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Enthalpy of formation of 6-(4-methoxyphenyl)-1,5-diazabicyclo[3.1.0]-hexane: determination by experimental and computational methods

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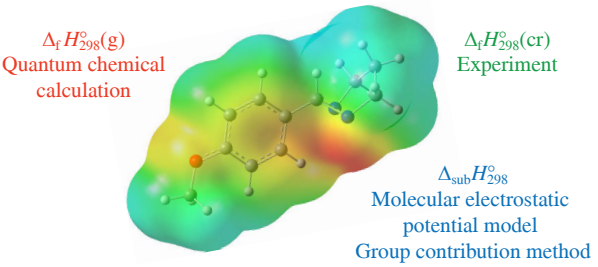
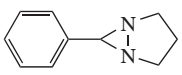
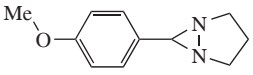
The bicyclic diaziridine derivative 6-(4-methoxyphenyl)-1,5-diazabicyclo[3.1.0]hexane was synthesized, purified and characterized. Its standard specific energy in the crystalline state at 298.15 K was determined by static bomb combustion calorimetry, from which the standard enthalpies of combustion and formation were calculated. The enthalpy of formation in the gas phase was calculated using the DLPNO-CCSD(T_1)/CBS method in combination with isodesmic reactions; the molecular electrostatic potential and group additivity methods were used to estimate the enthalpy of sublimation.



Keywords: diaziridine derivatives, 6-(4-methoxyphenyl)-1,5-diazabicyclo[3.1.0]hexane, synthesis, combustion calorimetry, standard enthalpy of formation, quantum chemical calculations.

Various transformations of 6-phenyl-1,5-diazabicyclo[3.1.0]hexane (PDABH) revealed in synthetic studies are applied to prepare precursors or intermediates in technologies for the production of a wide range of materials.[1–5] This bicyclic diaziridine derivative was recently selected by us for the determination of its enthalpies of combustion and formation, and to our knowledge, those measurements[6] remain the only experimental thermochemical study of diaziridine derivatives.


PDABH


MPDABH

In this work, we carried out a calorimetric investigation of another PDABH derivative, 6-(4-methoxyphenyl)-1,5-diazabicyclo[3.1.0]-hexane (MPDABH), which, like some other PDABH derivatives, is an important intermediate and precursor in organic synthesis.[1,5,7–10] The experimental value of the enthalpy of formation of MPDABH obtained in this work will allow us to test the reliability of the previously proposed scheme for estimating the enthalpies of formation of crystalline compounds using the molecular electrostatic potential (MEP) model. For greater reliability of the results, theoretical estimates were also performed for several other PDABH derivatives such as 2,4-dimethoxy-, 4-ethoxy-, 3,4,5-trimethoxy-, 4-isopropoxy- and 4-nitro-PDABH. Additionally, for all the compounds considered, the enthalpies of formation in the gas and solid phases were also estimated using the group additivity method.

MPDABH was synthesized according to the described method[11] and purified by vacuum sublimation at $p = 7.6$ Torr and $T = 30$ °C in a vacuum drying chamber (Table S3).[†,‡,12] The structure of the synthesized compound was controlled by spectroscopic methods.

Using differential scanning calorimetry, it was found that MPDABH melts at a temperature of 373.1 ± 0.2 K with a melting enthalpy of 27642.7 J mol^{-1} (145.3 J g^{-1}) (Figure 1).[§] Thermogravimetric analysis showed that after reaching the melting point, the MPDABH sample decomposes at a temperature of 381.0 K (Figure S12).[†,¶]

Precision calorimeters[††] with a stationary self-sealing bomb were used to measure the combustion energy of MPDABH. The results and data processing of the calorimetric determination of the combustion energy of MPDABH are presented in Table S3.[†,6] The standard molar energy, enthalpy of combustion and enthalpy of formation of MPDABH in the crystalline state are given in Table 1.

The gas-phase enthalpy of formation of MPDABH and some other PDABH derivatives was calculated from isodesmic reactions. The electron energies required to evaluate the enthalpies of these reactions were determined using the DLPNO-CCSD(T_1) level of theory.[13] The molecular electrostatic potential (MEP) model was used to estimate the enthalpy of sublimation of the compounds under consideration. The MEP model was based on experimental data for 400 CHNO compounds. All calculation details were described earlier when considering the parent molecule PDABH.[6] Gaussian 16[14] and ORCA 5.0.3[15] programs were used for quantum chemical calculations. Molecular surface analysis based

† For details, see Online Supplementary Materials.

‡ The sample was characterized by elemental analysis. Found (wt%): C, 69.54 ± 0.2; H, 7.30 ± 0.3; N, 14.89 ± 0.3. Calc. for $C_{11}H_{14}N_2O$ (wt%): C, 69.45; H, 7.42; N, 14.73. The purity of 100.00 ± 0.04 wt% was estimated by the gravimetric method for gaseous combustion products (carbon dioxide).[12]

§ A NETZSCH DSC 204 F1 Phoenix® differential scanning calorimeter was used.

¶ NETZSCH TG 209 F1 Iris® thermobalances were used.

†† Dickinson and Parr 6200 calorimeters were used.

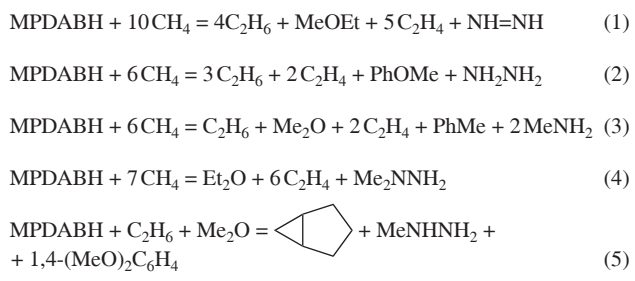
Table 1 Values of standard molar energy ($\Delta_c U_m^\circ$), enthalpy of combustion ($\Delta_c H_m^\circ$) and enthalpy of formation ($\Delta_f H_m^\circ$) of MPDABH in the crystalline phase at $T = 298.15$ K.[a]

$\Delta_c U_m^\circ$(cr)/kJ mol^{-1}	$\Delta_c H_m^\circ$(cr)/kJ mol^{-1}	$\Delta_f H_m^\circ$(cr)/kJ mol^{-1}
–6394.0 ± 3.8	–6398.9 ± 3.8	69.6 ± 4.1

[a] All uncertainties are the combined expanded uncertainties (U_c) at a confidence level of 0.95. Uncertainties in the determination of the energy equivalent and combustion energies of benzoic acid and MPDABH were taken into account in the calculation of $U_c[\Delta_c H_m^\circ(\text{cr})]$.[6]

on the Multiwfn program[16] was applied to obtain MEP descriptors. The gas-phase and solid-phase enthalpies of formation of PDABH derivatives were also estimated by the group additivity approach using the group contribution values determined by Domalski and Hearing.[17]

The enthalpies of formation of MPDABH (Table 2) and other PDABH derivatives (Table S4) were calculated using isodesmic reactions (1)–(5) involving different methoxy derivatives and nitrogen-containing compounds. As can be seen from Table 2, all five reactions give similar $\Delta_f H_m^\circ$(298.15 K) values despite using different reference compounds in each reaction. For other PDABH derivatives such as 2,4-dimethoxy-, 4-ethoxy-, 3,4,5-trimethoxy-, 4-isopropoxy- and 4-nitro-PDABH, the uncertainty in the calculated values is somewhat larger, especially for 2,4-dimethoxy- and 3,4,5-trimethoxy-PDABH for which reference compounds conveying the methoxy group interactions are difficult to find.



$$\text{MPDABH} + 10\,CH_4 = 4C_2H_6 + \text{MeOEt} + 5\,C_2H_4 + \text{NH=NH} \quad (1)$$

$$\text{MPDABH} + 6\,CH_4 = 3\,C_2H_6 + 2\,C_2H_4 + \text{PhOMe} + NH_2NH_2 \quad (2)$$

$$\text{MPDABH} + 6\,CH_4 = C_2H_6 + Me_2O + 2\,C_2H_4 + \text{PhMe} + 2\,\text{MeNH}_2 \quad (3)$$

$$\text{MPDABH} + 7\,CH_4 = Et_2O + 6\,C_2H_4 + Me_2NNH_2 \quad (4)$$

$$\text{MPDABH} + C_2H_6 + Me_2O = \text{[cyclopentane]} + \text{MeNHNH}_2 + \text{+ 1,4-(MeO)}_2C_6H_4 \quad (5)$$

To estimate the enthalpies of formation of PDABH derivatives in the solid phase, their enthalpies of sublimation were calculated using the MEP model, as was done previously for PDABH,[6] for which the experimental value of $\Delta_f H_m^\circ$(cr) was reproduced very well (Table 3). However, compared to PDABH, the sublimation enthalpy value of 109.0 ± 12.0 kJ mol^{-1} for MPDABH calculated using the MEP model is 12.1 kJ lower than the value of 121.1 ± 4.6 kJ mol^{-1} obtained from the experimental data as $\Delta_{sub} H_m^\circ = \Delta_f H_m^\circ(\text{g,calc}) - \Delta_f H_m^\circ(\text{cr,exp})$. Although this discrepancy lies within the error limits of the calculated MEP value, for an additional assessment of the accuracy of the data obtained in this work, $\Delta_f H_m^\circ$(cr) and $\Delta_f H_m^\circ$(g) were calculated using the group additivity method,[17] which should give reliable results, since there are sufficient experimental data are for methoxy derivatives of benzene.

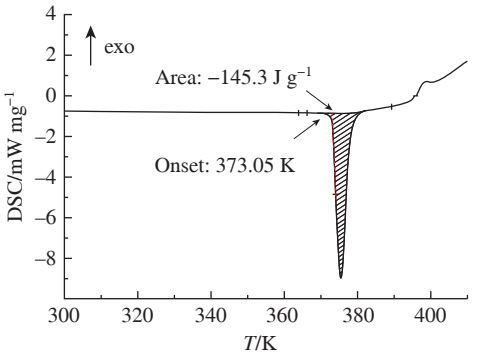


Figure 1 Melting temperature and melting enthalpy of MPDABH.

Table 2 Standard molar enthalpy of formation in the gas phase at 298.15 K for MPDABH calculated at the DLPNO-CCSD(T_1)/CBS//B3LYP-D3(BJ)/def2-TZVPP level using isodesmic reactions (1)–(5).

Entry	Reaction equation	$\Delta_r H_m^\circ$[a]/kJ mol^{-1}	$\Delta_f H_m^\circ$/kJ mol^{-1}
1	(1)	461.9	191.5
2	(2)	137.0	190.1
3	(3)	101.1	190.4
4	(4)	477.1	191.4
5	(5)	–4.6	190.1
6	Weighted average	–	190.7 ± 2.0[b]

[a] Enthalpy of reaction. [b] The uncertainty of the calculated value was defined as $s_d \times t$, where s_d is the standard deviation from the weighted average value and t is Student's coefficient for the 95% confidence level.

The results obtained using the group additivity calculation scheme are shown in Table 3. These estimations were based on the enthalpies of formation of PDABH[6] and the group contributions proposed by Domalski and Hearing[17] (for details, see Table S5). As can be seen from Table 3, the $\Delta_f H_m^\circ$(g) and $\Delta_f H_m^\circ$(cr) values for MPDABH calculated from the group contributions are in good agreement with those determined in the present work. Thus, the sublimation enthalpy value calculated from the MEP descriptors is clearly underestimated.

As for other PDABH derivatives, a large discrepancy between the enthalpies of sublimation calculated by the MEP and GA methods is observed for 2,4-dimethoxy- and 3,4,5-trimethoxy-PDABH. On the one hand, this may be due to the need to select the parameters of the MEP equation using a narrow set of test compounds that are most similar in structure to methoxy-substituted benzenes, similar to how this was done, for example, for tetrazine derivatives[18] and adamantanes.[19] On the other hand, it should be noted that corrections for *ortho*- and *meta*-interactions between two or more methoxy groups were not developed, and corrections for interactions between methoxy and carboxyl groups[17] were applied instead (see Table S5). This may be the reason for the inaccuracy of the GA values for 2,4-dimethoxy- and 3,4,5-trimethoxy-PDABH. For the remaining compounds in Table 3, 4-ethoxy-, 4-isopropoxy- and 4-nitro-PDABH, the discrepancies between the MEP and GA values of the enthalpies of sublimation do not exceed 4.9 kJ mol^{-1} and therefore the obtained estimates of $\Delta_f H_m^\circ$(cr) for these compounds can be considered reliable.

Using the approaches described earlier,[6] a thermochemical study of 6-(4-methoxyphenyl)-1,5-diazabicyclo[3.1.0]hexane was carried out by experimental and theoretical methods. The enthalpy of formation in the solid and gas phases at 298.15 K, the enthalpy of sublimation at 298.15 K, the melting point and the enthalpy of melting of this compound were determined for the first time. These values are fundamental physicochemical characteristics that can be used in thermodynamic modeling of processes involving MPDABH, as well as in evaluating other thermodynamic properties of this compound and other PDABH derivatives.

The quantum chemical method used in this work allows one to determine the enthalpy of formation in the gas phase for PDABH derivatives with sufficient accuracy, whereas the errors in determining the enthalpy of sublimation using the MEP model can reach 10–20 kJ mol^{-1}, as was the case with methoxy derivatives of PDABH. Therefore, as an additional check of the accuracy of the MEP values of the enthalpy of sublimation, it is recommended to use the group additivity approach. In this case, there is no need to perform calculations using group contributions, but it is sufficient, if the necessary experimental data are available, to compare the enthalpies of sublimation of related compounds. For example, for MPDABH, one can compare the enthalpies of sublimation of benzoic acid (90.4 kJ mol^{-1})[20] and 4-methoxybenzoic acid (112.2 kJ mol^{-1})[21] and assume that the enthalpy of sublimation of MPDABH should be approximately 22 kJ mol^{-1} higher than that of PDABH. Thus,

Table 3 Estimation of the enthalpy of sublimation and the enthalpy of formation in the solid phase for PDABH and its derivatives.

Entry	Molecule	Method[a]	$\Delta_f H_m^\circ$(g)/kJ mol^{-1}	$\Delta_{sub} H_m^{\circ b}$/kJ mol^{-1}	$\Delta_f H_m^\circ$(cr)[b]/kJ mol^{-1}
1	PDABH	QC + EXP	343.4 ± 1.9	(97.0 ± 2.6)	246.4 ± 1.8 (exp[6])
2		QC + MEP	343.4 ± 1.9	96.5 ± 12.0	(246.9 ± 12.1)
3	MPDABH	QC + EXP	190.7 ± 2.0	(121.1 ± 4.6)	69.6 ± 4.1 (exp)
4		QC + MEP	190.7 ± 2.0	109.0 ± 12.0	(81.7 ± 12.2)
5		GA	190.0	(118.7)	71.3
6	2,4-dimethoxy-PDABH	QC + MEP	39.2 ± 5.4	120.2 ± 12.0	(–81.0 ± 13.2)
7		GA	41.7	(140.6)	–98.9
8	4-ethoxy-PDABH	QC + MEP	157.6 ± 3.4	114.3 ± 12.0	(43.3 ± 12.5)
9		GA	157.1	(118.8)	38.3
10	3,4,5-trimethoxy-PDABH	QC + MEP	–84.3 ± 5.4	137.2 ± 12.0	(–221.5 ± 13.2)
11		GA	–86.7	(146.3)	–233.0
12	4-isopropoxy-PDABH	QC + MEP	124.7 ± 3.6	119.0 ± 12.0	(5.7 ± 12.5)
13		GA	128.3	(123.9)	4.4
14	4-nitro-PDABH	QC + MEP	323.7 ± 2.7	119.4 ± 12.0	(204.3 ± 12.3)
15		GA	328.1	(120.7)	207.4

[a] QC + EXP: The enthalpy of sublimation was estimated using the $\Delta_f H_m^\circ$(g) value determined from quantum chemical calculations and the experimental $\Delta_f H_m^\circ$(cr) value. QC + MEP: The enthalpy of formation in the solid phase was estimated using the $\Delta_f H_m^\circ$(g) value determined from quantum chemical calculations, and the $\Delta_{sub} H_m^\circ$ value was obtained from the MEP descriptors using the equation $\Delta_{sub} H_m^\circ = a\rho + bA_S + cV_S + d(\sigma_{tot}^2\nu) + e\Pi + f$, where ρ is the crystal density, A_S is the overall molecular surface area, V_S is the average value of the surface potential, $\sigma_{tot}^2\nu$ is the product of the variability of the molecular surface potential (σ_{tot}^2) and the degree of balance between the positive and negative regions (ν), and Π is the measure of local polarity.[6] GA: The enthalpies of formation in the gas and solid phases were calculated using group additivity values[17] (for details, see Table S5). [b] The values in parentheses were obtained from the equation $\Delta_f H_m^\circ$(cr) + $\Delta_{sub} H_m^\circ = \Delta_f H_m^\circ$(g) using the other two values in this equation.

it is quite possible to replace experimental studies of PDABH derivatives with theoretical calculations, as proposed in this work.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7770.

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