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ON THE AROMATICITY OF HETEROCYCLES CONTAINING THE AMINE NITROGEN OR THE ETHER OXYGEN*

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Abstract—A new method of predicting aromaticity [B. A. Hess, Jr. and L. J. Schaad, *J. Am. Chem. Soc.* **93**, 305 (1971)] is extended to conjugated heterocyclic systems containing the amine nitrogen or the ether oxygen. Coulomb and resonance integrals for these atoms were determined using experimental heats of atomization. Empirical π bond energies for the carbon-heteroatom bonds were determined from heteroatom containing acyclic molecules. These were in turn used to calculate the HMO π resonance energies of a wide variety of heterocyclic compounds. An excellent correlation between calculated resonance energy and experimental aromaticity was found.

INTRODUCTION

THE lack of correlation between computed Hückel MO delocalization energy and observed aromatic behavior has been quoted widely as a failure of the Hückel method. Recently Dewar,[1a] using the more elaborate PPP method, has for the first time obtained calculated resonance energies that do correlate well with experimental aromaticity for a wide range of compounds. He concludes that the simple Hückel method therefore no longer has a place in organic chemistry.[1b] However, not only has Dewar changed from the Hückel to the PPP approximation, but he has also changed the reference structure relative to which aromatic stabilization is computed. We have shown that it is this modification of the reference structure that is crucial.[2] Using the old Hückel method, but a reference structure analogous to Dewar's gives HMO π resonance energies that correlate at least as well as Dewar's with experimental properties for a wide variety of both alternant and nonalternant hydrocarbons.[3,4]

In the computation of the original Hückel delocalization energy, the π energy of an aromatic hydrocarbon with n double bonds was compared to the π energy of n isolated double bonds (ethylene). In our method, modeled after Dewar's, the HMO π energy is compared to the π energy of a "localized"[1] structure obtained by summing π bond energy terms with contributions from both single and double bonds.[2] In this method all acyclic polyenes have essentially zero resonance energy whereas cyclic hydrocarbons are found to have a wide and continuous variation in resonance energies from positive (aromatic) to zero (nonaromatic) to negative (antiaromatic).

Note that we have not modified the Hückel computation itself; only the reference structure. All the crudities of the Hückel wavefunction remain. In particular, charge

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distributions and dipole moments are inaccurately calculated. On the other hand, all the simplicity and ease of application of the Hückel method also remain. Should Hückel resonance energies be as accurate as those from more sophisticated methods, we feel that they are preferred, not only because the Hückel method is cheaper and easier to use, but also because the simpler Hückel model might be expected to provide easier insight into the physical basis of aromaticity.

Dewar's aromaticity can be approximated by the difference between heat of atomization of a compound and of its reference structure.[1,5] A given computational method might be able to reproduce this difference accurately without being able to compute the heats of atomization themselves. However, at present there are not available all the required experimental heats of atomization to check this point.[5] A method is therefore on firmer ground if it can give accurate individual heats of atomization. We have shown that the Hückel method can do so. This depends upon the fact that over a range of π bond order from 0·3 to 1·0, HMO π resonance energies are directly proportional to total resonance energy, thus explaining why the Hückel method which ignores σ effects is able to predict heats of atomization as accurately as more complete methods which consider these effects explicitly.[5]

The success of our method with the hydrocarbons raised the question of whether a similar approach might also be successful with conjugated heterocyclic compounds. We present here the results for cyclic compounds containing the amine nitrogen and the ether oxygen. These heterocyclic systems have been of considerable recent interest from both a synthetic and theoretical viewpoint.[5]

RESULTS AND DISCUSSION

Evaluation of Coulomb and resonance integrals

In order to perform HMO calculations on conjugated compounds containing heteroatoms, corrections must be made to the Coulomb integral (eq. 1) for

$$\alpha_X = \alpha + h_X\beta \tag{1}$$

each heteroatom and to the resonance integral (eq. 2) for each carbon–heteroatom

$$\beta_{C-X} = k_{C-X}\beta \tag{2}$$

bond. Although there are a number of values of $h_{\ddot{O}}$, $k_{C-\ddot{O}}$, $h_{\ddot{N}}$, and $k_{C-\ddot{N}}$ available from the literature,[7] the majority of these were determined using the eigenvectors and/or excited state properties. Since resonance energies are a ground state property and arise from the eigenvalues, we sought a method for the determination of the heteroatom parameters, h_X and k_{C-X}, which would be based on a ground state property and would make use of eigenvalues rather than the eigenvectors. Although Streitwieser noted the need for a systematic evaluation of these parameters over ten years ago[8] this has not been done extensively. He suggested that a correlation which had been established between an experimental property and a calculated quantity for hydrocarbons might be used for the systematic evaluation of h_X and k_{C-X} in heterosystems. We have recently developed such a correlation using experimentally determined heats of atomization of hydrocarbons.[5] Accurate heats of atomization can be calculated for a wide variety of hydrocarbons using the HMO method and equation 3 where E_{CH} is

$$\Delta H_a = -(n_{CC}E_{CC} + n_{CH}E_{CH} + P \cdot \beta) \tag{3}$$

the energy of each of the n_{CH} C—H bonds and E_{CC} is the σ energy of each of the n_{CC} C—C bonds. $P \cdot \beta$ is HMO π-binding energy. Note that in spite of C—C bonds of various lengths, only a single bond energy term is used. As mentioned above, changes in the σ compression energy are automatically taken into account by the Hückel π calculation. The values E_{CC}, E_{CH} and β were determined by a least squares fit of equation 3 to the observed heats of atomization for a series of conjugated cyclic hydrocarbons giving $-3{\cdot}48543$ eV, $-4{\cdot}27606$ eV and $-1{\cdot}33077$ eV, respectively.*

A similar treatment of conjugated systems which contain heteroatoms requires several additional bond energy terms (eq. 4).

$$\Delta H_a = -(n_{CC}E_{CC} + n_{CH}E_{CH} + n_{CX}E_{CX} + n_{XH}E_{XH} + P \cdot \beta) \tag{4}$$

The π binding energy $P \cdot \beta$ is the difference between the total π energy of the molecule and the energy of the same electrons in separated atoms. Each isolated carbon atom has π energy α, but that of a heteroatom contributing two electrons to the π system is $2(\alpha + h_X\beta)$. π binding energies and therefore calculated heats of atomization are functions of h_X and k_{CX}. Best values of these parameters were determined as follows. With some initial pair of h_X and k_{CX} and the previously determined values of E_{CH} and E_{CC},[5] the linear least squares method was used to determine E_{CX}, E_{XH} and β by a fit of experimental ΔH_a to that calculated by equation 4. The process was repeated

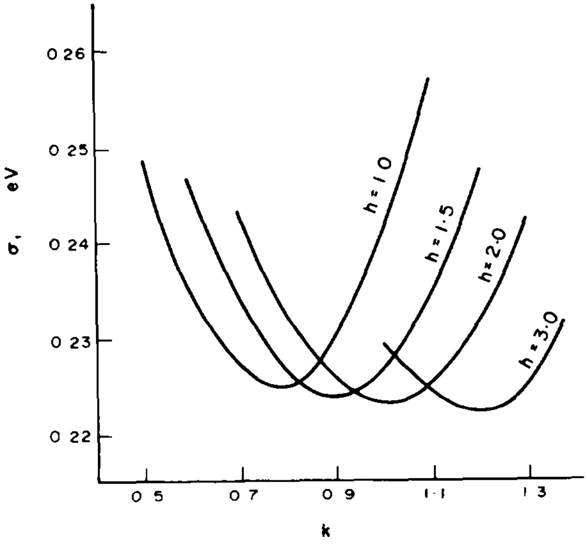

Fig 1. Accuracy of computed heats of atomization as a function of k_{C-N} and h_N

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* As revised heats of atomization were used,[9] these values differ slightly from those previously obtained.

with varying sets of h_X and k_{CX} to minimize the standard deviation σ between calculated and experimental ΔH_a's.

$$\sigma = \{\textstyle\sum_i[\Delta H_a{}^{expt}(i) - \Delta H_a{}^{calc}(i)]\}^{\frac{1}{2}} \tag{5}$$

Results for the amine nitrogen are shown in Fig 1. As can be seen there appears to be no unique set of $h_{\ddot{N}}$ and $k_{C-\ddot{N}}$ as for each $h_{\ddot{N}}$ chosen there is a $k_{C-\ddot{N}}$ value which gives essentially the same value of σ. It is interesting to note that Streitwieser has previously suggested that exactly such a situation might arise, *i.e.*, that no unique set of parameters might be found. A similar result is found in the evaluation of $h_{\ddot{O}}$ and $k_{C-\ddot{O}}$. This lack of a unique solution frustrated our attempt to obtain h_X and k_{C-X} more automatically by use of a pattern search computer program.

In the case of the amine nitrogen $h_{\ddot{N}} = 1{\cdot}5$ and $k_{C-\ddot{N}} = 0{\cdot}90$, and for ether oxygen $h_{\ddot{O}} = 2{\cdot}00$ and $k_{C-\ddot{O}} = 0{\cdot}34$ were chosen. Our value of $h_{\ddot{O}}$ is commonly used, but the corresponding resonance parameter $k_{C-\ddot{O}}$ is smaller than usually reported.[7] Alternatively, one could choose a set with $k_{C-\ddot{O}} \approx 1$ and $h_{\ddot{O}}$ greater than 2. Either set perhaps indicates oxygen to be more electronegative than has been assumed in earlier HMO treatments. It is clear that increasing electronegativity increases h, but it might also lead to a more negative p orbital exponent, smaller overlap with neighboring atoms and therefore a smaller k. This point becomes significant below in comparing the properties of 1*H*-azonine and oxonin. Although it makes no difference which set of parameters one chooses at the minimum σ as far as the calculation of heats of atomization is concerned, it may make a difference as far as the calculation of resonance energies is concerned (see below). The calculated heats of atomization obtained with the above parameters are listed in Table 1. As can be seen the agreement between experimental and calculated heats of atomization is excellent and as good as that obtained by Dewar using the Pariser–Parr method in a similar treatment.[6c] Table 2 lists the parameters used. However, because of the limited number of experimental heats of atomization, these parameters must be considered

Table 1. Observed and calculated heats of atomization

Compound	Obsd (eV)	Calcd (eV)	Diff (eV)
Pyrrole	44·78	44·69	0·09
Indole	78·20	78·37	−0·17
Carbazole	112·19	112·11	0·08
Diphenylamine	116·53	116·52	0·01
Aniline	64·38	64·38	0·00
α-Naphthylamine	97·87	97·93	−0·06
β-Naphthylamine	97·97	97·91	0·06
Furan	41·69	41·64	0·05
Phenol	61·70	61·64	0·06
Hydroquinone	66·03	66·06	−0·03
Divinyl Ether	45·99	46·02	−0·03
Diphenyl Ether	113·79	113·64	0·15
Dibenzofuran	108·92	109·09	−0·17

somewhat preliminary and subject to revision when more data become available. We hope that the initial success here in the calculation of heats of atomization will prompt the determination of heats of combustion of a much wider range of heterocyclics.

TABLE 2. PARAMETERS OBTAINED USING THE HEATS OF ATOMIZATION IN TABLE 1

Parameter	Amine Nitrogen	Ether Oxygen
h_X	1·50	2·00
k_{C-X}	0·90	0·34
E_{C-X}	−2·9175 eV	−4·0376 eV
E_{X-H}	−4·0808 eV	−4·7179 eV
β	−1·3276 eV	−1·3052 eV
σ	0·2239 eV	0·2477 eV

Resonance energies

Having obtained the necessary Coulomb and resonance integrals for the heteroatoms, we were then in a position to calculate resonance energies of heterocyclic systems. Our approach to the calculation of resonance energies was exactly analogous to our method used with the hydrocarbons.[2] The first step was to determine empirical additive π-bond energies for the carbon–heteroatom bonds. As in the case of the hydrocarbons we found it necessary to classify the bond types according to the number of adjacent conjugated atoms in order to achieve additivity in the acyclic systems. In Table 3 are listed all possible C—Ö and C—N̈ bonds according to this classification. HMO π-binding energies were calculated for a series of acyclics containing all possible C—Ö and C—N̈ bonds. With the previously obtained C—C bond energies these π-binding energies were fit by least squares to a sum of bond energy terms giving the results in Table 3. The additive model fit the HMO energies to 0·003 β per electron (standard deviation). Hence, as in the case of the hydrocarbons,

TABLE 3. EMPIRICAL π BOND ENERGIES OF CARBON–HETEROATOM BONDS

Designation	Bond Type	π-Bond Energy (β)
N̈3	$CH-NH_2$	0·2745
N̈2	CH—NH	0·2980
N̈2′	$C-NH_2$	0·3096
N̈1	CH—N	0·3101
N̈1′	C—NH	0·3137
N̈0	C—N	0·3187
Ö2	CH—OH	−0·0302
Ö1′	C—OH	0·0273
Ö1	CH—O	−0·0259
Ö0	C—O	0·0374

π-binding energies of heteroatoms containing acyclics can be calculated accurately in an additive fashion with these empirical bond energies. Because of the two linear dependencies among the bond types, two of the bond energy terms may be fixed arbitrarily (Appendix). For this reason physical significance must not be attached to individual terms. Other, equally valid, choices of the arbitrary parameters can lead to positive energies for all bonds or to single bond energy terms larger than double. All parameter choices give identical resonance energies for all molecules.

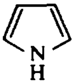
Having found additivity in the acyclics, one can now calculate resonance energies since the bond energies listed in Table 3 in conjunction with those previously obtained for C—C bonds[2] may be used to calculate the π-energy of "localized" cyclic models. The resonance energy of a heterocyclic compound is then the difference between the HMO π-binding energy of the compound and the energy of the "localized" model obtained in an additive fashion. In Table 4 are listed the π-binding energies, "localized" energies, resonance energies and resonance energies per π electron (REPE) for a wide variety of cyclic compounds which contain amine nitrogen or

TABLE 4. RESONANCE ENERGIES OF TWO ELECTRON NITROGEN AND OXYGEN HETEROCYCLES

Compound	π-Binding Energy (β)	Additive Energy (β)	Resonance Energy (β)	REPE (β)
1	5·435	5·202	0·233	0·039
2	7·447	7·738	−0·291	−0·036
3	10·413	10·274	0·139	0·014
4	11·236	10·770	0·466	0·047
5	11·019	10·727	0·292	0·029
6	10·892	10·625	0·267	0·027
7	17·082	16·367	0·715	0·051
8	13·469	13·306	0·163	0·014
9	12·977	13·263	−0·286	−0·024
10	13·438	13·260	0·178	0·015
11	19·417	18·874	0·543	0·034
12	19·036	18·831	0·205	0·013
13	19·407	18·858	0·549	0·034
14	18·845	18·812	0·033	0·002
15	14·136	13·661	0·475	0·040
16	15·875	15·860	0·015	0·001
17	18·689	18·733	−0·044	−0·003
18	4·598	4·554	0·044	0·007
19	7·039	7·090	−0·051	−0·006
20	9·627	9·626	0·001	0·000
21	10·526	10·170	0·356	0·036
22	10·096	10·079	0·017	0·002
23	16·470	15·815	0·655	0·047
24	12·993	12·706	0·287	0·024
25	12·573	12·615	−0·042	−0·004
26	12·928	12·612	0·316	0·026
27	18·914	18·238	0·676	0·042
28	18·521	18·230	0·291	0·018
29	18·888	18·257	0·631	0·039
30	18·189	18·164	0·025	0·002

ether oxygen. As before in cases where more than one localized structure can be written, the average of their energies (which never differ significantly) was used.[2]

Examination of the resonance energies of compounds **1–30** clearly indicates that their calculated resonance energies are in extremely good agreement with their experimental properties. Furthermore, the resonance energies obtained here closely parallel those obtained by Dewar using the PPP method.[10–12] We emphasize that the evaluation of the heteroatom parameters is based strictly on an experimental ground state property, heats of atomization. The resonance energies and the agreement between observed and experimental properties to be described below follow automatically; they were not obtained by a judicious manipulation of the Hückel parameters.



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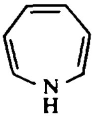

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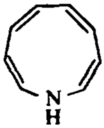

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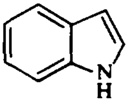

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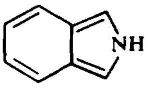

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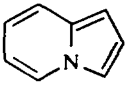

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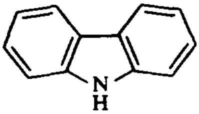

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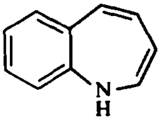

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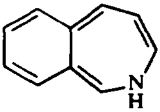

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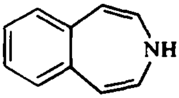

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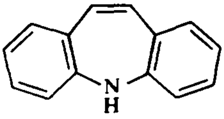

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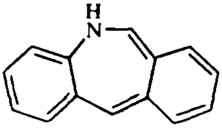

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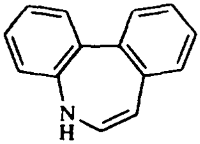

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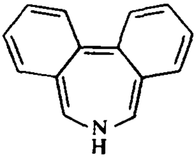

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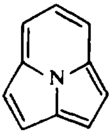

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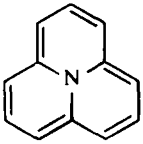

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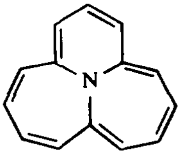

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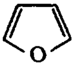

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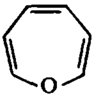

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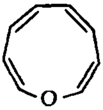

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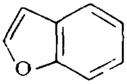

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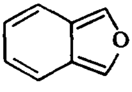

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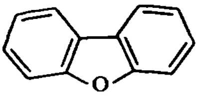

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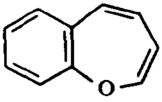

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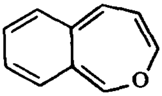

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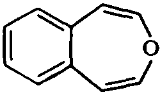

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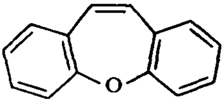

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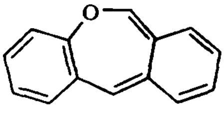

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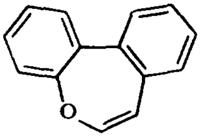

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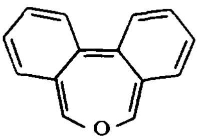

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It is interesting to make a comparison between the oxygen and nitrogen systems. Whereas pyrrole (**1**) has a substantial REPE (roughly two-thirds that of benzene), furan (**18**) has a very small REPE (0·007). Furan behaves much like a polyene as it undergoes Diels–Alder reactions readily.[13] The chemistry of pyrrole however is indicative of an aromatic compound, particularly its failure to undergo addition reactions.[14] The resonance energy of benzofuran (**21**) is very close to that of benzene[2] which implies that the furan ring is not aromatic whereas the resonance energy of indole (**4**) is greater than that of benzene. The chemistry of benzofuran is similar to that of styrene; the chemistry of indole is considerably different from styrene particularly in its resistance to addition reactions. Isoindole (**5**) has a significant REPE (0·029) but considerably lower than that of indole. On the other hand isobenzofuran (**22**) is predicted to be nonaromatic. Even though isoindole (**5**) is calculated to be aromatic, its potential conversion to a benzene derivative by an addition or Diels–Alder reaction is likely to make it a very reactive compound. Isobenzofuran (**22**) has recently been isolated[15] but its properties appear to be that of a reactive polyene. Isoindole has not been isolated, but its presence as a transient reaction intermediate has been noted.[16]

While azepine (**2**) is predicted to be substantially antiaromatic, oxepin (**19**) is predicted to be only slightly antiaromatic. Both compounds have been observed[17, 18] but are very reactive with oxepin somewhat more stable than azepine in agreement with their REPE's. On the other hand azonine (**3**) has a positive REPE (0·014) which suggests that it should be aromatic while oxonin (**20**) has a zero REPE and therefore it should be polyenic in nature. It is very gratifying to note that recent experimental studies by Anastassiou[19] have led him to charactize these 9-membered heterocycles in exactly this way as azonine is considerably more stable than oxonin. Had more usual oxygen HMO parameters been used, azonine and oxonin would be predicted to be similar and both aromatic. In Fig 2 a comparison of the REPE's of the amine and ether monocycles is shown.

Of the six benzo derivatives of azepine and oxepin (**8–10**, **24–26**) the 2,3- and 4,5-benzo derivatives have a significantly positive REPE. 4,5-Benzazepine (**10**),[20] 4,5-benzoxepin (**24**)[21, 22] and 2,3-benzoxepin (**26**)[23, 24] are known compounds. In contrast to the 2,3- and 4,5-benzo derivatives the 3,4-benzo derivatives of azepine and oxepin (**9** and **25**) have negative REPE. Neither is known. Similarly the dibenzo derivatives of azepine and oxepin (**11–14** and **27–30**) have the highest REPE when there is no substitution at the 3,4 position. Both 2,3,6,7-dibenzazepine (**11**)[25, 26] and 2,3,6,7-dibenzoxepin (**27**)[27–30] are known.

Cycl[3.2.2]azine **15** was prepared some years ago by Boekelheide[31] and is considered to be aromatic. Cycl[3.3.3]azine (**16**) has recently been synthesized[32] but is a reactive compound decomposing rapidly on exposure to air. Again we see the excellent correlation between the experimental properties and REPE as **15** has a very substantial REPE (0·040) whereas **16** has essentially zero REPE (0·001). Note that, cycl[4.4.3]azine (**17**) is predicted to be essentially nonaromatic even though it contains a 14-π periphery.

One question remains. In the evaluation of h_X and k_{C-X} above, we noted that there was no unique set of parameters for either the nitrogen or oxygen systems. In order to determine if resonance energies were dependent upon which set of parameters at the minimum σ were chosen, we also carried out the resonance energy calculation

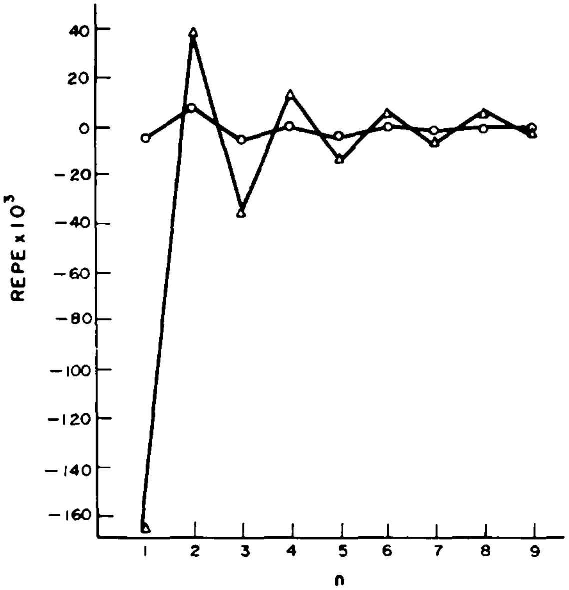

FIG 2. Resonance energy per π electron (REPE) *vs.* number of carbon–carbon double bonds (n) for completely conjugated monocycles containing one heteroatom (1-*H*-azirine, pyrrole, azepine ... =△; oxirene, furan, oxepin ... =○)

(including determination of a new set of π bond energies from the acyclics) with $h_{\dot{N}} = 3{\cdot}00$, $k_{C-\dot{N}} = 1{\cdot}20$, $h_{\dot{O}} = 1{\cdot}0$, $k_{C-\dot{O}} = 0{\cdot}26$. As can be seen in Table 5, there is no significant difference in REPE for the two different sets of parameters.

In conclusion we emphasize that earlier failures of the HMO method when applied to conjugated heterocyclics were not due to the failure of the HMO method itself

TABLE 5. COMPARISON OF REPE OBTAINED WITH DIFFERENT HETEROATOM PARAMETER VALUES

Compound	REPE[a] (β)	REPE[b] (β)
1	0·039	0·041
2	−0·036	−0·038
4	0·047	0·048
5	0·029	0·029
11	0·007	0·007
14	0·036	0·036

[a] $h_{\dot{N}} = 1{\cdot}50$, $k_{C-\dot{N}} = 0{\cdot}90$, $h_{\dot{O}} = 2{\cdot}00$, $k_{C-\dot{O}} = 0{\cdot}34$

[b] $h_N = 3{\cdot}00$, $k_{C-N} = 1{\cdot}20$, $h_O = 1{\cdot}00$, $k_{C-O} = 0{\cdot}26$

but to the incorrect association of delocalization energy with aromaticity and perhaps also to the use of incorrect values of h_X and k_{C-X}. The apparently widely held opinion[12] that the HMO method is very unreliable for heteroatom containing systems is unfounded as far as the ground state properties—heats of atomization and resonance energies—are concerned.

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APPENDIX

We have previously derived[2] the two linear relations connecting the numbers of C—C bond types in conjugated hydrocarbons

$$n(11) + 2n(12) = n(21) + 2n(22) + n(23) \qquad (A1)$$

$$2n(10) + 2n(11) + 2n(12) = 4n(20) + 3n(21) + 2n(22) + 2n(22') + n(23) \qquad \text{(A2)}$$

Our original derivation of (A2) made use of the general empirical formula for conjugated acyclic hydrocarbons. However, we have since derived it for all conjugated hydrocarbons. The derivation uses the number of carbon atoms in a fashion analogous to the use of the number of hydrogen atoms in the derivation of (A1).[2]

Similar linear relations are easily derived for conjugated amines

$$n(23) + 2n(22) + n(21) = 2n(12) + n(11) + n(\dot{N}3) + n(\ddot{N}2) + n(N1) \qquad \text{(A3)}$$

$$\begin{aligned} 2n(23) + 4n(22) + 2n(22') + 4n(21) + 4n(20) &= 4n(12) + 3n(11) + 2n(10) \\ &\quad + 2n(N3) + 2n(N2) + n(\dot{N}2') + 2n(\ddot{N}1) + n(\dot{N}1') + n(\ddot{N}0) \end{aligned} \qquad \text{(A4)}$$

and for conjugated ethers

$$n(23) + 2n(22) + n(21) = 2n(12) + n(11) + n(\ddot{O}1) + n(\ddot{O}2) \qquad \text{(A5)}$$

$$\begin{aligned} 2n(23) + 4n(22) + 2n(22') + 4n(21) + 4n(20) &= 4n(12) + 3n(11) + 2n(10) \\ &\quad + 2n(\ddot{O}2) + 2n(\ddot{O}1) + n(\ddot{O}1') + n(\ddot{O}0) \end{aligned} \qquad \text{(A6)}$$

Note added in proof: The synthesis of isoindole (5) has been reported.* Although it is not stable at room temperature for long periods, *N*-substituted derivatives are known to be quite stable.†

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