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Heteroaromaticity. 10. The Direct Calculation of Resonance Energies of Azines and Azoles from Molecular Dimensions

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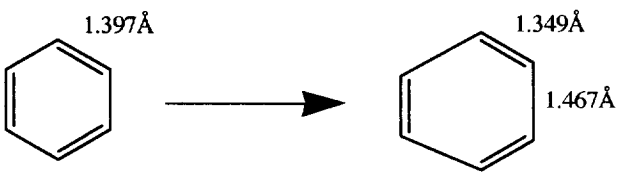
Abstract: A simple method is presented for the direct calculation of thermodynamic resonance energies of aza heterocycles from their molecular dimensions. This method, which is derived from the HOSE approach of Krygowski, provides values for a range of azines and fused azoles which are in satisfactory agreement with those obtained by other methods. In the case of 1,2-diazines an energy of repulsion of ca 9.5 Kcal. mole^{-1} between the nitrogen lone pairs has been estimated and some consequences of this observation for the stability of polyazines are discussed.

INTRODUCTION

The direct calculation of molecular heats of formation from measured bond lengths has received spasmodic attention[1] which has been mostly confined to hydrocarbons.While reasonably accurate predictions of heats of formation of most saturated molecules can be obtained using standard bond energy schemes this is not the case with conjugated systems for which a knowledge of the conjugation energy is also required. Such information is usually obtained either by subtracting the predicted heat of formation from the experimentally determined value or from the heat of hydrogenation[2]. These methods are of course not readily accessible to most organic chemists and the values obtained may also contain contributions from molecular strain energies *etc.* In contrast molecular dimensions are now readily available for a large and rapidly increasing range of molecules largely due to modern developments in X-ray crystallography. Additionally, as recent calculations have shown[3], molecules can undergo changes in dimensions and energies when subjected to differing environments. Consequently , a simple method for the calculation of the resonance energy of a molecule from its molecular dimensions would seem to be highly desirable.

Some years ago Krygowski and his colleagues[4,5,6] introduced what they termed the HOSE (Harmonic Oscillator Stabilisation Energy) defined as the negative value of energy necessary to deform the real molecule into its Kekulé or resonance structure as illustrated for benzene;



The bond lengths adopted for the cyclohexatriene structure were those for butadiene. The energy of deformation could then be derived from a simple harmonic oscillator relationship resulting in the expression:

$$E_{def} = -\,{}^{1}/_{2} \sum (R_r - R_0)^2 k_r \qquad (1)$$

where $R_0 = 1.337$Å for the n_2 shortest carbon-carbon bonds which are shrunk in the course of the deformation process, and $R_0 = 1.483$ Å for the n_1 longer carbon-carbon bonds which are lengthened during the deformation. Obviously $n_1 + n_2 = n$, the number of single (s) and double (d) bonds in the Kekulé structure. This expression is more conveniently written :

$$E_{def} = -\,{}^{1}/_{2} \left[\sum_{r=1}^{n_1} (R_r' - 1.467)^2 k_r' + \sum_{r=1}^{n_2} (R_r'' - 1.349)^2 k_r'' \right] \qquad (2)$$

where R_r' and R_r'' are the lengths of the bonds which are stretched and shortened respectively, and k_r' and k_r''. are the corresponding force constants for these bonds. These force constants, k_r' and k_r'', were calculated from the equation:

$$k_r = a + bR_r \qquad (3)$$

using $R_{C=C} = 1.349$ and $R_{C-C} = 1.467$ taken from buta-1,3-diene plus the corresponding $k_{C=C} = 9.6$ dyn cm^{-1} and $k_{C-C} = 4.5$ dyn cm^{-1}, resulting in the values a = 44.39 dyn cm $^{-1}$ and b = - 26.02 dyn cm^{-1}. Equation (3) then becomes:

$$HOSE = 301.15 (44.39 - 26.02 R_r) \left[\sum_{r=1}^{n_1} (R_r' - 1.467)^2 + \sum_{r=1}^{n_2} (R_r'' - 1.349)^2 \right] \qquad (4)$$

where the negative E_{def} is termed the stabilisation energy (HOSE) and the factor 301.15 permits the use of R in Å and gives HOSE-values in kJ $mole^{-1}$. These figures yield a HOSE for benzene of ca. 12 kcal. $mole^{-1}$. A corresponding set of values have been calculated[5] for a range of polybenzenoid hydrocarbons and correlated with the corresponding theoretical resonance energies of Hess and Schaad[8]. Of course in the case of molecules having several Kekulé structures of differing energies it is necessary to calculate HOSE values for each and then employ the weighted summation. The values for the individual resonance forms have been used to estimate their relative contributions to the overall picture. Comparable equations have also been derived for carbon-oxygen and carbon-nitrogen bonds[5].

RESULTS AND DISCUSSION

For reasons indicated in part above we were particularly interested in the possibility of calculating heats of formation or resonance energies directly from experimentally determined molecular dimensions and it occurred to us that the HOSE approach summarised above might provide a satisfactory basis for this purpose. As indicated it was originally constructed to provide Dewar type resonance energies[9] with the corresponding conjugated acyclic polyene as the reference structure rather than its totally unconjugated counterpart, which is the basis for the derivation of the thermodynamic values. Firstly , the carbon single and double bond lengths of ethane [10] and ethylene[11] were selected in place of those of butadiene. As anticipated employment of these in

equation (1) together with the respective force constants led to a resonance energy of 38.4 kcal. mole^{-1} for benzene rather than the current value[12] of 45.8. It is apparently well established[13] that experimentally determined force constants frequently need numerical adjustment so as to perform satisfactorily in molecular mechanics programmes. In the present situation the incorporation of a scaling factor of 1.194 sufficed to reproduce this value. A comparable approach was employed for the carbon-nitrogen bond, with the initial bond lengths and force constants selected being derived from methylamine [14] and formaldehyde imine[15]. These values gave a resonance energy of 52 kcal. mole^{-1} for 1,3,5-triazine rather than the experimental value[12] of 44.9 hence a scaling factor of 0.864 was introduced.The equation for calculating individual bond energy contributions, E,becomes:

$$E = F (R_s \text{ or } R_d - R)^2 (a - bR) \text{ kcal. mole}^{-1} \quad (5)$$

where R (Å) is the length of the bond. The lengths of the appropriate single (R_s) and double bonds (R_d) together with the values of the constants F, a and b are listed in Table 1.

Table 1. Constants used for bond energy calculations

Bond	R_s (Å)	R_d (Å)	F	a (x10^4 Pa)	b(x10^4 Pa)
CC	1.533	1.337	85.94	44.39	26.02
CN	1.474	1.274	62.19	43.18	25.73
NN	1.449	1.250	62.33	57.10	35.51

As will be seen later these constants give very satisfactory results for six-membered ring systems but in order to extend this treatment to five-membered rings it is necessary to make allowance for the bond angle strain introduced. Perhaps the simplest method of achieving this is to assume that this will be more or less constant and to calculate an appropriate energy increment using Dauben's potential function[16]:

$$V_s = 0.5 A\alpha^2 \quad (6)$$

where A is the bond angle deformation constant (0.026 kcal. mole^{-1}deg^2) and α is the bond angle deformation. This leads to a strain energy value of 9.36 kcal. mole^{-1}for a five-membered ring. Addition of this to the bond energy sums for 5-membered ring systems gives in general good agreement with anticipated values, *vide infra*.

As indicated earlier where more than one Kekulé form is possible a separate energy has to be calculated for each of these and the energies then summed according to the following expression:

$$\text{Resonance energy} = n E_i \left(1/E_i \div \sum_{i=1}^{i=n} 1/E_i \right) \quad (7)$$

As will be seen from the entries in Table 2 the calculated resonance energies obtained by this method in general show good agreement with those reported for a range of nitrogen heterocycles. In those instances where experimental heats of formation have not been reported use has been made of values obtained by the group additivity method[17] to estimate resonance energies. The accuracy of course depends on the quality of the structural determination and this has been extensively discussed[5] in the context of the HOSE method.

Table 2. Resonance Energies of Azaheterocycles Calculated from Molecular Dimensions

		Resonance energies (kcal mole^{-1})			
Entry	Compound	Calc.	Exptl.[43-45]	G.A.[h]	Ref.[i]
1	Pyridine	44.1	43.3	-	19
2	Pyrimidine	40.1	40.6	-	20
3	Pyrazine	38.8	40.9	-	21
4	1,3,5-Triazine	44.9	44.9	-	22
5	Quinoline[a]	81.6	81.0	-	23
6	Isoquinoline[b]	82.6	81.0	-	24
7	Quinazoline	74.8	76.5	-	25
8	1,5-Diazanaphthalene	79.0	-	75.3	26
9	1,8-Diazanaphthalene	79.5	-	75.6	27
10	2,6-Diazanaphthalene	74.0	-	75.1	26
11	2,7-Diazanaphthalene	81.0	-	75.1	28
12	Pteridine	69.9	-	70.8	29
13	Pyrrole	31.8	34.8	-	30
14	Imidazole	34.9	40.0	-	31
15	Indole	73.3	73.8	-	32
16	Isoindole[c]	62.5	62.4	-	33
17	Indolizine[d]	48.5	-	-	34
18	Benzimidazole	75.1	78.9	-	35
19	Purine	71.6	-	74.4	36
20	Carbazole	113.5	111.7	-	37
21	Acridine[e]	101.1	108.3	-	38
22	Phenazine	100.3	110.3	-	39
23	Phenanthridine	108.5	119.6	113.3	40
24	Benzo[h]quinoline[f]	110.9	122.7	114.3	41
25	1,10-Phenanthroline[g]	113.6	-	109.7	42

[a] Dimensions from 8,8'-biquinolyl; [b] dimensions from 3-methylisoquinoline; [c] dimensions from N-neopentyl-isoindole; [d] dimensions from bis(1,2-dimethylindolizin-3-yl)methane; [e] dimensions from 9-chloroacridine; [f] dimensions from 8,9,10,11-tetrahydrobenz[c]acridine; [g] dimensions from 2,9-dimethyl-1,10-phenanthroline; [h] calculated from heats of formation derived from group additivity method[17]; [i] reference to source of molecular dimensions.

Based upon this analysis a typical estimated standard deviation in bond lengths of 0.004 Å in the case of quinoline would result in a resonance energy change of about 1-2 kcal mole^{-1}. This would increase rapidly with increasing estimated standard deviations reaching about 3 kcal at 0.006 Å and around 5 kcal at 0.008 Å. In practice the estimated standard deviations of most modern X-ray structural determinations rarely exceed 0.005 Å.We note that doubt has been expressed[18] concerning the level of accuracy of heats of formation, and hence resonance energies, obtained by combustion methods for some nitrogen heterocycles. A particular case is provided by the benzoquinolines (entries 23 and 24) where we[17], and others[46], have previously drawn attention to apparent discrepancies in the reported heats of formation. The divergences displayed by pyrrole and imidazole (entries 13 and 14) may reflect an insufficient allowance for angle strain in five-membered rings, though this is not borne out by their benzo analogues.

Table 3. Resonance Energies of 1,2-Diazines Calculated from Molecular Dimensions.

		Resonance energies (kcal mole^{-1})					
Entry	Compound	Calc. I[a]	Calc. II[b]	Exptl.[c]	G.A.[d]	Δ	Ref.[e]
1.	Pyridazine	43.9	37.2	33.5	33.7	10.4	47
2	1,2,4-Triazine[f]	40.4	31.2	-	32.9	7.5	48
3	1,2,4,5-Tetrazine[g]	39.2	24.5	-	21.6	8.8	49
4	Phthalazine	87.4	83.4	80.1	80.1	7.3	50
5	Cinnoline[h]	83.4	75.8	69.8	69.3	13.6	51

[a] Including nitrogen-nitrogen bond contributions; [b] excluding nitrogen-nitrogen bond contributions; [c] references 43-45 ; [d] calculated from heats of formation derived from group additivity method[17]; [e] reference to source of molecular dimensions; [f] dimensions from 5-p-chlorophenyl-1,2,4-triazine; [g] dimensions from 3,6-dimethyl-1,2,4,5-tetrazine;[h] dimensions from 4-methylcinnoline.

An unexpected situation was uncovered in extending this treatment to 1,2-diazines. Calculation of the resonance energies of a selection of these compounds omitting any contribution from the nitrogen-nitrogen bond yielded values shown in column four of Table 3 which are slightly larger than the experimental ones. In order to calculate the nitrogen-nitrogen bond contributions the bond lengths and force constants for hydrazine[52] and *trans*-diimine[53] were adopted to calculate the constants "a" and "b" listed in Table 1. In the absence of any other obvious criterion to estimate the value of a potential scaling factor these constants were used to calculate the notional resonance energy of hexazine. A nitrogen-nitrogen bond length of 1.309 Å was calculated for hexazine from the Gordy relationship[54] assuming a bond order of 1.67. On this basis a resonance energy of 52.89 kcal. mole^{-1} was calculated. As benzene and 1,3,5-triazine have resonance energies of 45.8 and 44.9 kcal. mole^{-1} respectively[12], it seemed reasonable to assign a similar value to hexazine also, hence a scaling factor of 0.866 was chosen. The resulting resonance energies are shown in column three of

Table 3. The differences, Δ, between these values and those obtained either directly, or *via* heats of formation calculated by the group additivity method[17], are shown in the penultimate column. In each case the resonance energy calculated by the present method is greater than the experimental one by a weighted average of 9.0 kcal. which can be attributed to the so far neglected energy of repulsion between the adjacent nitrogen lone pairs of electrons. This phenomenon appears to go largely unremarked in discussions of diazine chemistry. However, we note that an energy difference of 7.2 kcal. has been deduced[55] between *cis*- and *trans*-diimine.

Table 4. Heats of Formation, Dissociation and Resonance Energies of Azines (kcal. mole^{-1}).

Entry	Compound	ΔH_f°	R.E.	ΔH_d
1	Pyridine	33.6[a]	43.3	107.8
2	Pyrimidine	46.8[a]	40.6	72.3
3	Pyrazine	46.9[a]	40.9	72.3
4	Pyridazine	66.5[a]	33.5	52.6
5	1,3,5-Triazine	54.0[a]	44.9	42.9
6	1,2,4-Triazine	79.9[b]	32.9	17.0
7	1,2,3-Triazine	97.3[b]	43.1	-10.5
8	1,2,4,5-Tetrazine	112.8[b]	21.6	-48.2
9	1,2,3,5-Tetrazine	110.7[b]	35.1	-46.1
10	1,2,3,4-Tetrazine	128.3[b]	29.7	-73.8
11	Pentazine	159.1[b]	16.5	-126.8
12	Hexazine	197.2[c]	-8.2	-197.2

[a] Experimental value; [b] from group additivities; [c] see text.

A frequently discussed problem in heterocyclic chemistry[56] is that of the possible synthesis of the polyazines. As yet no evidence has been reported for even the transitory existence of either 1,2,3,5-tetrazine, pentazine or hexazine, although fused examples of 1,2,3,4-tetrazine have been described and some derivatives of pentazole show modest thermal stability[57]. It is clear from the foregoing discussion that the repulsions between adjacent nitrogen lone pairs can play an important role in determining molecular stability. If we return to the case of hexazine discussed above the sum of the lone pair repulsion energies slightly exceeds the resonance stabilisation energy, and leads to a predicted heat of formation of hexazine of 197.2 kcal. mole^{-1}. This figure allows the assignment of a provisional N_A-$(N_A)_2$ group additivity value of 32.87 kcal. mole^{-1}. Using this value and those formerly reported[17] permits the prediction of the previously unknown heats of formation shown in Table 4 of the polyazines and their heats of dissociation to nitrogen, hydrogen cyanide and acetylene which have heats of formation of 0, 32.3 and 54.5 kcal. mole^{-1} respectively. Not surprisingly these values differ to some extent from those derived by various molecular orbital types of calculation[56], however the present estimates agree with previous ones in indicating the very high heats of dissociation associated with hexazine and pentazine and to a lesser extent with 1,2,3,4-tetrazine. Of course this does not directly reflect the

kinetic stability of these molecules but does suggest fairly low energies of activation towards dissociation.

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