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The Application of Group Additivity Parameters to the Prediction of the Enthalpies of Formation of Heteroaromatic Compounds

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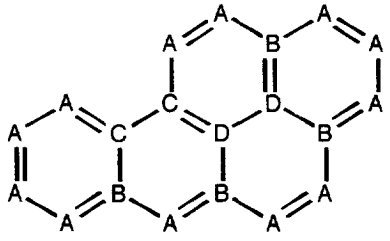
Abstract: Group additivity parameters have been devised which permit the prediction of the enthalpies of formation of azine heterocycles. Some applications of this approach to fused five-membered ring heterocycles are also presented. Copyright © 1996 Elsevier Science Ltd

The enthalpy of formation of a compound in its ideal-gaseous state is an important starting point for such diverse purposes as estimation of its resonance energy and prediction of its likely concentration among the products of a thermodynamically controlled reaction. As few laboratories have the appropriate facilities and expertise for the direct determination of this quantity such information is only available for a limited range of compounds. For example no information is available on such important ring systems as pteridine or purine. Consequently the derivation of group additivity approaches to the calculation of enthalpies of formation of organic compounds have received much attention[1]. However, most of this attention has been devoted to aliphatic compounds and heteroaromatic compounds have been largely neglected. A notable exception are the bond energy schemes of Joshi[2], which have mostly been applied to monocyclic systems. Some years ago[3] a group additivity approach was presented which enabled the prediction of the enthalpies of formation of



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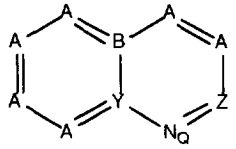
polycyclic aromatic hydrocarbons within experimental uncertainty. The approach used four groups, A to D, representing inherently different carbon atoms as illustrated for benzo[a]pyrene **1**. The values ascribed to these groups were A 3.30, B 4.80, C 3.70 and D 1.45 kcal mol^{-1}. In a recent paper[4] we showed that this group additivity method could be applied to fullerenes and related molecules with accuracies far superior to those provided by Molecular Orbital methods. In the present paper the group additivity method is extended to the prediction of enthalpies of formation of hetero-aromatic compounds.

Following this method inspection of the structures of the azaheterocycles listed in Table 1, for which enthalpies of formation are available[5,6], identified the additional groups for which values were required. Most of these are illustrated by the examples of quinoline **2**, quinazoline **3** and cinnoline **4** . Values were then selected for these groups so as to to provide the optimum reproduction with three exceptions,*vide infra*,of the experimental enthalpies of formation of the listed heterocycles.The values deduced for the individual groups are provided in Table 1. In the cases of the pairs of formally different groups C_B-$(C_B)_2$(H) , C_B-$(C_{BF})(C_B)$(H), and N_A-$(C_B)_2$, N-$(C_B)(C_{BF})$ the numerical differences were too small to justify the allocation of different values. The resulting predicted enthalpies are compared with the experimental ones in Table 2.which also includes entries for the corresponding carbocycles. In general the differences between calculated and experimental figures are comparable to the errors normally associated with experimental determinations. A perplexing anomaly is provided by phenanthridine and the isomeric benzo[f] and [h]quinolines listed at the end of Table 2 which show substantial deviations well outside the expected range. To a good approximation



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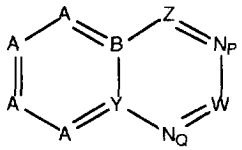

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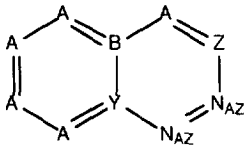

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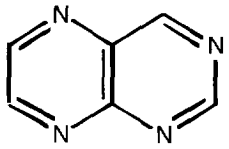

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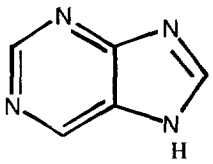

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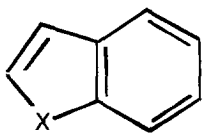


7 X = O

8 X = S

9 X = NH

introduction of an azine nitrogen into a benzenoid hydrocarbon increases the enthalpy of formation by about 14 Kcal. mole^{-1} leading to expected values, based upon that of phenanthrene, of about 64 Kcals. mole^{-1} for the enthalpies of formation of phenanthridine and its isomers in contrast to the reported values of 55-58 . In with that view of the success with which the group additivity values replicate the enthalpies of formation of all of the other systems presented here we are inclined to question the accuracy of the data for these compounds, all reported in the same paper, and surmise that they are subject to a common error. These group values lead to an enthalpy of formation of 89.7 Kcal. mole^{-1} for pteridine **5**.

So far parallel attempts to extend the group additivity treatment to five membered ring heterocycles has proved unpromising. However, inspection of Figure 1 shows that subtraction of the four A units from their benzo derivatives of established heats of formation[5,7] provides a very useful source of five-membered heterocycle sub-units. For example, from the fragment in the third entry it is possible to estimate an enthalpy of formation for purine **6** of 70.1 Kcal mole^{-1}. A value of 40.49±0.6 has been derived[8] for the solid state and the projected heat of sublimation of *ca.* 29 Kcal. mole^{-1} is comparable with that of *ca.* 25 Kcal. mole^{-1}

Table 1

Group	Label	$\Delta H_f^\circ_{298}$ kcal mol^{-1}	Ref.
C_B-(H)	A	3.30	5
C_{BF}-(C_B)$_2$(C_{BF})	B	4.80	5
C_{BF}-(C_B)(C_{BF})$_2$	C	3.70	5
C_{BF}-(C_{BF})$_2$	D	1.45	5
C_B-(C_{BF})$_2$(H)	-	4.40	This paper
C_{BF}-(C_B)(C_{BF})(N)	Y	5.10	This paper
C_B-(C_B)(N_A)	Z	3.70	This paper
C_B-(N_A)$_2$	W	4.00	This paper
N_A-(C_B)$_2$	N_P	16.10	This paper
N_A-(C_B)(C_{BF})	N_Q	16.10	This paper
N_A-(C_{BF})$_2$	-	17.70	This paper
N_A-(C_B)(N_A)	N_{AZ1}	26.20	This paper
N_A-(C_{BF})(N_A)	N_{AZ2}	25.20	This paper

Table 2

$\Delta H_f^\circ_{298}$ (Kcal. mole^{-1})

Entry	Compound	Exptl.[5,6]	Calc.	Error
1	Benzene	19.74±0.17	19.8	0.06
2	Pyridine	33.56 ± 0.17	33.4	-0.16
3	Pyridazine	66.52 ±0.24	66.3	-0.22
4	Pyrimidine	46.90 ± 0.33	46.9	0
5	Pyrazine	46.87 ± 0.31	47.0	+0.13
6	Naphthalene	35.92 ± 0.36	36.0	0.08
7	Quinoline	50.43 ± 0.2	49.5	-0.93
8	Isoquinoline	49.71 ± 0.2	49.6	-0.11
9	Phthalazine	82.53 ± 4.3	82.5	+0.03
10	Cinnoline	81.00 ± 2.0	81.5	+0.5
11	Quinazoline	61.81 ± 2.1	63.0	+1.19
12	Quinoxaline	63.00 ± 1.0	63.0	0.0
13	Anthracene	55.19 ± 0.53	54.4	-0.79
14	Acridine	69.55 ±0.24	68.3	-1.25
15	Phenazine	82.17 ±0.84	82.2	0.0
16	Phenanthrene	49.59 ±0.41	50.0	0.41
17	Benzo[c]cinnoline	94.81 ± 0.43	94.4	-0.4
18	Phenanthridine	58.20 ±1.27	64.5	+6.3
19	Benzo[f]quinoline	55.86± 1.72	63.5	+7.64
20	Benzo[h]quinoline	55.09±1.15	63.8	+8.71

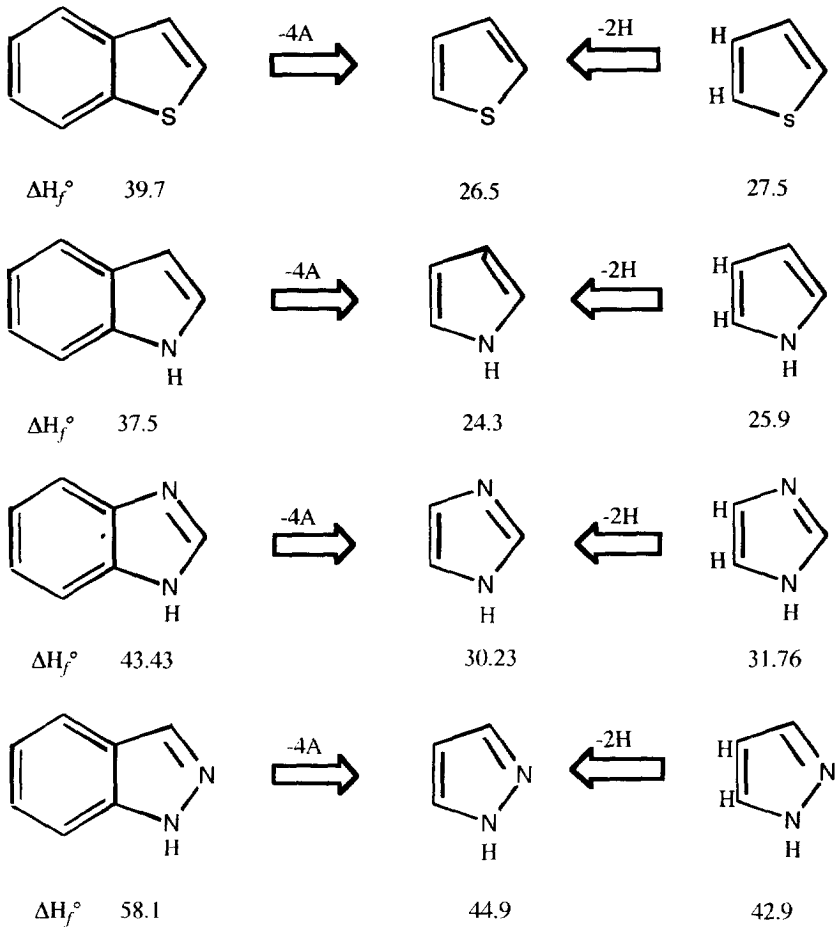
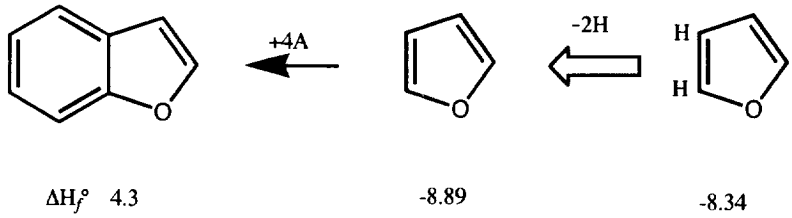
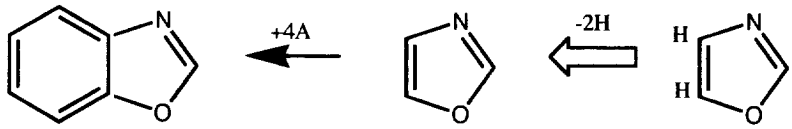


FIGURE 1

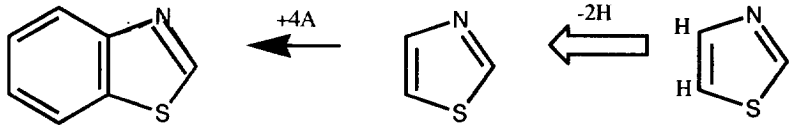
observed for benzimidazole. Since in arriving at these sub-units from the monocycle we are formally replacing two 'A/Z' groups by 'B/Y' ones or their five-membered ring equivalents we would anticipate that they would have enthalpies of formation *ca.*2-3 K.cals. higher than their parent heterocycles. Comparison of the heats of formation of these sub units in Figure 1 with those of the corresponding monocyclic heterocycles[5,7] indicates that the formal removal of two adjacent ring hydrogens results in enthalpy changes ranging from -1.6 to +2.0 with an average of -0.55 Kcal mole^{-1} This observation provides a means of access to several other systems shown in Figure 2 where enthalpies of formation are only available for the monocyclic heterocycle[5]. Thus enthalpies of formation of 4.3, 8.95, 31.45 and 31.8 Kcal. mole^{-1} can be deduced for benzofuran, benzoxazole, benzo[d]isoxazole and benzothiazole respectively. Conversely, an enthalpy of formation of 67.6 Kcal. mole^{-1} can be deduced for 1,2,3-triazole from the reported value[9] for benzotriazole. In a simlar fashion partial dissection of dibenzofuran, dibenzothiophene or acridine provides the 'building' units **7**, **8** and **9** with enthalpies of formation of 6.7, 35.8 and 36.9 Kcal. mole^{-1} respectively.



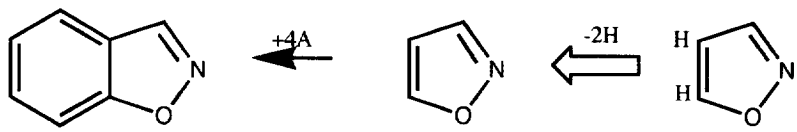
$\Delta H_f°$ 4.3 -8.89 -8.34



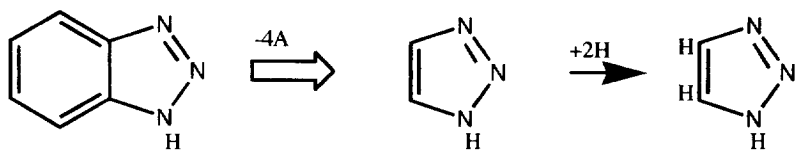
$\Delta H_f°$ 8.95 -4.25 -3.7



$\Delta H_f°$ 31.8 18.6 19.1

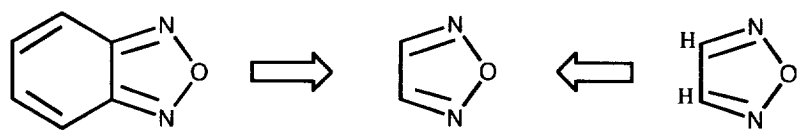


$\Delta H_f°$ 31.45 18.25 18.8



$\Delta H_f°$ 80.2 67.0 67.6

FIGURE 2



$\Delta H_f°$ 71.8 *ca.*9.2 10.4

FIGURE 3

As emphasised earlier the application of such group additivities in the situations discussed so far presupposes that each ring atom is essentially aromatic in character and that the group value incorporates its contribution to both σ and π bonds. A totally different balance of contributions arises for example in situations where the benzenoid ring is essentially *o*-quinonoid. For example, comparison of the enthalpies of formation of furazan, 10.4[10], and benzofurazan, 71.8[11], shows that they differ by 61.4 Kcal.mole^{-1}. This is far in excess of the foregoing allowances of *ca.*12 Kcal. mole^{-1}for fusion to a benzene ring and commensurate with the C_4H_4 fragment consisting of two relatively localised double bonds rather than 4 aromatic CH's. While further experimental evidence for the size of such an increment for fusion with an *o*-quinonoid benzenoid ring is desirable we note that this permits prediction of enthalpies of formation of 53.1, 88.9 and 87.3 Kcals. mole^{-1} for benzo[c]furan, benzo[c]thiophene and isoindole respectively. These values lead to corresponding resonance energies of 8.8, 20.6 and 23.9 Kcals. mole^{-1} for the foregoing heterocycles.

While there is obviously no completely satisfactory replacement for a direct determination of the enthalpy of formation of a compound the foregoing approach is expected to provide an acceptable substitute in many situations.

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