

Rediscovering the Wheel. Thermochemical Analysis of Energetics of the Aromatic Diazines

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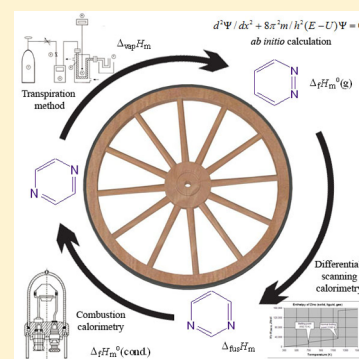
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Supporting Information

ABSTRACT: Thermochemical properties of pyrimidine, pyrazine, and pyridazine have been measured and re-evaluated to provide benchmark quality results. A new internally consistent data set of $\Delta_f H_m^\circ(g)$ has been obtained from combustion calorimetry and vapor pressure measurements. The gas and condensed phase enthalpies of formation of the parent diazines have been re-evaluated, and the results were compared to current theoretical calculations using the highly accurate first-principles methods: G3, G4, CBS-APNO, W1(RO). Simple "corrected atomization procedures" to derive theoretical $\Delta_f H_m^\circ(g)$ directly from the enthalpies H_{298} have been tested and recommended as an alternative to using the bond separation and isodesmic reaction models for organic cyclic and heterocyclic compounds containing one to three nitrogen atoms.



SECTION: Molecular Structure, Quantum Chemistry, and General Theory

Diazabenzene is a key building block used to develop compounds of biological, medicinal, and chemical interest. There are three isomeric diazabenzene or diazine: the 1,2-, more commonly known as pyridazine; the 1,3-, more commonly known as pyrimidine, and the 1,4-, more commonly known as pyrazine (Figure 1).

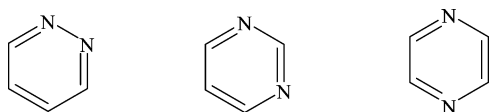


Figure 1. The structures of pyridazine, pyrimidine, and pyrazine.

The study of biochemistry is inseparable from that of pyrimidines. The simple pyrimidine derivatives thymine, cytosine, and uracil are three of the five key components of nucleic acids. The pyrimidine ring is also found as a substructure for purines, the other two key components of nucleic acids, as well as other biomolecules such as ATP and NADP(H). The pyrimidine ring is also a substructure for pteridines and their benzo derivatives, and therefore are ubiquitous as folic acid and flavin derivatives within the biochemical context, two inherent constituents of essential coenzymes. These latter folic and flavin species also contain a

pyrazine ring. Many other pyrimidines and pyrazines show biological activity and have natural functions. Additionally, alkyl derivatives of pyrazines are also commonplace ingredients of the human diet as they arise from the cooking process. By contrast, pyridazines are almost unknown in the natural setting.

Does any of this disparity between the abundance of pyrimidines, pyrazines and pyridazines reflect differences in their inherent chemical stability? Thermodynamics is able to provide a plausible explanation, provided that reliable data are available. Physical and chemical properties of benzene and its simple heteroatom nitrogen derivatives are textbook knowledge, and their properties should be known with impeccable quality. Much to our surprise and disappointment, this is still not the case for diazabenzene. The previous comprehensive experimental study of both the condensed and gas phase enthalpies of formation of all three diazines was reported by Tjebbes in 1962.¹ These and some recent other measurements¹⁻⁷ on these species are collected in Table 1. Tjebbes' results were then commonly accepted. In 1989, using theoretical calculations on all three diazines at the MP3/6-

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Table 1. Compilation of Thermochemical Data for Diazines (in $\text{kJ}\cdot\text{mol}^{-1}$ at $T = 298.15\text{ K}$)

compounds	$\Delta_f H_m^\circ(\text{l or cr})$	$\Delta_{\text{cr}}^\circ H_m$	$\Delta_f^\circ H_m(298\text{ K})$	$\Delta_f H_m^\circ(\text{g})$	$\Delta_f H_m^\circ\text{calc}$
pyridazine (l)	224.9 ± 0.9 [1]		53.5 ± 0.4 [1]	278.3 ± 1.3 [30,31]	279.5 ± 2.9 [8] ^e
	226.9 ± 1.3 ^a		46.5 ± 2.2 [3] ^b	281.5 ± 1.3 ^a	
			52.7 ± 4.5 [7]		
			52.8 ± 3.8 [7]		
			60.6 [6] ^d		
recommended ^a	(225.9 ± 1.6)		54.6 ± 0.2 ^a		281.7 (G4) ^a
	225.6 ± 0.7		54.6 ± 0.2	280.2 ± 0.7	280.1 ^g
pyrimidine (l)	146.6 ± 0.8 [1]		50.0 ± 0.3 [1]	195.7 ± 1.4 [30,31]	182.8 ± 2.9 [8] ^e
	143.2 ± 1.8 [2]		49.9 ± 0.6 [2]		187.4 ± 4.2 [9] ^f
	144.9 ± 1.0 ^a		41.0 ± 1.9 [3]		
			44.0 [6] ^d		
			44.1 ± 0.4 ^a	189.0 ± 1.1 ^a	187.8 (G4) ^a
recommended ^a	145.6 ± 0.6	58.3 ± 0.6 ^a	44.1 ± 0.4	189.7 ± 0.7	187.9 ^g
pyrazine (cr)	139.8 ± 1.2 [1]	55.3 ± 1.7 [3]	40.5 ± 1.7 [3]	196.1 ± 1.3 [30,31]	200.2 ± 2.9 [8] ^e
		56.3 ± 0.5 [1]	41.8 ± 0.7 [1] ^c		
			41.0 ± 0.1 [4]		
			40.2 ± 0.2 [5]		
			39.9 [6] ^d		
recommended ^a	145.7 ± 1.3 ^a	57.5 ± 0.4 ^a	42.0 ± 0.8 ^{a,c}	203.2 ± 1.5 ^a	206.5 (G4) ^a
	145.7 ± 1.3	57.5 ± 0.4	42.0 ± 0.8	203.2 ± 1.5	206.4 ^g

^aThis work; values given in italics were averaged and the averaged values are given in parentheses. ^bThis value was measured in ref 3 but was considered unreliable. ^cFrom the difference between $\Delta_{\text{cr}}^\circ H_m$ and $\Delta_{\text{cr}}^1 H_m$. ^dFrom Monte Carlo simulations. ^eCalculated using the MP3/6-31G(d,p) method in ref 8. ^fA weighted average calculated using the CBS-APNO, G3, and G3B3LYP method in ref 9. ^gMean values obtained from G4 and W1 calculations given in Table S9.

31G(d,p) level, Wiberg et al.⁸ concluded that the experimental gas phase enthalpy of formation of pyrimidine was in error. Using CBS-APNO, G3, and G3B3LYP methods, Da Silva et al.⁹ later suggested that the available measured enthalpy of formation of pyrimidine is high by 4–12 $\text{kJ}\cdot\text{mol}^{-1}$. Recently, Lipkind and Chickos^{3,10} presented new vaporization enthalpies of all three diazines using the technique of correlation-gas chromatography, and their results cast additional doubt on the accuracy of the literature vaporization enthalpy measured for pyrimidine. As indicated in Table 1, the experimental $\Delta_f H_m^\circ(\text{g})$ value reported for pyrimidine were in good agreement but differed from the calculated results by more than 10 $\text{kJ}\cdot\text{mol}^{-1}$. The ambiguity of the thermochemical properties of pyrimidine and perhaps the other diazines initially prompted this work. Our interest has been reinforced by our current activities on the field of ionic liquids (ILs).¹¹ This field is currently dominated by low melting imidazolium, pyridinium, pyrrolidinium, and alkyl ammonium salts.^{12–15} However, the ease with which the six-membered 1,2-, 1,3-, and 1,4- diazines undergo quaternization reactions significantly extends the variety of ILs with promising practical properties.¹² Pyridazinium-, pyrimidinium-, and pyrazinium-based ILs demonstrate high thermal, radiative, and chemical stability and thus offer many opportunities for wide application as liquid crystals, dye-stuffs, fluoroplastics, anesthetics, and as chemotherapeutic agents.¹³ These ILs can also be used as industrial solvents, especially as ligands for efficient catalyst recycling,¹⁴ or heat-resistant thermally stable explosives. They are also suitable candidates for high-energy density materials with higher performance and/or decreased sensitivity with respect to thermal, shock, and friction stability.¹⁵ Use of the three diazines as precursors for ILs raised the necessity of reliable thermochemical properties,

which is indispensable for proper temperature management of the highly exothermic ILs synthesis reactions.¹⁶

The current study investigates the energetics of diazines from both calorimetric and first principle computational perspectives where the comparison of these archetypical heterocycles will help benchmark contemporary calculational protocols. More precisely, we investigate the enthalpies of formation of pyridazine, pyrimidine, and pyrazine in both the condensed and gaseous state where our results and accompanying analysis has ramifications for both the biochemical and computational chemistry communities.

Materials. All compounds were purchased from Aldrich or Acros Ltd. Gas–liquid chromatography (GLC) analyses of the as-purchased samples gave an average mass fraction of 0.99, in agreement with specifications. Liquid compounds were fractionally distilled under flowing dry N_2 , after being dried with molecular sieves (0.4 nm). Solid pyrazine was sublimed under reduced pressure to remove any traces of solvent. The determination of purity was carried out by GLC. No impurities (≥ 0.01 mass percent) could be detected in samples used in this study. The samples were stored cold in the dark, either at reduced pressure or in a nitrogen atmosphere.

Combustion Calorimetry. For measurements of the enthalpies of combustion of the diazines, an isoperibolic calorimeter with a static bomb and a stirred water bath was used. The samples were placed (under an inert atmosphere in a glovebox) in polythene capsules and burned in oxygen at 3.04 MPa pressure. The detailed procedure has been described previously,^{11,17} and it is briefly given in the Supporting Information. The combustion procedure has been tested successfully on the secondary reference material, nicotinic acid. For the reduction of the data to standard conditions, conventional procedures^{18,19} were used. The auxiliaries are given in Table S1 (Supporting

Information). The values of the standard specific energy of combustion, $\Delta_c u^\circ$, the standard molar enthalpy of combustion, $\Delta_c H_m^\circ$, and the standard molar enthalpy of formation in the crystalline state $\Delta_f H_m^\circ(\text{cr})$ or in the liquid state $\Delta_f H_m^\circ(\text{l})$ were based on the reaction: $\text{C}_4\text{H}_4\text{N}_2 + 5 \text{O}_2 = 4 \text{CO}_2 + 2 \text{H}_2\text{O} + \text{N}_2$. Values of the molar enthalpies of formation, $\Delta_f H_m^\circ(\text{l or cr})$ of the compounds under study have been obtained from the enthalpic balance for reaction 1 above according to Hess's law using the molar enthalpies of formation of $\text{H}_2\text{O}(\text{l})$ and $\text{CO}_2(\text{g})$ as assigned by CODATA.²⁰ The results of the combustion experiments for the three diazines are given in Tables S2–S4 (Supporting Information). The uncertainties assigned to $\Delta_f H_m^\circ$ are twice the overall standard deviation and include the uncertainties from calibration, from the combustion energies of the auxiliary materials, and the uncertainties of the enthalpies of formation of the reaction products H_2O and CO_2 .

Transpiration Method. Vapor pressures, enthalpies of sublimation ($\Delta_{\text{cr}}^{\text{g}} H_m$), and enthalpies of vaporization ($\Delta_{\text{cr}}^{\text{l}} H_m$) of the diazines were determined using the method of transpiration in a saturated stream of nitrogen. The method has been described before^{21,22} (details are given in the Supporting Information) and has proven to give results in agreement with other established techniques. The temperature dependence of the vapor pressures

$$R \cdot \ln p_i^{\text{sat}} = a + \frac{b}{T} + \Delta_{\text{cr}}^{\text{g}} C_p \cdot \ln \left(\frac{T}{T_0} \right) \quad (1)$$

was used to determine the enthalpies of vaporization/sublimation of the diazines. Experimental results are presented in Table S5. The vapor pressure measurements on the diazines have been performed in the temperature range as close as possible to the reference temperature, $T = 298 \text{ K}$. Molar enthalpies of sublimation and vaporization of the compounds under study (Figure S1 and S2, Supporting Information) were obtained from the temperature dependence of the vapor pressure. New enthalpies of vaporization/sublimation as well as those known from the literature (see Table 1) were adjusted to $T = 298 \text{ K}$ using the experimental isobaric molar heat capacities according to the procedure described by Chickos and Acree.^{23,24}

Differential Scanning Calorimetry (DSC). The melting temperature and enthalpies of the solid phase transition and fusion of pyrazine and pyrimidine have been measured using DSC. For pyrazine, a solid phase transition, $\Delta H_{\text{tr}} = 1.0 \text{ kJ}\cdot\text{mol}^{-1}$ between 301.3 and 305.6 K, has been detected. An enthalpy of fusion $\Delta_{\text{cr}}^{\text{l}} H_m(327 \text{ K}) = 15.3 \pm 0.4 \text{ kJ}\cdot\text{mol}^{-1}$ measured by DSC was obtained at the melting temperature, $T_{\text{fus}} = 326.5 \text{ K}$. This value is in agreement with the fusion enthalpy, $14.7 \pm 0.4 \text{ kJ}\cdot\text{mol}^{-1}$ at 325.5 K, reported by Steele et al.⁴ The experimental enthalpy of fusion adjusted to $T = 298.15 \text{ K}$, $\Delta_{\text{cr}}^{\text{l}} H_m(298.15 \text{ K}) = 14.5 \pm 0.4 \text{ kJ}\cdot\text{mol}^{-1}$, using the procedure suggested by Chickos et al.²⁵ (details are given in the Supporting Information).

For pyrimidine, a solid phase transition, $\Delta H_{\text{tr}} = 2.6 \text{ kJ}\cdot\text{mol}^{-1}$, between 235.5 and 241.3 K has been detected. An experimental enthalpy of fusion, $\Delta_{\text{cr}}^{\text{l}} H_m(294 \text{ K}) = 13.0 \pm 0.5 \text{ kJ}\cdot\text{mol}^{-1}$, measured by DSC was obtained at the melting temperature $T_{\text{fus}} = 294.3 \text{ K}$ and adjusted to the reference temperature $\Delta_{\text{cr}}^{\text{l}} H_m(298.15 \text{ K}) = 13.1 \pm 0.5 \text{ kJ}\cdot\text{mol}^{-1}$ as described above.²⁵ These results are summarized in Table S6 (Supporting Information).

Computational Details. Standard ab initio molecular orbital calculations were performed with the Gaussian 09²⁶ series of programs. The energies of the compounds studied were calculated using different theoretical model chemistry methods: the Gaussian- n methods of Pople, Curtiss, and co-workers, at the G3²⁷ and G4²⁸ levels; the complete basis set (CBS) model chemistries of Petersson and co-workers, at the CBS-APNO²⁹ level, and the Weizmann- n (W n) theories of Martin and co-workers, at the W1(RO)³⁰ level (see details in the Supporting Information). The enthalpy value of the compounds studied at $T = 298 \text{ K}$ was evaluated according to standard thermodynamic procedures.³¹

Considerable activity has taken place with respect to the thermochemical property measurements on the diazabenzene. However, the mutual consistency of the data sets available from the literature is insufficient, especially for enthalpies of sublimation and enthalpies of formation (see Table 1). The additional thermochemical research reported here has helped to validate results previously generated for these compounds.

As indicated in Table 1, the two earlier $\Delta_f H_m^\circ(\text{l})$ values reported for pyrimidine were in good agreement, and as can be also seen from Table 1, our new combustion results for pyridazine and pyrimidine are in excellent agreement with those from previous studies. However, our new value $\Delta_f H_m^\circ(\text{cr})$ for pyrazine is about $6 \text{ kJ}\cdot\text{mol}^{-1}$ less negative than the earlier result. We suppose that some ill defined impurities and/or incomplete combustion of the earlier sample caused this difference.

Enthalpies of vaporization and enthalpies of sublimation at $T = 298.15 \text{ K}$ were derived from the temperature dependence of the vapor pressures (see Table 1). Experimental vapor pressures were fitted by eq 1 and they are given below:

$$\text{pyridazine } \Delta_{\text{cr}}^{\text{l}} H_m(298.15 \text{ K}) = 54.62 \pm 0.22 \text{ kJ}\cdot\text{mol}^{-1}$$

$$\ln(p/\text{Pa}) = \frac{259.54}{R} - \frac{68094.52}{R \cdot (T, \text{K})} - \frac{45.2}{R} \ln \left(\frac{T, \text{K}}{298.15} \right)$$

$$\text{pyrimidine } \Delta_{\text{cr}}^{\text{l}} H_m(298.15 \text{ K}) = 44.10 \pm 0.40 \text{ kJ}\cdot\text{mol}^{-1}$$

$$\ln(p/\text{Pa}) = \frac{253.70}{R} - \frac{57580.37}{R \cdot (T, \text{K})} - \frac{45.2}{R} \ln \left(\frac{T, \text{K}}{298.15} \right)$$

$$\text{pyrimidine } \Delta_{\text{cr}}^{\text{g}} H_m(298.15 \text{ K}) = 58.30 \pm 0.63 \text{ kJ}\cdot\text{mol}^{-1}$$

$$\ln(p/\text{Pa}) = \frac{273.10}{R} - \frac{63098.28}{R \cdot (T, \text{K})} - \frac{16.1}{R} \ln \left(\frac{T, \text{K}}{298.15} \right)$$

$$\text{pyrazine (cr I) } \Delta_{\text{cr}}^{\text{g}} H_m(298.15 \text{ K}) = 57.47 \pm 0.41 \text{ kJ}\cdot\text{mol}^{-1}$$

$$\ln(p/\text{Pa}) = \frac{269.76}{R} - \frac{62270.83}{R \cdot (T, \text{K})} - \frac{16.1}{R} \ln \left(\frac{T, \text{K}}{298.15} \right)$$

$$\text{pyrazine (cr II) } \Delta_{\text{cr}}^{\text{g}} H_m(298.15 \text{ K}) = 56.43 \pm 0.82 \text{ kJ}\cdot\text{mol}^{-1}$$

$$\ln(p/\text{Pa}) = \frac{266.47}{R} - \frac{61232.93}{R \cdot (T, \text{K})} - \frac{16.1}{R} \ln \left(\frac{T, \text{K}}{298.15} \right)$$

Pyridazine and pyrimidine are quite volatile liquids, and it would appear that their vapor pressures and vaporization enthalpies would not be difficult to measure with conventional methods. Surprisingly, the spread of the vaporization enthalpy data for these compounds is over $10 \text{ kJ}\cdot\text{mol}^{-1}$. In contrast, available experimental vaporization enthalpies for pyrazine are in good agreement, all within $1\text{--}2 \text{ kJ}\cdot\text{mol}^{-1}$. Recently, Lipkind and Chickos³ derived vaporization enthalpies of all three diazines using the technique of correlation-gas chromatography.

In this study they concluded that, based on evaluated vapor pressure and boiling temperature estimates, their result for pyridazine was in error and subsequently re-evaluated this result by using the same technique with different standards.⁷ As can be seen in Table 1, our new results measured by transpiration for all three diazines are in very good agreement with the data derived in refs 3 and 7 using correlation-gas chromatography. In a recent study, Rai and Siepmann⁶ calculated a vaporization enthalpy of all three diazines using Monte Carlo simulations. Their results for pyrimidine and pyrazine were in good agreement with the value measured in this study. However, vaporization enthalpy for pyridazine of 60.6 kJ·mol⁻¹ was significantly larger in comparison to other values (see Table 1).

Internal Consistency of the Phase Change Enthalpies of Pyrazine and Pyrimidine. As a result of the large spread of the available phase change data for the diazines as shown in Table 1, an additional test for consistency of our new experimental data was desirable. In order to ascertain our results, we deliberately measured vapor pressures of pyrazine and pyrimidine of the solid as well as of the liquid sample and derived enthalpies of vaporization and enthalpies of sublimation for both diazines (see Table S5, Supporting Information). In combination with additional DSC measurements of both the fusion enthalpy and solid–solid phase transition (see Table S6, Supporting Information), we have tested the phase transitions data for internal consistency as follows.

The value of $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (58.3 \pm 0.6)$ kJ·mol⁻¹ for pyrimidine was obtained in this work from measurements in the temperature range $T = (275.1\text{--}291.8)$ K of the solid sample. The value of $\Delta_{\text{f}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (44.1 \pm 0.4)$ kJ·mol⁻¹ for pyrimidine was obtained in this work from measurements in the temperature range $T = (293.5\text{--}328.1)$ K of the liquid sample. Using these values, the enthalpy of fusion, $\Delta_{\text{cr}}^{\text{l}}H_{\text{m}}(298\text{ K}) = \Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298\text{ K}) - \Delta_{\text{f}}^{\text{g}}H_{\text{m}}(298\text{ K}) = 58.3 - 44.1 = 14.2 \pm 0.7$ kJ·mol⁻¹, was calculated, which is in very close agreement with the value measured by DSC, $\Delta_{\text{cr}}^{\text{l}}H_{\text{m}}(298\text{ K}) = (13.1 \pm 0.5)$ kJ·mol⁻¹, in this work.

Pyrazine in the solid state exists in two crystal modifications, cr II and cr I, with a phase transition enthalpy, $\Delta_{\text{cr}}^{\text{cr2}}H_{\text{m}}(T_{\text{tr}}) = (0.9 \pm 0.1)$ kJ·mol⁻¹ at 300.7 K (see Table S6, Supporting Information). The value of $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (56.4 \pm 0.8)$ kJ·mol⁻¹ for pyrazine was obtained from measurements in the temperature range $T = (303\text{--}314)$ K of the sample in the cr II phase. The value of $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (57.5 \pm 0.4)$ kJ·mol⁻¹ for pyrazine was obtained from measurements in the temperature range $T = (274.5\text{ to }300.3)$ K of the sample in the cr I phase. The sublimation enthalpies obtained from either side of the transition differ by about 1 kJ·mol⁻¹, and this difference exactly can be attributed to the enthalpy of the solid–solid phase transition $\Delta_{\text{cr}}^{\text{cr2}}H_{\text{m}}(T_{\text{tr}})$ measured by DSC. Using $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (56.5 \pm 0.6)$ kJ·mol⁻¹ for cr I and the fusion enthalpy adjusted to $T = 298\text{ K}$, $\Delta_{\text{cr}}^{\text{l}}H_{\text{m}}(298\text{ K}) = 14.5 \pm 0.5$ kJ·mol⁻¹, a value for the vaporization enthalpy for pyrazine, $\Delta_{\text{f}}^{\text{g}}H_{\text{m}}(298\text{ K}) = (42.0 \pm 0.8)$ kJ·mol⁻¹ is calculated, which is in very close agreement with the results reported in the literature.^{3–5} Thus, the phase transition data measured in this work possess internal consistency and can now be used together with the results from combustion experiments for calculation of the standard gas phase enthalpy of formation, $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ at $T = 298\text{ K}$, of all three diazines. The resulting experimental values of $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ are given in the column 5 in Table 1, and they can be now

compared with previous experimental results as well as with the theoretical results from quantum chemical calculations.

Experimental Gas Phase Enthalpies of Formation of the Diazines. The experimental enthalpies of formation, $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$, of the three diazines that are the subject of this work are reported in Table 1. This table also includes previous literature values evaluated in the commonly acknowledged comprehensive thermochemical data compilations by Cox and Pilcher³² as well as by Pedley et al.³³ In comparison to the $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ values recommended earlier, our results are significantly different for pyrimidine by 6.7 kJ·mol⁻¹ lower, and for pyrazine by 7.1 kJ·mol⁻¹ higher. The results for pyridazine basically remain unchanged. With respect to very carefully purified and sufficiently attested samples used in this work, as well as due to internal consistency of vapor pressure results, our new thermochemical results together with some earlier values (see Table 1) can be now recommended as the benchmark thermochemical properties for the diazines studied in this work. Table 1 summarizes the recommended phase change enthalpies and enthalpies of formation. Not all the experimental literature values were necessarily included in the generation of the recommended value. For pyridazine, the recommended value for $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ is the sum of the average values for $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{l})$ and the vaporization enthalpy measured in this work. For pyrimidine, the average $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{l})$ value is indistinguishable from the one measured in this work. The value chosen for the vaporization enthalpy is also the one measured in this work. This value was chosen on the basis of the consistent results obtained from the thermochemical cycle described above. This value resolves the contradictions due to the wide divergence of the values from the literature. The recommended $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ value for pyrazine was based on the thermochemical results evaluated by this work.

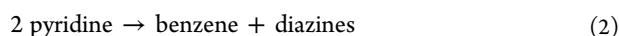
Calculation of the Gas Phase Enthalpies of Formation: Quantum Chemical Calculations. Recent development of the quantum chemistry methods have been designed for predicting enthalpies of formation $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ with “chemical accuracy”, which is usually defined as within ± 4 kJ·mol⁻¹ (± 1 kcal·mol⁻¹) of the experimental value. It means that the validation of these method have to be performed with highly accurate experimental values of benchmark quality.

Reliable calculations of enthalpies of formation for small rings and aromatic compounds have been a popular but challenging endeavor for quantum chemists.^{27–30} Although the average absolute deviation from experiment for hydrocarbons is on the level of experimental accuracy of 3–5 kJ·mol⁻¹, the deviations are much larger for unsaturated ring systems than for saturated systems. For example, the enthalpy of formation even of benzene calculated by the modern composite G2 method differs from experiment by 16.3 kJ·mol⁻¹, and only the incorporation of the special correction taking into account some core-related correlation²⁷ improved the deviation to 2.9 kJ·mol⁻¹. Having in mind these inherent complications of the quantum chemical methods, the experimental data used for the design of such a “special correction” should only be of impeccable quality. The consistent experimental data set for the diazines derived in this work has allowed a test of some of the most popular quantum chemical methods: G3, G4, CBS-APNO, and W1(RO) to predict $\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$ for these species.

Enthalpies of formation of diazines calculated by Wiberg⁸ using the MP3/6-31G(d,p) method are nowadays only of historical interest as the first indication of the possible disarray of experimental data. In this work, we have selected the best

modern G3, G4, CBS-APNO, and W1(RO) methods, which are claimed to predict $\Delta_f H_m^\circ(\text{g})$ values at the desired level.

We have calculated the total energies E_0 at $T = 0$ K and enthalpies H_{298} at $T = 298$ K using four first-principle methods (Table S2, Supporting Information). In order to convert the H_{298} values into theoretical standard enthalpies of formation, $\Delta_f H_m^\circ(\text{g})$, construction of model reactions with simple molecules is usually required. However, it is well established that the enthalpies of formation obtained from the first-principle calculations are very sensitive to the choice of the bond separation or isodesmic reactions used for this purpose.³⁴ The possible reasons usually account for the large number of small molecules and the different quality of their experimental data, as well as an imbalance of electronic energies between the left and the right side calculated for the reaction participants. For example, we calculated the gaseous enthalpies of formation, using a very well balanced isodesmic reaction (see Table S7)



In spite of the high quality of the enthalpies of formation of benzene, pyridine, and the diazines, the spread of the theoretical values calculated by our four selected methods was on the order of 4–5 $\text{kJ}\cdot\text{mol}^{-1}$, among them as well as with the experimental values. In contrast to the bond isodesmic reactions, the atomization reaction suggests that the quality of the data on the right side (the constituent atoms) is the same for all compounds under study.³⁴ From our experiences with these first-principle methods, we have noticed that for certain classes of organic compounds (e.g., for C, H, N, and O containing molecules of the parent structure and similar in size), very often the enthalpies of formation derived with the atomization procedure deviate systematically from the experimental values. Fortunately, it has turned out that a simple linear-type correlation could be found between experimental enthalpies of formation and those calculated by the atomization procedure (see Table S8) for each computational method.³⁵ In this work we have collected a set of 18 small heterocyclic compounds similar in shape to the diazines. The following linear correlations have been obtained (in the case of W1(RO) calculations, there are only 8 compounds in the correlations due to the very expensive computational cost of this method, see below):

$$\begin{aligned} \Delta_f H_m^\circ(\text{g})(\text{exp})/\text{kJ}\cdot\text{mol}^{-1} \\ = (0.988 \pm 0.006)\Delta_f H_m^\circ(\text{g})(\text{G3}) - (1.3 \pm 0.7) \end{aligned} \quad (3)$$

$$n = 18 \quad R = 0.9995$$

$$\begin{aligned} \Delta_f H_m^\circ(\text{g})(\text{exp})/\text{kJ}\cdot\text{mol}^{-1} \\ = (0.010 \pm 0.003)\Delta_f H_m^\circ(\text{g})(\text{G4}) - (0.7 \pm 0.4) \end{aligned} \quad (4)$$

$$n = 18 \quad R = 0.9998$$

$$\begin{aligned} \Delta_f H_m^\circ(\text{g})(\text{exp})/\text{kJ}\cdot\text{mol}^{-1} \\ = (0.957 \pm 0.008)\Delta_f H_m^\circ(\text{g})(\text{CBS} - \text{APNO}) \\ + (11.4 \pm 0.9) \end{aligned} \quad (5)$$

$$n = 18 \quad R = 0.9990$$

$$\begin{aligned} \Delta_f H_m^\circ(\text{g})(\text{exp})/\text{kJ}\cdot\text{mol}^{-1} \\ = (0.977 \pm 0.005)\Delta_f H_m^\circ(\text{g})(\text{W1}(\text{RO})) + (10.5 \pm 0.6) \end{aligned} \quad (6)$$

$$n = 8 \quad R = 0.9998$$

These correlations derived for each of the selected quantum chemical methods now open a new option for calculating more precisely the theoretical enthalpies of formation of diazines using the results from the atomization procedure (see Table S9), and most of these “corrected” values are now in good agreement with the experimental results for diazines (within the error bars of 1–2 $\text{kJ}\cdot\text{mol}^{-1}$). In our opinion, the combination of the first-principle methods with such a “corrected atomization procedure” could be generally recommended for reliable calculations of $\Delta_f H_m^\circ(\text{gas}, 298 \text{ K})$ of organic compounds. Indeed, using the enthalpies H_{298} calculated by G3, G4, CBS-APNO, W1(RO), or any other method can be converted to enthalpies of formation without creating any “suitable” sophisticated bond separation or isodesmic reaction. Having established the corrected atomization procedure for all 4 computational methods, we are able to set priorities among them. As a rule, the best method should be accurate and less time-consuming. The computational cost of these methods follows the order: G3 < G4 ~ CBS-APNO \ll W1(RO), and it is apparent that the W1(RO) method is much more expensive than the others.

Results of quantum chemical calculations collected in Tables S8 and S9 have revealed that G4 is the best method for calculation of various azines and diazines and their parent compounds. The linear correlation (eq 4) has the best fit to the experimental data. This method also has acceptable CPU time consumption for the heterocycles studied in Table S8. The following values for the studied diazines: pyridazine 281.7 $\text{kJ}\cdot\text{mol}^{-1}$, pyrimidine 187.8 $\text{kJ}\cdot\text{mol}^{-1}$, and pyrazine 206.5 $\text{kJ}\cdot\text{mol}^{-1}$, were calculated by G4 (see Table 1 and S9). The next accurate method for calculating nitrogen containing heterocycles is W1(RO). However, the usual university computational resources are very restricted for the broad application of this method to molecules larger than the diazabenzene studied in this work. Mean values obtained from G4 and W1 calculations are considered as the recommended best “theoretical” values for the diazines studied (see Table 1).

Thermochemical properties for three diazabenzene have been measured using well-established experimental techniques. Data are tested for the internal consistency and the new data set of $\Delta_f H_m^\circ(\text{g})$ of benchmark quality have been used to evaluate the most accurate first-principles methods currently available: G3, G4, CBS-APNO, and W1(RO). A simple “corrected atomization procedure” to derive theoretical $\Delta_f H_m^\circ(\text{g})$ directly from the enthalpies H_{298} has been tested and recommended as an alternative to the bond separation and isodesmic reactions for calculations of organic cyclic and heterocyclic compounds containing one to three nitrogen atoms.

■ ASSOCIATED CONTENT

Supporting Information

Experimental and theoretical details and additional data of the calculations performed here. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

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