Structure and Reactivity of Dipolar Heterocycles

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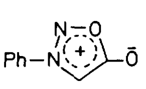
Summary A general theory of the structure and reactivity of those heterocyclic betaines which are isoelectronic with odd alternant hydrocarbon anions is described; two distinct types of dipolar heterocycles are recognised and a rule for predicting novel systems which may be reactive 1,3-dipoles is presented.

FIVE-membered heterocyclic systems which can only be represented by dipolar structures are described as mesoionic and this class of molecule is exemplified by *N*-phenylsydnone (**1**) and dehydrodithizone (**2**).[1] Extensive studies of a wide variety of mesoionic systems have been reported and their participation in 1,3-dipolar cycloaddition reactions is of particular interest.[1] Recently attention has been directed to six-membered heterocycles which also can only be represented by dipolar canonical forms.[2] We now demonstrate that these mesomeric betaines belong to a general class of heterocyclic molecules which are isoelectronic with odd alternant hydrocarbon (AH) anions.

For convenience we describe odd AH anions which contain an inactive even AH segment[3] (linked to an unstarred atom of a smaller odd AH fragment) as reducible odd AH (ROAH) anions (*e.g.* **3**); the even and odd fragments of these species are cross-conjugated.[3] Odd AH anions which do not contain an inactive segment we describe as irreducible odd AH (IOAH) anions (*e.g.* **4**, **7**, **9**, and **11**).

To represent neutral heteroconjugated species which are isoelectronic with IOAH anions by non-polar structures, the lone pair of electrons must be associated with its parent heteroatom and the remaining even AH network represented by double bonds drawn between atoms of opposite parity. This is only possible if the heteroatom contributing the lone pair is one of the m starred atoms of the IOAH skeleton *e.g.* 2-pyridones derived from the benzyl anion (**7**). When the lone pair originates at one of the $m - 1$ unstarred positions the remaining AH network is composed of unequal numbers of atoms of opposite parity (m starred and $m - 2$ unstarred): it follows that only polar canonical forms can be drawn for these species. Pyridinium-3-olates (**5**)[2] and pyridazinium-3-olates (**6**),[4] isoelectronic with the benzyl anion (**7**), are examples of dipolar species of this type. Other examples include azomethine ylides (**8**)[5] derived from the heptatrienyl anion (**9**) and triazaphenalenes (**10**)[6] derived from the perinaphthenyl anion (**11**). This principle can be summarised as a general rule: *neutral heterosystems isoelectronic with IOAH anions cannot be represented by non-polar structures if the lone pair originates at an unstarred position.* The recognition of this general principle provides the opportunity of systematically predicting and preparing new mesomeric betaines which are associated with four and six-membered rings. We now demonstrate that these novel systems may be valuable synthons.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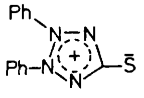
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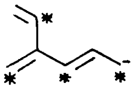
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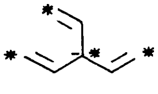
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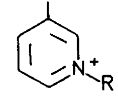
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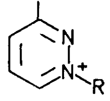
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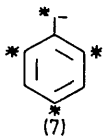
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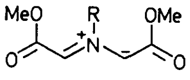
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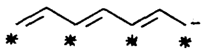
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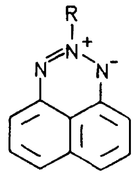
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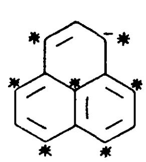
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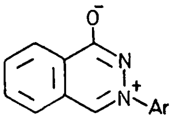
Since the NBMO of an odd AH vanishes at unstarred positions, a heteronucleus introduced at these positions will have little effect on the energy of this orbital. Consequently, mesomeric betaines derived in accord with the above rule will be associated with a HOMO which is high in energy and has the topological features of a NBMO. The orbital symmetry of these mesomeric betaines is favourable for [3 + 2] cycloaddition reactions across starred positions.[7] Since the rate of 1,3-dipolar cycloadditions is governed by HOMO–LUMO interactions[8] these mesomeric betaines (high energy HOMO) might generally be predicted to participate in 1,3-dipolar cycloaddition reactions with electron-deficient dipolarophiles (low energy LUMO). Examples of this type of reactivity are certainly known[2,4,5–7,9] and new heterocyclic 1,3-dipoles may now be designed. Introduction of heteroatoms at starred positions will reduce the orbital energy of the HOMO and this heteratom effect can be expected to diminish 1,3-dipolar reactivity by reducing HOMO–LUMO interactions in the transition state. This effect may well account for the previously unexplained lack of reactivity of the pyridazium-3-olates (**6**) towards 1,3-dipolarophiles.[4]

It also follows generally that the total π-electron energy of mesomeric betaines derived from IOAH anions will be higher than that of isoconjugate covalent isomers. This relatively high π-electron energy may be an important factor governing the tendency of mesomeric betaines to rearrange to thermodynamically more stable isomers. A striking example is the Rowe rearrangement (**12** → **13**).[10]

Neutral heteroconjugated systems isoelectronic with ROAH anions will have properties as described above if the heteroatom donating the lone pair is located in the IOAH fragment; an example is the *N*-phenylpyridinium-3-olate (**5**; R = Ph) which behaves as a reactive 1,3-dipole.[2] Alternatively, if the heteroatom donating the lone pair is located in one of the even AH fragments of the ROAH skeleton a fundamentally different dipolar species is obtained in which the positive and negative fragments are cross-conjugated. Examples of this type are the natural product trigonelline (**14**)[11] and the pyridinium phenolate (**15**; R = NO_2).[12] These cross-conjugated dipoles or inner salts (*e.g.* **14** and **15**) should be recognised as being quite distinct from the conjugated dipoles (**1**, **2**, **5**, **6**, **8**, **10**, and **12**) and these two discrete types of dipolar species, which have not previously been formally recognised, can be expected to be associated with different chemical properties.



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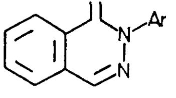

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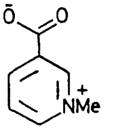

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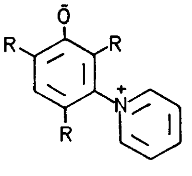

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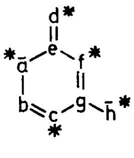

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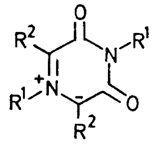

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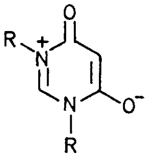

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Dipolar derivatives of dianionic species may also be predicted. The pyrazinium-2,6-diolates (**17**)[13] can be considered as being derived from the dianionic system (**16**) in which an allyl anion fragment ($\bar{a}$–b=c) and a pentadienyl anion fragment (d=e–f=g–$\bar{h}$) are cross-conjugated and, for a discussion of collective properties of the species (**16**), can be considered as independent IOAH fragments. In the molecule (**17**) a lone pair originates at an unstarred position of one of the IOAH components (*i.e.* the allylic fragment) and predictably the resulting mesomeric betaine (**17**) participates in 1,3-dipolar cycloaddition reactions.[13] The subtle difference between these reactive conjugated dipoles (**17**) and the fundamentally different cross-conjugated dipoles (**18**),[14] which are stable crystalline compounds, should now be recognised. Other dipolar systems related to the dianions of non-Kekulé AH[3] (*e.g.* **16**) can now be predicted.

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