies, $\Delta_{\text{cr}}^g H_m^o$, and vaporization enthalpies, $\Delta_1^g H_m^o$, are usually measured directly calorimetrically or derived from the vapour pressure temperature dependences, whereby these two phase transition enthalpies are related to each other by Eq. (3):

$$\Delta_{\text{cr}}^g H_m^o = \Delta_1^g H_m^o + \Delta_{\text{cr}}^1 H_m^o \quad (3)$$

where $\Delta_{\text{cr}}^1 H_m^o$ is the standard molar enthalpy of fusion, easily measurable using differential scanning calorimetry (DSC). In thermochemistry, it is common to adjust all enthalpies involved in Eqs. (1)–(3) to an arbitrary but common reference temperature. In this work, we have chosen $T = 298.15 \text{ K}$ as the reference temperature.

There is a long tradition in science of relying on experimental results rather than empirical or theoretical knowledge. Authors follow this tradition unreservedly. However, all experimental enthalpies involved in Eqs. (1)–(3) could be affected by occasional or systematic errors due to equipment defects or malfunctions or insufficient sample purity. For this reason,

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any single value available in the literature should be considered suspect until some sort of validation is performed on that value. The straightforward validation consists in repeating the enthalpy measurement (preferably with a different technique). The agreement of old and new results is the best way to dispel suspicion. But what to do if the results are different? Which result is preferred? In our experience, the most recent result is most commonly used for chemical engineering calculations. Is that right? Obviously not, as both results have to be checked for consistency with the entire network of experimental thermochemical properties already available. Only after the test has been passed can the old or new value be regarded as reliable.

Structure–property relationships in physical chemistry are the most recognized empirical tool to test and establish useful regularities within the set of structurally similar molecules. These relationships are quite important from an educational point of view, as they facilitate the understanding of the available data. In addition, they also allow a reasonable prediction of properties that have not yet been studied. The best textbook example that supports these ideas is the chain length dependence of boiling points in *n*-alkanes.

One of the most popular modifications of structure–property relationships is a group additivity methodology. This methodology can be easily understood in analogy to the LEGO® game, in which any desired construction is built from a certain number of differently shaped bricks. In a highly simplified form, we could roughly estimate a property of a molecule by only collecting contributions from the constituent atoms according to the chemical formula, without considering bonding types within a molecule. It is obvious that such a primitive procedure is of little interest in chemistry, since the neighborhood of the atom generally determines the nature and strength of the bonds between atoms. For this reason, the first-order group additivity schemes, where nearest-neighbor interactions are taken into account (see Fig. 1 a and b), receive more attention.

Many different schemes of fragmentation of molecules have been proposed in the past to adequately account for the atomic environment and nearest or non-nearest neighbor interactions (e.g., Bernstein [1], Laidler [2], Allen [3]). However, Cox and Pilcher [4] show that these three methods are mathematically equivalent. It is not the subject of this work to analyze the advantages and disadvantages of these additive schemes, as a historical winner among them was ultimately the modification proposed by Benson and Buss [5]. They proposed the most practical method for predicting enthalpies of formation, entropies, heat capacities, and enthalpies of vaporization of organic compounds [5–8]. A group is defined by Benson [5, 6] as “a polyvalent atom (ligancy ≥ 2) in a molecule together with all of its ligands.” The group is written as $X-(A)_i(B)_j(C)_k(D)_l$, where X is the central atom attached to i A atoms, j B atoms, etc., as it shown in Fig. 1b. Nevertheless, the successful application of all schemes that take into account the first environment (including Benson’s) is limited to relatively simple molecules (e.g., aliphatic compounds with different functional groups). But even for the cyclic, aromatic, heterocyclic, or sterically congested molecules, the use of the Benson-like schemes is thwarted with complications. The reason for this is that the second environment is not negligible when the molecule is cyclic or complex. In the case of Benson’s scheme, numerous correction terms are proposed (e.g., ring strains for three-, four-, and five-membered rings or the gauche interaction), which partially reduce the limitations. However, the specifics of structures in organic chemistry are dimensionless and it is impractical to design countless correction terms as they generally require additional experiments. One of the possible ways to overcome the limitations of the Benson-like additive schemes could be to construct the procedure considering the second environment and a large number of parameters responsible for the non-bonded interactions. A visualization of this method is shown in Fig. 2a.

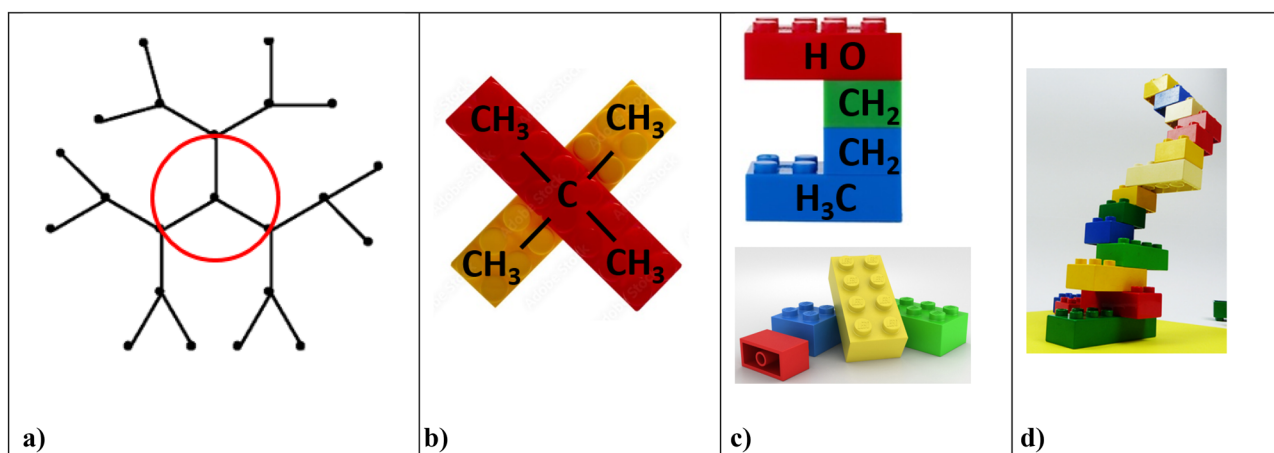


Fig. 1 Visualization of the first-order group additivity techniques

Second-order group contribution techniques incorporate important non-nearest neighbor interactions (see Fig. 2b). This methodology can also be easily understood in analogy to the PLUS-PLUS[®] game, in which any constructions are built from a large number of different fragments, which are more complex in shape than LEGO bricks (see Fig. 2c). In principle, there is no limit to the number of interaction groups which can be included (see Fig. 2d) nor to the accuracy which can be obtained when these interactions are taken into consideration. There are two limitations to this approach, however. First, there are only limited thermodynamic data available to determine the interaction contributions. Secondly, one must recognize the interactions of importance a priori, or resulting estimates will be less accurate than anticipated. The pioneering work on such a method was published by Tatevskii [9–11]. He developed remarkable bonding networks and even proposed numerical solutions for a series of aliphatic hydrocarbons [11], which, unfortunately difficult to apply to calculations of thermochemical properties because the amount of the experimental data required for the parametrization of such a method, more or less sufficient for hydrocarbons, is not sufficient even for their functionally substituted derivatives.

From this plaintive introduction, it is clear that the group additivity methodology, based solely on experimental data, fails to fulfil our expectation to accurately predict the thermochemical property of any organic molecule of interest. However, this pessimistic statement reflects the state of the art in the twentieth century. As early as the last decade of the twentieth century, enormous progress was made in the development of quantum chemical methods, which, together with the rapidly growing computing capabilities, led to previously unbelievable situations in which, for example, gas-phase enthalpies of formation can be calculated with a “chemical accuracy” of $\pm 4\text{--}5\text{ kJ}\cdot\text{mol}^{-1}$ [12]. Admittedly, the quantum-chemical (QC) methods are not free from limitations either. For example, if the calculations of relatively

“small” molecules give results on enthalpies of formation with comparable accuracy to experiment, the results for “large” molecules (with 14–20 heavy atoms) might be questionable.

The reason for the ambiguity that arises is the accumulation of possible systematic errors by simplifications specific to each QC method. However, the current state of the art in the twenty-first century opens new horizons for thermochemistry, as we believe that through a meaningful combination of the quantum chemical and the empirical structure–property methods, it is possible to combine the advantages of both methods and to overcome many of their specific limitations.

The empirical group additivity (GA) methods can hardly help the theoretical QC methods, but in contrast, the theoretical methods could contribute significantly to the development of GA. A possible way to do this is to calculate the enthalpies of formation of molecules with rare fragments for which experimental data required for parameterization is lacking or questionable. For example, the imines [13] or azides [14]. This is the subject of our upcoming publication. In this paper, the focus is on another option where the combination of the QC and GA methods is extremely fruitful. Admittedly, quality of the experimental data used for structure–property correlations is always crucial for robust conclusions. However, the last compilation of evaluated thermochemical data (enthalpies of formation and enthalpies of vaporization/sublimation) was printed in 1994 [15]. This compilation contains truly validated data for about 3000 organic compounds, since the main entries are taken from “classic” thermochemical books compiled by Cox and Pilcher [4] and by Pedley et al. [16]. It is known that Cox and Pilcher devoted their entire lives to thermochemistry. With their impeccable experience, they collected primary sources and, analyzed and recalculated the results and uncertainties according to the norms and requirements. Finally, they selected and recommended the evaluated values in

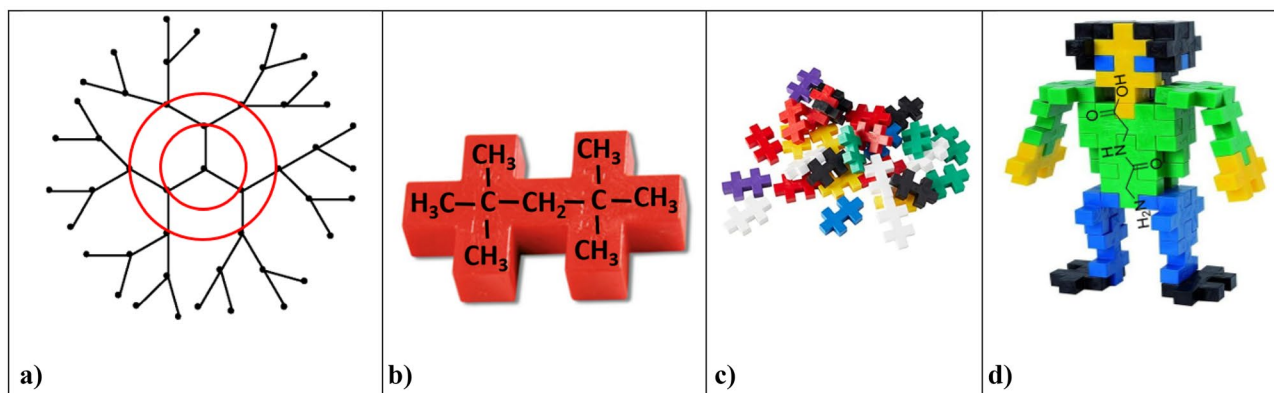


Fig. 2 Visualization of the second-order group additivity techniques

those cases where few results were available for a particular compound. But they were helpless with recommendations in cases where only a single experimental enthalpic result was found in the literature. The benefit of the subsequent books by Pedley et al. [15, 16] is that there, simple group additivity was applied to the homologous series of compounds. The apparent additivity outliers were shown to raise doubts about the quality of the experimental measurements.

As printed books become outdated in the twenty-first century, electronic databases (usually commercial ones) are coming in their place. To avoid any discussion of the content and quality of the commercial databases available, we will base our discussion on only one free database maintained by NIST Webbook [17]. This database is often used at universities to quickly obtain information about enthalpies of formation and enthalpies of phase transitions of organic compounds. However, this database is incomplete. Since 1994, hundreds of new experimental thermochemical data, mainly from Porto, Madrid, Lisbon, and Rostock, have been published in the open literature. In our experience, most of these results are still not included in the webbook, and searching for references with up-to-date thermochemical information becomes a time-consuming task in the absence of freely accessible electronic sources. However, even if the new data are found, evaluation of consistency of the new results with the existing network of thermochemical data is of paramount importance in modern science. Are the appropriate tools already available to carry out such an evaluation? This is essentially the main purpose of this work, to show that the combination of QC methods with structure–property relationships and with group additivity methodology provides a reliable diagnostics of the quality of thermochemical data for any organic molecule of interest. Since this combination encompasses the computational algorithms from simple least squares treatment of the data matrices to the quantum chemical calculations, we refer to this combination as “in silico” assisted diagnostics of available enthalpy data involved in Eqs. (1)–(3). This diagnostics, as developed in our lab, comprises a few steps.

Step I first, it is convenient to collect and analyze vaporization enthalpies, $\Delta_1^g H_m^o(298.15\text{ K})$ for a series of structurally similar molecules. In fact, among the enthalpies of phase transitions (liquid–gas, crystal–gas, and crystal–liquid), only the vaporization enthalpy obeys the additive rules and can be easily validated by this methodology. Moreover, the enthalpy of vaporization tends to correlate with physico–chemical properties (e.g., normal boiling temperatures [18] and surface tension [19]), with measurable quantities such as gas chromatographic retention indices [20] or with structural units such as the number of CH_2 groups in homologous series [21]. These different types of correlations cross-link the vaporization enthalpy of the test molecule with the network of reliable data and provide consistency or inconsistency of its numerical value.

Step II the vaporization enthalpy, $\Delta_1^g H_m^o(298.15\text{ K})$, validated in this way is helpful for the second step—diagnostics of the enthalpies of the crystal–gas and crystal–liquid phase transition enthalpies according to Eq. (3). Typically, the DSC measurements of the fusion enthalpy, $\Delta_{\text{cr}}^l H_m^o$, are less demanding compared to the sophisticated sublimation enthalpy, $\Delta_{\text{cr}}^g H_m^o$, measurements. Due to very low volatility of the crystalline compounds, the experimental sublimation enthalpies could be subject to a systematic error. But with the validated $\Delta_1^g H_m^o(298.15\text{ K})$ value from the first step and the fusion enthalpy, $\Delta_{\text{cr}}^l H_m^o$, (adjusted to 298.15 K), the “expected” sublimation enthalpy, $\Delta_{\text{cr}}^g H_m^o(298.15\text{ K})$, can be calculated with Eq. (3) and compared with the experimental result, giving the desired confidence also for this type of phase transition enthalpy.

Step III in the third step, the “in silico” diagnostics is continued by using Eqs. (1) and (2). For this purpose, few mid-level G^* -family composite QC methods of, e.g., G3MP2 [22], G4MP2 [23], G4 [24], as well as the CBS-APNO [25] method, are used to derive the gas-phase enthalpies of formation, $\Delta_f H_m^o(g, 298.15\text{ K})$, for several similarly shaped molecules for which reliable experimental data are available. Since the G^* methods are similarly composed, their possible systematic errors may be the same or close in magnitude. In addition, to independently confirm the correctness of $\Delta_f H_m^o(g, 298.15\text{ K})_{\text{theor}}$ obtained from the G^* methods, the enthalpy of formation should be calculated using the mid-level composite method CBS-APNO, which differs from G^* in a number of computational steps. Usually, the chosen QC methods agree well with experiment and validate the calculations for the desired subclass of molecules and in particular the “theoretical” $\Delta_f H_m^o(g, 298.15\text{ K})$ value for the molecule of interest.

Step IV in step four, depending on the physical state of the compound, the condensed state enthalpies of formation, $\Delta_f H_m^o(\text{liq or cr}, 298.15\text{ K})$, are estimated with Eqs. (1) and (2) as the difference between the “theoretical” gas-phase enthalpy of formation and the $\Delta_1^g H_m^o(298.15\text{ K})$ or $\Delta_{\text{cr}}^g H_m^o(298.15\text{ K})$ values validated in steps one and two. The “theoretical” condensed state enthalpies of formation derived in this way are compared with the experimental result available for the molecule of interest. Provided that the combustion experiments were carried out correctly and with sufficient purity of the sample, the agreement between “theoretical” and experimental results is usually within the “chemical accuracy” of ± 4 to $5\text{ kJ}\cdot\text{mol}^{-1}$ and, in our experience, even better.

In our practice, however, agreement was sometimes not reached. Which method is wrong? To answer this question, a more careful search for stable conformers is performed and the QC calculations are repeated using other appropriate methods. In the case that the combustion experiments were

carried out in our laboratory, the sample was additionally purified and carefully analyzed for impurities and traces of water, and the measurements were repeated under changed experimental conditions (e.g., higher or lower pressure in the bomb, addition of auxiliary materials). As a rule, this additional effort resulted in reasonable agreement between the experimental and the QC-predicted value.

In addition to the QC methods, other “in silico” methods are also used for diagnostics of the gas-phase and the liquid-phase formation enthalpies. These values also obey group additivity rules [26] and if the new enthalpy of formation deviates from the expected model without obvious structural peculiarities, this value should be considered questionable. One of the best flags to possible experimental errors is a large discrepancy between experimental and GA calculated values—especially if other, closely related compounds show no such discrepancy. Moreover, different types of structure–property correlations could also be applied to understand if the new value fits into the network of data already available. For example, structure–property analysis of thermodynamic properties (enthalpies of vaporization and enthalpies of formation) in chemical families of *R*-substituted benzamides and *R*-substituted benzoic acids, as well as *R*-substituted benzenes, has revealed the general linear interrelations between these chemical families [27]. These linear correlations can be used to establish the internal consistency of the experimental results available for each chemical series and provide a simple way to predict the thermodynamic properties of benzenes with different combinations of substituents *R* in the benzene ring.

This paper is written for a special collection “Bonding and Structure” dedicated to Prof. Vladimir M. Tatevsky (1914–1999) who significantly contributed to the development of quantum mechanical theory and methods for calculating the properties of molecules based on classical chemical structure theory. In this context, it is important to acknowledge his contributions both to the development of the current QC method and to the development of property predictions. Our work has benefited directly from modern

trends in quantum chemistry. However, we are more grateful to Tatevsky for inspiration related to his idea of group additivity regarding the “second-order” environment as shown in Fig. 2. Predicting properties using this idea in Tatevsky’s original form is impractical. However, we have modified this idea and developed a “centerpiece” approach [28, 29], in which the role of the “first-order” environment is played by a large molecule (see Fig. 3a) with well-defined experimental data.

The role of the necessary “second-order” environment is delegated to various substituents (see Fig. 3b and c) attached to this “centerpiece” molecule. Details of this approach will be discussed using thermochemical data on alkyl-substituted benzophenones (see Fig. 4).

The aim of this work is to demonstrate how to apply “in silico” methods and the “centerpiece” approach for the diagnostics of thermochemical properties available for a set of alkyl-substituted benzophenones (see Fig. 4), where there are some experimental data of questionable quality.

We hope that despite the complex four-step procedure proposed in this work, in silico diagnostics in general could be useful for data evaluation and recommendation of reliable thermodynamic information needed for quantitative understanding of structure–property relationships in molecules and for high-quality chemical-engineering calculations.

Materials and methods

Commercially available samples of benzophenone (Sigma-Aldrich, ReagentPlus®, 99%) and 3'-methylbenzophenone (Sigma-Aldrich, 99%) have been used in this work. Samples were used for vapor pressure measurements without additional purification. However, before starting the vapor pressure measurements using the transpiration method, the samples were conditioned “in situ” in the saturator, as described in the Electronic Supporting Materials (ESI). No impurities (greater than 0.001 mass fraction) were detected in samples using a gas

Fig. 3 Visualization of the second-order “centerpiece” group additivity approach

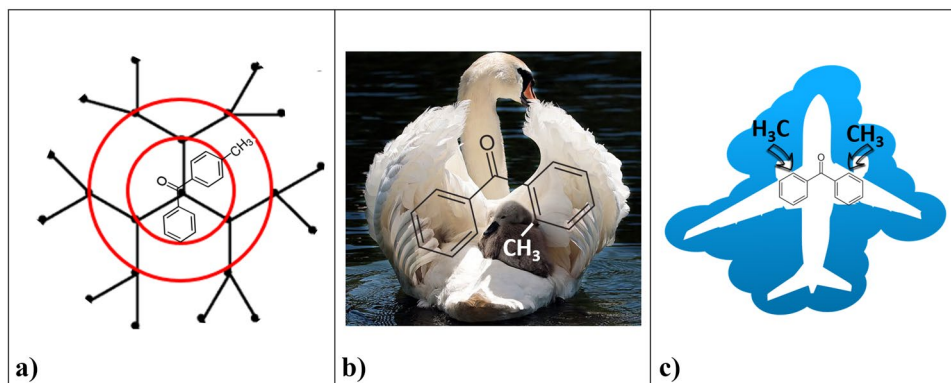
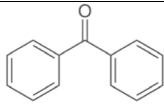
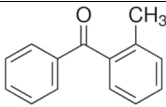
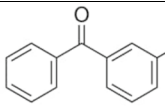
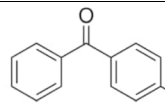
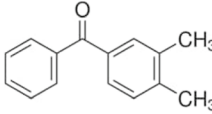
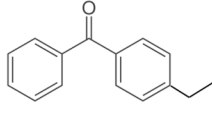
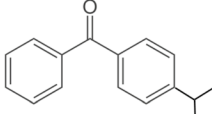
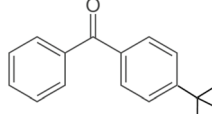


Fig. 4 Alkyl-substituted benzophenones studied in this work

			
benzophenone	2-methyl-benzophenone	3-methyl-benzophenone	4-methyl-benzophenone
			
3,4-dimethyl-benzophenone	4-ethyl-benzophenone	4-iso-propyl-benzophenone	4-tert-butyl-benzophenone

chromatograph equipped with a capillary column HP-5 and a flame ionization detector. Vapor pressures of benzophenones at different temperatures were measured by using the transpiration method [30, 31]. The standard molar enthalpies of vaporization, $\Delta_1^g H_m^o$, were derived from the temperature dependences of vapor pressures. The quantum-chemical composite G4 [24] method from Gaussian 16 software [32] was used for calculations of enthalpy H_{298} values, which were finally converted to the $\Delta_f H_m^o(g)$ and discussed.

Results and discussion

Absolute vapor pressures and thermodynamics of vaporization/sublimation

The experimental vapor pressures, p_i , at different temperatures measured in this work for benzophenone and 3'-methyl-benzophenone are given in Table 1, and they were approximated by the following equation [30]:

$$R \times \ln(p_i/p_{\text{ref}}) = a + \frac{b}{T} + \Delta_1^g C_{p,m}^o \times \ln\left(\frac{T}{T_0}\right) \quad (4)$$

where $\Delta_1^g C_{p,m}^o$ is the difference of the molar heat capacities of the gas and the liquid phases respectively (see Table S1), a and b are adjustable parameters, $R = 8.31446 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ is the molar gas constant, and the reference pressure $p_{\text{ref}} = 1 \text{ Pa}$. The arbitrary temperature T_0 given in Eq. (4) was chosen to be $T_0 = 298.15 \text{ K}$. The results of the vapor pressure measurements by the transpiration method are given in Table 1.

Vapor pressure measured at different temperatures, T , measured in this work, as well as those available from the literature, has been used to derive the enthalpies of sublimation/vaporization using the following equation:

$$\Delta_{\text{cr,l}}^g H_m^o(T) = -b + \Delta_{\text{cr,l}}^g C_{p,m}^o \times T \quad (5)$$

Sublimation entropies at temperatures T were also derived from the vapor pressure temperature dependences using Eq. (6):

$$\Delta_{\text{cr,l}}^g S_m^o(T) = \Delta_{\text{cr,l}}^g H_m^o/T + R \ln(p_i/p^o) \quad (6)$$

with $p^o = 0.1 \text{ MPa}$. The original absolute vapor pressures available in the literature have been also treated by using Eqs. (5) and (6) in order to evaluate enthalpies of sublimation/vaporization at 298.15 K (see Table 2) in the same way as our own results. Uncertainties of the literature results have been also re-assessed in the same way [33, 34], as for our own experimental results.

Our new complementary measurements have helped to ascertain the available vaporization enthalpies for benzophenone and for 3-methyl-benzophenone. The vaporization enthalpies obtained from different methods for each alkyl-substituted benzophenone were evaluated and the agreed values averaged using the experimental uncertainties as a weighting factor (see Table 2).

Step I: diagnostics of consistency of vaporization enthalpies

Kovats's retention indices for diagnostics of consistency of vaporization enthalpies

One of the methods successfully used for diagnostics of consistency of the available $\Delta_1^g H_m^o(298.15 \text{ K})$ values (see Table 2) is the method based on chromatographic retention indices [20] [43]. It is known, that the $\Delta_1^g H_m^o(298.15 \text{ K})$ values correlate linearly with Kovats's indices for various homologous series of alkanes, alkylbenzenes, aliphatic ethers, and alcohols or in a series of structurally similar compounds [20]. The following linear correlation was obtained when the $\Delta_1^g H_m^o(298.15 \text{ K})$ values are correlated with the J_x values for the benzophenones collected in Table 3:

$$\Delta_1^g H_m^o(298.15 \text{ K})/(\text{kJ}\cdot\text{mol}^{-1}) = 33.7 + 0.0276 \times J_x \text{ with } (R^2 = 0.922) \quad (7)$$

The vaporization enthalpies for the set of the methyl-substituted benzophenones derived from the J_x correlation (see Table 3, column 4) are in agreement with those from

Table 1 Results of the transpiration method for benzophenones: absolute vapor pressures p , standard molar vaporization enthalpies, and standard molar vaporization entropies

T (K) ^a	m (mg) ^b	$V(N_2)$ (dm ³) ^c	T_a (K) ^d	Flow (dm ³ ·h ⁻¹)	p (Pa) ^e	$u(p)$ (Pa) ^f	$\Delta_1^g H_m^o(T)$ (kJ·mol ⁻¹)	$\Delta_1^g S_m^o(T)$ (J·K ⁻¹ ·mol ⁻¹)
Benzophenone: $\Delta_1^g H_m^o(298.15 \text{ K}) = (78.5 \pm 0.7) \text{ kJ}\cdot\text{mol}^{-1}$								
$\ln(p/p_{\text{ref}}) = \frac{335.3}{R} - \frac{104806.2}{RT} - \frac{88.1}{R} \ln \frac{T}{298.15}$; $p_{\text{ref}} = 1 \text{ Pa}$								
324.1	7.40	59.05	293.2	1.14	1.77	0.05	76.3	144.4
330.8	9.60	42.86	292.2	1.53	3.07	0.08	75.7	142.4
336.2	7.10	20.44	292.2	6.13	4.72	0.12	75.2	140.9
341.2	11.00	21.05	292.2	1.63	7.05	0.20	74.8	139.6
346.1	6.90	9.247	291.7	1.52	10.01	0.28	74.3	138.2
347.0	10.70	13.33	292.7	1.86	10.81	0.30	74.2	138.0
351.2	10.90	10.03	291.7	1.52	14.54	0.39	73.9	136.9
351.5	11.50	10.37	292.2	5.76	14.87	0.40	73.8	136.8
352.4	9.00	7.523	293.2	1.53	16.10	0.43	73.8	136.7
354.0	12.70	9.405	292.2	5.64	18.08	0.48	73.6	136.4
355.4	11.60	7.905	291.7	1.53	19.61	0.52	73.5	135.9
356.2	10.90	7.013	292.2	1.53	20.80	0.55	73.4	135.7
357.2	14.00	8.286	292.2	1.63	22.61	0.59	73.3	135.6
359.6	13.60	6.792	292.2	1.63	26.77	0.69	73.1	135.0
360.3	11.10	5.250	292.2	4.09	28.26	0.73	73.1	134.9
362.7	7.00	2.875	292.2	1.50	32.53	0.84	72.9	134.1
367.6	11.10	3.250	292.2	1.95	45.60	1.16	72.4	133.1
369.2	9.00	2.340	292.2	1.95	51.33	1.31	72.3	132.8
373.1	5.60	1.138	292.2	1.95	65.67	1.67	71.9	131.9
3'-Methyl-benzophenone: $\Delta_1^g H_m^o(298.15 \text{ K}) = (80.4 \pm 0.6) \text{ kJ}\cdot\text{mol}^{-1}$								
$\ln(p/p_{\text{ref}}) = \frac{340.1}{R} - \frac{108842.0}{RT} - \frac{95.4}{R} \ln \frac{T}{298.15}$; $p_{\text{ref}} = 1 \text{ Pa}$								
303.2	0.13	18.91	297.5	4.93	0.085	0.007	79.92	147.4
308.2	0.13	11.51	295.3	4.93	0.142	0.009	79.44	145.8
308.3	0.02	2.140	295.8	3.05	0.142	0.009	79.43	145.7
313.2	0.14	7.371	296.6	3.05	0.236	0.011	78.97	144.5
318.2	0.12	3.863	296.9	3.05	0.376	0.014	78.49	142.8
320.2	0.14	3.863	297.0	4.93	0.458	0.016	78.30	142.3
323.2	0.15	3.152	296.1	3.05	0.577	0.019	78.01	141.1
323.2	0.14	3.152	297.4	3.05	0.574	0.019	78.01	141.1
328.2	0.16	2.237	296.8	3.05	0.892	0.027	77.54	139.6
333.2	0.23	2.135	299.5	3.05	1.346	0.039	77.06	138.1
338.2	0.21	1.271	297.5	3.05	2.072	0.057	76.58	136.8
341.2	0.24	1.162	295.6	3.03	2.618	0.070	76.29	135.9
344.2	0.24	0.909	296.2	3.03	3.288	0.087	76.01	135.0
347.2	0.25	0.720	296.8	1.96	4.324	0.113	75.72	134.6
350.2	0.25	0.589	297.4	1.96	5.270	0.157	75.44	133.5
353.2	0.25	0.467	297.9	1.00	6.852	0.196	75.15	133.1
356.2	0.25	0.383	298.4	1.00	8.316	0.233	74.87	132.1
359.2	0.24	0.292	298.7	1.00	10.281	0.282	74.58	131.3
362.2	0.25	0.250	298.9	1.00	12.417	0.335	74.29	130.4

^aSaturation temperature measured with the standard uncertainty ($u(T) = 0.1 \text{ K}$)^bMass of transferred sample condensed at $T = 273 \text{ K}$ ^cVolume of nitrogen ($u(V) = 0.005 \text{ dm}^3$) used to transfer m ($u(m) = 0.0001 \text{ g}$) of the sample. Uncertainties are given as standard uncertainties^d T_a is the temperature of the soap bubble meter used for measurement of the gas flow^eVapor pressure at temperature T , calculated from the m and the residual vapor pressure at the condensation temperature calculated by an iteration procedure^fStandard uncertainties were calculated with $u(p_i/\text{Pa}) = 0.005 + 0.025(p_i/\text{Pa})$ for pressures below 5 Pa and with $u(p_i/\text{Pa}) = 0.025 + 0.025(p_i/\text{Pa})$ for pressures from 5 to 3000 Pa. The standard uncertainties for T , V , p , and m are standard uncertainties with 0.683 confidence level. Uncertainty of the vaporization enthalpy $U(\Delta_1^g H_m^o)$ is the expanded uncertainty (0.95 level of confidence) calculated according to procedure described elsewhere [33, 34]. Uncertainties include uncertainties from the experimental conditions and the fitting equation, vapor pressures, and uncertainties from adjustment of vaporization enthalpies to the reference temperature $T = 298.15 \text{ K}$

conventional methods (see Table 2). Such good agreement can be seen as additional validation of the experimental data measured and evaluated in this work. It can be seen from Table 3 that differences between experimental vaporization enthalpies and values calculated according to Eq. (7) are mostly below $0.5 \text{ kJ}\cdot\text{mol}^{-1}$. Hence, the uncertainties of the “empirical” enthalpies of vaporization which are estimated from the correlation of $\Delta_1^g H_m^o(298.15 \text{ K})$ with Kovats’s indices are evaluated with an uncertainty of $\pm 0.5 \text{ kJ}\cdot\text{mol}^{-1}$.

Normal boiling temperatures for diagnostics of vaporization enthalpies

Another possible option for determining the consistency of the experimental results on vaporization enthalpies for alkyl-substituted benzophenones is also the correlation of enthalpies of vaporization with their normal boiling temperatures [18]. The literature data [42] available on the normal boiling temperatures, T_b , for acetophenone, benzophenone, and alkyl-substituted benzophenones were taken for correlation with the $\Delta_1^g H_m^o(298.15 \text{ K})$ values (see Table 4) evaluated in our recent work [45]. The $\Delta_1^g H_m^o(298.15 \text{ K})$ values correlated with the T_b values with the following linear correlation:

$$\Delta_1^g H_m^o(298.15 \text{ K})/(\text{kJ}\cdot\text{mol}^{-1}) = 0.2204 \times T_b - 49.2$$

with ($R^2 = 0.985$) (8)

The vaporization enthalpies for methyl-benzophenones derived from the correlations with T_b (see Table 4, column 4) agree sufficiently with those evaluated in Table 2. This correlation was useful to estimate the vaporization enthalpies of 3,4-dimethyl-benzophenone, 4-ethyl-benzophenone, 4-iso-propyl-benzophenone, and 4-tert-butyl-benzophenone (see Table 4, column 4) where the results of the conventional methods were not available. The $\Delta_1^g H_m^o(298.15 \text{ K})$ estimates for 3,4-dimethyl-benzophenone, 4-ethyl-benzophenone, 4-iso-propyl-benzophenone, and 4-tert-butyl-benzophenone derived using normal boiling temperatures agree well with results obtained from other methods (see Table 2). The uncertainties of the “empirical” enthalpies of vaporization which are estimated from the correlation of $\Delta_1^g H_m^o(298.15 \text{ K})$ with T_b are assigned to be of $\pm 2.0 \text{ kJ}\cdot\text{mol}^{-1}$.

Structure–property correlation between families for diagnostics of consistency of vaporization enthalpies

The evaluation of the thermochemical properties of substituted acetophenones was the subject of our recent study [45]. We can benefit from the use of the evaluated vaporization enthalpies of the alkyl-substituted acetophenones (see Table 5, column 2), to correlate

with the alkyl-substituted benzophenones (see Table 5, column 3), which is under study in this work. Structure–property analysis of vaporization enthalpies in chemical families of R-substituted acetophenones and R-substituted benzophenones has revealed the linear interrelationships between these chemical families with the following equation:

$$\Delta_1^g H_m^o(298.15 \text{ K})/(\text{kJ}\cdot\text{mol}^{-1}) = 1.3316 \times \Delta_1^g H_m^o(298K, R - acetophenone) + 1.1 \text{ with } (R^2 = 0.979) \quad (9)$$

As can be seen from results in Table 5, very good correlation between the vaporization enthalpies evaluated for both families can be taken as evidence of the internal consistency of the $\Delta_1^g H_m^o(298.15 \text{ K})$ values within each data set. The estimated vaporization enthalpies of the alkyl-benzophenones (see Table 5, column 4) agree (within the assigned uncertainties of $\pm 1.0 \text{ kJ}\cdot\text{mol}^{-1}$, 0.95 level, $k = 2$) with the results of other methods given in Table 2.

Step II: diagnostics of consistency of phase transitions

Benzophenone, 4-methyl-benzophenone, and 3,4-dimethyl-benzophenone are solids at room temperature. The experimental sublimation enthalpies for these benzophenones are now known from the literature. The diagnostics of their consistency with the vaporization enthalpies evaluated in Step I is performed in this section.

According to most recent precise DSC studies, there are two polymorphs α and β that can exist at room temperature for benzophenone [37]. Polymorph α melts at $321.3 \pm 0.3 \text{ K}$ with an enthalpy of fusion of $\Delta_{cr}^l H_m^o = 18.6 \pm 0.3 \text{ kJ}\cdot\text{mol}^{-1}$. Polymorph β melts at $298.3 \pm 0.3 \text{ K}$ with an enthalpy of fusion of $\Delta_{cr}^l H_m^o = 14.5 \pm 0.3 \text{ kJ}\cdot\text{mol}^{-1}$. The enthalpy of sublimation of benzophenone in the polymorphic α -form, $\Delta_{cr}^g H_m^o(298.15 \text{ K}) = 95.0 \pm 0.1 \text{ kJ}\cdot\text{mol}^{-1}$, was measured using the static method [37]. The enthalpy of fusion of the α -form of benzophenone was adjusted to the reference temperature $T = 298.15 \text{ K}$ as it shown in Table 6 with the result $\Delta_{cr}^l H_m^o(298.15 \text{ K}) = 17.4 \pm 0.5 \text{ kJ}\cdot\text{mol}^{-1}$.

With these results using Eq. (10), we can calculate the enthalpy of vaporization of benzophenone as follows:

$$\Delta_1^g H_m^o(298.15K) = \Delta_{cr}^g H_m^o(298.15K, \alpha) - \Delta_{cr}^l H_m^o(298.15K, \alpha)$$

$$= (95.0 - 17.4) = 77.6 \pm 0.5 \text{ kJmol}^{-1} \quad (10)$$

This result is in excellent agreement with those measured by conventional methods (see Table 2), demonstrating the reliability of phase transitions for benzophenone. Unfortunately, the enthalpies of fusion for 4-methyl-benzophenone and 3,4-dimethyl-benzophenone cannot be found in the

Table 2 Compilation of enthalpies of vaporization/sublimation $\Delta_{l,cr}^g H_m^o$, $\Delta_l^g H_m^o$ for the benzophenone derivatives derived in this work and from the data available in the literature

Compound CAS	M^a	T range K	$\Delta_{l,cr}^g H_m^o(T_{av})$ kJ·mol ⁻¹	$\Delta_{l,cr}^g H_m^o(298.15\text{ K})^b$ kJ·mol ⁻¹	Ref
Benzophenone (liq) 119–61-9	IP/E	355–579	64.8 ± 0.3	78.4 ± 2.7	35 [35]
	S	308.2–384.8	73.7 ± 0.1	77.9 ± 0.8	36 [36]
	S	293.1–364.48	75.6 ± 0.2	78.1 ± 0.5	37 [37]
	PhT			77.6 ± 0.5	Table 6
	T	324.1–373.1	74.2 ± 0.6	78.5 ± 0.7	Table 1
				78.0 ± 0.2 ^c	Average
2-Methyl-benzophenone (liq) 131–58-8	n/a	435–580	64.4 ± 2.0	84.4 ± 2.3	38 [38]
	C	523	141.8 ± 1.7	81.2 ± 1.7	39 [39]
	J_x			80.7 ± 0.5	Table 3
				80.9 ± 0.5 ^c	Average
3-Methyl-benzophenone (liq) 643–65-2	n/a	445–585	67.8 ± 2.0	(88.5 ± 2.3)	38 [38]
	C	523	146.2 ± 1.2	85.6 ± 1.7	39 [39]
	T	303.2–362.2	77.2 ± 0.5	80.4 ± 0.6	Table 1
	J_x			80.5 ± 0.5	Table 3
				80.7 ± 0.4 ^c	Average
4-Methyl-benzophenone (cr) 134–84-9	C	401	120.8 ± 1.0	97.3 ± 1.0	39 [39]
	SC			98.5 ± 1.0	40 [40]
				97.9 ± 0.7 ^c	Average
4-Methyl-benzophenone (liq)	n/a	450–492	71.9 ± 2.0	(88.4 ± 2.3)	38 [38]
	PhT			80.0 ± 1.5	Table 6
	J_x			80.5 ± 0.5	Table 3
				80.5 ± 0.5 ^c	Average
3,4-Dimethyl-benzophenone (cr) 2571–39-3	C	401	134.5 ± 0.8	107.9 ± 5.4	41 [41]
	PhT			90.7 ± 5.5	Table 6
3,4-Dimethyl-benzophenone (liq)	BP	411–614	68.0 ± 1.6	88.8 ± 2.0	Table S2
	T_b			87.9 ± 2.0	Table 4
	CP			87.6 ± 1.0	Table S3
					87.9 ± 0.8 ^c
4-Ethyl-benzophenone 18220–90-1	SPC			87.1 ± 1.0	Table 5
	BP	447–605	64.2 ± 2.4	86.7 ± 3.0	Table S2
	T_b			87.0 ± 2.0	Table 4
4-Iso-propyl-benzophenone 18864–76-1	CP			86.4 ± 1.0	Table S3
				86.5 ± 0.9 ^c	Average
	SPC			87.3 ± 1.0	Table 5
4-Tert-butyl-benzophenone 22679–54-5	T_b			86.5 ± 2.0	Table 4
	CP			89.3 ± 1.0	Table S3
				88.7 ± 0.9 ^c	Average
4-Tert-butyl-benzophenone	SPC			88.8 ± 1.0	Table 5
	BP	424–648	68.3 ± 2.8	94.9 ± 3.0	Table S2
	T_b			91.4 ± 2.0	Table 4
	CP			91.6 ± 1.0	Table S3
				91.8 ± 0.9 ^c	Average
	SPC			91.7 ± 1.0	Table 5

^aTechniques: T transpiration method, C Calvet microcalorimetry, SC method based on solution calorimetry, IP inclined-piston gauge manometry, E ebulliometry, n/a not available, J_x from correlation of experimental vaporization enthalpies with Kovats's indices (see text), S static method, PhT calculated as the difference of phase transitions (see Table 6), BP from boiling points at different temperatures available from the literature [42], T_b from correlation of experimental vaporization enthalpies with normal boiling temperatures (see text), CP derived according to the “centerpiece” approach (see text), SPC derived from structure–property correlations (see text)

^bVapor pressures available in the literature were treated using Eqs. (2) and (3) with help of heat capacity differences from Table S1 to evaluate the enthalpy of vaporization at 298.15 K in the same way as our own results in Table 1. Uncertainties of the vaporization/sublimation enthalpies $U(\Delta_{l,cr}^g H_m^o, \Delta_l^g H_m^o)$ are the expanded uncertainty (0.95 level of confidence) calculated according to procedure described elsewhere [33, 34]

^cWeighted mean value (uncertainties were taken as the weighing factor). Values in parenthesis were excluded from the calculation of the mean. Values in bold are recommended for further thermochemical calculations

Table 3 Correlation of vaporization enthalpies, $\Delta_1^g H_m^o$ (298.15 K), of benzophenones with their Kovats's indices (J_x)

Compound	J_x^a	$\Delta_1^g H_m^o(298\text{ K})_{\text{exp}}^b$ kJ·mol ⁻¹	$\Delta_1^g H_m^o(298\text{ K})_{\text{calc}}^c$ kJ·mol ⁻¹	Δ^d kJ·mol ⁻¹
Benzophenone	1603	78.1 ± 0.5	77.9	0.2
2-Methyl-benzophenone	1704	81.2 ± 1.7	80.7	0.5
3-Methyl-benzophenone	1694	80.4 ± 0.6	80.5	-0.1
4-Methyl-benzophenone	1694	80.0 ± 1.5	80.5	-0.5

^aKovats's indices, J_x , on the standard non-polar column SE-30[44]^bSelected experimental data (given in italic in Table 2)^cCalculated using Eq. (7): $\Delta_1^g H_m^o(298.15\text{ K}) / (\text{kJ}\cdot\text{mol}^{-1}) = 33.7 + 0.0276 \times J_x$ with ($R^2 = 0.922$) and with the assessed uncertainty of $\pm 0.5\text{ kJ}\cdot\text{mol}^{-1}$ (expanded uncertainty 0.95 level of confidence)^dDifference between columns 3 and 4 in this table

literature. Only the melting temperatures were found (see Table 6). For this reason, the diagnosis of phase transitions for these compounds was performed using the enthalpies of fusion estimated according to Walden's rule, as described below.

In 1908, Walden found that the ratio according to Eq. (11) can be considered a constant (Walden's constant) [46]:

$$\text{WC} = \frac{\Delta_{\text{cr}}^1 H_m^o}{T_{\text{fus}}} = \Delta_{\text{cr}}^1 S_m^o = 56.5 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1} \quad (11)$$

This observation was supported by experimental results from 35 compounds. A prerequisite for this constancy is that the compounds in the liquid state do not associate. Equation (12) is known as Walden's rule for thermochemistry [48]. Walden's rule is derived from the general Gibbs–Helmholtz thermodynamic equation:

$$\Delta_{\text{cr}}^1 G_m^o = \Delta_{\text{cr}}^1 H_m^o - T_{\text{fus}} \times \Delta_{\text{cr}}^1 S_m^o \quad (12)$$

where $\Delta_{\text{cr}}^1 G_m^o$ is the standard molar Gibbs energy of the solid–liquid phase transition and $\Delta_{\text{cr}}^1 S_m^o$ is the standard molar fusion entropy. At equilibrium, $\Delta_{\text{cr}}^1 G_m^o = 0$ and Walden's

constant is equal to $\Delta_{\text{cr}}^1 S_m^o$. The fundamental meaning of the latter equality is that the structure of the solid and liquid phase is in principle very close and determined (e.g., by “non-associated” compounds) mainly by the weak van der Waals forces. The “classic” contribution of $56.5\text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ suggested by Walden may be considered a constant entropic “penalty” for the re-organization of both “non-associated” phases during fusion [48].

In a series of our recent work, we have shown that the “classic” Walden constant is also valid for different families of organic compounds, such as R-acetanilides with R = alkyl, F, Cl, Br, NO₂, NH₂, OH, OCH₃ [49], R-substituted benzamides [50], and even for nucleobases [48]. We have found that for these series, the WC deviates from the “classic” value of $56.5\text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ by only about $\pm 10\text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$. Such a “modified” Walden constant helps not only in evaluating the consistency of experimental fusion data within a set of similarly structured compounds, but Walden's rule also serves as a valuable tool for estimating missing fusion enthalpies of organic compounds of interest (e.g., for 4-methyl-benzophenone and 3,4-dimethyl-benzophenone in this work) provided their melting temperatures are available.

Table 4 Correlation of vaporization enthalpies, $\Delta_1^g H_m^o$ (298.15 K), of acetophenone and benzophenone derivatives with their normal boiling temperatures (T_b)

Compound	T_b^a K	$\Delta_1^g H_m^o(298\text{ K})_{\text{exp}}$ kJ·mol ⁻¹	$\Delta_1^g H_m^o(298\text{ K})_{\text{calc}}^b$ kJ·mol ⁻¹	Δ^c kJ·mol ⁻¹
Acetophenone	475.8	55.4 ± 0.3 [45]	55.6	-0.2
Benzophenone	578.6	78.0 ± 0.2 [Table 2]	78.3	-0.3
2'-Methyl-benzophenone	582.7	81.2 ± 1.7 [39]	79.2	2.0
3'-Methyl-benzophenone	586.2	80.4 ± 0.6 [Table 1]	79.9	0.5
4'-Methyl-benzophenone	599.2	81.0 ± 0.9 [45]	82.8	-1.8
3,4-Methyl-benzophenone	622	-	87.9 ± 2.0	-
4'-Ethyl-benzophenone	618	-	87.0 ± 2.0	-
4'-Iso-propyl-benzophenone	616	-	86.5 ± 2.0	-
4'-Tert-butyl-benzophenone	638	-	91.4 ± 2.0	-

^aNormal boiling temperatures, T_b , [42]^bCalculated using Eq. (8): $\Delta_1^g H_m^o(298.15\text{ K}) / (\text{kJ}\cdot\text{mol}^{-1}) = 0.2204 \times T_b - 49.2$ with ($R^2 = 0.985$) and with the assessed uncertainty of $\pm 2.0\text{ kJ}\cdot\text{mol}^{-1}$ (expanded uncertainty 0.95 level of confidence)^cDifference between columns 3 and 4 in this table

Table 5 Correlation of evaluated vaporization enthalpies, $\Delta_1^g H_m^o(298.15\text{ K})$, of alkyl-substituted acetophenones and alkyl-substituted benzophenone families (in $\text{kJ}\cdot\text{mol}^{-1}$)

R	4-R-Acetophenone	4-R-Benzophenone		Δ^b
	$\Delta_1^g H_m^o(298.15\text{ K})$	$\Delta_1^g H_m^o(298.15\text{ K})$ (Table 2)	$\Delta_1^g H_m^o(298\text{ K})_{\text{calc}}^a$	
R = Me	61.5 ± 0.3 [45]	80.5 ± 0.5	80.8 ± 1.0	-0.3
R = Et	66.4 ± 0.6 [45]	86.5 ± 0.9	87.3 ± 1.0	-0.8
R = iso-Pr	67.5 ± 1.3 (Table S5)	88.7 ± 0.9	88.8 ± 1.0	-0.1
R = t-Bu	69.7 ± 1.3 (Table S5)	91.8 ± 0.9	91.7 ± 1.0	0.1
R = 2,3-diMe	66.2 ± 2.0 (Table S7)	87.9 ± 0.8	87.1 ± 1.0	0.8

^aCalculated using Eq. (9): $\Delta_1^g H_m^o(298.15\text{ K}) / (\text{kJ}\cdot\text{mol}^{-1}) = 1.3316 \times \Delta_1^g H_m^o(298.15\text{ K}, \text{R-acetophenone}) + 1.1$ with ($R^2 = 0.979$)

^bDifference between columns 3 and 4 in this table

Moreover, the “modified” Walden rule often helps to evaluate available phase transition data according to the general equation Eq. (3) as shown above for benzophenone.

We used the Walden constant = $57.9\text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ calculated from the fusion data available for benzophenone (see Table 6) and calculated the required fusion enthalpies for 4-methyl-benzophenone and 3,4-dimethyl-benzophenone for diagnostic purposes (see Table 6, column 3). These fusion enthalpies were adjusted to $T = 298.15\text{ K}$ and used in Eq. (3) to estimate the $\Delta_1^g H_m^o(298.15\text{ K})$ values for both compounds (see Table 6, column 7). The resulting values are compared in Table 2 with those derived by other techniques and they show good agreement, reflecting the consistency of the phase transitions (liquid–gas, solid–gas, and solid–liquid) also for 4-methyl-benzophenone and 3,4-dimethyl-benzophenone.

Step III: gas-phase standard molar enthalpies of formation from quantum chemistry

As already mentioned in introduction, the recent development of quantum chemistry methods in twentieth and twenty-first

centuries makes it promising to calculate enthalpies of formation $\Delta_f H_m^o(\text{g})$ at the level of “chemical accuracy” [12, 51]. In particular, this success has made the composite methods of the G*-family a valuable tool for the cross-validation of results from experimental and computational thermochemistry. Agreement between the experimental and theoretical $\Delta_f H_m^o(\text{g}, 298.15\text{ K})$ values could provide a criterion for mutual validation of both results. In addition, this valuable information helps in evaluating the quality of the thermochemical data for compounds under study.

Stable conformers were found by using a computer code named CREST (conformer-rotamer ensemble sampling tool) [52] and optimized with the B3LYP/6-31 g(d,p) method [53]. The energies E_0 and the enthalpies H_{298} of the most stable conformers (see Table 7 and Table S8) were finally calculated by using the G4 method.

The H_{298} values were converted to the standard molar enthalpies of formation $\Delta_f H_m^o(\text{g}, 298.15\text{ K})_{\text{theor}}$ with help of the experimental gas-phase standard molar enthalpies of formation of auxiliary compounds (see Table S9) by using the enthalpies

Table 6 Phase transitions thermodynamics of benzophenones (in $\text{kJ}\cdot\text{mol}^{-1}$)^a

Compounds	$T_{\text{fus}}(\text{K})$	$\Delta_{\text{cr}}^l H_m^o$ at T_{fus}	WC ^b	$\Delta_{\text{cr}}^l H_m^o$ ^c	$\Delta_{\text{cr}}^g H_m^o$ 298.15 K	$\Delta_1^g H_m^o$ ^d
1	2	3	4	5	6	7
Benzophenone [37]	321.0 ± 0.3	18.6 ± 0.3	57.9	17.4 ± 0.5	95.0 ± 0.1	77.6 ± 0.5
4-Methyl-benzophenone	327.0 ± 1.0 [42]	18.9 ± 1.0 ^e		17.3 ± 1.1	97.3 ± 1.0 [39]	80.0 ± 1.2
3,4-Dimethyl-benzophenone	320.7 ± 1.0 [42]	18.6 ± 1.0 ^e		17.2 ± 1.1	107.9 ± 5.4 [41]	90.7 ± 5.5

^aUncertainties are presented as expanded uncertainties (0.95 level of confidence with $k = 2$)

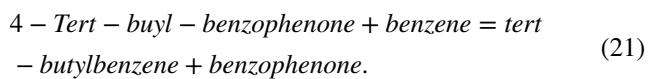
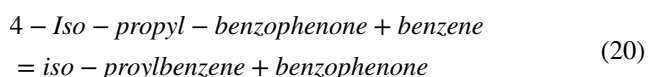
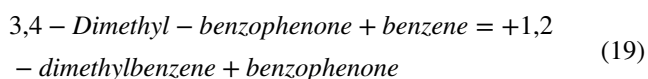
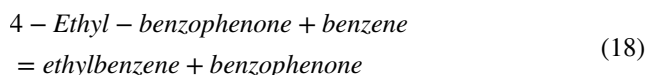
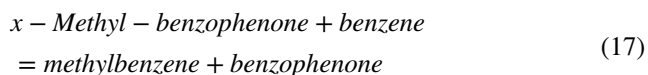
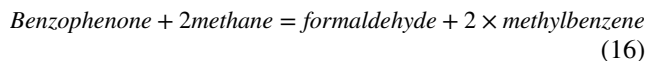
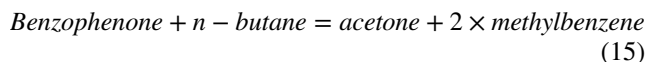
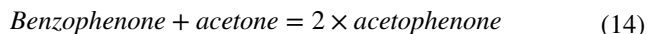
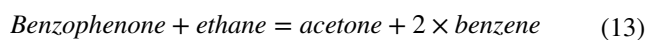
^bWalden’s constant (WC) [46] calculated according to Eq. (11)

^cThe experimental enthalpies of fusion $\Delta_{\text{cr}}^l H_m^o$ measured at T_{fus} were adjusted to $T = 298.15\text{ K}$ with help of the following equation [47]: $\Delta_{\text{cr}}^l H_m^o(298.15\text{ K}) / (\text{J}\cdot\text{mol}^{-1}) = \Delta_{\text{cr}}^l H_m^o(T_{\text{fus}}/\text{K}) - (\Delta_{\text{cr}}^g C_{\text{p,m}}^o - \Delta_1^g C_{\text{p,m}}^o) \times [(T_{\text{fus}}/\text{K}) - 298.15\text{ K}]$, where $\Delta_{\text{cr}}^g C_{\text{p,m}}^o$ and $\Delta_1^g C_{\text{p,m}}^o$ were taken from Table S1. Uncertainties in the temperature adjustment of fusion enthalpies from T_{fus} to the reference temperature are estimated to account with 30% to the total adjustment [47]

^dCalculated according to the following equation: $\Delta_1^g H_m^o(298.15\text{ K}) = \Delta_{\text{cr}}^g H_m^o(298.15\text{ K}) - \Delta_{\text{cr}}^l H_m^o(298.15\text{ K})$, as the difference between columns 6 and 5 in this table

^eCalculated according to Walden’s rule with the WC from benzophenone (column 4 in this table)

of following well-balanced reactions (WBR) for benzophenone and alkyl-benzophenones (see Table S10):



Results of the quantum-chemical calculations of the theoretical gas-phase enthalpies of formation of benzophenone are given in Table 8.

For this “centerpiece” molecule, we performed a careful search for the stable conformers using the G3MP2 method (see Fig. 5). It turned out that Conformer I and Conformer II are energetically barely distinguishable with a small difference of 1.2 kJ·mol⁻¹. Conformer III is less stable at 7.5 kJ·mol⁻¹ and practically absent in the gas-phase equilibrium mixture of conformers. As can be seen in Table 8, the G4 calculated results for benzophenone are very close regardless of the type of reactions used to convert H_{298} to enthalpies of formation. In addition, the theoretical enthalpy of formation of benzophenone calculated using the G4MP2 [54] (see Table 8) agrees with the G4 results. An average value $\Delta_f H_m^{\circ}(\text{g}, 298.15 \text{ K})_{\text{theor}} = 49.4 \pm 0.8 \text{ kJ}\cdot\text{mol}^{-1}$ was calculated for benzophenone and is recommended for thermochemical calculations.

All quantum-chemical enthalpies of formation of the alkyl-substituted benzophenones calculated by the G4 method with help of reactions 14–18 are summarized in Table 9. As can be seen from this table, the theoretical values, $\Delta_f H_m^{\circ}(\text{g}, 298.15 \text{ K})_{\text{theor}}$, are in good agreement with the experimental values, $\Delta_f H_m^{\circ}(\text{g}, 298.15 \text{ K})_{\text{exp}}$, for 3-methyl- and 4-methyl-benzophenone, and 3,4-dimethyl-benzophenone, as well as for

4-iso-propyl-benzophenone. The theoretical and experimental results for 2-methyl-benzophenone and 4-methyl-benzophenone are still fairly consistent within their combined uncertainties. However, the theoretical $\Delta_f H_m^{\circ}(\text{g}, 298.15 \text{ K})$ values for benzophenone, 4-ethyl-benzophenone and 4-tert-butyl-benzophenone are significantly more negative compared to the experiment, which raises certain doubts about the quality of the samples used for the combustion experiments. This issue is discussed in detail in the following section.

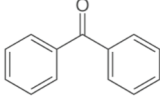
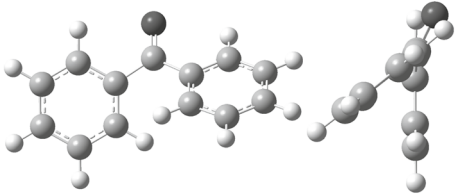
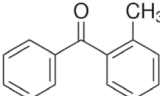
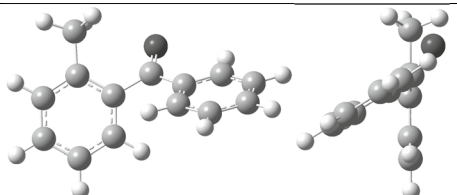
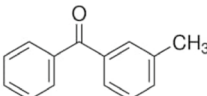
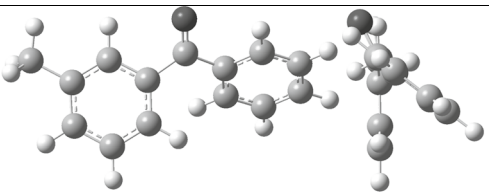
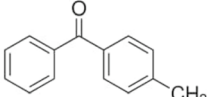
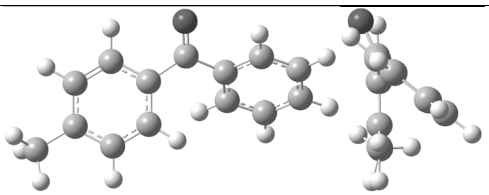
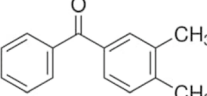
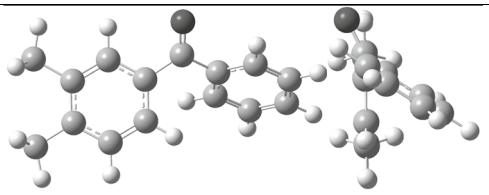
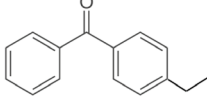
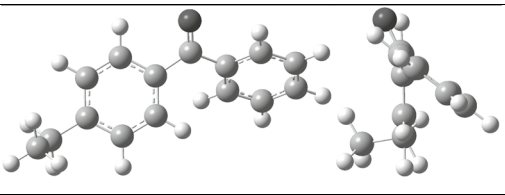
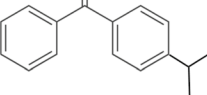
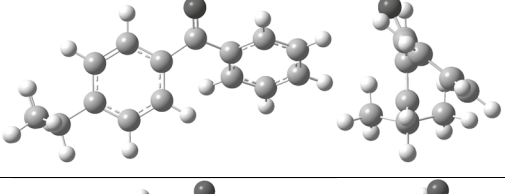
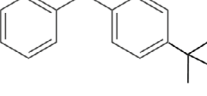
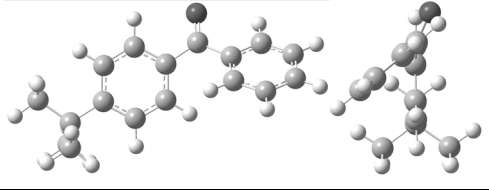
Step IV: diagnostics of condense state standard molar enthalpies of formation

The agreement between G4-calculated and experimental enthalpies of formation demonstrated for the five benzophenones shown in Table 9 can be viewed as a manifestation of the reliability of the experimental results collected for these compounds in Table 9. The discrepancy between G4-calculated and experimental enthalpies of formation found for the other three benzophenones is also essential to show the usefulness of the composite methods for diagnostics available $\Delta_f H_m^{\circ}(\text{g})_{\text{exp}}$ data, which are often in disorder or lying as single experimental determination.

In Step IV, we use the experimental data on vaporization/sublimation enthalpies already evaluated in Table 2 and proven reliable for the thermochemical calculations. The differences between the G4-theoretical enthalpies of formation (see Table 9, column 5) and the corresponding experimental vaporization/sublimation enthalpies (see Table 9, column 3) provide the numerical values of “theoretical” condensed state enthalpies of formation (see Table 9, column 2). The scarce numerical data on the condensed state standard molar enthalpies of formation, $\Delta_f H_m^{\circ}(\text{liq or cr})$, of the alkyl-substituted benzophenones reported in the literature from the combustion calorimetry experiments are also summarized in Table 9, column 2. With the exception of the benzophenone and the 4-methyl-benzophenone, only single values are available for other alkyl-derivatives.

Admittedly, benzophenone is recommended as the reference material for thermochemical measurements [60]. However, as can be seen from Table 9, the combustion results for the benzophenone differ by 18.5 kJ·mol⁻¹, although they generally agree within their combined experimental uncertainties. Such inaccuracy is hardly acceptable for a “reference” material. Furthermore, the polymorphism detected by DSC in the benzophenone at room temperature [37] and discussed in “Step II: diagnostics of consistency of phase transitions” makes this material questionable as a reference material, since the significant difference in lattice energy of the two polymorphs renders experiments with benzophenone ambiguous in the absence of XRD-determined structures. Both polymorphs can be easily obtained during purification of the sample prior to calorimetric studies. The

Table 7 Structures of the most stable conformers for alkylbenzophenones as calculated with the G4 and their gas-phase enthalpies of formation

Benzophenone	Structure	$\Delta_f H_m^0(\text{g})_{\text{G4}^{\text{a}}}$ kJ·mol ⁻¹
		50.1
		19.0
		16.0
		15.3
		-19.5
		-6.7
		-34.4
		-62.2

^a Calculated using the atomization procedure.

Table 8 Compilation of theoretical gas-phase enthalpies of formation of benzophenone calculated using quantum-chemical methods (at $T=298.15$ K, in $\text{kJ}\cdot\text{mol}^{-1}$)

Reactions	$\Delta_f H_m^{\circ}(\text{g})_{\text{theor}}^a$
Atomization (G4)	50.1 ± 3.5
Reaction 10 (G4)	48.1 ± 1.5
Reaction 11 (G4)	46.6 ± 1.6
Reaction 12 (G4)	49.3 ± 1.7
Reaction 13 (G4)	52.8 ± 1.7
Isodesmic reactions (G4MP2) [54]	49.3 ± 2.9
Weighted average	49.4 ± 0.8

^aUncertainties in this table represent two standard deviations. They were calculated using uncertainties of the reaction participants (see Table S9)

phenomenon of polymorphism of the benzophenone sample was overlooked in all five combustion calorimetry studies [35, 55–58]. On the one hand, this fact could explain the scatter of the available results; on the other hand, we can no longer rely on the crystalline enthalpies of formation, $\Delta_f H_m^{\circ}(\text{cr})$, of benzophenone since a variation of $4 \text{ kJ}\cdot\text{mol}^{-1}$ in general could be expected depending on which polymorph was used in the experiments. This ambiguity specific to benzophenone should attract the attention of experimentalists and prompt the redetermination of the crystal phase enthalpy of formation of benzophenone using a properly characterized polymorph. However, in this work, we overcame this obstacle by using the general thermochemical equation, Eq. (2). Indeed, the sublimation enthalpy of benzophenone as the α -polymorph was carefully characterized and measured recently using the static method. The value, $\Delta_{\text{cr}}^{\text{g}} H_m^{\circ}$ ($298.15 \text{ K}, \alpha$) = $95.0 \pm 0.1 \text{ kJ}\cdot\text{mol}^{-1}$, was recommended for thermochemical calculations. The gas-phase enthalpy of formation of benzophenone $\Delta_f H_m^{\circ}(\text{g}, 298.15 \text{ K})_{\text{theor}} = 4$

$9.4 \pm 0.8 \text{ kJ}\cdot\text{mol}^{-1}$ was derived theoretically and reported in Table 8. Using Eq. (2), we assessed the crystalline state enthalpy of formation of benzophenone, $\Delta_f H_m^{\circ}(\text{cr}, 298.15 \text{ K}, \alpha) = -45.6 \pm 1.4 \text{ kJ}\cdot\text{mol}^{-1}$ (see Table 9, column 2), as the α -polymorph at the reference temperature $T = 298.15 \text{ K}$. This value can now be taken as a preliminary guideline for future combustion experiments with the α -polymorph of benzophenone.

Returning to the other alkyl-substituted benzophenones collected in Table 9, we should note that both combustion results for 4-methyl-benzophenone [39, 58] are indistinguishable within their experimental uncertainties; therefore, the weighted average value, $\Delta_f H_m^{\circ}(\text{cr}, 298.15 \text{ K}) = -77.4 \pm 2.0 \text{ kJ}\cdot\text{mol}^{-1}$, could be taken as a reliable value for this compound. At the same time, the condensed state enthalpies of formation of 2-methyl-, 4-ethyl-, and 4-tert-butyl-benzophenone obtained as the difference between G4-calculated enthalpies of formation and vaporization enthalpies (see Table 9, column 2) should be considered more reliable as compared to the experimental combustion results. In addition, the supplementary evaluation of these questionable results according to the centerpiece approach is presented in the following section.

Development of the “centerpiece” group-contribution approach

The inconsistency of the experimental and theoretical results for 4-ethyl-benzophenone, 4-tert-butyl-benzophenone, 2-methyl-benzophenone, and 4-methyl-benzophenone on one hand and sufficient consistency of the experimental and theoretical results for 3-methyl-benzophenone, 4-methyl-benzophenone, 3,4-dimethyl-benzophenone, and 4-iso-propyl-benzophenone

Fig. 5 Stable conformers of benzophenone calculated using the G3MP2 method

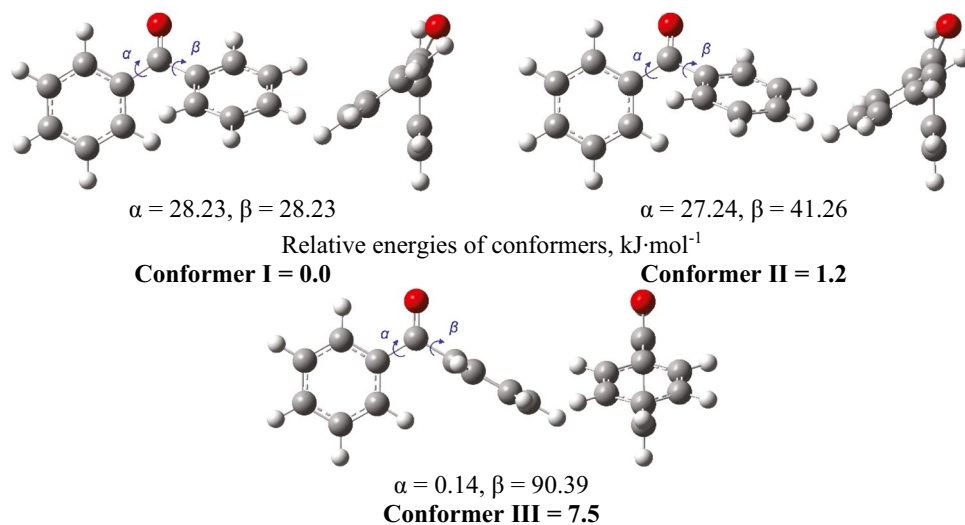


Table 9 Thermochemical data for benzophenones at $T=298.15\text{ K}$ ($p^\circ=0.1\text{ MPa}$, in $\text{kJ}\cdot\text{mol}^{-1}$)^a

Compound	$\Delta_f H_m^\circ(\text{cr/liq})^a$	$\Delta_{\text{l,cr}}^g H_m^\circ(298.15\text{ K})^b$	$\Delta_f H_m^\circ(\text{g})_{\text{exp}}$	$\Delta_f H_m^\circ(\text{g})_{\text{G4}}^c$
Benzophenone (cr, unknown)	-50.8 ± 8.5 [55]			
	-41.6 ± 6.3 [56]			
	-32.3 ± 3.3 [57]			
	-34.6 ± 2.6 [58]			
	-36.3 ± 2.5 [35]	93.1 ± 2.1 [59]	(56.8 ± 3.3)	$49.4 \pm 0.8^\circ$
Benzophenone (cr, α)	-45.6 ± 1.4^d	95.0 ± 0.1 [37]		$49.4 \pm 0.8^\circ$
2-Methyl-benzophenone (liq)	(-54.0 ± 3.3) [39]		(26.9 ± 3.3)	
	-62.0 ± 1.7^d	80.9 ± 0.5		18.9 ± 1.6
3-Methyl-benzophenone (liq)	-62.9 ± 3.8 [39]	80.7 ± 0.4	17.8 ± 3.8	15.9 ± 1.6
4-Methyl-benzophenone (cr)	-77.9 ± 2.8 [58]			
	-76.9 ± 2.8 [39]			
	-77.4 ± 2.0^f	97.7 ± 0.8	20.3 ± 2.2	15.2 ± 1.6
3,4-Dimethyl-benzophenone (cr)	-125.0 ± 2.8 [41]	107.9 ± 0.8 [41]	-17.1 ± 2.9	-16.6 ± 1.6
4-Ethyl-benzophenone (liq)	(-64.5 ± 3.0) [58]		(22.0 ± 3.1)	
	-91.4 ± 1.9^d	86.5 ± 0.9		-4.9 ± 1.7
4-Iso-propyl-benzophenone (liq)	-118.6 ± 3.3 [58]	88.7 ± 0.9	-29.9 ± 3.4	-30.9 ± 1.6
4-Tert-butyl-benzophenone (liq)	(-135.5 ± 3.5) [58]		(-43.7 ± 3.6)	
	-150.4 ± 1.8^d	91.8 ± 0.9		-58.6 ± 1.5

^aUncertainties in this table are twice standard deviations^bTaken from Table 2^cCalculated by the G4 method with help of reactions 14–18 using experimental $\Delta_f H_m^\circ(\text{g})$ values for the reaction participants from Table S9. The uncertainties calculated from uncertainties of the reaction participants^dDifference between columns 5 and 3. Values in brackets are considered questionable. Value in bold are recommended for thermochemical calculations^eTaken from Table 8^fWeighted mean value (uncertainties were taken as the weighing factor)

on the other have prompted the use of this data for the development of a “centerpiece” group-contribution approach. This approach serves as a complementary method for diagnosis of available thermochemical results for alkyl-benzophenones.

Construction of a strain-free theoretical framework

The basic idea of the “centerpiece approach” approach is to select a relatively large “centerpiece molecule” (rather than the traditional summation of group contributions) with well-known thermodynamic properties that structurally most closely resembles the molecule of interest [28, 29]. Related to the compounds discussed in this paper, benzophenone itself is the most suitable “centerpiece” molecule. Various substituents (e.g., methyl, ethyl, iso-propyl, tert-butyl) can be attached to the “centerpiece” at different positions on the benzene rings of the benzophenone (see Fig. 6).

The enthalpic contributions for these substituents can be easily quantified (see Fig. S1) from the differences between the enthalpy of the alkyl substituted benzene and the enthalpy of the benzene itself. Using this scheme, the contributions, e.g., $\Delta H(\text{H} \rightarrow \text{CH}_3)$, $\Delta H(\text{H} \rightarrow \text{ethyl})$, $\Delta H(\text{H} \rightarrow \text{iso-propyl})$, and $\Delta H(\text{H} \rightarrow \text{tert-butyl})$, were derived (see Table 10) using the

reliable thermochemical data for benzene, methylbenzene, 1,2-dimethyl-benzene, iso-propyl-benzene, and tert-butyl-benzene compiled in Table S9. These enthalpic contributions $\Delta H(\text{H} \rightarrow \text{CH}_3)$, $\Delta H(\text{H} \rightarrow \text{ethyl})$, $\Delta H(\text{H} \rightarrow \text{iso-propyl})$, and $\Delta H(\text{H} \rightarrow \text{tert-butyl})$ can be now applied to construct a framework of any desired alkyl-substituted benzophenone (e.g., 4-ethyl-, 4-iso-propyl- or 4-tert-butyl-benzophenone), starting from the benzophenone as the “centerpiece” (see Fig. 6). As a rule, this framework can energetically predict at a rough level the vaporization or formation enthalpies. But this framework is not perfect since it lacks the energetics of the interactions between the carbonyl and the alkyl substituents attached to the phenyl rings of benzophenone. For a more accurate assessment, the pairwise nearest and non-nearest neighbor interactions of substituents on the “centerpiece” framework should also be taken into account as follows.

Pairwise interactions of substituents on the benzene ring

The nearest (e.g., ortho-interactions) interactions of substituents or non-nearest neighbor (e.g., meta- or para-interactions) interactions of substituents on the benzene ring are an

indispensable part of the energetics of aromatic molecules. However, quantitatively, they are strictly dependent on the type and position of the substituent. As a rule, *ortho*-interactions are more profound, and *meta*- or *para*-interactions are less pronounced. There are two types of groups relevant to this work: alkyl and carbonyl. In our previous work, the mutual pairwise enthalpic interactions of methyl and carbonyl substituents in the benzene ring were quantified using thermochemical data on substituted acetophenones [45]. How the pairwise interactions were derived is shown in Fig. 7.

Indeed, to quantify the enthalpic contribution in “*para* $C=O(CH_3)-CH_3$ ” for the non-bonded interaction of the carbonyl and CH_3 -group in the *para*-position on acetophenone (taken as the “centerpiece”), we must first construct the “theoretical framework” of 4-methyl-acetophenone (see Fig. 7). To do that, we simply add the contribution $\Delta H(H \rightarrow CH_3)$ from Table 10 to the experimental enthalpy (enthalpy of vaporization or enthalpy of formation) of the acetophenone from Table S9. This “theoretical framework” of 4-methyl-acetophenone does not contain the “*para* $C=O(CH_3)-CH_3$ ” interaction. However, this interaction is present in the real 4-methyl-acetophenone (it is symbolized in Fig. 7 with a blue arrow). The arithmetic difference between the experimental enthalpy of 4-methyl-acetophenone and the enthalpy of the “theoretical framework” therefore provides the quantitative size of the pairwise interaction “*para* $C=O(CH_3)-CH_3$ ” directly (see Table 10). Using the same logic, the enthalpic contributions for the “*ortho* $C=O(CH_3)-CH_3$ ” and “*meta* $C=O(CH_3)-CH_3$ ” were derived from experimental data for

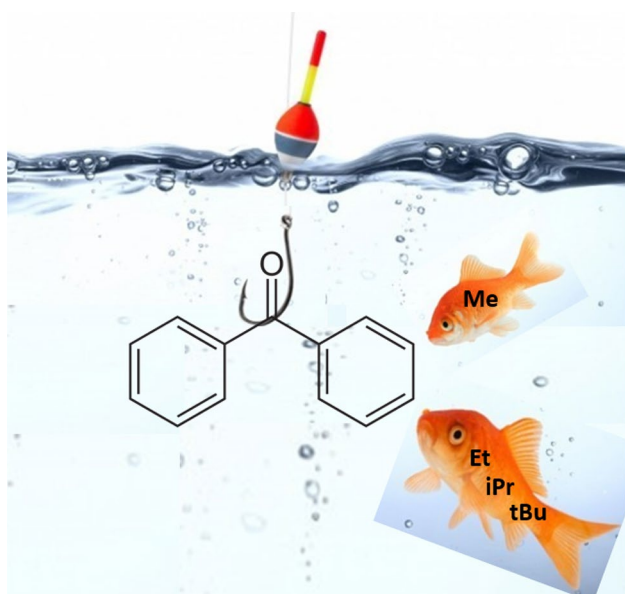


Fig. 6 Graphical presentation of the idea of a “centerpiece” group-contribution approach

Table 10 Parameters and pairwise nearest and non-nearest neighbor interactions of substituents on the “centerpiece” for calculation of thermodynamic properties of substituted benzenes and benzophenones at $T=298.15$ K (in $\text{kJ}\cdot\text{mol}^{-1}$)

Centerpiece	$\Delta_f H_m^o(\text{g})$	$\Delta_1^g H_m^o$
Benzene	82.9	33.9
Acetophenone	87.1	55.4
Benzophenone	49.4	78.0
<i>Contributions</i>		
$\Delta H(H \rightarrow C=O(CH_3))$	-170.0	21.5
$\Delta H(H \rightarrow CH_3)$	-32.8	4.2
$\Delta H(H \rightarrow \text{ethyl})^a$	-53.0	8.4
$\Delta H(H \rightarrow \text{iso-propyl})^a$	-78.9	11.3
$\Delta H(H \rightarrow \text{tert-butyl})^a$	-106.6	13.6
<i>Interactions</i> ^b		
<i>Ortho</i> $C=O(CH_3)-CH_3$	9.2	-0.4
<i>Meta</i> $C=O(CH_3)-CH_3$	-0.2	0.3
<i>Para</i> $C=O(CH_3)-CH_3$	-0.9	1.9
<i>Ortho</i> $C=O(C_6H_5)-CH_3$	2.3 ^c	-
<i>Meta</i> $C=O(C_6H_5)-CH_3$	-0.7 ^c	-
<i>Para</i> $C=O(C_6H_5)-CH_3$	-1.4 ^c	-

^aThe contributions were derived from the differences between the enthalpy of the alkyl substituted benzene and the enthalpy of benzene itself (see text)

^bThe pairwise interactions between carbonyl and methyl group were derived from the methyl-acetophenones in our previous work [45]. These interactions were supposed to be transferrable from acetophenone to the benzophenone system

^cCalculated from G4 using the inverse well-balanced reaction (14)

2-methyl- and 4-methyl-acetophenone by using the parameters $\Delta H(H \rightarrow CH_3)$ and $\Delta H(H \rightarrow C=O(CH_3))$, respectively. In the same way, the required enthalpy contributions for other pairwise interactions of substituents were estimated and summarized in Table 10. The quantities of these interactions derived from substituted acetophenones have been propagated to the alkyl-substituted benzophenones.

Practical application of the centerpiece approach for prediction of enthalpies of substituted benzophenones

As can be seen from Table 10, the magnitudes of the pairwise interactions in terms of $\Delta_1^g H_m^o$ are rather negligible given the uncertainties of the species involved in estimating the contributions. This observation greatly simplified the application of the “centerpiece” approach to the assessment of vaporization enthalpies of alkyl-substituted benzophenones. We just have to add the corresponding alkyl contribution to the enthalpy of vaporization of benzophenone. The estimates derived in this way are marked “CP” in Table 2 and agree well with the results of other methods.

As can also be seen from Table 10, the magnitudes of the pairwise interactions in terms of $\Delta_f H_m^o(\text{g})$ are also negligible (except for “*ortho* $\text{C}=\text{O}(\text{CH}_3)\text{—CH}_3$ ”) taking into account the combined uncertainties of the species involved in estimating the contributions. It is interesting, that the *ortho*-interaction of the methyl and carbonyl group “*ortho* $\text{C}=\text{O}(\text{CH}_3)\text{—CH}_3$ ” with $9.2 \text{ kJ}\cdot\text{mol}^{-1}$ is significantly larger than the *ortho*-interaction of the methyl and phenyl ring “*ortho* $\text{C}=\text{O}(\text{C}_6\text{H}_5)\text{—CH}_3$ ” with $2.3 \text{ kJ}\cdot\text{mol}^{-1}$ (see Table 10). But this difference can be explained by the twisting of the phenyl group attached to the carbonyl group as it shown in Table 7.

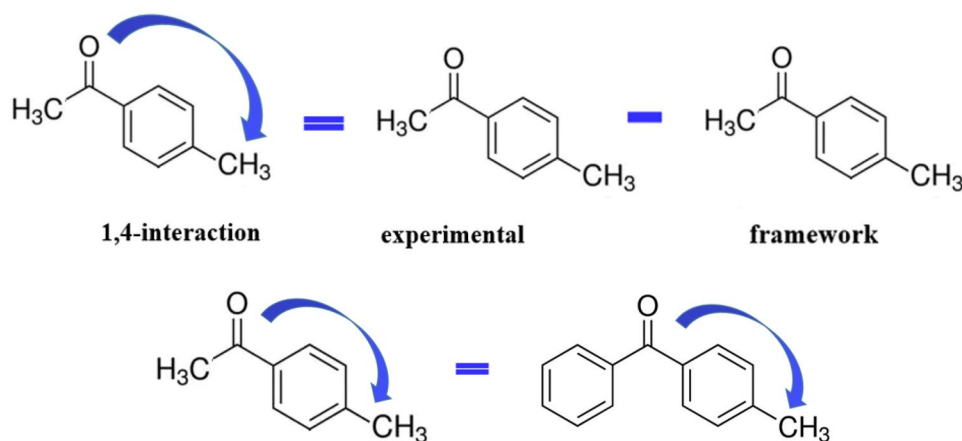
In “Step III: gas-phase standard molar enthalpies of formation from quantum chemistry” and “Step IV: diagnostics of condense state standard molar enthalpies of formation,” we noticed that the G4-calculated enthalpies of formation of 2-methyl-benzophenone, 4-ethyl-benzophenone, and 4-tert-butyl-benzophenone should be considered more reliable compared to the experimental results. The “centerpiece” approach provides an independent way to obtain the gas-phase enthalpies of formation for these compounds for comparison. For example, for 2-methyl-benzophenone:

$$\Delta_f H_m^o(\text{g})_{\text{CP}} = \Delta_f H_m^o(\text{g})_{\text{benzophenone}} + \Delta H(\text{H} \rightarrow \text{CH}_3) + "$$

$$\text{ortho } \text{C}=\text{O}(\text{C}_6\text{H}_5)\text{—CH}_3'' = 49.4 + (-32.8) + 2.3 = 18.9 \text{ kJ}\cdot\text{mol}^{-1},$$

and this result is indistinguishable from the value calculated by the G4 method (see Table 9, last column). The calculation according to “centerpiece” approach for 4-ethyl-benzophenone gives $\Delta_f H_m^o(\text{g})_{\text{CP}} = -5.0 \text{ kJ}\cdot\text{mol}^{-1}$, and for 4-tert-butyl-benzophenone gives $\Delta_f H_m^o(\text{g})_{\text{CP}} = -58.0 \text{ kJ}\cdot\text{mol}^{-1}$. These two results are practically identical to the results of the G4 method (see Table 9, column 5). Therefore, we can conclude that the results of combustion calorimetry in these three species are “unreliable” and should be repeated. Such good agreement between two independent methods for validating the experimental data sets allows proposing the “centerpiece” approach as an additional fifth “in silico” step for diagnostics of thermochemical data. The usefulness of this suggestion is demonstrated in the next section.

Fig. 7 Example for a quantification of the 1,4-non-nearest neighbor interactions of the carbonyl-group with the CH_3 -substituent in 4-methyl-acetophenone. This quantity was propagated to alkyl-substituted benzophenones. The scheme is valid for the standard molar enthalpies of vaporization, as well as for the gas-phase standard molar enthalpies of formation



Diagnostic check for the gas-phase enthalpies of formation of substituted benzophenones reported in the literature

There are two experimental data sets for nitro-substituted [61] and chloro-substituted [62] benzophenones available in the literature. Structures of these compounds are given in Fig. 8. For the first set of experimental data, the G4 calculations of the enthalpies of formation of three nitro-benzophenones were reported (see Table 11, column 3) by Suntsova and Dorofeeva [54]. They designed 26 isodesmic reactions with these species, and all isodesmic reactions gave the $\Delta_f H_m^o(\text{g})_{\text{G4}}$ values less positive than the experimental ones (see Table 11, column 2). They concluded that the reported experimental values [61] were overestimated and recommended the theoretical enthalpies of formation for 3-nitro-benzophenone, 4-nitro-benzophenone, and 3,3'-dinitro-benzophenone as more reliable values [54]. Does the “centerpiece” approach support this conclusion or defend the experiments? The results of the estimations are given in Table 11, column 4.

It is evident that the results of the centerpiece approach agree with the G4 calculations and not with experiment for the nitro-benzophenones, supporting the conclusion of Suntsova and Dorofeeva [54].

For the second set of experimental data, the experimental enthalpies of formation for four chloro-substituted benzophenones given in Fig. 8 were reported by Ribeiro da Silva et al. [62] and listed in Table 11 (column 2). The results of estimations are given in Table 11, column 4. It turned out that in this case, the results of the centerpiece approach, the G4 calculations, and experiment are in a good agreement within the boundaries of the combined uncertainties. Therefore, with this successful diagnostic check, the thermochemical data reported for the set of chloro-substituted benzophenones can be recommended for additional thermochemical calculations. These two examples distinctly show that diagnostic steps four and five developed in this work are complementary “in silico” tools that together are able to resolve contradictory results in reported experimental data.

Fig. 8 Structures of nitro-substituted [61] and chloro-substituted [62] benzophenones available in the literature

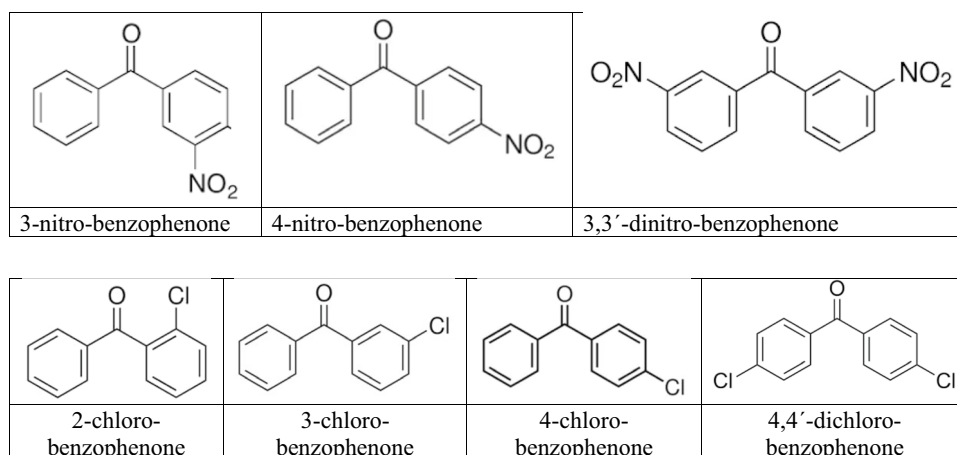


Table 11 Diagnostic check of the gas-phase enthalpies of formation, $\Delta_f H_m^o(g)$, of formation of substituted benzophenones available in the literature (at 298.15 K in $\text{kJ}\cdot\text{mol}^{-1}$)^a

Compound	$\Delta_f H_m^o(g)_{\text{exp}}$	$\Delta_f H_m^o(g)_{\text{QC}}^b$	$\Delta_f H_m^o(g)_{\text{CP}}^c$
2-Methyl-benzophenone	26.9 ± 3.3 (Table 9)	18.9 ± 1.6 (Table 9)	18.9 ± 2.1
3-Methyl-benzophenone	18.0 ± 3.8 (Table 9)	15.9 ± 1.6 (Table 9)	15.9 ± 2.1
4-Methyl-benzophenone	20.3 ± 2.2 (Table 9)	15.2 ± 1.6 (Table 9)	15.2 ± 2.1
4-Ethyl-benzophenone	(22.0 ± 3.1) (Table 9)	-4.9 ± 1.7 (Table 9)	-5.0 ± 2.1
4-Iso-propyl-benzophenone	-29.9 ± 3.4 (Table 9)	-30.9 ± 1.6 (Table 9)	-30.9 ± 2.1
4-Tert-butyl-benzophenone	(-43.7 ± 3.6) (Table 9)	-58.6 ± 1.5 (Table 9)	-58.0 ± 1.9
3-Nitro-benzophenone	(44.2 ± 2.3) [61]	37.6 ± 5.0 [54] ^d	37.1 ± 2.3
4-Nitro-benzophenone	(48.8 ± 2.6) [61]	39.2 ± 5.0 [54] ^d	37.4 ± 2.3
3,3'-Di-nitro-benzophenone	(43.0 ± 4.8) [61]	26.6 ± 5.0 [54] ^d	24.8 ± 3.0
2-Chloro-benzophenone	35.6 ± 2.3 [62]	34.5 ± 2.2 ^e	33.7 ± 2.2
3-Chloro-benzophenone	24.0 ± 2.4 [62]	21.8 ± 2.2 ^e	21.0 ± 2.2
4-Chloro-benzophenone	21.0 ± 2.6 [62]	19.8 ± 2.2 ^e	19.8 ± 2.2
4,4'-Di-chloro-benzophenone	-0.4 ± 2.4 [62]	-9.0 ± 2.7 ^e	-11.4 ± 2.7

^aUncertainties are expanded uncertainties (0.95 level of confidence, $k=2$). Values in bold are considered questionable and require additional measurements

^bCalculated using quantum-chemical methods

^cCalculated using the “centerpiece” approach using the enthalpy of formation of benzophenone and the NO_2 - and Cl- contributions derived in Tables S11 and S12

^dCalculated using G4MP2 by Suntsova and Dorofeeva [54]

^eDerived in this work from enthalpies of well-balanced reactions calculated by Ribeiro da Silva et al. [62] using B3LYP/6-311 + G(2d,2p)//B3LYP/6-31G-(d) and the enthalpies of formation of reference compound from Table S9

Conclusions

Quo vadis in the twenty-first century with the evaluation of available thermochemical data? In this work, a multi-step *in silico* assisted diagnostic was proposed and applied to conflicting experimental data for alkyl-substituted benzophenones.

In the first step, the vaporization enthalpies obtained with different methods were evaluated for each alkyl-substituted benzophenone and values in agreement were averaged using the experimental uncertainties as a weighting factor. The structure–property correlations were used to derive the vaporization enthalpies of 3,4-dimethyl-benzophenone, 4-ethyl-benzophenone, 4-*iso*-propyl-benzophenone, and 4-*tert*-butyl-benzophenone where experimental results were lacking in the literature.

In the second step, the phase transition data for solid samples of benzophenone, 4-methyl-benzophenone, and 3,4-dimethyl-benzophenone were evaluated and used to establish the consistency of the phase transitions for these compounds.

In the third step, we calculated the gas-phase formation enthalpies of benzophenone and its alkyl derivatives using quantum chemical methods. These methods were particularly useful for benzophenone as they helped uncover inconsistencies in thermochemical data for this important compound.

In the fourth step, the thermochemical data evaluated in the previous steps were used for diagnostics of the quality of condensed state enthalpies of formation. It turned out that combustion calorimetry experiments should be repeated for the α -polymorph of benzophenone, as well as for 2-methyl-, 4-ethyl-, and 4-*tert*-butyl-benzophenone.

The consistent set of thermochemical data evaluated in this work for alkyl-benzophenones was used to develop the “centerpiece” group-contribution approach as the complementary fifth “*in silico*” step for the diagnosis of available thermochemical information. This approach can be used for a quick appraisal of vaporization or formation enthalpies and is very useful for pre-planning experiments.

In the last decade, *in silico* assisted diagnostics of available thermochemical data has been used systematically in our laboratory and it has been shown to be able to reduce the experimental efforts and to avoid measuring properties where consistent data are already available in the literature.

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Author contribution S.P.V. and A.A.S. wrote and edited the main manuscript text. A.A.S. measured vapor pressures. S.P.V. and A.A.S. were responsible for conceptualization and methodology. S.P.V. and A.A.S. were responsible for formal analysis and validation. All authors reviewed the manuscript.

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Data availability All data sets used are given in the main text and in the electronic supporting information and can be accessed from the online version of this article.

Declarations

Ethics approval and consent to participate Not applicable.

Competing interests The authors declare no competing interests.

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References

- Bernstein HJ (1952) The physical properties of molecules in relation to their structure. I. Relations between additive molecular properties in several homologous series. *J Chem Phys* 20:263–269. <https://doi.org/10.1063/1.1700389>
- Laidler KJ (1956) A system of molecular thermochemistry for organic gases and liquids. *Can J Chem* 34:626–648. <https://doi.org/10.1139/v56-086>
- Allen TL (1959) Bond energies and the interactions between next-nearest neighbors. I. Saturated hydrocarbons, diamond, sulfanes, S8, and organic sulfur compounds. *J Chem Phys* 31:1039–1049. <https://doi.org/10.1063/1.1730501>
- Cox JD, Pilcher G (1970) Thermochemistry of organic and organometallic compounds. Academic Press, New York, pp 1–636
- Benson SW, Buss JH (1958) Additivity rules for the estimation of molecular properties. Thermodynamic properties. *J Chem Phys* 29:546–572. <https://doi.org/10.1063/1.1744539>
- Benson SW (1976) Thermochemical kinetics, 2nd edn. John Wiley & Sons, New York-London-Sydney-Toronto, pp 1–320
- Domalski ES, Hearing ED (1993) Estimation of the thermodynamic properties of C-H-N-O-S-Halogen Compounds at 298.15 K. *J Phys Chem Ref Data* 22:805–1159. <https://doi.org/10.1063/1.555927>
- Cohen N (1996) Revised group additivity values for enthalpies of formation (at 298 K) of carbon-hydrogen and carbon-hydrogen-oxygen compounds. *J Phys Chem Ref Data* 25:1411–1481. <https://doi.org/10.1063/1.555988>
- Tatevskii VM (1950) *Doklady Akad Nauk S.S.S.R.* 25:819–822

10. Tatevskiy VM (1953) Chemical structure of hydrocarbons and regularities in their physical and chemical properties. M.: MGU. 1–320
11. Tatevskii VM, Benderskii VA, Yarovoi SS (1961) Rules and methods for calculating the physico-chemical properties of paraffinic hydrocarbons. Pergamon Press, Oxford, pp 1–128
12. Zheng P, Yang W, Wu W, Isayev O, Dral PO (2022) Toward chemical accuracy in predicting enthalpies of formation with general-purpose data-driven method. *J Phys Chem Lett* 13:3479–3491. <https://doi.org/10.1021/acs.jpcllett.2c007341>
13. Verevkin SP, Morgenthaler J, Rüchardt C (1997) Thermochemistry of imines: experimental standard molar enthalpies of formation. *J Chem Thermodyn* 29:1175–1183. <https://doi.org/10.1006/jcht.1997.0242>
14. Verevkin SP, Emel'yanenko VN, Algarra M et al (2011) Vapor pressures and enthalpies of vaporization of azides. *J Chem Thermodyn* 43:1652–1659. <https://doi.org/10.1016/j.jct.2011.05.028>
15. Pedley JB. Thermochemical data and structures of organic compounds, Vol I, TRC Data Series, College Station, pp 1994 1–571
16. Pedley JB, Naylor RD, Kirby SP (1986) Thermochemical data of organic compounds. Chapman and Hall, New York, pp 1–792
17. <https://webbook.nist.gov/chemistry/>. (visited 26.09.2022)
18. Verevkin SP, Turovtsev VV, Andreeva IV et al (2021) Webbing a network of reliable thermochemistry around lignin building blocks: tri-methoxy-benzenes. *RSC Adv* 11:10727–10737. <https://doi.org/10.1039/D1RA00690H>
19. Zaitsau DH, Pohako-Esko K, Arlt S et al (2017) Thermodynamics of imidazolium based ionic liquids with cyano containing anions. *J Mol Liq* 248:86–90. <https://doi.org/10.1016/j.molliq.2017.10.004>
20. Verevkin SP (2006) Vapour pressures and enthalpies of vaporization of a series of the linear n-alkyl-benzenes. *J Chem Thermodyn* 38:1111–1123. <https://doi.org/10.1016/j.jct.2005.11.009>
21. Zaitsau DH, Pimerzin AA, Verevkin SP (2019) Fatty acids methyl esters: complementary measurements and comprehensive analysis of vaporization thermodynamics. *J Chem Thermodyn* 132:322–340. <https://doi.org/10.1016/j.jct.2019.01.007>
22. Curtiss LA, Redfern PC, Raghavachari K et al (1999) Gaussian-3 theory using reduced Mo/ller-Plesset order. *J Chem Phys* 110:4703–4709. <https://doi.org/10.1063/1.478385>
23. Dandu NK, Assary RS, Redfern PC et al (2022) Improving the accuracy of composite methods: a G4MP2 method with G4-like accuracy and implications for machine learning. *J Phys Chem A* 126:4528–4536. <https://doi.org/10.1021/acs.jpca.2c01327>
24. Curtiss LA, Redfern PC, Raghavachari K (2007) Gaussian-4 theory. *J Chem Phys* 126:084108. <https://doi.org/10.1063/1.2436888>
25. Ochterski JW, Petersson GA, Montgomery JA (1996) A complete basis set model chemistry. V. Extensions to six or more heavy atoms. *J Chem Phys* 104:2598–2619. <https://doi.org/10.1063/1.470985>
26. Verevkin SP, Emel'yanenko VN, Diky V et al (2013) New group-contribution approach to thermochemical properties of organic compounds: hydrocarbons and oxygen-containing compounds. *J Phys Chem Ref Data* 42:033102. <https://doi.org/10.1063/1.4815957>
27. Verevkin SP, Emel'yanenko VN, Zaitsau DH (2018) Thermochemistry of substituted benzamides and substituted benzoic acids: like tree, like fruit? *ChemPhysChem* 19:619–630. <https://doi.org/10.1002/cphc.201701132>
28. Verevkin SP, Andreeva IV, Zherikova KV, Pimerzin AA (2022) Prediction of thermodynamic properties: centerpiece approach—how do we avoid confusion and get reliable results? *J Therm Anal Calorim* 147:8525–8534. <https://doi.org/10.1007/s10973-021-11115-4>
29. Verevkin SP, Konnova ME, Turovtsev VV et al (2020) Weaving a network of reliable thermochemistry around lignin building blocks: methoxy-phenols and methoxy-benzaldehydes. *Ind Eng Chem Res* 59:22626–22639. <https://doi.org/10.1021/acs.iecr.0c04281>
30. Kulikov D, Verevkin SP, Heintz A (2001) Determination of vapor pressures and vaporization enthalpies of the aliphatic branched C 5 and C 6 alcohols. *J Chem Eng Data* 46:1593–1600. <https://doi.org/10.1021/je010187p>
31. Verevkin SP, Emel'yanenko VN (2008) Transpiration method: vapor pressures and enthalpies of vaporization of some low-boiling esters. *Fluid Phase Equilib* 266:64–75. <https://doi.org/10.1016/j.fluid.2008.02.001>
32. Frisch MJ, Trucks GW, Schlegel HB et al (2016) Gaussian 16, Revision C.01 Gaussian, Inc., Wallingford CT
33. Verevkin SP, Sazonova AY, Emel'yanenko VN et al (2015) Thermochemistry of halogen-substituted methylbenzenes. *J Chem Eng Data* 60:89–103. <https://doi.org/10.1021/je500784s>
34. Emel'yanenko VN, Verevkin SP (2015) Benchmark thermodynamic properties of 1,3-propanediol: comprehensive experimental and theoretical study. *J Chem Thermodyn* 85:111–119. <https://doi.org/10.1016/j.jct.2015.01.014>
35. Steele WV, Chirico RD, Hossenlopp IA et al (1994) DIPPR project 871. Determination of ideal-gas enthalpies of formation for key compounds. The 1990 project results. *DIPPR Data Ser* 2:188–215
36. Monte MJS, Santos LMNBF, Fulem M et al (2006) New static apparatus and vapor pressure of reference materials: naphthalene, benzoic acid, benzophenone, and ferrocene. *J Chem Eng Data* 51:757–766. <https://doi.org/10.1021/je050502y>
37. Štefja V, Fulem M, Růžička K, Morávek P (2016) New static apparatus for vapor pressure measurements: reconciled thermo-physical data for benzophenone. *J Chem Eng Data* 61:3627–3639. <https://doi.org/10.1021/acs.jced.6b00523>
38. Stephenson RM, Malanowski S (1987) Handbook of the thermodynamics of organic compounds. Springer, Netherlands, Dordrecht
39. Ribeiro da Silva MA, Amaral LMPF, Guedes FCR, Gomes JRB (2006) Standard molar enthalpies of formation of methylbenzophenones. *J Phys Org Chem* 19:689–696. <https://doi.org/10.1002/poc.1117>
40. Nagrimanov RN, Samatov AA, Buzyorov AV, Solomonov BN (2017) Determination of sublimation enthalpies of substituted benzophenones, fluorenes and diphenyl ethers by solution calorimetry approach. *Thermochim Acta* 655:358–362. <https://doi.org/10.1016/j.tca.2017.08.003>
41. Gomes JRB, Amaral LMPF, Ribeiro Da Silva MAV (2008) Standard molar enthalpies of formation of dimethylbenzophenones. *J Phys Org Chem* 21:365–371. <https://doi.org/10.1002/poc.1342>
42. SciFinder - Chemical Abstracts Service (2022) <http://scifinder.cas.org/>
43. Kováts E (1958) Gas-chromatographische Charakterisierung organischer Verbindungen. Teil 1: Retentionsindices aliphatischer Halogenide, Alkohole, Alkohole, Aldehyde und Ketone. *Helv Chim Acta* 41:1915–1932. <https://doi.org/10.1002/hlca.19580410703>
44. Vinogradov BA (2004) Production, composition, properties and application of essential oils, retrieved from <http://viness.narod.ru>
45. Andreeva IV, Verevkin SP (2022) Thermochemistry of substituted benzenes: acetophenones with methyl, ethyl, cyano and acetoxy substituents. *J Therm Anal Calorim* 147:11401–11415. <https://doi.org/10.1007/s10973-022-11326-3>
46. Walden P (1908) Über die Schmelzwärme, spezifische Kohäsion und Molekulargröße bei der Schmelztemperatur. *Zeitschrift für Elektrotechnik und Elektrochemie* 14:713–724. <https://doi.org/10.1002/bbpc.19080144302>
47. Acree W, Chickos JS (2016) Phase transition enthalpy measurements of organic and organometallic compounds. sublimation, vaporization and fusion enthalpies from 1880 to 2015. Part 1. C

- 1 – C 10. *J Phys Chem Ref Data* 45:033101. <https://doi.org/10.1063/1.4948363>
48. Abdelaziz A, Zaitsau DH, Kuratieva NV et al (2019) Melting of nucleobases. Getting the cutting edge of “Walden’s Rule.” *Phys Chem Chem Phys* 21:12787–12797. <https://doi.org/10.1039/C9CP00716D>
49. Nagrimanov RN, Ziganshin MA, Solomonov BN, Verevkin SP (2019) Thermochemistry of drugs: experimental and theoretical study of analgesics. *Struct Chem* 30:247–261. <https://doi.org/10.1007/s11224-018-1188-z>
50. Verevkin SP, Emel’yanenko VN, Nagrimanov RN (2016) Nearest-neighbor and non-nearest-neighbor interactions between substituents in the benzene ring. Experimental and theoretical study of functionally substituted benzamides. *J Phys Chem A* 120:9867–9877. <https://doi.org/10.1021/acs.jpca.6b10332>
51. Zaitseva KV, Emel’yanenko VN, Agapito F et al (2015) Benchmark thermochemistry of methylbenzonnitriles: experimental and theoretical study. *J Chem Thermodyn* 91:186–193. <https://doi.org/10.1016/j.jct.2015.07.025>
52. Pracht P, Bohle F, Grimme S (2020) Automated exploration of the low-energy chemical space with fast quantum chemical methods. *Phys Chem Chem Phys* 22:7169–7192. <https://doi.org/10.1039/C9CP06869D>
53. Petersson GA, Bennett A, Tensfeldt TG et al (1988) A complete basis set model chemistry. I. The total energies of closed-shell atoms and hydrides of the first-row elements. *J Chem Phys* 89:2193–2218. <https://doi.org/10.1063/1.455064>
54. Suntsova MA, Dorofeeva OV (2016) Use of G4 Theory for the assessment of inaccuracies in experimental enthalpies of formation of aromatic nitro compounds. *J Chem Eng Data* 61:313–329. <https://doi.org/10.1021/acs.jced.5b00558>
55. Landrieu P, Blatt H (1924) Thermochemical study of diphenylphenylethynylcarbinol and its derivatives. *Bull Soc Chim Fr* 35:1424–1236
56. Beckers M (1931) *Bul Soc Chim* 40:518
57. Parks GS, Mosley JR, Peterson PV (1950) Heats of combustion and formation of some organic compounds containing oxygen. *J Chem Phys* 18:152–153. <https://doi.org/10.1063/1.1747444>
58. Colomina M, Cambeiro M, Perez-Ossorio R, Latorre C (1959) Estudios acerca de calores de combustion. II. Calores de combustion de benzofenona y sus p-alquilderivados. *An Real Soc Esp Fis y Quim LV (B)*:509–514
59. Verevkin SP (1998) Thermochemistry of aromatic ketones. Experimental enthalpies of formation and structural effects. *Thermochim Acta* 310:229–235. [https://doi.org/10.1016/s0040-6031\(97\)00231-1](https://doi.org/10.1016/s0040-6031(97)00231-1)
60. Sabbah R, Xu-Wu A, Chickos JS et al (1999) Reference materials for calorimetry and differential thermal analysis. *Thermochim Acta* 331:93–204. [https://doi.org/10.1016/s0040-6031\(99\)00009-x](https://doi.org/10.1016/s0040-6031(99)00009-x)
61. Ribeiro Da Silva MAV, Amaral LMPF, Ortiz RV (2011) Experimental study on the thermochemistry of 3-nitrobenzophenone, 4-nitrobenzophenone and 3,3'-dinitrobenzophenone. *J Chem Thermodyn* 43:546–551. <https://doi.org/10.1016/j.jct.2010.11.005>
62. Ribeiro da Silva MAV, Amaral LMPF, Gomes JRB (2007) Experimental and computational studies on the molecular energetics of chlorobenzophenones. *J Phys Chem B* 111:13033–13040. <https://doi.org/10.1021/jp076522j>

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