



IUPAC

**2nd International Symposium
on the Chemistry of
Nonbenzenoid Aromatic Compounds
(Lindau/Bodensee 1974)**

Butterworths

Plenary lectures presented at the

SECOND INTERNATIONAL SYMPOSIUM ON
THE CHEMISTRY OF NONBENZENOID
AROMATIC COMPOUNDS

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ORGANIC CHEMISTRY DIVISION

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THE CHEMISTRY OF
NONBENZENOID
AROMATIC COMPOUNDS—II

Plenary lectures presented at the

SECOND INTERNATIONAL SYMPOSIUM ON THE
CHEMISTRY OF NONBENZENOID AROMATIC COMPOUNDS

*held in Lindau/Bodensee, Germany
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SYNTHESIS AND STUDY OF SELECT HETEROCYCLES

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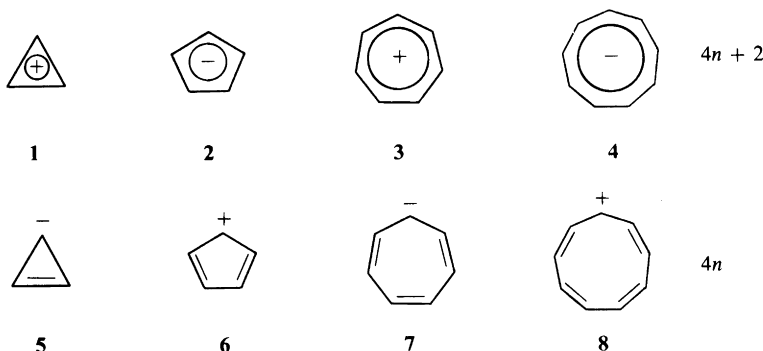
ABSTRACT

The central theme of this review is the synthesis and subsequent study of a variety of π heterocycles with particular emphasis placed on the recognition of key steric and electronic factors controlling the development of heteroaromaticity as well as its less conventional variants, heterohomoaromaticity and heterobicycloaromaticity. The first three sections are devoted to the hetero[9]-annulenes, their benzologues and the hetero[13]annulenes respectively and incorporate information attesting to the validity of Hückel's $4n + 2$ rule in spite of frequent need for rather major, potentially damaging, skeletal readjustments. In each case, there is also unmistakable indication of an inverse relationship between heteroatom electronegativity and the development of 'aromatic' character. Section D contains information establishing the existence of bicycloconjugation in the 9-heterobicyclo[4.2.1]nona-2,4,7-triene system. Lastly, section E deals with the 2-heterobicyclo[3.2.1]octa-3,6-diene skeleton, incorporating data which are indicative of the system's ability to realize a homoconjugated frame.

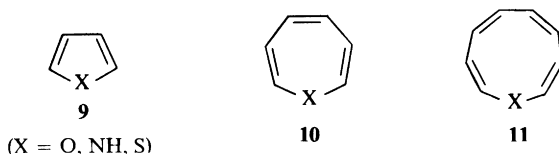
INTRODUCTION

The use of the lone pair as a double bond substitute has long intrigued chemists and certainly holds special fascination for those actively engaged in the study of 'aromaticity'. Undoubtedly, the origins of chemical awareness into the similarity between lone pair and double bond date back to the early work with the cyclopentadienyl anion¹ and certain π -excessive heterocyclic analogues, e.g. pyrrole (Bayer, 1870), furan (Bayer, 1877) and thiophene (Mayer, 1882), and has since been formalized theoretically by E. Hückel in his historic treatise on the theory of aromaticity, published some 40 years ago². And while the literature now abounds with such compounds as are frequently cited in support of Hückel's $4n + 2$ rule of 'aromaticity' none appears to illustrate its strength more convincingly than the electrically charged π monocycles shown in 1-8, each consisting of an acyclic array of conjugated double bonds joined at the termini by a single sp^2 hybrid. What is, doubtlessly, the most striking characteristic of these systems is the strict control imposed on their overall stability and shape by the occupancy of the p orbital associated with the bridging unit. It has thus been amply and in many instances dramatically demonstrated over the years that whereas the $4n + 2$ members of this

family, 1-4, are endowed with stable, fully delocalized, planar frames (e.g. D_{9h} for 4), the $4n$ counterparts, 5-8, are invariably plagued by pronounced instability, each member existing fleetingly at best and strongly resisting charge delocalization.



Extension of the lone pair concept to substances whose odd p ao is located on a heteroatom instead of carbon, offers valuable insight into the electronic properties of π -excessive heterocycles. The long known stability and to some extent aromatic characteristics of the general heterocyclic frame shown in 9 is thus ascribed to its 6π -electron potential, i.e. to its being iso- π -electronic with 2 and, to a less obvious degree, with benzene, while the well documented instability of its π -homologue, i.e. the heteropin frame (10) is best reasoned in terms of its 8π potential and its formal resemblance to the tropyli anion (7). The next member of the family, the nine-membered heteronin (11), is the heterocyclic analogue of the cyclononatetraenyl anion (4) which is now accepted as the largest possible C_nH_n molecule with access to a flat, fully delocalized all-*cis* frame, i.e. one where π stabilization clearly overrides the adverse effect of angle strain (180°) attending this geometry. Evidently then, the heteronin frame with its inherent ability for controlled variation of heteroatom electronegativity and, consequently, of lone pair availability, is ideally suited for the purpose of probing into the delicate balance of opposing structural factors, i.e. π stabilization with its tendency to flatten the system and skeletal strain with its strong demand for a puckered frame. In other words the heteronin family occupies a position of prominence among π -excessive heteromonocycles in that it is endowed with such unique size as is necessary for the study of what is possibly the most fundamental question in the theory of heteroaromaticity, namely to what extent does heteroatom electronegativity influence the development of aromatic properties?



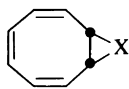
Seeking answers to this and other questions we have, over the past few years, devoted a major portion of our research activities to the synthesis and study of the heteronin system and of choice benzologues, vinylogues and valence tautomers thereof. Now, since much of our work with the heteronins has already been reviewed elsewhere³ we give here only a brief account of the subject chiefly emphasizing findings not previously discussed. For the most part, then, the present account deals with several extensions of our heteronin experiences into other related molecules which have recently attracted our attention. In specific terms, section B deals with the benzoheteronin system, section C describes our recent experience with 13-membered π -excessive molecules and sections D and E address themselves, respectively, to the questions of bicycloconjugation and homoconjugation as applied to heterocyclic systems. Finally, section F incorporates recently acquired information directly relating to the areas of research described under the previous headings. Obviously, our work in the area is far from complete. Nevertheless, we find the information collected thus far to be sufficiently straightforward to permit rational interpretation. We might also note at this point that while the account is primarily devoted to a description of our own discoveries in the area it does incorporate in its main text any directly pertinent *original* information contributed by other groups as well. Finally, in order to properly credit the individuals directly associated with the various areas of research, each heading and/or subheading is accompanied by a list of contributors from within our own research group.

A. THE HETERONINS

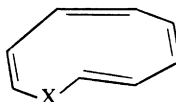
(1) Synthesis

Work by: R. P. Cellura, S. W. Eachus, J. H. Gebrian and V. Orfanos

In our quest for a convenient general entry into the heteronin frame we reached the early decision that classical synthetic methods would be unnecessarily cumbersome if not altogether inadequate. As a result, we resolved to explore the use of symmetry-controlled valence isomerization as a means of realizing our synthetic goal expeditiously and, most important, in the absence of potentially harmful reagents. To this end, we concentrated our attention on the readily available 9-heterobicyclo[6.1.0]nona-2,4,6-triene skeleton **12**⁴ about which we had earlier theorized⁵, on the basis of orbital symmetry⁶, the possibility of conrotatory opening to the mono-*trans* heteronin skeleton **13** under thermal activation and of disrotatory retroelectrocyclization to the all-*cis* frame **11** under the influence of light.



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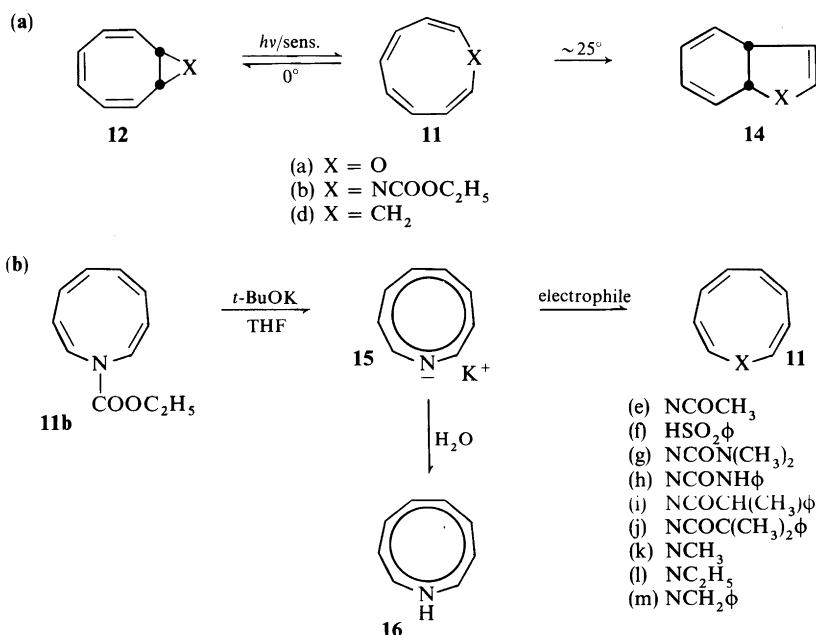


13

- (a) X = O
- (b) X = NCOOC₂H₅
- (c) X = NCN

Now, since we were, for obvious reasons, primarily concerned with the preparation of the all-*cis* variant we pursued the photochemical route⁷ and soon realized the photosynthesis of two heat-sensitive all-*cis* heteronins, *N*-carbethoxazonine (**11b**)⁸ and oxonin (**11a**)⁹ from bicyclic progenitors **12b** and **12a** respectively. Urethane **11b** was then converted to the parent amine (**16**) as well as to a host of *N*-substituted derivatives (**11d–11l**) on successive low-temperature (-78° to -20°) exposure to potassium *t*-butoxide and an appropriate electrophile¹¹. Moreover, the intermediacy of the azoninyl anion **15** in the synthetic sequence was securely established by its isolation in association with a variety of gegenions (Li^+ , Na^+ , K^+ , Rb^+ , Cs^+)¹². For purposes of classification of the various available heteronins it was of course also necessary to prepare the previously unknown classical polyenic model of the series, namely *cis*⁴-1,3,5,7-cyclononatetraene. This was soon realized, both here¹³ and elsewhere^{14–16}, by the low-temperature protonation of its aromatic conjugate base **4**.

Scheme 1



(2) The Question of Aromaticity

Work by: R. P. Cellura, S. W. Eachus, H. Yamamoto and J. H. Gebrian

Once the rather wide selection of heteronins, described in the previous section, became available in our laboratories attention was naturally given to the classification of the various members along the wide spectrum of properties bordered by the aromatic anion **4** on one end and its polyenic

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conjugate acid **11d** on the other. Our efforts along these lines centred on three key criteria: (i) thermal stability, (ii) n.m.r. characteristics and (iii) u.v. spectral properties, which we shall now briefly discuss.

In terms of physical properties the heteronins may be grouped in two basic categories, each differing from the other on several counts. First, we note that there are striking differences in thermal sensitivity. It is immediately seen for example from the thermal stability data collected in *Table 1* that the two parent

Table 1. Thermal activation constants^a

No.	Substance X	$\Delta H^\ddagger$ (kcal/mol) ^b	$\Delta S^\ddagger$ (eu)	$\Delta F^\ddagger(30^\circ)$ (kcal/mol)	$t_{\frac{1}{2}}(50^\circ)$
11a	O	18.2	-13	22.2	3 min
11c	CH ₂	19.8 ^c	-10.4	23.0	10 min
11b	NC ₂ OOC ₂ H ₅	21.2	-7	23.3	14 min
11f	NSO ₂ Ph	22.3	-3	23.0	8 min
11e	NCOCH ₃	23.4	0	23.5	13 min
11g	NCON(CH ₃) ₂	24.8	+3	24.1	32 min
11m	NCH ₂ Ph	—	—	—	~70 min
11k	NCH ₃	—	—	—	~4 h
11l	NC ₂ H ₅	—	—	—	~4 h
16	NH	—	—	—	>100 h
15	NK	—	—	—	stable

^a The first six entries were evaluated by monitoring the conversion of **11** to **14** by n.m.r. 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 n.m.r. in acetone-d₆ at ca. 50°.

^b A maximum error of ten per cent is associated with these values.

substances, oxonin (**11a**; $t_{\frac{1}{2}} \sim 3$ min, at 50°) and azonine, in conjugate acid (**16**; $t_{\frac{1}{2}} > 12000$ min, at 50°) or conjugate base (**15**; stable at 100°) form, show significant variation in thermal stability, with oxonin closely resembling the polyenic model, **11d** ($t_{\frac{1}{2}} \sim 10$ min, at 50°) both in the degree and nature (disrotation to **14**) of its thermal response. Oxonin may thus be safely classed as a polyenic heterocycle while 1H-azonine (**16**) and its conjugate base (**15**) are seen to possess a significantly more stable π system, i.e. one endowed with the type of thermal stability one normally attributes to the presence of aromatic character. Similar, albeit less pronounced, differences are also seen to exist between the two sets of *N*-substituted azonines, with the members bearing electron-withdrawing *N*-appendages (**11b**, **11e–11g**), i.e. groups characterized by positive σ_p^- terms, resembling oxonin in general thermal behaviour (rapid disrotation to the *cis*-fused bicycle **14**) and those carrying electron-donating groups (**11k–11m**) responding in manner reminiscent of parent azonine.

N.m.r. spectroscopy fully confirms the notion that oxonin (*Figure 1a*) and *N*-substituted azonines **11b** (*Figure 1b*), **11e**, **11f** and **11g** are no more than mere polyenes and, most important, offers unambiguous demonstration that 1H-azonine (*Figure 1c*) and its anion (*Figure 1d*) are endowed with significant ring diamagnetism and are thus securely classed as aromatic. Interestingly,

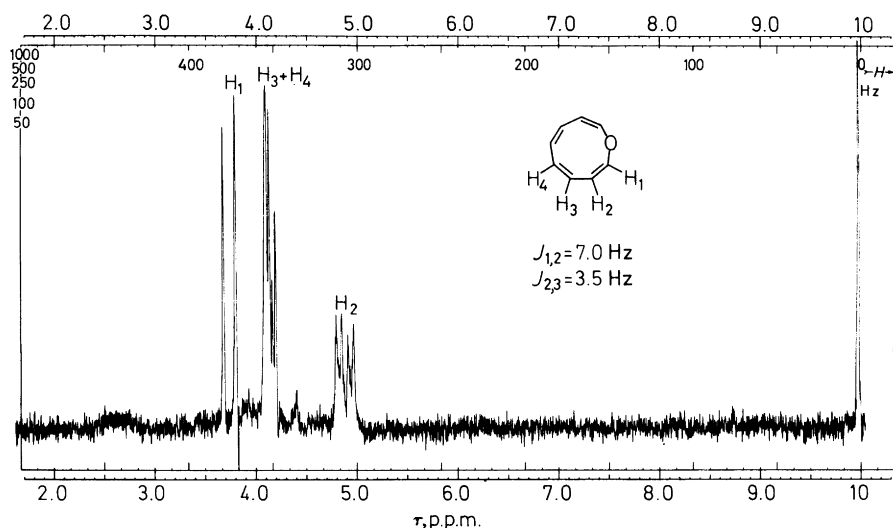
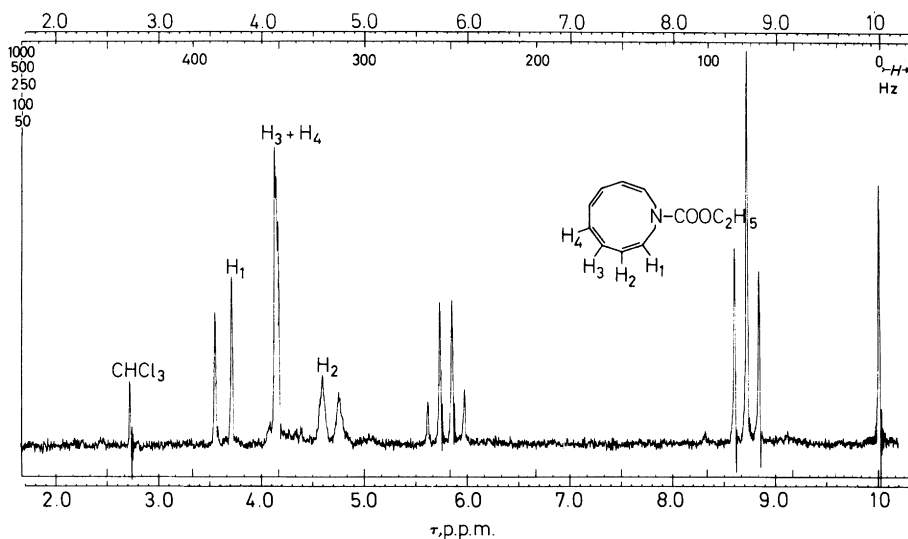


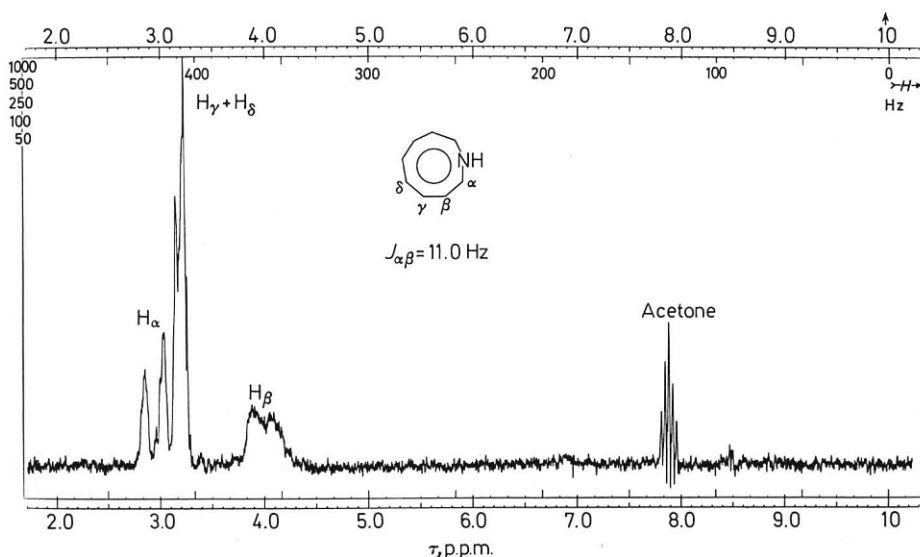
Figure 1. The n.m.r. spectra (60 MHz) of (a) oxonin, **11a** (in CDCl_3).



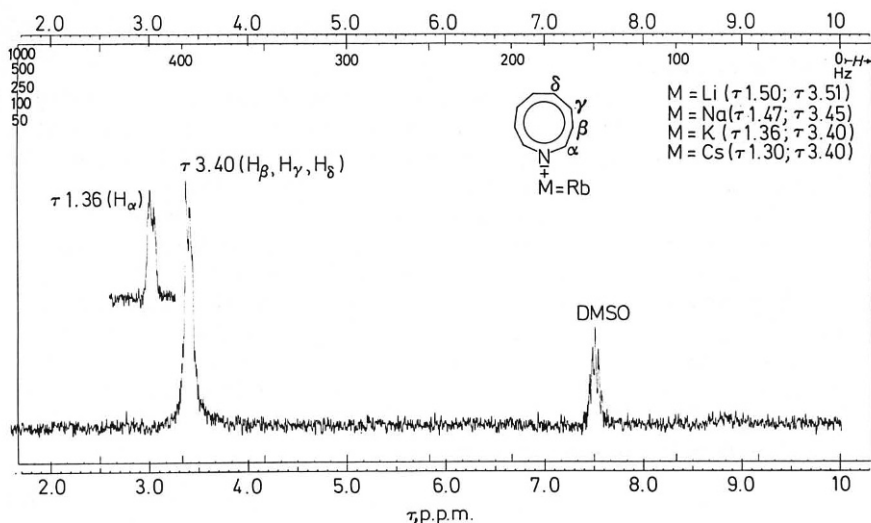
(b) *N*-ethoxycarbonyl azonine, **11b** (in CDCl_3).

the *N*-alkyl counterparts **11k** (Figure 1e), **11l** and **11m** show n.m.r. characteristics (the H_α resonance appearing, in each case, at higher field than the $H_\gamma + H_\delta$ band) indicative of mild ring diamagnetism within a frame which is slightly buckled due to the steric interference between *N*-alkyl and adjacent ring hydrogens (H_α)¹⁷. The differences between the two types of heteronin indicated by the n.m.r. spectra receive added confirmation from more direct

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(c). 1H-azonine, **16** (in acetone- d_6).



(d). Alkali metal azonides, **15** (in DMSO- d_6).

measurement of ring current as given by the n.m.r. solvent shift (S) parameters¹⁸. 1H-azonine (**16**) was thus found¹⁹ to possess an S value which is both large and positive (+1.35), i.e. one indicative of extensive ring diamagnetism, the N -methyl derivative (**11k**) one which is small and positive (+0.34), i.e. one reflective of but mild diamagnetism, and the polyenic counterparts, oxonin (**11a**) and CNT (**11d**) to be associated with negligibly small *negative* S values