

t_R 30.3 min. Anal. Calcd for $C_{31}H_{50}O_6$: C, 71.77; H, 9.71; M - CH_3CO_2H , 458.33959. Found: C, 71.84; H, 9.56; M - CH_3CO_2H , 458.3397.

3 β ,6 ξ -Diacetoxy-10-hydroxy-6 ξ -methoxy-5,6,5,10-disecocholestan-5-oic Acid Lactone (5 \rightarrow 10) (12). The second main fraction eluted from silica gel after **8** β -acetate and **10** derived from **6b** gave 18.4 mg (31.2%) of **12** as an oil: IR (CCl_4) 1755, 1745, 1245 cm^{-1} ; 1H NMR 0.68 (3 H, s, C-18), 1.40 (3 H, s, C-19), 2.06 (6 H, s, CH_3CO), 3.00 (2 H, ABX, $J = 1.7, 9.0, 14.1$ Hz, 4- CH_2), 3.30 (3 H, s, OCH_3), 5.12 (1 H, m, $W_{1/2}$ 10.3 Hz, 3 α -H), 5.87 ppm (1 H, dd, $J = 4.6, 7.4$ Hz, 6 ξ -H); ^{13}C NMR 42.00 (C-4), 55.94 (OCH_3), 66.73 (C-3), 87.06 (C-10), 98.92 (C-6), 169.48 (C-5), 170.79 and 171.84 ppm (CH_3CO); EI mass spectrum, m/z (%) 518 (0.1) (M - CH_3OH) $^+$, 490 (3.0) (M - CH_3CO_2H) $^+$, 458 (1.5) (M - CH_3OH - CH_3CO_2H) $^+$, 430 (M - 2 CH_3CO_2H) $^+$, 398 (4.7) (M - CH_3OH - 2 CH_3CO_2H) $^+$, 263 (51.7), 249 (4.0), 248 (5.5), 247 (5.3), 143 (100), 135 (63.3), 125; R_f 0.13 (system IV), 0.41 (system III); t_R

25.5 min. Anal. Calcd for $C_{32}H_{54}O_7$: M - CH_3CO_2H , 490.3658 00. Found: M - CH_3CO_2H , 490.3652.³⁸

In like manner, 50 mg of **6b** β -acetate yielded 16.2 mg (29.6%) of **12**.

Acknowledgment. The kind assistance of Dr. Jan St. Pyrek, Department of Gastroenterology, University of Texas Health Science Center, Houston, TX, in recording mass spectra is gratefully acknowledged.

Registry No. **1a**, 57-88-5; **1b**, 604-35-3; **3**, 81811-27-0; **5**, 20104-87-4; **5** 3,6-diacetate, 84680-99-9; **6a**, 81811-27-0; **6b**, 84681-00-5; **6b** 3-acetate, 84711-19-3; **6c**, 84681-01-6; **6c** 3-acetate, 84681-02-7; **6d**, 84681-03-8; **7a**, 1250-95-9; **7b**, 4025-59-6; **8**, 84681-04-9; **8** acetate, 84681-05-0; **10**, 84681-06-1; **11**, 84681-07-2; **12**, 84693-96-9.

Topological Charge Stabilization

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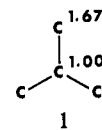
Abstract: The pattern of charge densities in a molecule is determined, at least in part, by the connectivity or the topology of the molecule. For the class of planar alternant hydrocarbons it is well-known that the calculated π -electron charge densities are all equal. But in nonalternant systems or in alternant systems for which the number of π electrons is not equal to the number of atomic orbitals that make up the system, the charge densities are not uniform. Many examples suggest that nature prefers to place atoms of greater electronegativity in those positions where the topology of the structure and the electron-filling level tend to pile up extra charge in the isoelectronic hydrocarbon. Since such heteroatomic systems are preferentially stabilized by molecular topology, the effect can be called the *rule of topological charge stabilization*. That such a rule indeed operates can be seen by comparing trends in calculated and empirical resonance energies, experimental heats of formation, and known relative molecular stabilities and reactivities to the patterns of charge densities calculated for the isoelectronic hydrocarbons. The topological charge stabilization rule has great potential value as a guide to synthetic efforts and as a quick way to rank the stabilities of positional isomers. It is easy to apply. Although more limited in its applicability than are energy quantities, the rule is often more direct because while energy is the property of a molecule as a whole, charge density is a property of an atom in a molecule. From a pattern of charge densities one can see immediately what is favorable or destabilizing about a particular arrangement of atoms. The simplicity and utility of this topological charge stabilization rule have gone largely unappreciated, although the idea was noticed at least as early as 1950 by Longuet-Higgins, Rector, and Platt.

The pattern of charge densities in a molecule is determined, at least in part, by the connectivity or the topology of the molecule. For the class of planar conjugated alternant hydrocarbons one can show quite generally that the simple Hückel π -electron charge densities are the same at all atoms in the molecule. But in nonalternant hydrocarbon systems or in alternant systems for which the number of π electrons is not equal to the number of atomic orbitals in the system, the charge densities are not all equal. These nonuniform charge densities arise solely from the way the atoms are connected and the number of electrons that fill the MO system. In this paper I will show many examples that suggest that nature prefers to place atoms of greater electronegativity in those positions where the topology of the structure tends to pile up extra charge. Since such heteroatomic systems are preferentially stabilized by molecular topology I call this the *rule of topological charge stabilization*.

Charge densities calculated for a heteroatomic molecule depend on the choice of semiempirical parameters, but in the isoelectronic hydrocarbon all Coulomb integrals are uniform and charge densities are determined only by topology and electron-filling level. To emphasize this fact I will refer to the isoelectronic hydrocarbon as the *uniform reference frame*, and all calculated charge densities reported here will be those calculated without assuming any heteroatomic parameters.¹

Examples

Consider the case of the trimethylenemethyl dianion $C(CH_2)_3^{2-}$, in which a central carbon is connected to three peripheral carbons in planar geometry (1). The π -electron system is composed of



six electrons moving through four atomic orbitals of the same type. The calculated Hückel π -electron charge densities are greater on the peripheral atoms (1.67) than on the central atom (1.00). The difference in charge densities can be easily understood from the nodal structure of the occupied molecular orbitals.² Recall that in simple Hückel theory charge density q_r at atom r is given by

$$q_r = \sum_i n_i c_{ir}^2 \quad (1)$$

where c_{ir} is the coefficient of atomic orbital r in the molecular orbital i and n_i is the number of electrons in orbital i . Even for

(1) Most Hückel charge densities mentioned here were taken from "Supplemental Tables of Molecular Orbital Calculations", A. Streitwieser, Jr., and J. I. Brauman, Eds., with a "Dictionary of π -Electron Calculations", C. A. Coulson and A. Streitwieser, Jr., Eds., Pergamon, Press, Oxford, 1965.

(2) B. M. Gimarc, "Molecular Structure and Bonding", Academic Press, New York, 1979, p 171.

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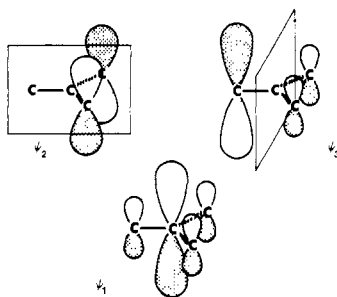


Figure 1. The occupied π MOs of $C(CH_2)_3^{2-}$.

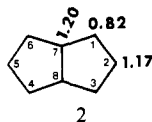
the uniform reference frame (1) the coefficients on the lowest energy molecular orbital ψ_1 (see Figure 1) will be larger than those on the peripheral atoms. But in the higher occupied orbitals, ψ_2 and ψ_3 , nodal surfaces pass through the central atom and prevent the participation of the 2p AO from the central atom, thereby eliminating central atom charge density contributions from ψ_2 and ψ_3 . The net result is a larger charge density on each of the peripheral atoms compared to that of the central atom, as indeed the calculated values demonstrate. Common species that have this particular electron configuration include CO_3^{2-} , NO_3^- , and SO_3 . In each of these examples nature puts the more electronegative atoms in the peripheral positions where topology and electron-filling level tend to distribute more charge density. The uniform reference frame, trimethylenemethyl dianion, is unknown. The topological charge stabilization rule is that those molecules are favored in which constituent atoms are arranged such that their electronegativities match the pattern of charge densities of the uniform reference frame.

The total π -electron energy can be expressed as a sum of atomic charge densities times associated Coulomb integrals plus a sum of bond orders times corresponding resonance energies (eq 2).³

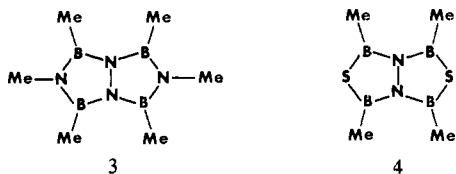
$$E = \sum_r q_r \alpha_r + 2 \sum_{r<s} p_{rs} \beta_{rs} \quad (2)$$

The first sum in this equation can provide a rationale for the topological charge stabilization rule. For alternant hydrocarbons all q_r are unity, all Coulomb integrals α_r are equal, and the first sum becomes $N\alpha$, where N is the number of π -electrons. For nonalternant hydrocarbons or for alternants in which the number of electrons differs from the number of orbitals, the charge densities are no longer uniform but the Coulomb integrals are all still equal and the sum is still $N\alpha$. Now imagine replacing one of the carbons by a heteroatom of greater electronegativity than carbon. One might expect to achieve the maximum energy stabilization by introducing the heteroatom at the site that already has the largest charge density in the isoelectronic hydrocarbon system.

The pentalene frame (2) is composed of two fused five-mem-



bered rings and 8- π electrons. Differences between largest and smallest charge densities are sizable. Attempts to prepare pentalene itself have failed, although 1,3,5-tri-*tert*-butylpentalene has been synthesized.⁴ The inorganic analogues 3 and 4 have been



(3) C. A. Coulson, B. O'Leary, and R. B. Mallion, "Hückel Theory for Organic Chemists", Academic Press, New York, 1978, p 126.

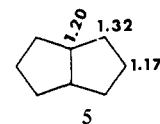
Table I. Calculated Resonance Energies^a of Isomeric Thienothiophenes, Pentalene, and Pentalene Dianion

structure	TRE ^a	RE ^b
	0.031	0.022
	0.031	0.020
	0.026	0.015
	0.004	
	-0.024	-0.018
	0.046	

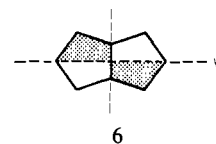
^a Units of β . ^b Reference 9. ^c Reference 10.

made.^{5,6} In these examples the electronegativity patterns match the charge density distributions of 2.

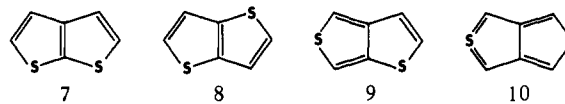
Next, consider the pentalene uniform reference frame but with ten electrons in the eight-orbital system (5). Here the largest



charge densities are at positions 1, 3, 4, and 6, while those at other positions are the same as they were in 2. The change can be easily understood from the nodal pattern of ψ_5 (6), which is occupied



in 5 but vacant in 2. Coefficients at 2, 5, 7, and 8 are 0, so occupation of ψ_5 makes no change in charge densities at these positions. Coefficients at 1, 3, 4, and 6 must be equal, and MO normalization requires that their squares sum to unity. Therefore each square must be 0.25. Since ψ_5 is doubly occupied in 5, the contributions from this MO to charge densities at positions 1, 3, 4, and 6 are $2 \times 0.25 = 0.50$, as seen. Although large differences in charge densities still exist in 5, these differences are smaller than the ones in 2. In fact, the pentalene dianion has been reported.⁷ But consider the series of isomeric, isoelectronic thienothiophenes (7-10). All four isomers have now been pre-



pared, although 10 is known only as the tetraphenyl-substituted derivative.⁸ The selenium analogues of 7-9 have been made, but not that of 10.⁸ When these structures are compared with the charge distribution in 5, it would appear that 7 and 8 should be of comparable stability with 9 and 10 successively less so. Table I lists some calculated resonance energies per electron (in units of β) for these systems.^{9,10} The results are in excellent agreement

(4) K. Hafner and H. U. Süss, *Angew. Chem., Int. Ed. Engl.*, **12**, 576 (1973).

(5) D. Nölle and H. Nöth, *Z. Naturforsch., B*, **27B**, 1425 (1972).

(6) H. Nöth and R. Ullmann, *Chem. Ber.*, **108**, 3125 (1975).

(7) T. J. Katz and M. Rosenberger, *J. Am. Chem. Soc.*, **84**, 865 (1962).

(8) V. P. Litvinov and Ya. L. Gol'dfarb, *Adv. Heterocycl. Chem.* **19**, 123 (1976).

(9) I. Gutman, M. Milun, and N. Trinajstić, *J. Am. Chem. Soc.*, **99**, 1692 (1977).

Table II. Calculated Resonance Energies Per Electron^a for Isomeric Species

normal	TRE ^b	RE ^c	isoconjugate	TRE ^b	RE ^c
indole (14)	0.038	0.047	isoindole (17)	0.032	0.029
benzofuran (15)	0.027	0.036	isobenzofuran (18)	0.011	0.002
thionaphthalene (16)	0.035		isothionaphthalene (19)	0.029	

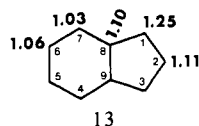
^a Units of β . ^b Reference 9. ^c Reference 10.

with what one would expect from the pattern of charge densities in the uniform reference frame. Still another set of semiempirically calculated resonance energies of the four thienothiophenes show the same order of stabilities, reinforcing these conclusions.¹¹

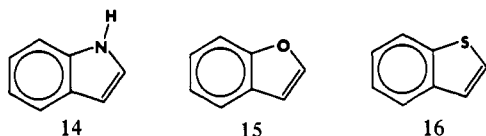
Other known heteroatomic systems follow the density distribution of **5**. For example, the unsubstituted imidazo[4,5-*d*]-imidazole (**11**) has been prepared.¹² A less convincing species is **12**.¹³



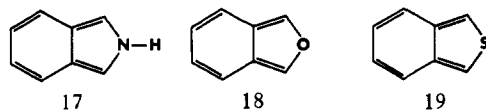
The uniform reference frame of the indenyl anion (**13**, 10 π



electrons over nine orbitals) has largest charge density at positions 1 and 3 of the five-membered ring. The isoelectronic molecules indole (**14**), benzofuran (**15**), and thionaphthalene (**16**) are all

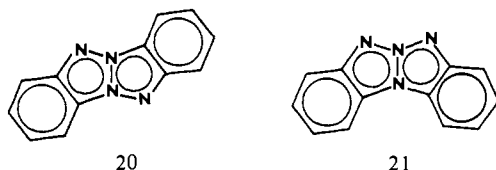


stable compounds that have been known since the 19th century. In each case, the heteroatom is located at one of the positions of maximum charge density in the uniform reference frame **13**. In contrast the isomers **17**, **18**, and **19** with the heteroatom located



at the 2-position are all reactive compounds that have been synthesized only in recent years after a long series of failures. Table II compares resonance energy per electron calculated by two different methods. Again the charge densities of the uniform reference frame correctly order the relative stabilities of isomers and correlate qualitatively with the calculated resonance energies.

The isomeric tetraazapentalenes (**20**, **21**) are known and their



heats of formation (ΔH_f) have been measured, corrected to the

(10) B. A. Hess, Jr., L. J. Schaad, and C. W. Holyoke, Jr., *Tetrahedron*, **28**, 3657 (1972); **31**, 295 (1975).

(11) M. J. S. Dewar and N. Trinajstić, *J. Am. Chem. Soc.*, **92**, 1453 (1970).

(12) J. P. Ferris and F. R. Antonucci, *J. Chem. Soc., Chem. Commun.*, 126 (1972); *J. Am. Chem. Soc.*, **96**, 2010, 2014 (1974).

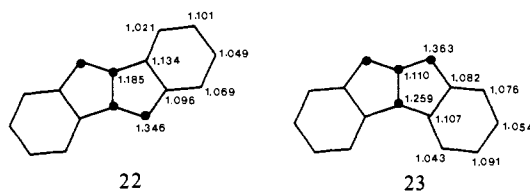
(13) C. L. Kwan, M. Carmack, and J. K. Kochi, *J. Phys. Chem.*, **80**, 1786 (1976).

Table III. Empirical Heats of Formation and Resonance Energies^a of Dibenzotetraazapentalenes^b

compd	ΔH_f	ERE
20	142.8 \pm 1.3	122.9
21	132.1 \pm 1.5	133.6

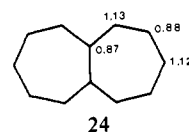
^a Units of kcal/mol. ^b Reference 14.

gas phase, and used to calculate empirical resonance energies.¹⁴ These data, displayed in Table III, show that **21** is more stable than **20**. The charge densities of the corresponding uniform reference frames (**22** and **23**, 18 electrons over 16 orbitals) reveal

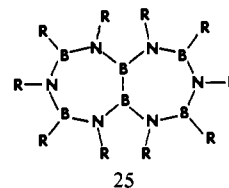


that the four nitrogens in each isomer occupy the sites of largest charge density in the corresponding uniform reference frames. The sums of the charge densities of the four sites are 5.062 (**22**) and 5.095 (**23**). Perhaps we can correlate the more stable tetraazapentalene (**21**) with the uniform reference frame with the larger sum of charge densities (**23**) in the heteroatom positions.

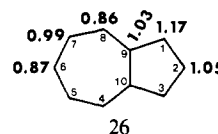
Heptalene (**24**, 12 electrons over 12 orbitals) shows considerable



variation of charge densities, thought not so large as those in pentalene (**2**). Unsubstituted heptalene has only recently been synthesized.¹⁵ The pattern of alternant charge densities in **24** suggests an inorganic analogue such as **25** as a possible synthetic goal.



In azulene (**26**, 10 electrons over 10 orbitals) the charge density



variations are as large as those in heptalene, yet azulene is a well-known molecule, unexpected from the topological charge stabilization rule alone. Azulene is considered to be aromatic, while heptalene is not. The rule of topological charge stabilization cannot differentiate between stabilities of aromatic, nonaromatic, and antiaromatic structures. The largest charge densities are at

(14) Y. T. Chia and H. E. Simmons, *J. Am. Chem. Soc.*, **89**, 2638 (1967).

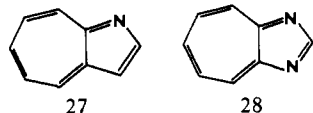
(15) L. A. Paquette, A. R. Browne, and E. Chamot, *Angew. Chem., Int. Ed. Engl.*, **18**, 546 (1979).

Table IV. Resonance Energies per Electron^a of Cycl[3.2.2]- and Cycl[3.3.3]azines

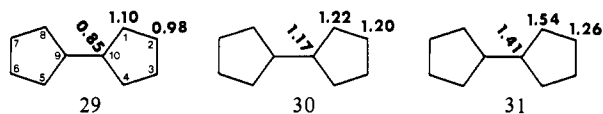
compd	TRE ^b	RE ^c
39	0.033	0.040
43	0.010	0.015

^a Units of β . ^b Reference 9. ^c Reference 10.

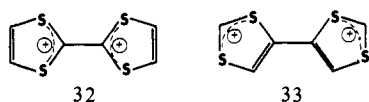
positions 1 and 3 on the five-membered ring. Indeed, both 1-azaazulene (**27**) and 1,3-diazaazulene (**28**) are known.¹⁶



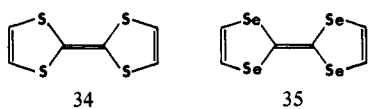
The fuvalene system (**29**) has 10 electrons in 10 orbitals. In



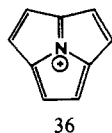
the 12-electron system (**30**) sites 1, 4, 5, and 8 carry very little more charge than do 2, 3, 6, and 7. Locations of sulfurs at both kinds of sites are known in the dicationic systems **32** and **33**. At the



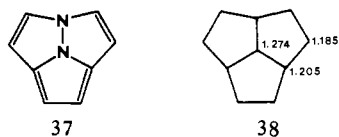
14-electron level (**31**) sites 1, 4, 5, and 8 have considerably higher charge densities than do the other locations. The known compounds have sulfurs (**34**) or seleniums (**35**) at only those positions.



The cycl[2.2.2]azinium cation (**36**) is unknown. Simple Hückel

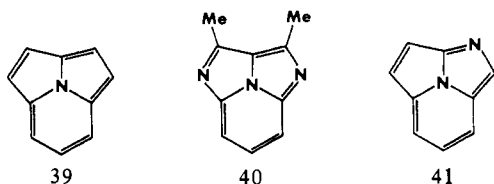


calculations show that this system with 10 electrons in 10 orbitals would have an open-shell electron configuration that would be highly reactive. But compounds with two nitrogens (**37**, 12



electrons in 10 orbitals) are known.¹⁷ The uniform reference frame (**38**) has largest charge densities at just those positions where nitrogens occur in the known compound.

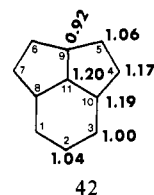
The cycl[3.2.2]azines **39**, **40**, and **41** have been synthesized and studied extensively.¹⁸⁻²⁰ The charge densities of the uniform



(16) T. Nozoe, S. Seto, S. Matsumura, and T. Terasania, *Chem. Ind. (London)*, 1357 (1954); T. Nozoe, T. Mukai and I. Murata, *J. Am. Chem. Soc.*, **76**, 3352 (1954).

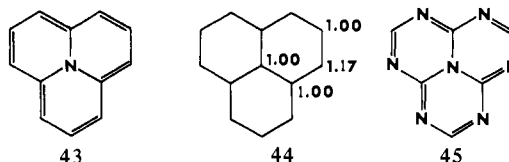
(17) V. Boekelheide and N. A. Fedoruk, *Proc. Natl. Acad. Sci. U.S.A.*, **55**, 1385 (1966).

reference frame (**42**, 12 electrons) show that the most favorable



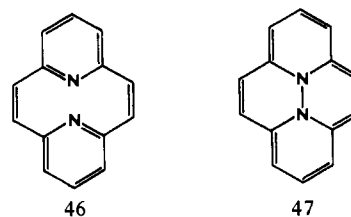
position for a nitrogen would be at the central 11-position. Although the topological charge stabilization rule suggests the location of a nitrogen at positions 8, 9, or 10 might be favorable, a nitrogen in one of those trivalent sites would contribute two electrons to the pi system instead of one.

The cycl[3.3.3]azine (**43**) has been prepared only rather recently after many failures.²¹ Charge densities of the uniform reference

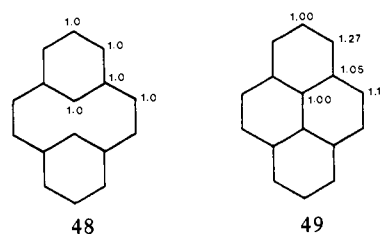


frame are larger at external positions than at the center. A report of the synthesis and structure of tri-*s*-triazine (**45**) has very recently appeared.²² In this molecule six of the seven nitrogens are located at the sites that have the larger charge density in the uniform reference frame (**44**). Table IV compares calculated resonance energies per electron for **39** and **43**. The relative values of resonance energies for these heteroatomic systems are consistent with the patterns of charge densities of the uniform reference frame.

Consider the valence tautomers **46** and **47**. Although **46** has



been synthesized, there is no evidence for tautomerization to **47**.²³ Note that **46** is an alternant system in which the number of π electrons equals the number of orbitals. Although **47** is also alternant, this system holds two additional π electrons. Calculations show that **47** has a larger resonance energy than **46**. Charge density patterns for the corresponding uniform reference frames are shown in **48** (16 electrons) and **49** (18 electrons). All



charge densities in **48** are unity. In **49** the smallest charge densities are at the internal sites with much larger charges at external locations.

Simple Hückel calculations indicate that the neutral triangulene molecule would have an open-shell π -electron configuration. Its dianion (**50**) serves as the uniform reference frame for the known

(18) V. Boekelheide and R. J. Windgassen, Jr., *J. Am. Chem. Soc.*, **80**, 2020 (1958).

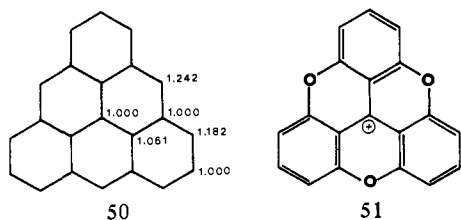
(19) K. Valentin and A. Taurins, *Tetrahedron Lett.*, 3621 (1966).

(20) O. Fuentes and W. W. Paudler, *J. Org. Chem.*, **40**, 1210 (1975).

(21) D. Farguhar and D. Leaver, *J. Chem. Soc. D*, 24 (1969); M. A. Jessep and D. Leaver, *ibid.*, 790 (1970).

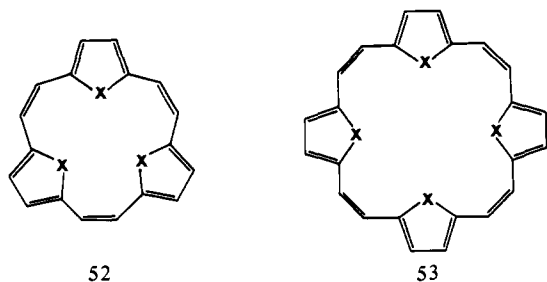
(22) R. S. Hosmane, M. R. Rossman, and N. J. Leonard, *J. Am. Chem. Soc.*, **104**, 5497 (1982).

(23) V. Boekelheide and J. A. Lawson, *J. Chem. Soc. D*, 1558 (1970).

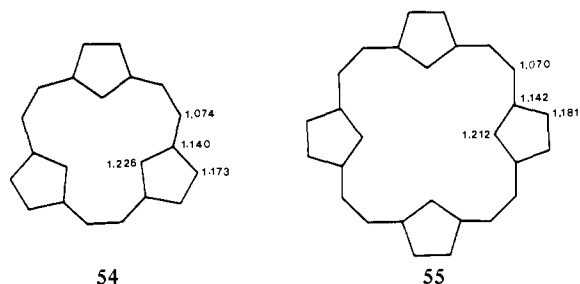


heteroatomic cation (**51**).²⁴ The oxygen atoms in **51** occupy sites that have greatest charge in **50**.

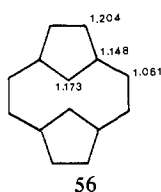
The macrocycles **52** and **53** ($X = O$ or S) are five-membered furan or thiophene rings linked together by ethylene bridges. The



corresponding uniform reference frames **54** (24 electrons) and **55**

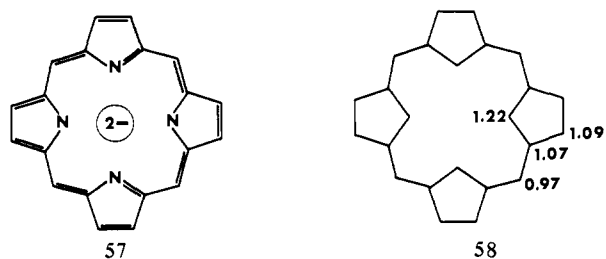


(32 electrons) have largest charge densities on the unique atom of the five-membered rings. The related structure composed of only two five-membered rings held together by ethylene bridges is unknown. In the uniform reference frame (**56**, 16 electrons over



14 orbitals) the largest charge density is not at the unique five-membered ring position.

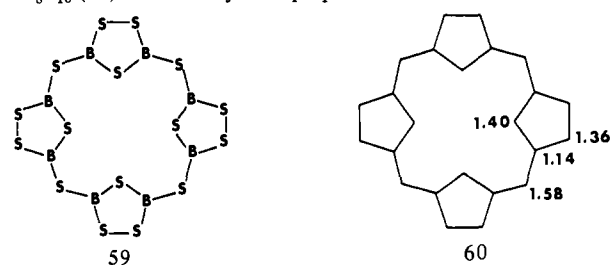
The macrocycle **53** is reminiscent of the porphine dianion (**57**).



The pyrrole nitrogens of porphine are located at those positions that have greatest charge density in the uniform reference frame (**58**, 26 electrons in 24 orbitals). This observation was made over 30 years ago by Longuet-Higgins, Rector, and Platt,²⁵ who introduced the idea of topological charge stabilization.

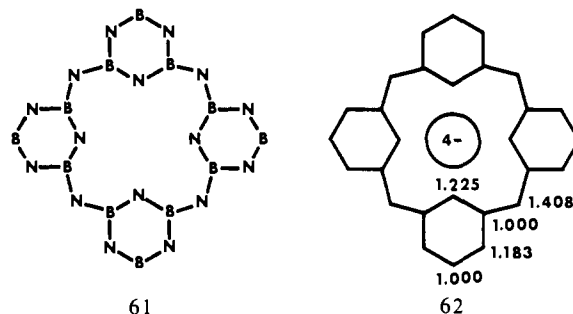
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(25) H. C. Longuet-Higgins, C. W. Rector, and J. R. Platt, *J. Chem. Phys.*, **18**, 1174 (1950).

B_8S_{16} (**59**) has recently been prepared and characterized.²⁶ This



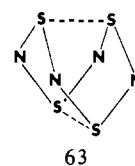
planar macrocycle has six more π electrons than does porphine. In the uniform reference frame (**60**, 32 electrons in 24 orbitals) those positions of largest charge densities correspond to locations of sulfurs in B_8S_{16} , and sites with smallest charge density are those where the borons occur.²⁷

The boron-nitrogen macrocycle (**61**) has been prepared.²⁸

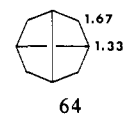


Substituents on ring nitrogens and external borons are methyl groups; hydrogens are on the four nitrogens that link the four six-membered rings. The planarity of the structure is perturbed by the internal methyl substituents. For the uniform reference frame (**62**, 32 electrons in 28 orbitals), those sites with the least charge density correspond to the positions where borons are located in the known macrocycle **61**.

What about three-dimensional systems? No survey has been made of such structures, but in a recent review Burdett²⁹ has reported an interesting result for the cage-shaped S_4N_4 molecule (**63**). From an extended Hückel calculation on an isoelectronic,



isostructural uniform reference frame X_8 , Burdett found that atoms at the two-coordinate sites carried the negative charges, and it would therefore be those positions that should attract the more electronegative atoms. This is indeed the case for the known molecules S_4N_4 , Se_4N_4 , P_4S_4 , As_4S_4 , and As_4Se_4 . The same result shows up at the purely topological level. Since planar cyclic $S_4N_4^{2+}$ has 10- π electrons, consider the uniform reference frame (**64**) with

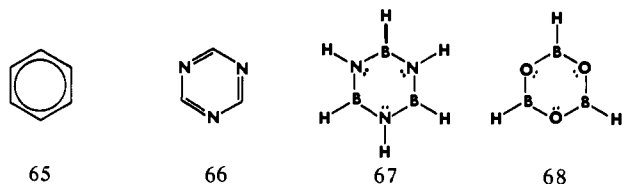


12 electrons in 8 orbitals as the appropriate analogue of S_4N_4 . Simple Hückel calculated charge densities are larger at the two-coordinate sites.

The rule of topological charge stabilization does not imply that heteroatoms cannot be introduced into stable systems for which

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the uniform reference frame has uniform charge densities. Countless examples of such systems exist. For example, all π charge densities in benzene (**65**) are unity. The isoelectronic,



heteroatomic systems **66**, **67**, and **68** are all known. The topological charge stabilization rule suggests a decrease in stability through this series, following the trend of increasing localization of charge on more electronegative atoms.

Conclusion

The topological charge stabilization rule has potential value as a guide for synthetic efforts and as a quick way to rank the

stabilities of positional isomers. It is easy to apply. Although more limited in its applicability, the rule is often more direct than a comparison of energy quantities because while energy is a property of a molecule as a whole, charge density is a property of an atom in a molecule. From the pattern of charge densities one can sense what is right or wrong with the location of an individual atom in a particular structure. Much further work remains to be done to learn the limitations of the rule, including a more quantitative sense of the effect of the magnitude of differences in charge densities. More applications need to be made to systems of low symmetry, to chain and branched structures, and to three-dimensional structures.

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Successive Displacements of Phenoxy by Methoxy Groups in Triphenyl Phosphite Ozonide: Mechanism of the Accelerated Singlet Oxygen Formation with Pyridine and Methanol

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Abstract: The ozonides from triphenyl phosphite, methyl diphenyl phosphite, and phenyl dimethyl phosphite form a series (1–3) which liberate singlet oxygen thermally at rates increasing by an order of magnitude for each substitution of methoxy for phenoxy. Trimethyl phosphite ozonide (**4**) fits in this series, although the very low temperature limit of its stability has not been determined. When triphenyl phosphite ozonide (**1**) is treated with methanol and pyridine in methylene chloride¹¹ and yields singlet oxygen at an accelerated rate, the phenyl methyl phosphates **6** and **7** and trimethyl phosphate (**8**) are produced in a total amount corresponding to the singlet oxygen evolved. The lower the temperature, the greater the predominance of trimethyl phosphate (**8**) in the product. Each of the mixed phosphite ozonides **2** and **3** is in turn subject to accelerated singlet oxygen formation by the action of methanol and pyridine; in each case the phosphates formed contain at least one more methoxy group than the starting ozonide. These facts establish the mechanism of the accelerated singlet oxygen liberation as a successive displacement of phenoxy by methoxy groups on the initial phosphite ozonide, each newly formed aliphatic–aromatic phosphite ozonide decomposing thermally at its own increased rate.

Phosphite ozonides have acquired great mechanistic interest in connection with the thermal generation of singlet oxygen (¹ Δ_g). Triphenyl phosphite ozonide (TPPO, **1**) at its thermal decomposition point³ of about -15°C gives high yields of singlet oxygen,⁴ which can be used preparatively with reactive singlet oxygen acceptors or diagnostically to identify the singlet oxygen component in complex photochemical reaction sequences.⁵ Cyclic triaryl or trialkyl phosphite ozonides having the phosphorus atom at a bridgehead,^{6,7} or the ozonides from triaryl phosphites having a

quinoline nitrogen available for chelation with P,⁸ show enhanced thermal stability, while triethyl phosphite ozonide can be detected only at -95°C or below.⁹

Although a direct reaction has been observed between triphenyl phosphite ozonide and certain oxidizable substrates at temperatures far below the decomposition point of the ozonide,¹⁰ the preparative and diagnostic usefulness of the phosphite ozonides centers about their use for the controlled thermal generation of singlet oxygen at temperatures where this can be made the dominant reaction. For that reason the usefulness of this way of generating singlet oxygen has been greatly increased by the discovery¹¹ of a simple way to generate singlet oxygen from triphenyl phosphite ozonide

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