

The Heteronins

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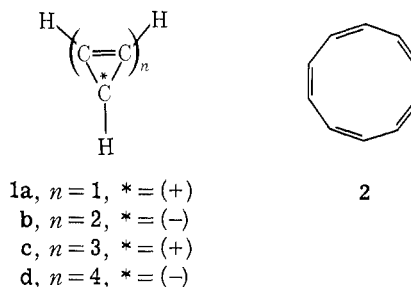
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Ever since the original formulation, some 40 years ago, of Hückel's " $4n + 2$ " theory of aromaticity,¹ experimentalists have engaged in testing its applicability and its limitations. Over the years the theory has withstood the test remarkably well, and it is now generally agreed that Hückel's prediction of an energetically beneficial electron-delocalization effect within planar monocyclic systems containing a total of " $4n + 2$ " π electrons has proven entirely correct. Not surprisingly, much of the crucial experimentation in this area was executed quite recently, for only in recent years have adequate isolation and spectral techniques become available.

Perhaps the most striking success of Hückel's theory has been in the area of electrically charged " π " monocycles where the " $4n + 2$ " frames of **1a**–**1d** have been synthesized and were found to be both stable² and planar.³ Further, the requirement of planarity for " π " stabilization within these systems is obvious, inasmuch as the natural propensity of a carbocyclic system the size of **1d** is to assume a puckered arrangement. Actually, **1d** appears to represent an upper size limit for the skeletal strain introduced by a planar all-cis arrangement to be offset by the aromatic stabilization enjoyed by a planar system; the next larger potentially aromatic all-cis carbomonocycle, cyclodecapentaene (**2**), was in fact generated⁴ but could not be effectively isolated owing to its pronounced thermal lability.

Apostolos G. Anastassiou received his undergraduate training at the American University of Beirut, Lebanon, and his Ph.D. degree from Yale University in 1963. He then joined Du Pont's Central Research Department where his research activities centered chiefly on the chemistry of cyanogen azide and cyanonitrene. Over the past 6 years he has been a member of the chemistry faculty at Syracuse University, where his active group of graduate students is mainly concerned with the synthesis and study of theoretically significant structures and the study of molecular rearrangements and electron-deficient intermediates.



Once the predictive value of Hückel's theory was recognized, application of the $4n + 2$ rule was naturally extended to heterocyclic systems as well. Thus, the long-known stability of the π -excessive heterocycles **3a**, **3b**, and **3c** was reasonably traced to their being iso- π -electronic and skeletally isoatomic with the cyclopentadienyl anion (**1b**). Nonetheless, these heterocycles ought to differ from their carbocyclic analog (**1b**) in terms of overall π delocalization chiefly because of differences in electronegativity between carbon and the respective heteroatoms. Specifically, one would expect π -electron delocalization and thus overall "aromaticity" to increase in the order **3a**, **3b** or **3c**, **1b** since in terms of electronegativity $O > N \sim S > C$. This indeed appears to be the case among the three heterocycles; pyrrole (**3b**) and thiophene (**3c**) are believed to be more

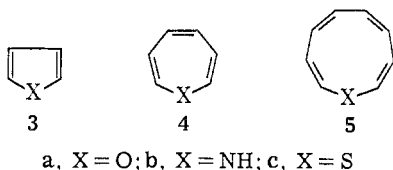
(1) (a) E. Hückel, *Z. Phys.*, **70**, 204 (1931); (b) *ibid.*, **76**, 628 (1932).

(2) The term denotes *thermodynamic* stability.

(3) For a review, see: P. J. Garratt and M. V. Sargent, *Advan. Org. Chem.*, **6**, 1 (1969).

(4) E. E. van Tamelen and T. L. Burkoth, *J. Amer. Chem. Soc.*, **89**, 151 (1967); S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969); E. E. van Tamelen and R. H. Greeley, *ibid.*, 601 (1971). Very recently the $(CH)_{10}$ monocycle was reportedly isolated at sub-zero temperatures in two distinct geometric forms: S. Masamune, K. Hojo, K. Hojo, G. Bigam, and D. L. Rabenstein, *J. Amer. Chem. Soc.*, **93**, 4966 (1971).

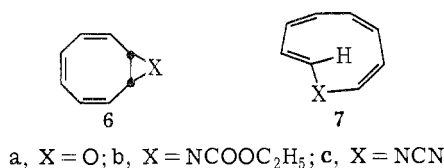
"aromatic" than furan (**3a**).⁵ Furthermore, the general applicability of Hückel's rule to π -excessive heterocycles has received strong support in recent years from work dealing with the $4n$ π systems **4a**, **4b**, and **4c** which led to their classification as strictly nonaromatic.^{6,7}



For all these reasons, we became quite interested in the new family of potential 10π ($4n + 2$; $n = 2$) systems represented by structure **5**, *i.e.*, the heteronins.⁸ Further, because of their ring size, which ought to allow for both planar and puckered arrangements, these substances appeared ideally suited for studying the effect that heteroatom electronegativity has on the development of aromatic properties.

Synthesis

Straightforward application of the Woodward-Hoffmann orbital symmetry rules⁹ to the hypothetical retroelectrocyclization of a 9-heterobicyclo[6.1.0]nona-2,4,6-triene (**6**) into the corresponding heteronin reveals that rupture of the key cross-link ought to proceed conrotatorily in the ground state and disrotatorily in the first excited state.⁸ In other words **6** ought to produce **7** thermally and **5** photochemically.



Indeed we soon discovered that sensitized irradiation of **6b** produces *N*-carbethoxyazonine (**5d**)¹⁰ and that similar exposure of the epoxide of cyclooctatetraene (**6a**) to light leads to oxonin (**5a**);¹¹ it was also shown by other workers that these transformations occur on direct 2537-Å irradiation as well.^{12,13} The two heteronins thus prepared, **5a** and **5d**, proved disappointing, however, inasmuch as (i) they are thermally labile and (ii) they possess the spectral characteristics expected of unexceptional cyclic polyenes. In fact, these two

(5) See, for example, L. A. Paquette, "Modern Heterocyclic Chemistry," W. A. Benjamin, New York, N. Y., 1968, Chapter 4.

(6) For a review, see: L. A. Paquette, in "Nonbenzenoid Aromatics," Vol. I, J. P. Snyder, Ed., Academic Press, 1969, pp 249-310.

(7) In fact, when compared to the known stability of tropilidene (**4**, X = CH₂), the elusiveness of parent azepine and the propensity of its oxygen relative (**4a**) to valence tautomerize suggest that these two heterocycles are antiaromatic.

(8) A. G. Anastassiou, *J. Amer. Chem. Soc.*, **90**, 1527 (1968). See also A. G. Anastassiou, "12th Annual Report on Research," Petroleum Research Fund, Washington, D. C., 1967, p 81.

(9) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970.

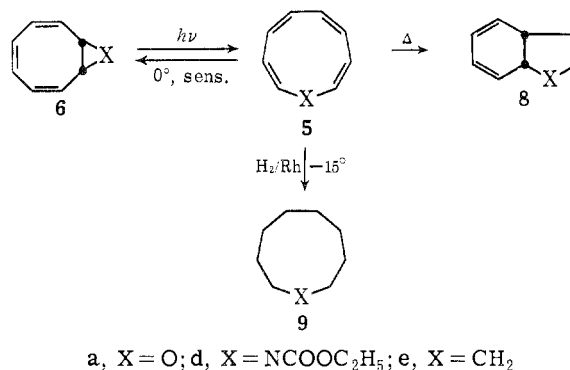
(10) A. G. Anastassiou and J. H. Gebrian, *J. Amer. Chem. Soc.*, **91**, 4011 (1969).

(11) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 903 (1969).

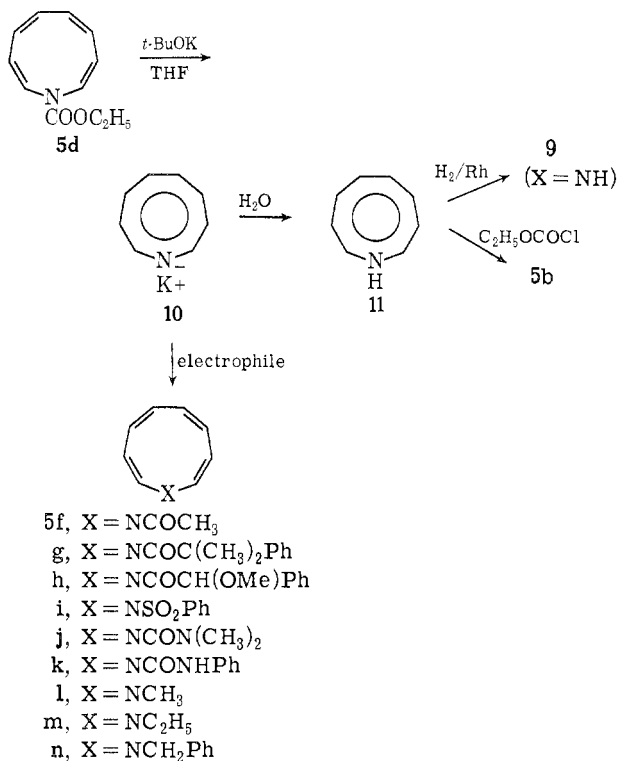
(12) S. Masamune, K. Hojo, and S. Takada, *ibid.*, 1204 (1969).

(13) S. Masamune, S. Takada, and R. S. Seidner, *J. Amer. Chem. Soc.*, **91**, 7769 (1969).

substances proved to be fundamentally similar to *cis*-4-cyclononatetraene (CNT) (**5e**), the classical model of the series which became available at approximately the same time¹⁴⁻¹⁷ (*vide infra*).



Next, our attention turned to the possible conversion of urethane **5d** to parent azonine which incorporates an effectively less electronegative heteroatom than either **5a** or **5d** and must thus resemble a true 10π system such as **1d** more closely than either of its two relatives. The conversion of **5d** into 1*H*-azonine (**11**) was easily accomplished by subzero alcoholysis of the urethane followed by aqueous work-up.¹³ Further, the actual intermediacy of potassium azonide (**10**) in the synthesis of **11** was established through its isolation¹⁹ as a thermally stable, moisture-sensitive white solid.



(14) G. Boche, H. Böhme, and D. Martens, *Angew. Chem.*, **81**, 565 (1969).

(15) P. Radlick and G. Alford, *J. Amer. Chem. Soc.*, **91**, 6529 (1969).

(16) A. G. Anastassiou, V. Orfanos, and J. H. Gebrian, *Tetrahedron Lett.*, 4491 (1969).

(17) S. Masamune, P. M. Baker, and K. Hojo, *Chem. Commun.*, 1203 (1969).

(18) A. G. Anastassiou and J. H. Gebrian, *Tetrahedron Lett.*, 825 (1970).

Table I
Thermal Activation Constants and Uv Absorption Characteristics of the Heteronins

No.	Substance X	Thermal activation data ^a				Uv spectra		
		ΔH^\ddagger , kcal/mole ^{b,c}	ΔS^\ddagger , eu ^c	ΔF^\ddagger (30°), kcal/mole	$t_{1/2}$ (50°)	Solvent	Weak band, nm (ϵ)	Strong band, nm (ϵ)
5a	O	18.2	-13	22.2	3 min	C ₆ H ₁₄	253 sh (4300)	218
5e	CH ₂	19.8 ^d	-10.4 ^d	23.0	10 min	C ₆ H ₁₄	248 sh (2500)	205
5d	NCOOC ₂ H ₅	21.2	-7	23.3	14 min	C ₆ H ₁₄	265 sh (2200)	220 (9000)
5h	NSO ₂ Ph	22.3	-3	23.0	8 min	C ₆ H ₁₄	270 sh (6000)	219
5f	NCOCH ₃	23.4	~0	23.5	13 min	C ₆ H ₁₄	270 sh (4400)	223 (9000)
5j	NCON(CH ₃) ₂	24.8	+3	24.1	32 min	C ₆ H ₁₄	288 (2900)	225 (11,200)
5n	NCH ₂ Ph				~70 min			
5l	NCH ₃				~4 hr	C ₆ H ₁₄	303 (3100)	223 (12,000)
5m	NC ₂ H ₅				~4 hr	C ₆ H ₁₄	306 (3500)	223 (10,000)
11	NH				>100 hr	C ₆ H ₁₄	335 (2700)	252 (20,500)
						Et ₂ O	344 sh (1500)	233 (24,500)
							328 (2200)	
							298 (2930)	
10	N-K ⁺				Stable	THF	330 (4500)	
							339 sh (3900)	?

^a The first six entries were evaluated by monitoring the **5** to **8** rearrangement by nmr spectroscopy in CDCl₃ at three or more different temperatures while the remaining five values were determined by following the rate of decomposition of the azonine by nmr in acetone-*d*₆ at ca. 50°. ^b The maximum error associated with these values is <10%. ^c Some of the values differ slightly from those originally recorded^{20,34} because of certain computational errors. ^d Reported by Boche, *et al.*¹⁴

Finally, **10** was conveniently employed in the preparation of the various N-substituted azonines, **5f** to **5n**.^{20,21}

The Question of Aromaticity in the Heteronins

Once these several heteronins became available, attention was focused on formulating an internally consistent classification in terms of their aromaticity or their lack thereof. They were judged comparatively with respect to three criteria: thermal stability, nmr characteristics, and uv spectral properties.

Thermal Stability. Pertinent information is collected in the first four data columns of Table I. Brief inspection of these findings reveals that differences do indeed exist and further that these are most extreme for the two parents, *i.e.*, where X = O and NH or N-M⁺. For example, whereas oxonin enjoys only fleeting existence at 50° ($t_{1/2}$ ~ 3 min), azonine and the various alkali metal azonides are inert at the same temperature. This pronounced difference in thermal stability is all the more meaningful in light of the thermal response [$t_{1/2}$ (50°) ~ 10 min] of all-cis CNT (**5e**), the classical model of the family, which closely parallels that of oxonin. Hence, in terms of thermal stability oxonin is truly polyenic in character whereas, by comparison, azonine and its salts appear to be aromatic.

A similar though less extreme difference in thermal stability appears to exist among the various N-substituted azonines. The members of the series incorporating electron-withdrawing substituents, *i.e.*, compounds **5d**, **5f**, **5i**, and **5j**, clearly parallel oxonin

and CNT in their thermal behavior [$t_{1/2}$ (50°) 3 min to 32 min] while their *N*-alkyl counterparts, **5l**, **5m**, and **5n**, are decidedly more heat resistant. In fact, the members of this latter group resemble the parent azonine in being exceedingly air sensitive and in tending to decompose into uncharacterizable tars when heated. In contrast, the *N*-substituted azonines that bear substituents which are electron withdrawing behave entirely in the manner of oxonin and CNT when heated, *i.e.*, they undergo clean and irreversible bond relocation to bicyclic compounds of structure **8**. A consistent pattern thus appears to emerge whereby thermal stability within the heteronin family is a sensitive function of heteroatom electronegativity, the two evidently bearing an inverse relationship.

This inverse relationship also emerges clearly, albeit less conspicuously, on comparison of the various thermally unstable members of the family. Now, since all these substances thermolyze to the same type of bicyclic structure (**8**), the ΔH^\ddagger term characterizing this conversion must in each case provide a reasonably sensitive measure of ground-state stability of the heteronin.²² Indeed, simple inspection of the tabulated values reveals a consistent *increase* in ΔH^\ddagger with *decreasing* effective electronegativity of X, the $\Delta\Delta H^\ddagger$ term between the two extremes, where X = O and NCON(CH₃)₂, being a substantial 6 kcal/mole.

Nmr Characteristics. Nmr spectroscopy confirms the inherent dissimilarity between azonine and its thermally unstable relatives and, in addition, provides insight into the origin of this difference. The nmr spectra of the thermally unstable heteronins are exemplified by those of oxonin and *N*-carbethoxy-azonine, whereas the spectrum of azonine is shifted in its entirety to lower fields by ca. 30-50 Hz; *cf.* Table

(19) (a) A. G. Anastassiou and S. W. Eachus, *J. Amer. Chem. Soc.*, **94**, 2537 (1972). (b) Much of the information disclosed in the original manuscript of this Account (submitted Aug 25, 1971) and subsequently published in ref 19a was later reported by others (R. T. Seidner and S. Masamune, *Chem. Commun.*, 149 (1971)) as well.

(20) A. G. Anastassiou, S. W. Eachus, R. P. Cellura, and J. H. Gebrian, *ibid.*, 1133 (1970).

(21) A. G. Anastassiou and S. W. Eachus, unpublished results.

(22) ΔH^\ddagger constitutes a more reliable measure of ground-state stability than does ΔF^\ddagger which also incorporates attendant geometry changes in the form of ΔS^\ddagger .

Table II
Nmr Characteristics of Certain Representative Heteronins^a

No.	Substance X	-Ring proton, τ -		
		α	β	$\gamma + \delta$
5a ^b	O	3.75 (d, $J = 7.0$ Hz)	4.90 (dd, $J = 7.0, 3.2$ Hz)	4.08-4.24 (m)
5d ^b	NCOOC ₂ H ₅	3.63 (d, $J = 9.6$ Hz)	4.68 (d, $J = 9.6$ Hz)	4.13 (m, $W_{1/2} \sim 3$ Hz)
5l ^c	NCH ₃	4.15 (d, $J = 10.5$ Hz)	5.12 (dd, $J = 10.5, 4.3$ Hz)	3.87-4.06 (m)
11 ^c	NH	2.93 (d, $J = 11.0$ Hz)	4.00 (broad d, $J \sim 11.0$ Hz)	3.03-3.30 (m)
10 ^c	N-K ⁺	1.36 (m, $W_{1/2} \sim 3$ Hz)	3.37 (m, $W_{1/2} \sim 5$ Hz)	

^a Spectrum determined in ^b CDCl₃, ^c acetone-*d*₆.

II. This pronounced shift to lower fields effectively places all the resonances displayed by this molecule in the region normally reserved for π -excessive heteroaromatics. 1*H*-Azonine thus appears to sustain ring diamagnetism and may on this basis be classed as aromatic.²³

Interestingly, the nmr characteristics of the *N*-alkylazonines (5l, 5m, and 5n) do not appear to satisfy the nmr criterion for aromaticity; the various resonances appear in a region of the spectrum normally associated with unexceptional polyenes. Nonetheless, the spectra of these substances do differ significantly from those of the polyenic heteronins in that their α protons resonate at an abnormally high field. Now, since the *N*-alkylazonines are quite stable thermally, it is possible that the abnormal shift of their α -proton pairs to high field is due to the shielding influence that ring diamagnetism is known to exert on atoms not contained within the molecular plane. Significantly, the α -hydrogen pair is the pair most likely to be forced out of plane on going from azonine to *N*-alkyl derivatives because of non-bonded interactions with the alkyl groups which ought to be severe in the case of an all-*cis* planar ring the size of a heteronin.²⁵ That the *N*-alkylazonines are indeed less planar than the parent substance is indicated by the uv characteristics of these heteronins, to be discussed shortly.

The nmr characteristics of the azonide ion¹⁹ (Table II) differ substantially from those of all other heteronins in two respects: (i) in the appearance of the α pair of hydrogens at exceedingly low field (τ 1.4 in (CH₃)₂SO-*d*₆) and (ii) in the virtual coincidence of the β , γ , and δ resonances. The first of these phenomena obviously arises from the deshielding influence that the positive gegenion exerts on the most closely located protons, while the coincidence of β , γ , and δ resonances is no doubt due to greater delocalization in the azonide system than in azonine, owing to the greater availability in the former of the nitrogen lone pair for over-all contribution into the " π " system.

Finally, comparison of certain key heteronins in terms of ring anisotropy, as assessed by their "shift"

capacity when employed as nmr solvents,²⁶ established weakly paramagnetic π frames for *cis*⁴-CNT [$S(0^\circ) = -0.05$] and oxonin [$S(0^\circ) = -0.07$], a weakly diamagnetic skeleton for *N*-methylazonine [$S(0^\circ) = +0.34$], and a strongly diamagnetic " π " system for 1*H*-azonine [$S(0^\circ) = +1.35$].²⁷ Significantly, 1*H*-azonine emerges as more effectively aromatic than pyrrole [$S = +0.82$]²⁶ and oxonin as much less so than furan [$S = +0.42$]²⁶ by this criterion. The *S* value of 1*H*-azonine suggests aromaticity appropriate to its 10 π -electron frame as it is quite similar to that [$S = +1.34$]²⁶ for naphthalene.

Uv Spectral Properties. The ultraviolet spectra of the heteronins (Table I) are generally characterized by two distinct absorptions, of which the higher energy one is invariably the more intense. Further, brief inspection of the values collected in Table I reveals that the two types of heteronin differ most markedly in terms of the position of the lower energy band which appears between 240 and 290 nm for the thermally labile heteronins and CNT and above 300 nm for the more stable members. The basis for these differences is revealed by the results of SCF-CI calculations²⁸ which place the lowest energy excited singlets of *planar delocalized* azonine and oxonin at 323 and 346 nm, respectively.²⁹ Comparison of these values with those actually recorded for 11 (335 nm) and 5a (252 nm) reveals a remarkable agreement between theory and experiment in the case of azonine and a sharp disagreement in the case of oxonin. When translated into molecular shape, these findings obviously require that azonine be planar or very nearly so and that oxonin be heavily puckered.

This conclusion is strongly supported by the close similarity of the uv spectrum of azonine to that of *D*_{9h} cyclononatetraenide [250 nm (ϵ 66,300), 320 (6700)]³⁰ and the near identity in this context of oxonin with CNT; cf. Table I.

The notion of a planar azonine receives added

(26) F. A. L. Anet and G. E. Schenck, *J. Amer. Chem. Soc.*, **93**, 556 (1971).

(27) A. G. Anastassiou and H. Yamamoto, *Chem. Commun.*, 286 (1972).

(28) H. E. Simmons, private communication.

(29) Simple Hückel theory also predicts that *planar delocalized* oxonin ought to absorb at lower energies than its nitrogen analog. This difference in the amount of energy required to reach the first excited state may be traced to the greater electronegativity of oxygen compared to nitrogen which operates to reduce the energy of the key LUMO (ψ_6) while leaving the corresponding HFMO (ψ_5) unchanged,⁸ hence, the predicted lowering of ΔE ($\psi_5 \rightarrow \psi_6$) with increasing heteroatom electronegativity.

(30) H. E. Simmons, D. B. Chesnut, and E. A. LaLancette, *J. Amer. Chem. Soc.*, **87**, 982 (1965).

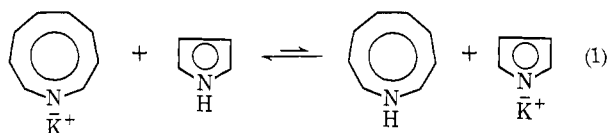
(23) Although temperature invariant in terms of general appearance,¹⁸ the nmr resonances of azonine do move to lower fields with decreasing temperature.²⁴ This shift is most pronounced for the β hydrogens and in strongly hydrogen-bonding solvents such as tetrahydrofuran, methanol, and acetone.

(24) A. G. Anastassiou and H. Yamamoto, unpublished observations.

(25) For a description of the effect of ring size on nonbonded H-H interactions see H. E. Simmons and J. K. Williams, *J. Amer. Chem. Soc.*, **86**, 3222 (1964).

credence from the fact that the position of its low-energy band is strongly solvent dependent, its maximum shifting to higher energies by as much as 36 nm on going from *n*-hexane to such hydrogen bonding media as tetrahydrofuran, ether, methanol, and water. The observed solvent shift is, for reasons discussed earlier, entirely consistent with the expected *decrease* in effective electronegativity of the N-H function on being hydrogen bonded in the manner: $\delta\text{-N}\cdots\text{H}\cdots\text{O}^{\delta+}$.

The uv spectral characteristics of the remaining heteronins (Table I) fall into a well-defined pattern whereby a decrease in the effective electronegativity of the heteroatom is associated with a shift of the lower energy band to higher wavelength, a phenomenon which is best accounted for in terms of progressive molecular "flattening" on going from oxonin to the *N*-alkylazonines. This change in overall geometry is also suggested from a comparison of the ΔS^\ddagger terms controlling the thermal rearrangement of the various heat-sensitive heteronins to **8** which may be construed, for the most part, as a measure of the degree of "unfolding" these systems must undergo in order to attain energetically comparable ($\Delta\Delta F^\ddagger < 2$ kcal/mole) transition states. The values tabulated show that an *increase* in heteroatom electronegativity is consistently paralleled by increasingly negative ΔS^\ddagger terms; the two extreme cases, **5a** and **5j**, differ by 16 eu.



Acidity measurements relating to the N-H function normally present in π -excessive azacyclics provide yet another means of classifying such systems in terms of overall π delocalization. N-H acidity is a sensitive function of overall electron density on nitrogen which, in turn, is heavily controlled by the extent to which the lone pair is delocalized into the π system. Hence, an increase in overall delocalization ought to manifest itself in a corresponding enhancement in N-H acidity. In the present instance the availability of both azonine and its conjugate base allowed for a direct comparison between this system and pyrrole. Thus, appropriate exchange experiments between potassium azonide and pyrrole in $(\text{CH}_3)_2\text{SO}-d_6$ established 1*H*-azonine to be *more* acidic than pyrrole by *ca.* 1.8 p*K*_a units.^{19a} Hence, to the extent that electron delocalization is responsible for the acidity difference, the π system of azonine appears to be more extensively delocalized than that of pyrrole.

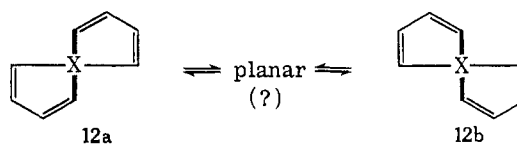
Thus, *all* currently available information points to striking and fundamental differences between the two parent heteronins. Oxonin reveals itself as a heavily distorted (uv, ΔS^\ddagger), thermally labile polyene (nmr), but azonine and its alkali metal salts emerge as planar or very nearly so (uv), thermally stable and decidedly aromatic (nmr, p*K*_a). The sharp dissimilarities between these two substances are best attributed to

differences in electronegativity between the respective heteroatoms. Thus, the strongly electronegative oxygen appears to inhibit delocalization of its lone electron pair into the π system of oxonin, whereas the less demanding nitrogen readily permits this process to occur in azonine. This "electronegativity" effect also emerges, though less dramatically, from the properties of the various *N*-substituted azonines studied to date, where an increase in effective heteroatom electronegativity is invariably associated with a decrease in both thermodynamic stability (ΔH^\ddagger) and overall planarity (ΔS^\ddagger , uv).

With regard to the shape of the nonplanar heteronins, examination of Dreiding molecular models reveals a symmetrical arrangement which, in the extreme, is represented by **12a** or **12b**. The suggested shape is helical and hence it ought to allow for optical isomerism should the interconversion of the two forms, **12a** and **12b**, happen to be slow. A few attempts have been made²¹ to observe these forms by low-temperature nmr spectroscopy in the cases of two especially constructed heteronins, **5g** and **5h**,²¹ but the results have, so far, proven inconclusive, inasmuch as a single sharp methyl resonance was observed in each case throughout a 100° temperature range (+35 to -65°).

Nonetheless, the nmr spectra of these substances as well as those of *N*-acetylazonine (**5f**) and *N*-carbethoxyazonine (**5d**) do display a temperature dependence whereby each portion of the symmetrically disposed doublets due to the α and β protons undergoes further splitting on cooling. A study of **5d** in this connection³¹ revealed that molecular asymmetry sets in at low temperatures mostly because of changes localized within the NCOOC_2H_5 portion of the molecule. Since the coalescence of signals relating to this spectral change set in at lower temperatures in the more polar media, it was concluded,³¹ for obvious electrostatic reasons, that the observed asymmetry originates not so much from hindered rotation about the N-COOC₂H₅ bond as from suppression of nitrogen inversion at the lower temperature. Nevertheless, the same data were employed more recently³² in an attempt to implicate hindered rotation as the cause of the nmr temperature dependence of **5d**.

Perhaps the most useful outcome of these studies is the realization that lack of appropriate models precludes a safe choice between mechanisms which quite possibly are further complicated in the present instance by skeletal effects as well.²¹ It is hoped that X-ray studies currently in progress³³ will clarify the situation.



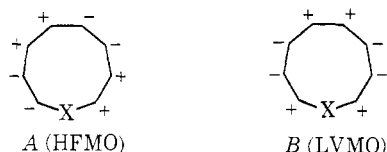
(31) A. G. Anastassiou, R. P. Cellura, and J. H. Gebrian, *Chem. Commun.*, 375 (1970).

(32) K. Hojo and S. Masamune, *J. Amer. Chem. Soc.*, **92**, 6690 (1970).

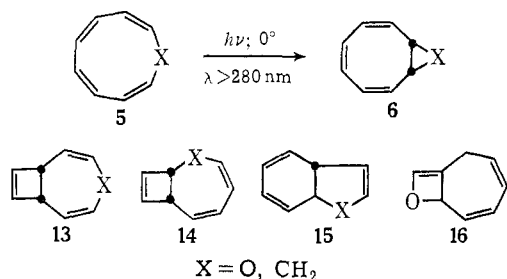
(33) Work conducted in collaboration with Professor I. C. Paul.

Chemical Studies

Thus far, chemical studies relating to the heteronins have been limited to molecular rearrangements and cycloadditions, *i.e.*, types of reactions best understood in terms of orbital symmetry⁹ whereby ground- and excited-state processes are controlled by frontier MO's A and B, respectively.⁸



Molecular Rearrangements. When warmed to ambient temperature, cyclononatetraene and the various thermally labile [$t_{1/2}(50^\circ) < 60$ min] heteronins rearrange cleanly and exclusively to cis-fused bicyclics of structure **8**. Inspection of key MO A reveals that thermal disrotation within an all-cis heteronin to produce **8** is indeed allowed by symmetry. In fact, **8** is the only cis-fused bicycle that can form under the control of A.



Conversely, excited-state rearrangements of the heteronins and CNT must be controlled by the nodal distribution shown in B which allows the monocycle to electrocyclicize disrotatorily to **6**, **13**, and **14** or conrotatorily to **15**. In actual fact, direct Pyrex-filtered illumination of either CNT¹⁶ or oxonin³⁴ with a medium-pressure mercury arc at *ca.* 0° leads cleanly and exclusively to bicyclic structure **6**.³⁵ In turn, irradiation of **6** (X = O, CH₂) with 2537-Å light at -80° generates a product mixture believed to consist of **5** as well as its *cis*,*trans* counterpart **7**.^{13,17} However, the evidence for **7** (X = O, CH₂) is tenuous, inasmuch as its presence was hypothesized solely on the basis of partial thermolytic (0°) conversion of the original photolysate into **15**.^{13,17}

Finally, a brief clarifying note regarding the first recorded photolysis of epoxide **6a**³⁶ is pertinent: two products of this reaction initially formulated as **15** (X = O) and **16** and viewed to form from electronically excited oxonin³⁶ were later revised to **8a**^{13,34,37} and **15**¹³

(34) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 1521 (1969).

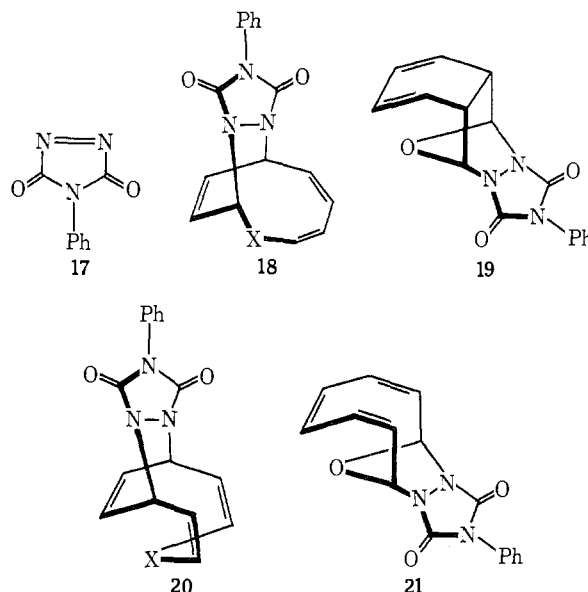
(35) Azonine and its urethane (**5d**) behave likewise when exposed to irradiation, but here the formation of **6** appears not to be exclusive of other, as yet unidentified, products. Interestingly, 9-azabicyclo-[6.1.0]nona-2,4,6-triene (**6**, X = NH) displays no tendency to thermally isomerize to azonine at ambient temperature.²¹

(36) J. M. Holovka, P. D. Gardner, C. B. Strow, M. L. Hill, and T. V. van Auken, *J. Amer. Chem. Soc.*, **90**, 5041 (1968).

(37) J. M. Holovka, R. R. Grabbe, P. D. Gardner, C. B. Strow, M. L. Hill, and T. V. van Auken, *Chem. Commun.*, 1522 (1969).

(X = O), respectively, and shown to materialize from thermally activated monocycle instead.^{11,13,34}

Cycloadditions. The response of all-*cis* CNT, oxonin, and two azonines, **5f** and **5j**, to electrophilic cycloaddition was recently examined by employing 4-phenyl-1,2,4-triazoline-3,5-dione (**17**), a powerful dienophile which readily forms 1:1 cycloadducts with these substances even at -78°. The adducts formed are **18a**,³⁸ **18b**, and **18c**,³⁹ respectively, from CNT and the two azonines examined, and **19** from oxonin.⁴⁰



a, X = CH₂; b, X = NCOCH₃; c, X = NCON(CH₃)₂; d, X = O

The formation of adducts **18a**, **18b**, and **18c** implies a symmetry-allowed [$\pi^2_s + \pi^4_s$] process whereby the nine-membered tetraene supplies the π^4_s segment. Although it is not entirely clear why **17** does not also cycloadd to the remote butadiene segment of these monocycles to yield the symmetrical structure **20**, inspection of Dreiding molecular models reveals that any "flattening" of the molecule away from the extreme helical geometry of **12** will be chiefly reflected along the four-carbon array that does indeed react, the ethylene moieties of the remote butadiene segment remaining very nearly orthogonal to one another during the early stages of this "flattening" process. Moreover, in the cases of the two azonines studied in this connection, the butadiene segment that does actually participate in cycloaddition is directly linked to nitrogen. It should on this basis be more electron rich and thus more reactive as a " π " donor than the alternate C₄ segment of the molecule. The importance of one or both of these factors is inferred from the fact that **5j**, which is believed to possess a frame that is less distorted and more electron rich than that of **5f**, is also the more reactive (*ca.* 18 × at -78°) of the two toward **17**.³⁹

(38) A. G. Anastassiou and R. P. Cellura, *Tetrahedron Lett.*, 911 (1970).

(39) A. G. Anastassiou, R. P. Cellura, J. M. Spence, and S. W. Eachus, *Chem. Commun.*, 325 (1972).

(40) A. G. Anastassiou and R. P. Cellura, *ibid.*, 484 (1970).

Formally, adduct **19** may be viewed to arise either by a direct $[\pi 2_s + \pi 2_s + \pi 2_s]$ process or by way of one or more thermally labile intermediates. The second possibility appears more realistic on the basis of both kinetic evidence⁴⁰ and direct low-temperature detection (nmr) of an intermediate which readily undergoes thermolytic rearrangement to **19** when warmed to *ca.* -50° . A mechanistically plausible formulation for this intermediate is structure **21**,⁴⁰ *i.e.*, the product of $[\pi 2_s + \pi 8_s]$ cycloaddition between **17** and oxonin. More information is needed, however, if the primary cycloadduct is to be securely formulated.

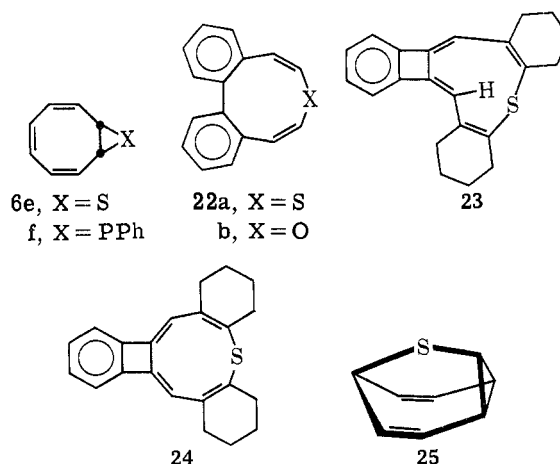
Concluding Remarks

Other Heteronins. Thionin (**5c**) is the most coveted member of the heteronin family yet to be synthesized. The most serious complication encountered in attempts to synthesize **5c** in the manner of **5a** and **5d** resides in the inherent weakness of the C-S link. Specifically, sensitized irradiation of the recently synthesized⁴¹ episulfide of cyclooctatetraene (**6e**) leads not to thionin but to the intriguing valence tautomer **25** instead.⁴² On the other hand, benzannelated derivatives **22**,⁴³ **23**, and **24**⁴⁴ have been prepared recently. With regard to thermodynamic stability, one conjectures that, owing to its *less* electronegative heteroatom, thionin ought to be *more* stable than its first-row relative, oxonin.⁴⁵

Phosponin (**5**; X = PH) represents yet another potentially "aromatic" second-row heteronin. Synthesis of *P*-phenylphosponin from its known valence tautomer (**6f**)⁴⁶ might be subject to the complicating factors noted for thionin.

Boronin (**5**; X = BH) would represent an 8π member of the heteronin family and might thus be expected to exhibit antiaromatic properties if planar. This molecule should therefore exist in a heavily distorted arrangement, perhaps one resembling the helical shape of **12**, which may conceivably provide for some nonbonded stabilization of the electron-deficient center by the ethylene units. Nonetheless, it is doubtful whether a molecule the size of boronin would be sufficiently flexible to benefit from the type of π stabilization expected of a Möbius-like distortion⁴⁷ of its various p

centers. In fact, the cyclononatetraenyl cation (**5**; X = C+H), which is iso- π -electronic with boronin, was recently described⁴⁸ as antiaromatic on the basis of its pronounced thermal sensitivity.



Heteroannulenes with More than Nine Peripheral Atoms. The general procedure employed in the initial construction of the heteronin frame, *i.e.*, photoinduced ring opening, has now been successfully extended⁴⁹ to the synthesis of the larger members of the series of structure **26** and **27**. These substances, while endowed with considerable thermal stability, display spectral characteristics normally associated with nonaromatic polyenes.

In sharp contrast to the general photosynthetic entry into the monocyclic heteroannulenes, intermolecular condensation has been uniformly practiced in the synthesis of annelated and/or bridged variants. Among the rich variety of such compounds now available,⁵⁰⁻⁵⁵ the polyenic substances of structure **28** possibly incorporate the least perturbed " π " frame while the two heavily functionalized counterparts **29**⁵⁴ and **30**⁵⁵ appear to be the only currently known members of this general family of pseudo monocycles which sustain a ring current. As expected, this current is paramagnetic in the case of **29** (16π system) and diamagnetic in the case of **30** (18π system) and no doubt materializes in each case from extensive participation of the lone pair into the π system as a result of conformational factors which force the key frame into an essentially planar geometry.

(41) A. G. Anastassiou and B. Chao, *Chem. Commun.*, 979 (1971).

(42) A. G. Anastassiou and B. Chao, *ibid.*, 277 (1972).

(43) A. P. Bindra, J. A. Elix, P. J. Garratt, and R. H. Mitchell, *J. Amer. Chem. Soc.*, **90**, 7372 (1968); the synthesis of the polyenic annelated oxonin **23b** is also described in this paper.

(44) P. J. Garratt, A. B. Holmes, F. Sondheimer, and K. P. C. Vollhardt, *J. Amer. Chem. Soc.*, **92**, 4492 (1970).

(45) The prediction was recently made⁴⁴ that thionin would be devoid of aromaticity since its annelated relatives, **23** and **24**, are polyenic in character. It is doubtful, however, that this extrapolation is valid inasmuch as even the all-cis frames of **22a** and **24** incorporate features which may be detrimental to any tendency thionin may have toward a delocalized arrangement. For example, it is obvious from simple "resonance" considerations that the two benzene moieties in **22a** would tend to localize the two remote double bonds of the thionin segment. Similarly, the bis(*exo*-methylene)benzocyclobutene portion of **24** will no doubt remain strongly localized if the molecule is to be spared an energetically uncomfortable benzocyclobutadiene-like arrangement.

(46) T. J. Katz, C. R. Nicholson, and C. A. Reilly, *J. Amer. Chem. Soc.*, **88**, 3832 (1966).

(47) (a) E. Heilbronner, *Tetrahedron Lett.*, 1923 (1964); (b) H. E. Zimmerman, *J. Amer. Chem. Soc.*, **88**, 1564 (1966).

(48) A. G. Anastassiou and E. Yakali, *Chem. Commun.*, 92 (1972).

(49) Personal communication from Professor G. Schröder; G. Schröder, G. Plinke, and J. F. M. Oth, *Angew. Chem.*, **84**, 472 (1972); G. Schröder, G. Heil, H. Röttele, and J. F. M. Oth, *ibid.*, **84**, 474 (1972).

(50) Personal communication from Professor E. Vogel; E. Vogel, R. Feldman, H. Düwel, H. D. Cremer, and H. Günther, *Angew. Chem.*, **84**, 207 (1972).

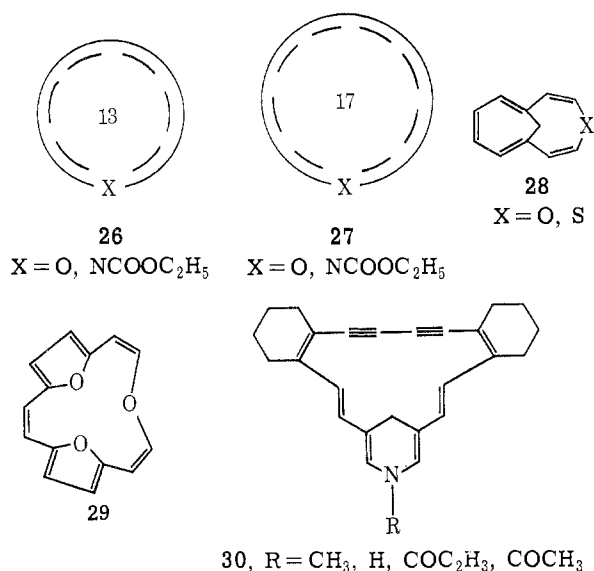
(51) A. B. Holmes and F. Sondheimer, *J. Amer. Chem. Soc.*, **92**, 5284 (1970).

(52) A. B. Holmes and F. Sondheimer, *Chem. Commun.*, 1434 (1971).

(53) T. M. Cresp and M. V. Sargent, *ibid.*, 1458 (1971).

(54) H. Ogawa, M. Kubo, and H. Saikachi, *Tetrahedron Lett.*, 4859 (1971).

(55) P. J. Beeby and F. Sondheimer, *J. Amer. Chem. Soc.*, **94**, 2128 (1972).



Future Outlook

It is appropriate to close with a few predictive remarks regarding such future heteronin chemistry as is likely to deepen insight into both the π -electronic structure and the synthetic utility of the various known members of the family. What comes immediately to mind is an assessment of the behavior of the various heteronins toward electrophilic and perhaps also radical reagents. In theory, such substances should, if sufficiently mild, react by substitution with azonine and the azonides and by overall addition with oxonin and those unstable azonines which may not derive any energetic benefit by regenerating the initial π frame. Nevertheless, the exact position of substitution cannot be predicted with any confidence at present. Although both HMO theory and nmr spectroscopy clearly point to the β position as the carbon site of highest electron density, complexation of the incoming electrophile by the lone pair on nitrogen would undoubtedly activate the α carbon as well.⁵⁶ Preferred

(56) Concerning radical attack, HMO theory predicts the α position of a planar delocalized heteronin to be the carbon site of highest free valency.

attack at the α position is also expected on the basis of π -localization energetics.

Metal complexation is yet another type of process which might prove a useful probe of " π " electronics. Whereas the thermally sensitive members of the series are expected to incorporate such metal carbonyls as iron and molybdenum in the manner of normal polyenes, their "aromatic" counterparts may conceivably behave as 10π units under proper conditions of complexation.⁵⁷

From a synthetic viewpoint, the heteronins presently on hand may be regarded as reasonable intermediates for the construction of larger heteroannulenes. For example, one may visualize the conversion of the azonide system, and perhaps of azonine itself, to azacyclodecapentaene (**31**)⁵⁸ under the Reimer-Tiemann conditions which convert pyrrole to pyridine. Moreover, the similarity of the polyenic heteronins to cyclooctatetraene suggests that treatment of these substances with alkali metals in a proper environment may lead to relatively stable homoaromatic dianions of type **32**. These, besides being interesting in their own right, are obviously ideally structured for ring enlargement as well as 10π metal complexation.



I thank my coworkers whose names are associated with the heteronin project. In particular I wish to single out Drs. Robert P. Cellura and Spencer W. Eachus for their competence and perseverance. I also wish to express my appreciation to Dr. Howard E. Simmons who supplied us with the SCF-CI results and to the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (GP 9404 and GP 26347) for the support that made this work possible.

(57) One might expect the aromatic heteronins to behave in the manner of cyclooctatetraene dianion toward complexation with metals such as uranium and thorium (A. Streitwieser, Jr., and U. Muller-Westerhoff, *J. Amer. Chem. Soc.*, **90**, 7364 (1968)).

(58) This 10π system may be "aromatic" in the geometry of structure **31**, which should be free of the nonbonded H-H repulsions that have long plagued the cyclodecapentaene problem. Indeed, interaction between the nitrogen lone pair (δ^-) and the "inner" hydrogen (δ^+) ought to be stabilizing.

Additions and Corrections

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Page 283. The last reference of footnote 19 should read: "... (R. T. Seidner and S. Masamune, *J. Chem. Soc., Chem. Commun.*, 149 (1972)) as well."