5230 *J. Chem. Eng. Data* **2010,** *55,* 5230–5236

Thermodynamic Study of the Three Fluorobenzamides: Vapor Pressures, Phase Diagrams, and Hydrogen Bonds

Ana R. R. P. Almeida and Manuel J. S. Monte*

Centro de Investigação em Química, Department of Chemistry and Biochemistry, Faculty of Science, University of Porto,
Rua do Campo Alegre, 687, P-4169-007 Porto, Portugal

A static method was used to measure the vapor pressures of crystalline and liquid phases of *ortho*-, *meta*-, and *para*-fluorobenzamides, in the temperature ranges (318.0 to 412.2) K, (336.8 to 432.0) K, and (344.8 to 437.8) K, respectively. The vapor pressures of the crystalline phase of the *ortho*- and *meta*-isomers were also measured using the Knudsen effusion method in the pressure ranges (0.1 to 1) Pa. From the experimental results, the standard molar Gibbs energies and enthalpies of sublimation and of vaporization, at $T = 298.15$ K, and the triple-point results (p, T) for the three compounds were derived. The temperatures and molar enthalpies of fusion were also determined using differential scanning calorimetry and were compared with the values derived from the vapor pressure measurements. The enthalpy of the intermolecular hydrogen bonds N−H···O in the studied compounds will be discussed and compared with the values derived for benzamide.

Introduction

The present work is a continuation of a previous study[1] in which the enthalpy of the intermolecular hydrogen bonds N−H···O in benzamide and *N*-methylbenzamide was determined. In order to compare these results with the enthalpies of intermolecular hydrogen bonds in other substituted benzamides it was decided to perform an experimental study on the sublimation of the three isomers of fluorobenzamide. The high electronegativity of fluorine might be expected to cause different properties of the compounds where hydrogen atoms were replaced by fluorine atoms. This has been the subject of several biochemistry studies in the past few years.[2–8] The main purpose of the present study is to evaluate if the intermolecular hydrogen bonds in benzamides are affected by the replacement of a benzenic hydrogen by a fluorine atom. As before our approach for determining the enthalpies of the hydrogen bonds is based on the determination of the enthalpies of sublimation and of vaporization from the measurements of vapor pressures of the crystalline and liquid phases of the compounds studied.

Experimental Section

Materials. The compounds studied in this work are commercial products from Aldrich Chemical Co. with the following molar purity certificates: *o*-fluorobenzamide (CAS Registry No. 445-28-3), 98 %; *m*-fluorobenzamide (CAS Registry No. 455-37-8), 99 %; and *p*-fluorobenzamide (CAS Registry No. 824-75-9), 99.6 %. The samples were further purified by sublimation under reduced pressure, and the final purities determined by gas chromatography (GC) were 99.78 % for *o*-fluorobenzamide, 99.81 % for *m*-fluorobenzamide, and 99.85 % for *p*-fluorobenzamide. GC analyses were performed using a Hewlett-Packard 4890 gas chromatograph equipped with column HP5 cross-linked 5 % PH ME siloxane, length 30 m, film thickness 0.25 μm, i.d. 0.32 mm, and an FID detector.

Differential Scanning Calorimetry (DSC). The temperature and enthalpy of fusion of the samples (sealed in aluminum crucibles) were measured using a Setaram DSC 141 apparatus, under a heating rate of $3.3 \cdot 10^{-2}$ K·s^{-1}. The calibration of the power scale of the calorimeter was performed using high-purity indium (mass fraction > 0.99999). The temperature scale of the calorimeter was calibrated by measuring the melting temperature of the following high purity reference materials:[9] naphthalene, benzoic acid, and indium. For each compound at least four independent runs were performed. Mean results and experimental uncertainties (calculated as twice the standard deviations) of the temperatures of fusion (observed at the onset of the calorimetric peaks), T_{fus}, and of the molar enthalpies of fusion, $\Delta_{\text{cr}}^{\text{l}}H_{\text{m}}^{\text{o}}(T_{\text{fus}})$, are presented in Table 9. No crystalline transitions were detected between the temperature 298 K and the temperature of fusion of the *meta*- and *para*-fluorobenzamides. For the *ortho* isomer a double peak was observed during the fusion process which may be due to a premelting step.

Vapor-Pressure Measurements. The vapor pressures of the three isomers were measured at different temperatures in both crystalline and liquid phases using a static apparatus based on capacitance diaphragm gauges that was previously described in detail.[10] The two capacitance diaphragm absolute gauges used in this apparatus were commercially available from MKS Instruments, Inc. They operate at self-controlled constant temperatures: gauge I, Baratron 631A01TBEH ($T_{\text{gauge}} = 423$ K) for measuring pressures in the range (0.4 to 133) Pa and in the temperature range (253 to 413) K; gauge II, Baratron 631A11TBFP ($T_{\text{gauge}} = 473$ K) capable of measuring pressures in the range (3 to 1330) Pa and in the temperature range (253 to 463) K.

A platinum resistance thermometer (PRT) Pt100 class 1/10 (in a four-wire connection) was used to measure the temperatures of the condensed samples. This thermometer was calibrated by comparison with a standard PRT (25 Ω; Tinsley, 5187A). The tubing between the cell containing the condensed sample and the pressure gauge is kept at a temperature higher than the

---

* Author for correspondence. E-mail: mjmonte@fc.up.pt (M. J. S. Monte).

10.1021/je100801s

Table 1. Effusion Vapor-Pressure Results for Crystalline *o*-Fluorobenzamide[a]

T/K	303.12	305.21	307.19	309.12	311.20	313.29	315.11	317.20	319.18	321.11	323.18	325.18
p/Pa	0.102	0.130	0.166	0.213	0.270	0.341	0.429	0.540	0.668	0.843	1.059	1.295

[a] For each temperature, the presented vapor pressures are the mean of the results obtained with three different effusion orifices.

Table 2. Effusion Vapor-Pressure Results for Crystalline *m*-Fluorobenzamide[a]

T/K	323.10	325.17	327.18	329.08	331.13	333.18	337.28	339.17	341.08	343.13	345.18
p/Pa	0.090	0.114	0.143	0.183	0.229	0.286	0.461	0.559	0.688	0.842	1.032

[a] For each temperature, the presented vapor pressures are the mean of the results obtained with three different effusion orifices.

Table 3. Experimental Effusion Results for *o*-Fluorobenzamide Where a and b Are from the Clausius−Clapeyron Equation $\ln(p/\text{Pa}) = a - b\cdot(\text{K}/T)$ and $b = \Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{0}(\langle T\rangle)/R$

a	b	$\frac{\langle T\rangle}{\text{K}}$	$\frac{p(\langle T\rangle)}{\text{Pa}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(\langle T\rangle)}{\text{kJ}\cdot\text{mol}^{-1}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(298.15\text{ K})^{a}}{\text{kJ}\cdot\text{mol}^{-1}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}G_{\text{m}}^{\text{o}}(298.15\text{ K})^{a}}{\text{kJ}\cdot\text{mol}^{-1}}$	R^2
35.39 ± 0.10	11422 ± 32	314.15	0.380	95.0 ± 0.3	95.4 ± 0.3	35.78 ± 0.01	0.9999

[a] $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(298.15\text{ K})$ and $\Delta_{\text{cr}}^{\text{g}}G_{\text{m}}^{\text{o}}(298.15\text{ K})$ were derived from the Clarke and Glew eq 2 considering the reference pressure $p^{\text{o}} = 0.1$ MPa.

Table 4. Experimental Effusion Results for *m*-Fluorobenzamide Where a and b Are from the Clausius−Clapeyron Equation $\ln(p/\text{Pa}) = a - b\cdot(\text{K}/T)$ and $b = \Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{0}(\langle T\rangle)/R$

a	b	$\frac{\langle T\rangle}{\text{K}}$	$\frac{p(\langle T\rangle)}{\text{Pa}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(\langle T\rangle)}{\text{kJ}\cdot\text{mol}^{-1}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(298.15\text{ K})^{a}}{\text{kJ}\cdot\text{mol}^{-1}}$	$\frac{\Delta_{\text{cr}}^{\text{g}}G_{\text{m}}^{\text{o}}(298.15\text{ K})^{a}}{\text{kJ}\cdot\text{mol}^{-1}}$	R^2
35.98 ± 0.16	12405 ± 55	334.14	0.318	103.1 ± 0.5	104.1 ± 0.4	42.52 ± 0.05	0.9998

[a] $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(298.15\text{ K})$ and $\Delta_{\text{cr}}^{\text{g}}G_{\text{m}}^{\text{o}}(298.15\text{ K})$ were derived from the Clarke and Glew eq 2 considering the reference pressure $p^{\text{o}} = 0.1$ MPa.

temperature of the sample and lower than the temperature of the gauge. The uncertainty of the temperature measurements is estimated to be better than ± 0.01 K, and the uncertainty in the pressure measurements is adequately described by the expressions $\sigma(p/\text{Pa}) = 0.01 + 0.0025(p/\text{Pa})$ for gauge 1 and $\sigma(p/\text{Pa}) = 0.1 + 0.0025(p/\text{Pa})$ for gauge 2.

The vapor pressures of crystalline *ortho*- and *meta*-fluorobenzamide isomers were measured as a function of temperature in the range (0.10 to 1.30) Pa and (0.09 to 1.03) Pa, respectively, using an apparatus based on the mass-loss Knudsen effusion method, previously described in detail.[11] This technique was not used for measuring the vapor pressures of the *para*-isomer due to lack of enough purified sample of this compound for using both experimental techniques. The Knudsen effusion apparatus enables, in each experiment, the simultaneous use of nine effusion cells which are placed in cylindrical holes inside three temperature-controlled aluminum blocks. During an effusion experiment, each aluminum block, containing three effusion cells, is kept at a constant temperature, different from the other two blocks. Three different groups of effusion cells according to their different areas of effusion orifices were used: one "small" ($A_{\text{o}} \approx 0.5$ mm^2: series A), one "medium" ($A_{\text{o}} \approx 0.8$ mm^2: series B), and one "large" ($A_{\text{o}} \approx 1.1$ mm^2: series C). The exact areas and Clausing factors of each used effusion orifice, made in platinum foil of 0.0125 mm thickness, are presented in the Supporting Information, Table S1. In each effusion experiment, the mass loss of the crystalline samples, Δm, was measured by weighing the cells with a sample, within ± 0.01 mg, before and after a convenient effusion time period, t, in a system evacuated to a pressure near $1\cdot10^{-4}$ Pa. For the temperature T, measured with an accuracy of ± 0.01 K, the vapor pressure p of the crystalline sample contained in each effusion cell is calculated by eq 1 where M is the molar mass of the effusing vapor, R is the gas constant, A_{o} represents the area of the effusion orifice, and w_{o} is the respective Clausing factor. The accuracy of the measured pressures is estimated to be better than ± 0.02 (p/Pa).

$$p = (m/A_{\text{o}}w_{\text{o}}t)\cdot(2\pi RT/M)^{1/2} \qquad (1)$$

Results and Discussion

Effusion Vapor Pressures. The mean pressures derived from the effusion results at several temperatures for *ortho*- and *meta*-fluorobenzamides are presented in Tables 1 and 2, respectively. Tables S2 and S3, presented in Supporting Information, report experimental effusion results in detail. Tables 3 and 4 present the following thermodynamic parameters derived from the mean vapor pressures of *o*- and *m*-fluorobenzamides, respectively: the detailed parameters of the Clausius−Clapeyron equation, $\ln(p/\text{Pa}) = a - b(\text{K}/T)$, where a is a constant and $b = \Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\text{o}}(\langle T\rangle)/R$; the standard molar enthalpy of sublimation at the mean temperature of the experiments $T = \langle T\rangle$ and at $\theta = 298.15$ K; and the Gibbs energy of sublimation at the reference temperature 298.15 K. The values at $\theta = 298.15$ K were derived fitting the experimental results of the vapor pressures by the truncated form of Clarke and Glew equation (eq 2),[12]

$$R\ln\left(\frac{p}{p^{o}}\right) = -\frac{\Delta_{\text{cd}}^{\text{g}}G_{\text{m}}^{\text{o}}(\theta)}{\theta} + \Delta_{\text{cd}}^{\text{g}}H_{\text{m}}^{\text{o}}(\theta)\left(\frac{1}{\theta} - \frac{1}{T}\right) + \Delta_{\text{cd}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(\theta)\left[\left(\frac{\theta}{T}\right) - 1 + \ln\left(\frac{T}{\theta}\right)\right] \qquad (2)$$

where p is the vapor pressure at the temperature T, p^{o} is a selected reference pressure ($p^{\text{o}} = 10^5$ Pa in this work), θ is a selected reference temperature ($\theta = 298.15$ K in this work), R is the molar gas constant (8.31447 J$\cdot$K$^{-1}\cdot$mol^{-1}), $\Delta_{\text{cd}}^{\text{g}}G_{\text{m}}^{\text{o}}(\theta)$ is the difference in molar Gibbs energy between the gaseous and the crystalline or liquid phases (condensed phases) at the selected reference pressure. $\Delta_{\text{cd}}^{\text{g}}H_{\text{m}}^{\text{o}}(\theta)$ is the difference in molar enthalpy between the gas and the condensed phases, and $\Delta_{\text{cd}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(\theta)$ is the difference in molar heat capacity at constant pressure between the gaseous and the condensed phase. The results related to the small, medium, and large orifices for these two isomers are listed in Supporting Information, Table S4.

Static Vapor Pressures and Phase Diagrams. The vapor-pressure measurements using the static method were performed

Table 5. Static Vapor-Pressure Results for *o*-Fluorobenzamide

T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p^a$
Crystalline Phase								
317.98	0.60	−1.5	335.32	3.80	0.1	357.75	31.16	1.2
320.48	0.80	−0.4	337.75	4.84	0.2	360.13	37.77	−0.1
322.94	1.05	0.0	340.21	6.17	0.4	362.71	47.53	0.8
325.41	1.37	0.1	342.70	7.85	0.6	365.10	57.35	−0.5
327.86	1.75	−1.2	345.32	10.02	0.2	370.04	85.97	−0.7
330.38	2.33	1.2	350.20	15.81	0.7	372.63	105.8	−0.8
332.86	3.00	1.2	355.69	25.44	−1.0	377.60	157.2	−0.4
Liquid Phase								
358.65	59.79	−0.3	380.43	225.0	0.2	402.34	712.4	−0.5
361.55	72.25	0.0	385.38	297.2	0.4	404.79	806.4	−0.1
364.59	88.14	0.7	391.35	408.1	0.0	407.26	911.5	0.2
367.55	104.8	−0.4	394.82	489.2	0.0	409.66	1024	0.4
370.55	126.0	−0.2	397.41	557.2	−0.3	412.16	1147	0.0
375.47	168.8	−0.1	399.81	630.2	−0.1			

[a] $\Delta p = p - p_{\text{calc}}$.

Table 6. Static Vapor-Pressure Results for *m*-Fluorobenzamide

T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p^a$
Crystalline Phase								
336.83	0.46	−1.1	354.65	3.00	0.8	375.47	20.67	0.2
339.76	0.63	−1.6	357.76	4.07	0.9	378.58	27.12	0.2
342.87	0.89	−0.3	360.59	5.35	0.6	384.49	44.71	−0.9
345.87	1.20	0.1	363.62	7.10	1.5	387.47	56.59	−0.3
348.82	1.66	0.4	366.55	9.41	0.2	390.45	72.58	−1.6
351.66	2.22	0.7	372.50	15.92	0.1	396.38	114.8	
Liquid Phase								
382.58	58.70	0.6	402.37	189.5	−1.0	422.04	547.2	−0.1
387.53	79.55	−0.1	407.27	251.4	−0.1	427.02	703.9	0.3
392.49	108.0	0.3	412.23	326.4	−0.8	432.00	900.6	0.8
397.43	144.4	0.2	417.16	426.2	−0.1			

[a] $\Delta p = p - p_{\text{calc}}$.

Table 7. Static Vapor-Pressure Results for *p*-Fluorobenzamide

T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p$	T/K	p/Pa	100 $\Delta p/p^a$
Crystalline Phase								
344.79	0.70	−1.5	371.58	9.00	−0.7	401.25	98.54	−1.9
347.76	0.97	0.9	374.54	11.67	−0.5	404.24	126.6	1.0
350.74	1.30	0.4	377.53	15.00	−1.0	407.22	156.8	0.6
353.73	1.74	0.1	380.48	19.34	−0.5	410.16	194.4	0.9
356.70	2.36	1.9	383.47	24.45	−1.8	413.14	239.6	0.7
359.68	3.13	1.9	386.43	31.34	−1.2	416.10	294.8	0.8
362.66	4.10	1.1	392.35	49.95	−1.7	419.06	363.7	1.4
365.63	5.35	0.5	395.33	62.99	−1.7	422.01	441.9	0.9
368.61	6.99	0.4	398.28	78.72	−2.0	424.99	538.0	0.7
Liquid Phase								
410.20	262.9	0.4	420.05	439.8	0.1	429.92	719.0	0.1
412.16	290.2	−0.2	422.03	486.2	0.0	431.89	787.9	−0.2
414.13	322.2	−0.3	424.02	538.2	0.2	433.87	870.8	0.4
416.11	358.4	0.0	426.00	593.0	0.1	435.84	950.8	−0.1
418.11	396.3	−0.4	427.93	652.4	0.1	437.82	1040	−0.3

[a] $\Delta p = p - p_{\text{calc}}$.

above the crystalline and the liquid (both stable and undercooled) phases of the three compounds studied. These results are summarized in Tables 5, 6, and 7. The experimental results of the static vapor pressures were also fitted by the Clarke and Glew equation (eq 2). The thermodynamic parameters derived from these fittings are presented in Table 8. The value $\Delta_{\text{cr}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(\theta) = -26\ \text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ inserted in eq 2 was estimated for the three isomers. This estimation was derived using eq 3 proposed by Chickos et al.[13] The value of the molar heat capacity of the crystalline fluorobenzamide isomers, $C_{p,\text{m}}^{\text{o}}(\text{g})(\text{cr}) = 165.8\ \text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$, inserted in eq 3, was calculated from the heat capacity of benzamide, $C_{p,\text{m}}^{\text{o}}(\text{g})(\text{cr}) = 153.8\ \text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$,[14] after corrections for the substitution of a benzenic hydrogen atom by a fluorine one, according to group contribution values recommended by Domalski and Hearing.[15]

$$\Delta_{\text{cr}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(\theta) = -\{0.75 + 0.15C_{p,\text{m}}^{0}(\text{cr})\}\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1} \tag{3}$$

The result of $\Delta_{\text{l}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(298.15\ \text{K}) = -(67.8 \pm 8.2)\ \text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ was derived for *o*-fluorobenzamide directly from the regression of the fittings of eq 2 to the liquid−vapor pressure−temperature data over the 53 K temperature interval. The short temperature range used in the study of liquid *p*-fluorobenzamide did not allow the derivation of a reliable value from the fitting of eq 2. As the value derived from such fitting for *m*-fluorobenzamide was also not reliable, the value $\Delta_{\text{l}}^{\text{g}}C_{p,\text{m}}^{\text{o}}(298.15\ \text{K}) = -(67.8 \pm 8.2)\ \text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$ (derived as explained above for *o*-fluorobenzamide) was estimated for these two isomers. Figures 1, 2, and 3 represent the pressure−temperature phase diagrams of the compounds studied.

For the same temperature, the static crystalline−vapor pressures of *o*-fluorobenzamide and *m*-fluorobenzamide exceed in less than 1 % the vapor pressures measured by the effusion method. The enthalpies of sublimation derived from the two different measuring methods for the two compounds are also in good agreement. This agreement validates the assumption of no dimerization in the gas phase: the effusion vapor pressures calculated using eq 1 depend on the molar mass of the effusing vapor, while those measured using the static method are not dependent on this mass. In view of this we assumed that dimerization is also not present in the gas phase of the *para*-isomer.

According to the values of $\Delta_{\text{cd}}^{\text{g}}G_{\text{m}}^{\text{o}}(\theta)$, listed in Table 8, both *meta*- and *para*-isomers of fluorobenzamide present similar volatilities either in crystalline or liquid phases, *o*-fluorobenzamide being clearly more volatile than those two isomers. The higher volatility of this isomer is a consequence of weaker intermolecular forces presented in its condensed phases which

Table 8. Parameters of Clarke and Glew Equation 2 Derived from Vapor-Pressure Results for Crystalline and Liquid *o*-Fluorobenzamide, *m*-Fluorobenzamide, and *p*-Fluorobenzamide ($p^0 = 10^5$ Pa)

phase	ΔT K	θ K	$\Delta_{cr}^{g}G_{m}^{o}(\theta)$ kJ·mol^{-1}	$\Delta_{cr,l}^{g}H_{m}^{o}(\theta)$ kJ·mol^{-1}	R^2	$-\Delta_{cr,l}^{g}C_{p,m}^{o}$ J·K^{-1}·mol^{-1}	s[a]
o-Fluorobenzamide							
crystalline	318 to 378	298.15	35.63 ± 0.01	94.3 ± 0.1	1.0000	26[b]	0.008
		347.79[c]	25.97 ± 0.05	93.0 ± 0.1			
		387.22[d]	18.42 ± 0.01	92.0 ± 0.1			
		298.15[e]	35.78 ± 0.01	95.4 ± 0.3	0.9999		0.008
liquid[f]	359 to 412	298.15	30.49 ± 0.01	73.6 ± 0.1	1.0000	67.8 ± 8.2[g]	0.003
		385.40[c]	18.66 ± 0.02	67.7 ± 0.1			
		387.22[d]	18.42 ± 0.01	67.6 ± 0.1			
m-Fluorobenzamide							
crystalline	337 to 396	298.15	42.41 ± 0.02	104.7 ± 0.1	1.0000	26[b]	0.009
		366.60[c]	28.29 ± 0.01	102.9 ± 0.1			
		404.35[d]	20.66 ± 0.02	102.0 ± 0.1			
		298.15[e]	42.52 ± 0.05	104.1 ± 0.4	0.9998		0.012
liquid[f]	383 to 432	298.15	36.24 ± 0.04	83.2 ± 0.2	1.0000	67.8 ± 8.2[h]	0.006
		407.29[c]	20.26 ± 0.01	75.8 ± 0.2			
		404.35[d]	20.66 ± 0.01	76.0 ± 0.2			
p-Fluorobenzamide							
crystalline	345 to 425	298.15	43.21 ± 0.03	102.8 ± 0.1	1.0000	26[b]	0.012
		384.89[c]	26.18 ± 0.01	100.5 ± 0.1			
		428.41[b]	17.84 ± 0.02	99.4 ± 0.1			
liquid[f]	410 to 438	298.15	36.55 ± 0.03	83.3 ± 0.1	1.0000	67.8 ± 8.2[h]	0.002
		424.01[c]	18.43 ± 0.01	74.7 ± 0.1			
		428.41[b]	17.84 ± 0.01	74.4 ± 0.1			

[a] s is the standard deviation of the fit defined as $s = [(\sum_{i=1}^{n}(\ln p - \ln p_{calc})_i^2)/(n - m)]^{1/2}$, where n is the number of experimental points used in the fit and m is the number of adjustable parameters of Clarke and Glew eq 2. [b] Estimated value. [c] Mean temperature. [d] Temperature of triple point. [e] Knudsen effusion (this work). [f] Including supercooled liquid. [g] Adjustable parameter. [h] Estimated value.

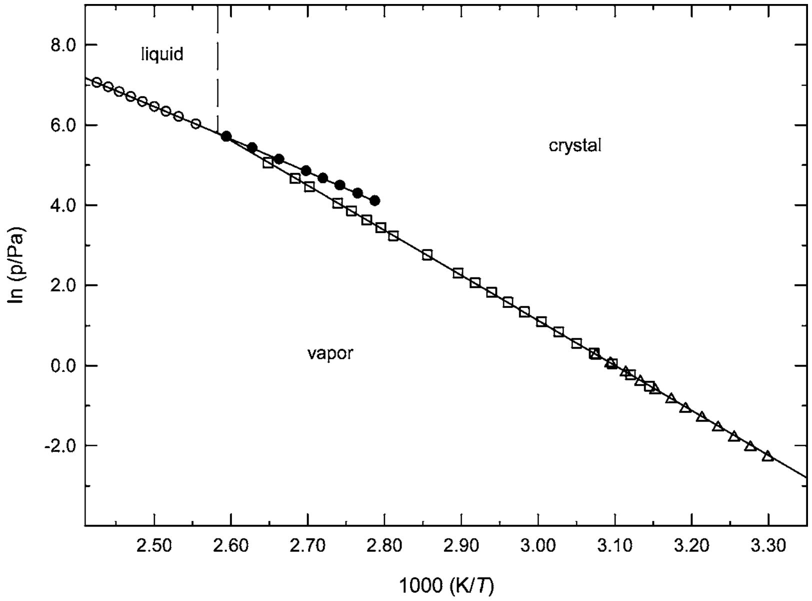

Figure 1. Phase diagram of *o*-fluorobenzamide. ○, static liquid−vapor pressures; ●, undercooled liquid−vapor pressures; □, static crystalline−vapor pressures (this study); △, effusion vapor pressures (mean of small, medium, and large orifices results from this study). Triple-point coordinates: $T = 387.22$ K, $p = 331.2$ Pa.

are reflected on the values of the enthalpies of sublimation and of vaporization of the three compounds.

Triple Points and Fusion. For the *ortho*-, *meta*-, and *para*-fluorobenzamides, the values of the temperature and pressure of the triple point (derived from the vapor-pressure measurements) and of the temperatures and enthalpies of fusion (derived from the calorimetric experiments) are summarized in Table 9. For the *o*-isomer the temperature of the triple point is 1.3 K lower than the value of the temperature of fusion obtained through the DSC experiments. The enthalpy of fusion derived from the enthalpies of sublimation and of vaporization (presented in Table 8) is in excellent agreement with the DSC results (derived considering the area under the double peak observed in the thermogram of this compound, as referred before). The temperature of the triple point for *meta*-fluorobenzamide is 2.8 K higher than the DSC result, and the enthalpy of fusion derived from the static vapor pressures is 1.4 kJ·mol^{-1} higher than the value obtained from the DSC experiments. For *p*-fluorobenzamide, the temperature of the triple point is only 0.8 K lower than the value derived from the DSC experiments, and the enthalpies of fusion derived from the both techniques are equal inside of experimental error. The proximity between the values derived indirectly from the vaporization and sublimation curves and the calorimetric ones gives additional consistency to the results derived from the vapor-pressure study.

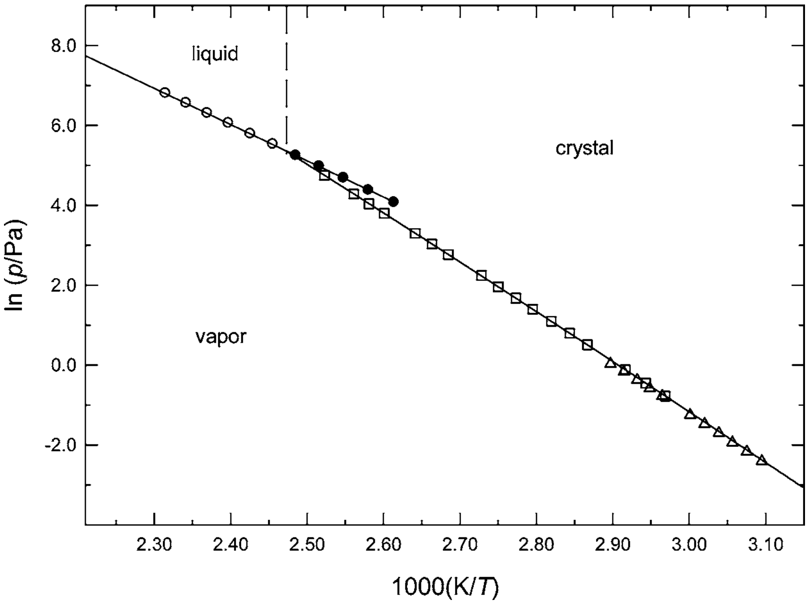

Figure 2. Phase diagram of *m*-fluorobenzamide. ○, liquid vapor pressures; ●, undercooled liquid−vapor pressures; □, crystalline−vapor pressures (this study); △, effusion vapor pressures (mean of small, medium, and large orifices results from this study). Triple-point coordinates: $T = 404.35$ K, $p = 218.0$ Pa.

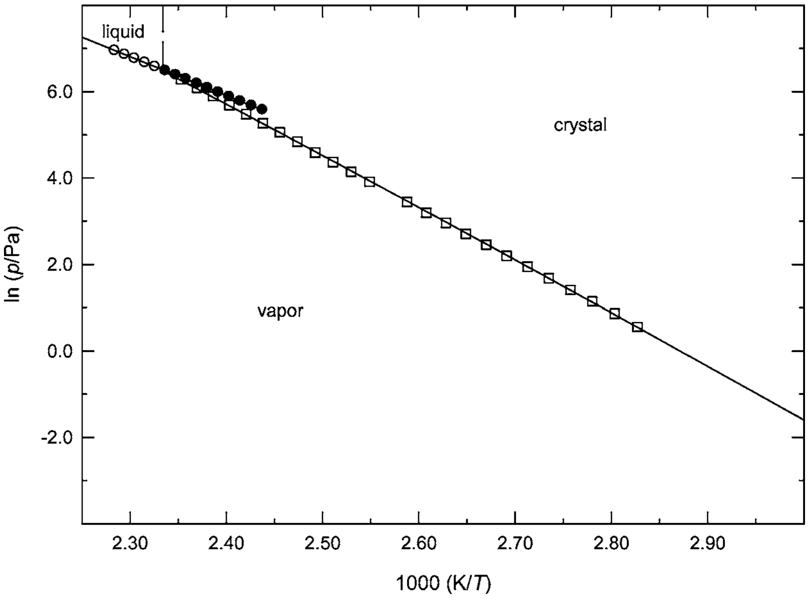

Figure 3. Phase diagram of *p*-fluorobenzamide. ○, liquid vapor pressures; ●, undercooled liquid vapor pressures; □, crystalline vapor pressures (this study). Triple-point coordinates: $T = 428.41$ K, $p = 678.9$ Pa.

Table 9. Triple-Point Coordinates (*p*,*T*), Temperature, and Molar Enthalpy of Fusion of the Studied Compounds

compound	T_{tp} K	$T_{fus.}$ K	$\Delta_{cr}^{l}H_{m}^{o}(T^{a})$ kJ·mol^{-1}	p_{tp} Pa	$\Delta_{cr}^{l}H_{m}^{o}(298.15\ K)$ kJ·mol^{-1}	method/reference
o-fluorobenzamide	-	388.49 ± 0.19	23.8 ± 0.4	-		DSC/this work
	387.22	-	24.4 ± 0.1	331.2	20.7 ± 0.1	static/this work
m-fluorobenzamide	-	401.58 ± 0.01	24.6 ± 0.2	-		DSC/this work
	404.35	-	26.0 ± 0.1	218.0	21.5 ± 0.1	static/this work
p-fluorobenzamide	-	429.19 ± 0.05	24.9 ± 0.1	-	-	DSC/this work
	428.41	-	25.0 ± 0.1	678.9	19.5 ± 0.3	static/this work

[a] Temperature of fusion or temperature of the triple point.

Hydrogen Bonds in the Crystalline Packing. From a recent study,[1] the enthalpy of sublimation, at $T = 298.15$ K, of benzamide is $\Delta_{cr}^{g}H_{m}^{o} = 102.6$ kJ·mol^{-1}. Crystalline benzamide forms two intermolecular N−H···O hydrogen bonds per molecule, being the mean enthalpy of these two bonds $(\Delta_{HB}H)_{m} = 15.1$ kJ·mol^{-1}.[1]

According to the crystal structures of benzamide,[16] *m*-fluorobenzamide[17] and *p*-fluorobenzamide,[18] represented schematically in Figure 4 (parts a, c, and d, respectively), the two intermolecular hydrogen bonds N−H···O, per molecule, in the crystals of these three compounds, have only slightly different lengths intra dimers (i.d.) and between dimers (b.d.): for

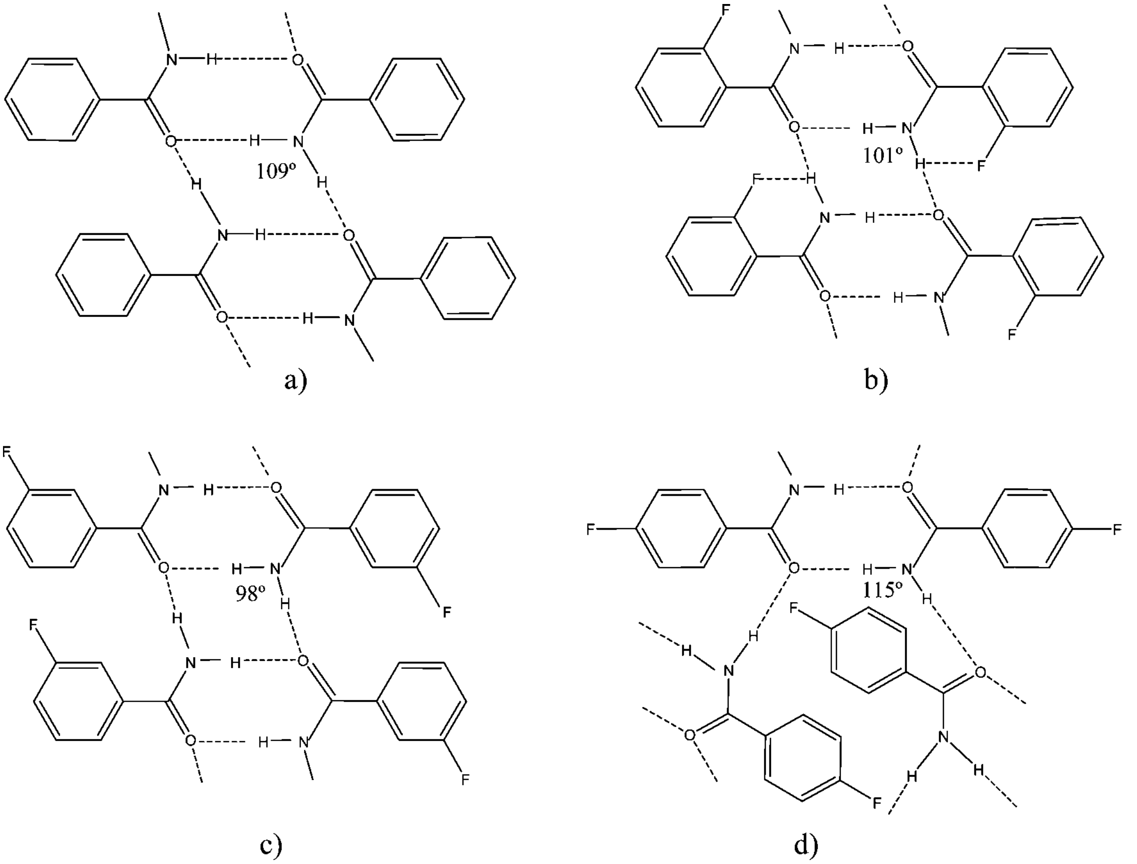

Figure 4. Schematic representation of the crystalline packing arrangements of (a) benzamide (adapted from ref 16); (b) *o*-fluorobenzamide (adapted from ref 19); (c) *m*-fluorobenzamide (adapted from ref 17); and (d) *p*-fluorobenzamide (adapted from ref 18).

Table 10. Group Contributions for Enthalpies of Formation, According to Domalsky and Hearing,[15] and for Enthalpies of Vaporization and Sublimation

	$\Delta_f H^o$(g) / kJ·mol^{-1}	$\Delta_f H^o$(l) / kJ·mol^{-1}	$\Delta_f H^o$(cr) / kJ·mol^{-1}	$\Delta_l^g H_m^o$ / kJ·mol^{-1}	$\Delta_{cr}^g H_m^o$ / kJ·mol^{-1}
$C_B-(H)(C_B)_2$	13.81	8.16	6.53	5.65	7.28
$C_B-(F)(C_B)_2$	−181.26	−191.20	−194.00	9.94	12.74

benzamide, l = 296 pm i.d. and l = 291 pm b.d.; for *m*-fluorobenzamide, l = 295 pm i.d. and l = 291 pm b.d.; and l = 292 pm i.d. and l = 293 pm b.d., for the *p*-fluorobenzamide. For *o*-fluorobenzamide, the proximity between the fluorine atom and the amino group (Figure 4b)[19] allows the establishment of an intramolecular N−H···F hydrogen bond which weakens the intermolecular N−H···O bonds inside and/or between dimers (l = 295/298 pm i.d. and l = 292/294 pm b.d.).

If the mean enthalpies of the intermolecular hydrogen bonds in benzamide and in the fluorobenzamide isomers had the same value, the difference between the enthalpies of sublimation would only be due to the contribution of the replacement of a hydrogen atom by a fluorine atom in the benzamide molecules. This effect may be estimated from group contribution as $\Delta(\Delta_{cr}^g H_m^o)$ = (12.74 − 7.28) kJ·mol^{-1} = 5.5 kJ·mol^{-1}, accordingly to the values proposed by Domalski and Hearing,[15] which are presented in Table 10. So, if that assumption was correct, the enthalpy of sublimation of fluorobenzamide isomers would be 5.5 kJ·mol^{-1} higher than the enthalpy of sublimation of benzamide. Taking this into account and considering the values of enthalpies of sublimation derived in the present study, the following conclusions may be outlined (for the *ortho*- and *meta*-isomers the values of the enthalpy of sublimation determined using the static method were selected considering the wider temperature range of these measurements compared to the effusion measurements).

meta-Fluorobenzamide. The enthalpy of sublimation, at 298.15 K, derived in this work for *meta*-fluorobenzamide is $\Delta_{cr}^g H_m^o$ = 104.7 kJ·mol^{-1}. If the enthalpies of the intermolecular hydrogen bonds were the same as in benzamide, then $\Delta_{cr}^g H_m^o$ would be (102.6 + 5.5) kJ·mol^{-1} = 108.1 kJ·mol^{-1}. So, the weakening of the intermolecular hydrogen bonds can be estimated as (108.1 − 104.7) kJ·mol^{-1} = 3.4 kJ·mol^{-1}. Since there are two hydrogen intermolecular bonds per molecule in the crystals of *meta*-fluorobenzamide (Figure 4c), the mean bond enthalpy of these two hydrogen bonds will be 1.7 kJ·mol^{-1} lower than the value calculated for benzamide, yielding the value $(\Delta_{HB}H)_m$ = (15.1 − 1.7) kJ·mol^{-1} = 13.4 kJ·mol^{-1} for *meta*-fluorobenzamide.

para-Fluorobenzamide. The enthalpy of sublimation, at 298.15 K, derived in this study for *para*-fluorobenzamide is $\Delta_{cr}^g H_m^o$ = 102.8 kJ·mol^{-1}. The weakening of the intermolecular hydrogen bonds, compared to benzamide, can be estimated as (108.1 − 102.8) kJ·mol^{-1} = 5.3 kJ·mol^{-1}. Considering the two hydrogen intermolecular bonds per molecule (Figure 4c), the mean bond enthalpy of these hydrogen bonds will be 2.6 kJ·mol^{-1} lower than the value calculated for benzamide. So, for *para*-fluorobenzamide this value is $(\Delta_{HB}H)_m$ = (15.1 − 2.6) kJ·mol^{-1} = 12.5 kJ·mol^{-1}.

ortho-Fluorobenzamide. The enthalpy of sublimation, at 298.15 K, derived in the present study for *ortho*-fluorobenzamide is $\Delta_{cr}^g H_m^o$ = 94.3 kJ·mol^{-1}. The weakening of the intermolecular hydrogen bonds can be estimated as (108.1 − 94.3) kJ·mol^{-1} = 13.8 kJ·mol^{-1}. So, the mean bond enthalpy of the two hydrogen bonds will be 6.9 kJ·mol^{-1} lower than the value calculated for benzamide, leading to the value $(\Delta_{HB}H)_m$ = (15.1

Table 11. Mean Enthalpies of Intermolecular Hydrogen Bonds in Liquid and Crystalline Benzamide and Fluorobenzamides

	$\{\Delta_{\mathrm{HB}}H(\mathrm{crystal})\}_{\mathrm{m}}$ / $\mathrm{kJ\cdot mol^{-1}}$	$\{\Delta_{\mathrm{HB}}H(\mathrm{liquid})\}_{\mathrm{m}}$ / $\mathrm{kJ\cdot mol^{-1}}$
benzamide[1]	15.1	11.7
o-fluorobenzamide	8.2	3.1
m-fluorobenzamide	13.4	7.9
p-fluorobenzamide	12.5	7.9

$-$ 6.9) $\mathrm{kJ\cdot mol^{-1}} = 8.2\ \mathrm{kJ\cdot mol^{-1}}$. This relatively low value seems to be a consequence of the competition between the intramolecular and the intermolecular hydrogen bonds observed in the crystalline packing arrangement of this isomer.

Hydrogen Bonds in the Liquids. The enthalpy of vaporization, at $T = 298.15$ K, of benzamide was previously determined as $\Delta_{\mathrm{l}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}} = 86.5\ \mathrm{kJ\cdot mol^{-1}}$.[1] Assuming that the intermolecular hydrogen bonds observed in the crystalline phase remain in the liquid phase of benzamide, the value $\{\Delta_{\mathrm{HB}}H(\mathrm{liq})\}_{\mathrm{m}} = 11.7\ \mathrm{kJ\cdot mol^{-1}}$ was also derived.[1]

Making similar assumptions as above for the crystalline phases, the difference between the enthalpy of vaporization of fluorobenzamide isomers and the enthalpy of vaporization of benzamide may be estimated from the group contribution as $\Delta(\Delta_{\mathrm{l}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}) = (9.94 - 5.65)\ \mathrm{kJ\cdot mol^{-1}} = 4.3\ \mathrm{kJ\cdot mol^{-1}}$, accordingly to the values proposed by Domalski and Hearing,[15] presented in Table 10. So, the enthalpy of vaporization of fluorobenzamide isomers would be 4.3 $\mathrm{kJ\cdot mol^{-1}}$ higher than the enthalpy of vaporization of benzamide, that is, $\Delta_{\mathrm{l}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}} = 90.8\ \mathrm{kJ\cdot mol^{-1}}$. Considering the values of enthalpies of vaporization derived in the present study, for *meta*- and *para*-isomers of fluorobenzamide (83.2 and 83.3 $\mathrm{kJ\cdot mol^{-1}}$, repectively) and the existence of two hydrogen bonds NH···O per molecule in the crystals of these compounds, the mean intermolecular hydrogen-bond enthalpy in the *meta*- and *para*-isomers is 3.8 $\mathrm{kJ\cdot mol^{-1}}$ lower than in liquid benzamide, that is, $\{\Delta_{\mathrm{HB}}H(\mathrm{liq})\}_{\mathrm{m}} = 7.9\ \mathrm{kJ\cdot mol^{-1}}$. The enthalpy of vaporization of *ortho*-fluorobenzamide is 73.6 $\mathrm{kJ\cdot mol^{-1}}$, which is 17.2 $\mathrm{kJ\cdot mol^{-1}}$ lower than the enthalpy of vaporization of benzamide. Therefore, considering the value $\{\Delta_{\mathrm{HB}}H(\mathrm{liq})\}_{\mathrm{m}} = 11.7\ \mathrm{kJ\cdot mol^{-1}}$ derived for benzamide, the mean intermolecular hydrogen bond enthalpy, per molecule, in the liquid of *ortho*-fluorobenzamide is $\{\Delta_{\mathrm{HB}}H(\mathrm{liq})\}_{\mathrm{m}} = (11.7 - 8.6)\ \mathrm{kJ\cdot mol^{-1}} = 3.1\ \mathrm{kJ\cdot mol^{-1}}$.

Final Remarks

The values of the mean enthalpy of the intermolecular hydrogen bonds for crystalline and liquid phases of benzamide, determined previously,[1] and of the fluorobenzamide isomers calculated in this study are summarized in Table 11. It is interesting to note that the same value was obtained for liquid *meta*- and *para*-fluorobenzamide, while in the crystalline phase the difference between the values is 0.9 $\mathrm{kJ\cdot mol^{-1}}$. This difference seems to reflect the differences in the crystalline packing arrangements for these two isomers.

Acknowledgment

We are grateful to Dr. Luis Gales for very helpful discussions about the crystalline packing arrangement of the studied compounds.

Supporting Information Available:

Detailed data of the effusion orifices (diameter and Clausing factors) of the Knudsen apparatus and vapor-pressure results related to the small, medium, and large effusion orifices for *ortho*- and *meta*-fluorobenzamides. This section also presents the detailed parameters of the Clausius−Clapeyron equation, the standard molar enthalpies of sublimation at the mean temperature of the experiments, and the values of the standard enthalpy and Gibbs energy of sublimation at the reference temperature related to the small, medium, and large effusion orifices for these two compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Almeida, A. R. R. P.; Monte, M. J. S. Thermodynamic study of benzamide, *N*-methylbenzamide, and *N*,*N*-dimethylbenzamide: vapor pressures, phase diagrams, and hydrogen bond enthalpy. *J. Chem. Eng. Data* **2010**; DOI: 10.1021/je100175j.

(2) Mann, J. Modern methods for the introduction of fluorine into organic molecules: an approach to compounds with altered chemical and biological activities. *Chem. Soc. Rev.* **1987**, *16*, 381–436.

(3) Seebach, D. Organic Synthesis - Where now? *Angew. Chem., Int Ed. Engl.* **1990**, *29*, 1320–1367.

(4) Goldstein, J. A.; Cheung, Y.-F.; Marletta, M. A.; Walsh, C. Fluorinated substrate analogues as stereochemical probes of enzymatic reaction mechanisms. *Biochemistry* **1978**, *17*, 5567–5575.

(5) Abeles, R. H.; Alston, T. A. Enzyme inhibition by fluoro compounds. *J. Biol. Chem.* **1990**, *265*, 16705–16708.

(6) Hurley, T. J.; Carrel, H. L.; Gupta, R. K.; Schwartz, J.; Glusker, J. P. The structure of sodium β-fluoropyruvate: A *gem*-Diol. *Arch. Biochem. Biophys.* **1979**, *193*, 478–486.

(7) Kun, E. In *Biochemistry involving carbon fluorine bonds*; Filler, R., Ed.; ACS Symposium Series 28; American Chemical Society: Washington, DC, 1976; Chapter 1, pp 1−22.

(8) Marletta, M. A.; Srere, P. A.; Walsh, C. Stereochemical Outcome of Processing of Fluorinated Substrates by ATP Citrate Lyase and Malate Synthase. *Biochemistry* **1981**, *20*, 3719–3723.

(9) Sabbah, R.; Xu-wu, A.; Chickos, J. S.; Planas Leitão, M. L.; Roux, M. V.; Torres, L. A. Reference materials for calorimetry and differential thermal analysis. *Thermochim. Acta* **1999**, *331*, 93–204.

(10) Monte, M. J. S.; Santos, L. M. N. B. F.; Fulem, M.; Fonseca, J. M. S.; Sousa, C. A. D. New static apparatus and vapor pressure of reference materials: naphthalene, benzoic acid, benzophenone and ferrocene. *J. Chem. Eng. Data* **2006**, *51*, 757–766.

(11) Ribeiro da Silva, M. A. V.; Monte, M. J. S.; Santos, L. M. N. B. F. The design, construction and testing of a new Knudsen effusion apparatus. *J. Chem. Thermodyn.* **2006**, *38*, 778–787.

(12) Clarke, E. C. W.; Glew, D. N. Evaluation of thermodynamic functions from equilibrium constants. *Trans. Faraday Soc.* **1966**, *62*, 539–547.

(13) Chickos, J. S.; Hosseini, S.; Hesse, D. G.; Liebman, J. F. Heat capacity corrections to a standard state: A comparison of new and some literature methods for organic liquids and solids. *Struct. Chem.* **1993**, *4*, 271–278.

(14) Steele, W. V.; Chirico, R. D.; Nguyen, A.; Hossenlopp, I. A.; Smith, N. K. Determination of ideal-gas enthalpies of formation for key compounds. *AIChE Symp. Ser.* **1990**, 138–154. Cited by: Nist webbook: http://webbook.nist.gov/cgi/cbook.cgi?ID=C55210&Units=SI&Mask=4#Thermo-Phase.

(15) Domalski, E. S.; Hearing, E. D. Estimation of the thermodynamic properties of C-H-N-O-S-halogen compounds at 298.15 K. *J. Phys. Chem. Ref. Data* **1993**, *22*, 805–1159.

(16) Penfold, B. R.; White, J. C. B. The crystal and molecular structure of benzamide. *Acta Crystallogr.* **1959**, *12*, 130–135.

(17) Tanigushi, T.; Takaki, Y.; Sakurai, K. A reexamination of the crystal structure of *m*-fluorobenzamide. *Mem. Osaka Kyoiku Univ.* **1976**, *24*, 119–125.

(18) Takaki, Y.; Tanigushi, T.; Sakurai, K. The crystal structure of *p*-fluorobenzamide. *Mem. Osaka Gakugei Univ.* **1966**, *14*, 48–55.

(19) Kato, Y.; Sakurai, K. The crystal structure of *o*-fluorobenzamide. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1643–1644.

Received for review August 2, 2010. Accepted August 26, 2010. Thanks are due to Fundação para a Ciência e Tecnologia (FCT) Lisbon, Portugal, for financial support given to Centro de Investigação em Química of University of Porto. One of us, A.R.R.P.A, thanks FCT and the European Social Fund (ESF) under the Community Support Framework (CSF) for the award of a Ph.D. Research Grant (SFRH/BD/39210/2007).

JE100801S