



Dedicated to Professor Alexandru T. BALABAN  
on the occasion of his 90<sup>th</sup> anniversary

## THE STRUCTURE-ACTIVITY RELATIONSHIPS FROM DSC DATA

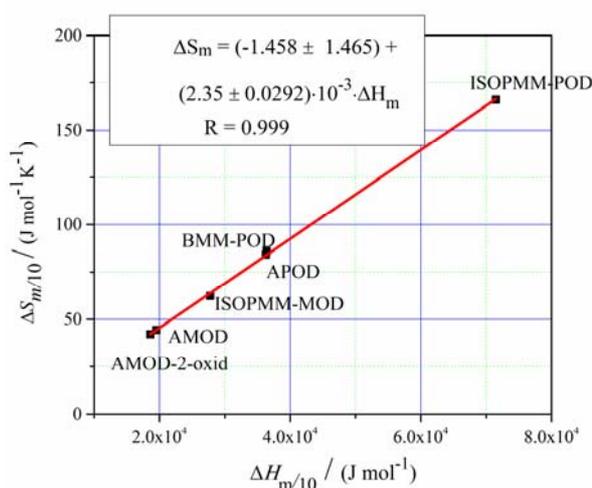
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The differential scanning calorimetry becomes nowadays an easily available technique able to provide experimental data which can be used to seek for possible correlations with molecular properties. Among these data, the entropy and enthalpy for different phase transition like melting or decomposition of various related compounds proved to be very fruitful. In the present paper, the enthalpy and entropy data for different phase transitions and decomposition of two classes of related energetic compounds (13 based on phenoxazone derivatives and 6 on substituted (*E*)-3-(azulen-1-yl-diazonyl)-1,2,5-oxadiazole) are analyzed and presented. The heats of decomposition seem to present no correlations as functions of molecular mass or melting temperature, while the heats of melting and the temperatures of melting present a fair correlation as a function of the molecular mass or melting temperature. A particularly good correlation is provided by the entropy of melting as a function of the enthalpy of melting, in accord with their significance for a process at equilibrium.



### INTRODUCTION

The subject dedicated to the relations between structure and properties of different compounds has been approached long time ago by several organic chemists and belong to basic principles of physical chemistry. Subsequently they substantiated the new discipline "Physical Organic Chemistry", dedicated to finding possible correlations between structural and measured properties. A step forward has been accomplished by using theoretical structural indexes.<sup>1</sup> A consistent contribution has been offered by several

seminal works of A. T. Balaban.<sup>2-4</sup> Some new works enlarged the knowledge in the field.<sup>5-9</sup> The subsequent pertinent papers have been dedicated to the experimental methods allowing for the measurements of different thermal properties, especially those based on differential scanning calorimetry (DSC). DSC is a useful technique able to rapidly provide all the thermodynamic parameters of different compounds.<sup>10,11</sup> The evaluation of quantitative structure-property relationship (QSPR) methods coupled with predictive methods (such as: molecular modeling methods, computer-assisted chemical risk

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assessment) mainly used to predict physico-chemical properties of energetic compounds are of a growing interest.<sup>12–15</sup> The extensive structure-properties relationships between various physico-chemical and structural parameters of different classes of energetic compounds was studied by different research groups.<sup>16–24</sup> The main advantage of quantitative structure-property relationships consists in establishment of a new structural model between various physical and chemical properties and the chemical structure. Moreover, the quantitative structure-property relationship can be useful to explain and to determine the structural and chemical properties of new chemical compounds with related molecular structure.<sup>25</sup>

Present research is focused on the study of structure-properties relationship of two sets of related energetic compounds (i) 13 based on phenoxazone derivatives and (ii) 6 based on substituted (*E*)-3-(azulen-1-ylidiazanyl)-1,2,5-oxadiazole. The data (melting temperature  $T_m$ , molar mass  $M$ , melting enthalpy  $\Delta H_m$ , and enthalpy of decomposition  $-\Delta H_{dec}$ ) used in these predictions are obtained from differential scanning calorimetry measurements, in our previous works.<sup>26,27</sup>

## RESULTS AND DISCUSSION

Figure 1 presents a typical DSC curve for (*E*)-3-(azulen-1-ylidiazanyl)-4-phenyl-1,2,5-oxadiazole (APOD) obtained in non-isothermal

heating mode, at a  $10 \text{ K min}^{-1}$  heating rate. The physical parameters such as: melting temperature ( $T_m$ ) and melting heat ( $\Delta H_m$ ), maximum decomposition temperature ( $T_{max}$ ) and decomposition heat ( $-\Delta H_{dec}$ ) were obtained from the experimental DSC curve.

The stability of a molecule is quantified by the standard free energy  $\Delta G$  with is the sum of two contributions according to equation (1):

$$\Delta G(T) = \Delta H(T) - T\Delta S(T) \quad (1)$$

where  $\Delta H$  and  $\Delta S$  are the enthalpy and the entropy changes at the temperature  $T$  at which  $\Delta G$  is being evaluated. At the melting point ( $T = T_m$ ), the whole system being at equilibrium (when  $\Delta G = 0$ ), and equation (2) can be obtained:

$$\Delta S_m = \frac{\Delta H_m}{T_m} \quad (2)$$

Consequently, the melting entropy of studied compounds can be calculated using the eq. (2), where  $T_m$  and  $\Delta H_m$  are the temperature and heat of melting, and  $\Delta S_m$  is the melting entropy. It is well known that both melting enthalpy and entropy are dependent on the chemical structure of compounds: the melting enthalpy is dependent on the intermolecular interaction between various functional groups of the molecule, whereas the melting entropy is dependent on the internal arrangement of the groups present in a molecule.<sup>14</sup>

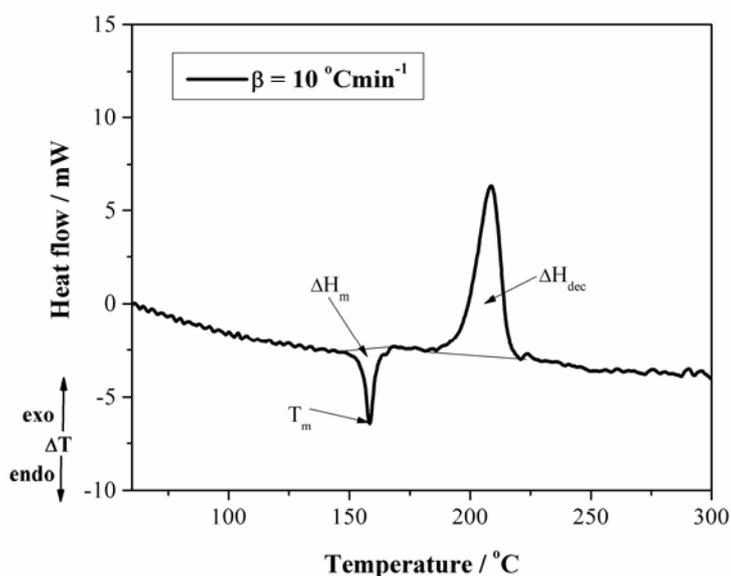


Fig. 1 – The DSC curve of (*E*)-3-(azulen-1-ylidiazanyl)-4-phenyl-1,2,5-oxadiazole (APOD) decomposition, recorded at  $10 \text{ K min}^{-1}$  heating rate and ambient pressure.

## RESULTS AND DISCUSSION

The necessary data for study of structure-properties relationship (melting temperature  $T_m$ , molar mass  $M$ , melting enthalpy  $\Delta H_m$ , melting entropy  $\Delta S_m$  and enthalpy of decomposition  $-\Delta H_{dec}$ ), obtained from previous studies<sup>26,27</sup> are shown in Tables 1 and 2. Since the DSC data exhibit slight variations with heating rate, the same heating rate of 10 Kmin<sup>-1</sup> was used throughout.

In Figs. 2 and 3, the correlations between the decomposition heat of studied compounds and molar masses or melting temperatures were analyzed.

The heat of decomposition values of the substituted oxadiazoles does not show any regularity, as shown in Fig. 2. The number of

studied oxadiazoles is too small to observe trends dependent on the molar masses. However, the effect of the nature of the substituents on both oxadiazole and azulenic cycles can be noticed. AMOD and ISOPMM-MOD have lower decomposition heats. The differences between the two compounds are given by the presence of isopropyl and two methyl groups on the azulenic cycles in the case of ISOPMM-MOD. In the middle, there are the compounds with a phenyl group on the oxadiazole cycle. The variation of  $-\Delta H_{dec}$  in this series is: BMM-POD < APOD < ISOPMM-POD. Differences between them are attributed to the presence of iso-propyl, tert-butyl and methyl groups from the azulenic cycle.

Table 1

The DSC experimental data ( $T_m$ ,  $\Delta H_m$ ,  $-\Delta H_{dec}$ ), molar masses ( $M$ ), and calculated ( $\Delta S_m$ ) for substituted (*E*)-3-(azulen-1-yl diazenyl)-1,2,5-oxadiazole, obtained at 10 K min<sup>-1</sup> heating rate<sup>26</sup>

Code	$M$ (g mol <sup>-1</sup> )	$T_{m/10}$ (K)	$\Delta H_{m/10}$ (J mol <sup>-1</sup> )	$\Delta S_{m/10}$ (J mol <sup>-1</sup> K <sup>-1</sup> )	$-\Delta H_{dec}$ (J mol <sup>-1</sup> )
APOD	300	431.5	36285	84.1	682.0
BMM-POD	384	423.8	36426	86.0	508.1
ISOPMM-POD	370	430.2	71503	166	772.9
AMOD	238	444.1	19530	44.4	325.7
ISOPMM-MOD	308	446.1	27784	62.23	247.26
AMOD-2-oxid	254	442.9	18621	42.1	826.49

*Notation:* APOD - (*E*)-3-(azulen-1-yl diazenyl)-4-phenyl-1,2,5-oxadiazole; BMM-POD - (*E*)-3-((6-tert-butyl-4,8-dimethylazulen-1-yl) diazenyl)-4-phenyl-1,2,5-oxadiazole; ISOPMM-POD - (*E*)-3-((5-iso-propyl-3,8-dimethylazulen-1-yl) diazenyl)-4-phenyl-1,2,5-oxadiazole; AMOD - (*E*)-3-(azulen-1-yl diazenyl)-4-methyl-1,2,5-oxadiazole; ISOPMM-MOD - (*E*)-3-((5-iso-propyl-3,8-dimethylazulen-1-yl) diazenyl)-4-methyl-1,2,5-oxadiazole; AMOD-2-oxid - (*E*)-4-(azulen-1-yl diazenyl)-3-methyl-1,2,5-oxadiazole-2 oxide.

Table 2

The DSC experimental data ( $T_m$ ,  $\Delta H_m$ ,  $-\Delta H_{dec}$ ), molar masses ( $M$ ), and calculated ( $\Delta S_m$ ) for phenoxazone derivatives at 10 K min<sup>-1</sup> heating rate<sup>27</sup>

Code	$M$ (g mol <sup>-1</sup> )	$T_{m/10}$ (K)	$\Delta H_{m/10}$ (kJ mol <sup>-1</sup> )	$\Delta S_{m/10}$ (J mol <sup>-1</sup> K <sup>-1</sup> )	$-\Delta H_{dec}$ (kJ mol <sup>-1</sup> )
AA-Ho	224.17	448.0	13.5	30.1	312
PA-Ho	238.203	426.0	26.3	62.1	362
BA-Ho	286.247	513.6	52.38	102	326
4CH <sub>3</sub> -BA-Ho	331.244	515.6	53.9	104.5	366
2NO <sub>2</sub> -BA-Ho	300.274	522.7	20.7	28.1	533
4CH <sub>3</sub> O-BA-Ho	316.273	524.0	16.51	21.2	399
3NO <sub>2</sub> -BA-Ho	331.244	568.0	30.9	54.4	-
4NO <sub>2</sub> -BA-Ho	331.244	600.0	13.5	22.5	-
Ac-Ho	238.203	398.0	33.5	84.2	189
Met-Et-Ket-Ho	252.23	386.0	32.4	84.1	353
AcPhen-Ho	300.274	521.0	51.6	98.9	363
5Cy-Ho	264.241	419.0	31.3	74.7	436
6Cy-Ho	278.268	436.0	40.1	92.3	440

*Notation:* Ho = 2, 4-dinitrophenylhydrazine; AA = acetaldehyde; PA = propionaldehyde; BA = benzaldehyde; Ac = acetone; Met-Et-Ket = methyl ethyl ketone; AcPhen = acetophenone; 5Cy = cyclopentanone; 6Cy = cyclohexanone

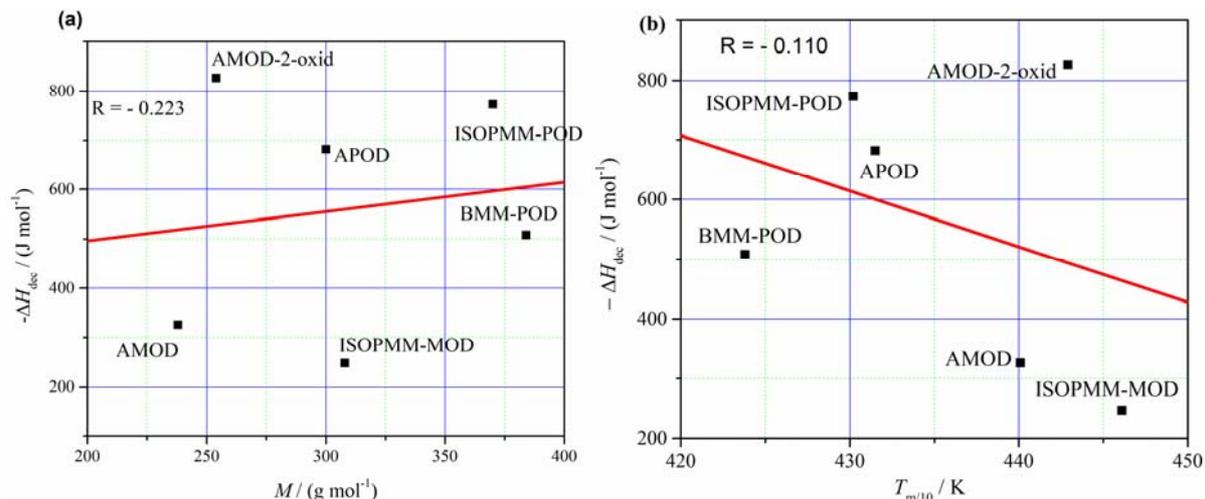


Fig. 2 – (a)  $-\Delta H_{dec}$  vs.  $M$  and (b)  $-\Delta H_{dec}$  vs.  $T_{m/10}$  for the substituted (*E*)-3-(azulen-1-ylidiazetyl)-1,2,5-oxadiazole.

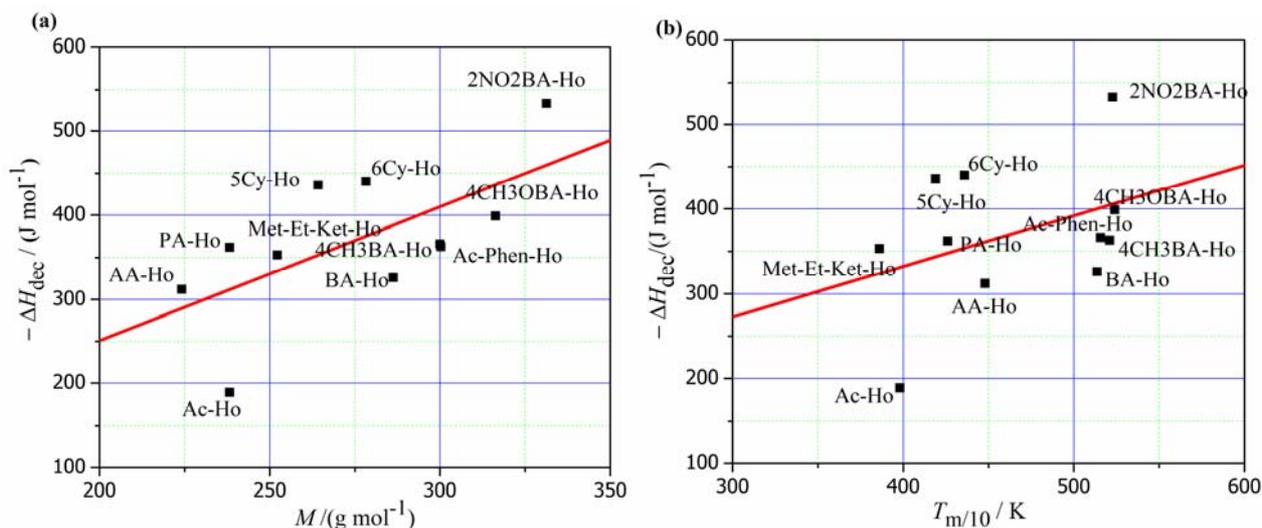


Fig. 3 – (a)  $-\Delta H_{dec}$  vs.  $M$  and (b)  $-\Delta H_{dec}$  vs.  $T_{m/10}$  for the phenoxazine derivatives.

For the phenoxazine derivatives one may notice a slight linear correlation between the heat of decomposition and the molar mass, according to

$$\Delta H_{dec} (kJ \cdot mol^{-1}) = -67.34 + 1.591M (g \cdot mol^{-1}) \quad (3)$$

Correlation with the melting temperatures (Fig. 3b) is practically non-existent according to equation (4):

$$\Delta H_{dec} (kJ \cdot mol^{-1}) = 94.06 + 0.596T_m (K) \quad (4)$$

which indicates a correlation coefficient  $R = 0.048$ .

Analyzing the data presented in Fig. 4(a) points to a slight linear correlation between melting heat of the substituted (*E*)-3-(azulen-1-ylidiazetyl)-

$$\Delta H_{m/10} (J \cdot mol^{-1}) = -41430.31 + 247.42 \times M (g \cdot mol^{-1}) \quad (5)$$

with a correlation coefficient  $R = 0.456$ . On the other hand, as seen in Fig. 4b, the melting heat

equation (3), with a correlation coefficient  $R = 0.345$  (Fig. 3a):

1,2,5-oxadiazole and the molar mass according to equation (5):

presents no correlation with the melting temperature.

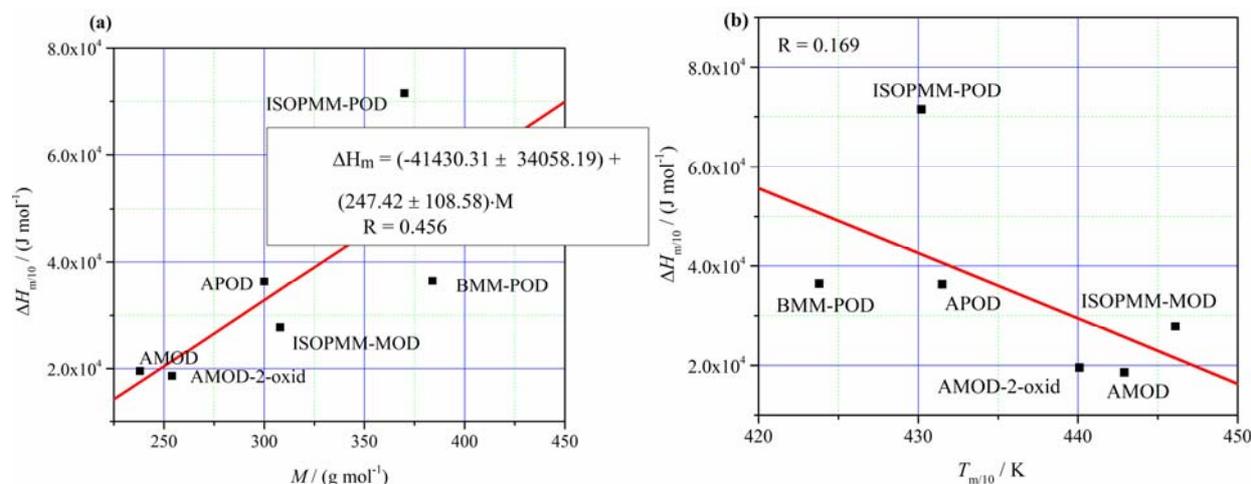


Fig. 4 – (a)  $\Delta H_{m/10}$  vs.  $M$  and (b)  $\Delta H_{m/10}$  vs.  $T_{m/10}$  for the substituted (*E*)-3-(azulen-1-ylidiazenyl)-1,2,5-oxadiazole.

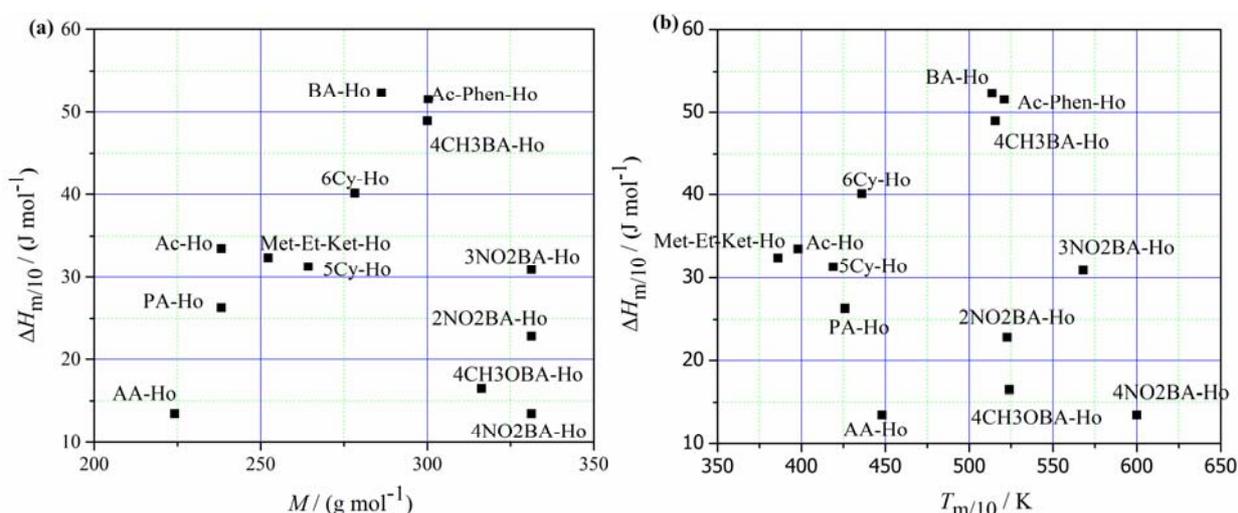


Fig. 5 – (a)  $\Delta H_{m/10}$  vs.  $M$  and (b)  $\Delta H_{m/10}$  vs.  $T_{m/10}$  for the phenoxazine derivatives.

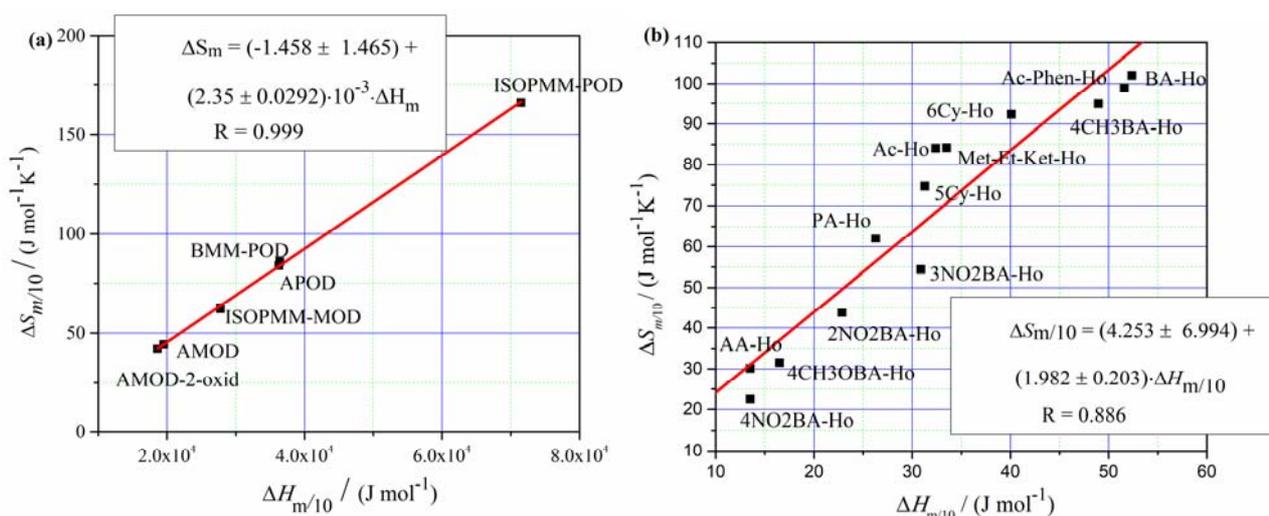


Fig. 6 –  $\Delta H_{m/10}$  versus  $\Delta S_{m/10}$  plot for (a) the substituted (*E*)-3-(azulen-1-ylidiazenyl)-1,2,5-oxadiazole and (b) the phenoxazine derivatives.

Figure 5 depicts the melting heat of phenoxazine derivatives as a function of their

molar masses or melting temperatures. No correlation can be inferred from data presented.

A statistically significant trend was found between  $\Delta H_{m/10}$  determined experimentally and calculated  $\Delta S_{m/10}$  from the equilibrium relationship  $\Delta G_m = 0$ . Analyzing the data from Fig. 6 linear

$$\Delta S_{m/10} \left( J \cdot mol^{-1} K^{-1} \right) = -1.458 + 2.35 \times 10^{-3} \times \Delta H_{m/10} \left( J \cdot mol^{-1} \right) \quad (6)$$

with a correlation coefficient  $R = 0.999$ ;

$$\Delta S_{m/10} \left( J \cdot mol^{-1} K^{-1} \right) = 4.253 + 1.982 \times \Delta H_{m/10} \left( J \cdot mol^{-1} \right) \quad (7)$$

with a correlation coefficient  $R = 0.886$ .

## CONCLUSIONS

The available experimental DSC data for two classes of related energetic compounds (6 based on substituted (*E*)-3-(azulen-1-yl diazenyl)-1,2,5-oxadiazole and 13 on phenoxazone derivatives have been systematized and critically evaluated. The present study is a first attempt to investigate if the heat of melting ( $\Delta H_m$ ) and heat of decomposition ( $\Delta H_{dec}$ ) of these compounds correlate with their molar masses and/or melting points. For the substituted (*E*)-3-(azulen-1-yl diazenyl)-1,2,5-oxadiazole, there are no correlations between the heats of decomposition as a function of either molar masses or the melting temperatures. There is a slight correlation for the phenoxazone derivatives.

A definite linear correlation between the entropy of melting and the enthalpy of melting was found for both classes of energetic compounds. This can be used to assess some thermodynamic and physical properties of related compounds (*e.g.* the heat of decomposition, the bond dissociation energy, the activation energy) using only a single energetic parameter, meaning  $\Delta H_m$ . Subsequently, this correlation between the two parameters can be further used to evaluate the relationship between physico-chemical properties and the structural characteristics of similar energetic compounds (*e.g.* nitroaromatic compounds, particularly nitrobenzene derivatives).

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