

Mesoionic Compounds

An Unconventional Class of Aromatic Heterocycles

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Bharati V Badami was a Professor of Organic Chemistry, Karnatak University, Dharwad. Her research interests are synthesis, reactions and synthetic utility of sydnone. She is currently working on electrochemical and insecticidal/antifungal activities for some of these compounds.

Mesoionic compounds are distinct types of heterocycles which belong to the class of non-benzenoid aromatics. *Sydnone*, the representative mesoionic compound has been extensively studied because of its unusual structure, chemical properties and synthetic utility. Sydnone is used as a versatile synthon in heterocyclic synthesis. This article gives a brief account of the comparative studies of the structural features of mesoionic compounds and other heteroaromatic systems. Some synthetically useful tandem reactions of sydnones are also discussed.

Aromatic Compounds

Benzene has played an important role in the development of the ideas concerning 'aromaticity'. Though benzene and its derivatives were considered to be the best examples of aromatic compounds, a number of heterocyclic systems are known to exhibit properties sufficiently similar to the benzenoid compounds, so that they are also classified as aromatic. There are, in addition, a large number of aromatic compounds structurally unrelated to benzene, and are classified as 'non-benzenoid aromatic compounds'. The criteria to identify the aromatic character of a planar, fully conjugated cyclic system are as follows.

- All the atoms comprising the ring must be sp^2 hybridised with a p-orbital for sideways overlapping.
- The ring must have $(4n+2)\pi$ electrons (Huckel's rule) delocalised over all the atoms of the ring.

The stability caused by this cyclic delocalisation of $(4n+2)\pi$ electrons, makes the ring susceptible to substitution rather than addition by electrophiles. However, this chemical reactivity is

Keywords

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not a deciding property in several cases. Instead, proton NMR property has been used to determine whether a compound is aromatic or not.

Mesoionic compounds are structurally very different from benzenoid compounds, but they fulfill most of the criteria of aromaticity and form a part of a variety of aromatic compounds, which can be classified as follows.

A) Benzenoid Compounds

i) Heterocyclic analogs of benzene in which one or more ring carbons are replaced by heteroatoms (*Figure 1a*).

ii) When the heteroatom is oxygen or sulfur, the ring shows aromatic properties only in its ionic form (*Figure 1b*).

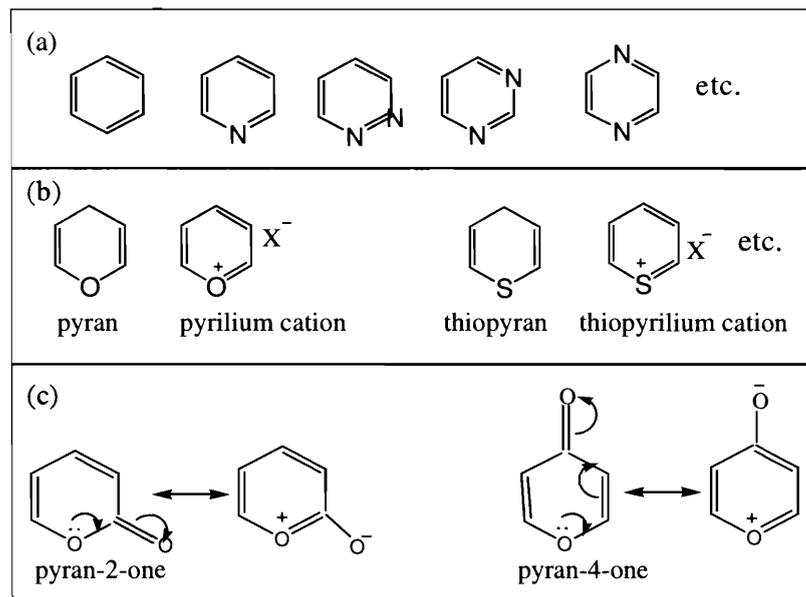
iii) For ring with an exocyclic atom, aromaticity is explained by the dipolar forms (*Figure 1c*).

B) Nonbenzenoid Compounds : Rings other than six-membered.

i. Ionic hydrocarbons (*Figure 2*)

Box 1.

When an external magnetic field is applied to an aromatic compound, the circulation of $(4n+2)\pi$ electrons in a particular direction produces a tiny magnetic field opposing the applied field in the middle of the ring but augmenting the applied field at the periphery where the ring hydrogens are located. The latter is known as 'deshielding effect' and the peripheral hydrogens require lower applied field to resonate compared to the vinylic hydrogens. This has allowed chemists to recognise many structurally variant molecules as aromatic.



Figures 1a-c. Benzene and benzene-like aromatic compounds.

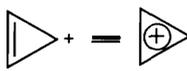
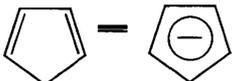
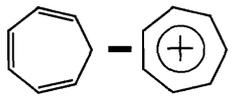
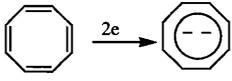
Ring size	$(4n+2)\pi$ electrons	Compounds	Name
Three	2		Cyclopropenium cation
Five	6		Cyclopentadienyl anion.
Seven	6		Cycloheptatrienyl cation. (Tropylium cation)
Eight	10		Cyclooctatetraenyl dianion.

Figure 2. Ionic compounds with $(4n+2)\pi$ electrons.

ii. Even a large ring compound like [18]annulene, (Figure 3) which follows Huckel's rule, is regarded as aromatic due to the presence of ring current inferred from its $^1\text{H-NMR}$ spectrum.

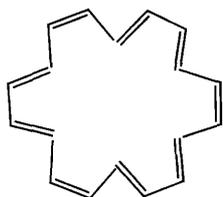


Figure 3. [18]annulene.

C) **Heterocycles:** Aromatic heterocycles comprise 2/3 of organic compounds and the majority of them are 5-membered.

D) **Mesoionic Compounds:** A number of 5-membered ionic heterocycles, with unusual structural features, have been recognised as members of a vast family of nonbenzenoid heterocycles, known as the 'Mesoionic Compounds'. Mesoionic compounds are defined as 'five membered heterocycles which cannot be satisfactorily represented by any one covalent or dipolar structure, but only as hybrids of polar structures and they possess a sextet of electrons'.

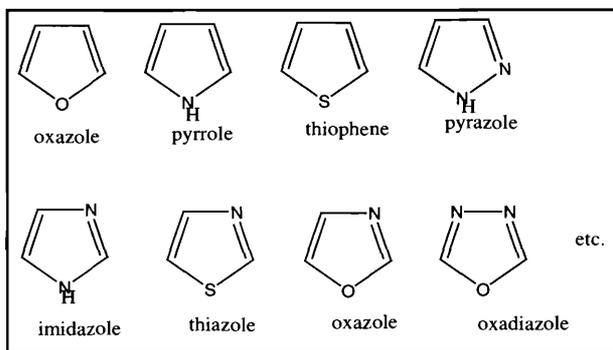
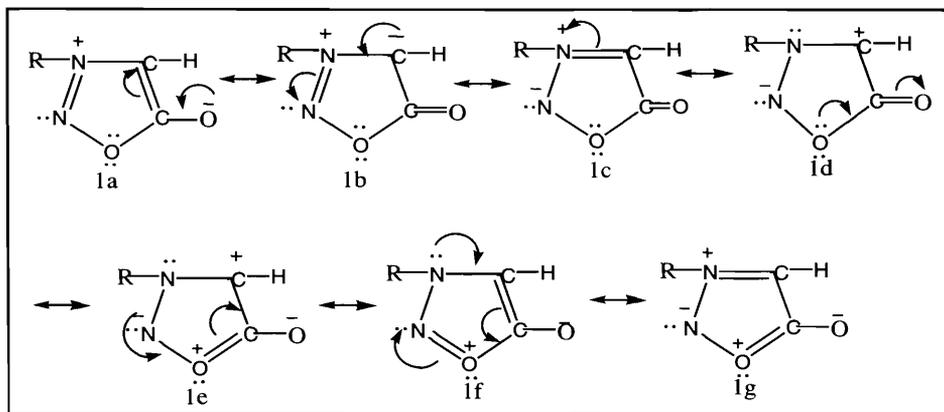


Figure 4. 5-membered heterocycles.



This definition, which makes them a distinct class of heterocycles, is illustrated with the *syndnone* ring – a representative mesoionic compound. As can be seen in the above resonance structures (Figure 5), it is not possible to write a covalent structure for syndnones without separating the positive and negative charges. The term ‘Mesoionic’ (mesomeric+ ionic) was coined by Baker *et al* in 1949 to indicate this peculiar ionic character of such heterocycles.

The aromaticity of the ring is explained by the classical sextet theory. A total of seven 2p_z electrons are contributed by the five atoms of the ring with one 2p_z electron on the exocyclic atom. A sextet of electrons will be obtained when one of the seven 2p_z electrons is paired with the single electron on the exocyclic atom. The ring will be positively charged, balanced by the negative charge on the exocyclic atom.

The circle indicates the delocalisation of 6 electrons which is detected as ring current by ¹H-NMR spectroscopy. This polarization of charges is evidenced by large dipole moments (4–6 D) for the mesoionic rings.

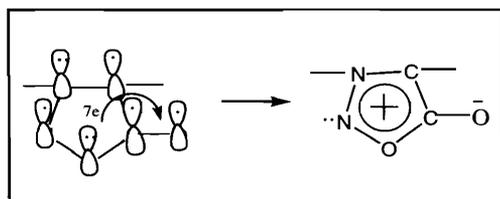


Figure 5. Resonance structures of syndnone.

A large ring compound like [18]-annulene, which follows Huckel's rule, is regarded as aromatic due to the presence of ring current in its ¹H-NMR spectrum.

Figure 6. Overlap of p-orbitals in syndnone ring.

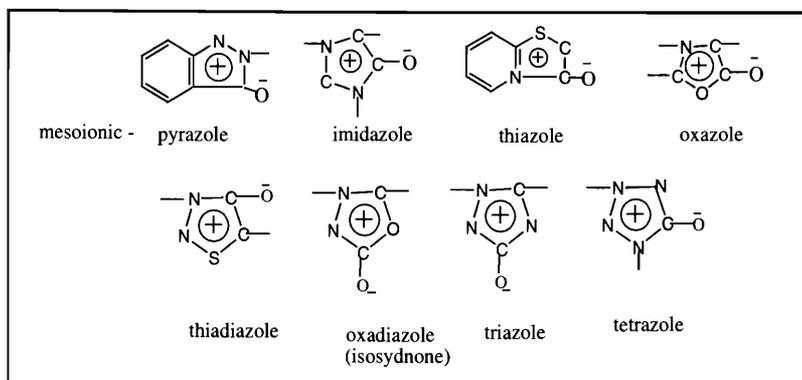


Figure 7. Some mesoionic compounds.

Mesoionic heterocycles contain two or more heteroatoms with an exocyclic heteroatom (oxygen, nitrogen, sulfur). All the 52 mesoionic heterocycles known so far are of *synthetic origin*, though they contain naturally occurring heterocyclic rings viz: pyrazole, imidazole, thiazole, oxazole, thiadiazole, oxadiazole, triazole, tetrazole etc.

Sydnone

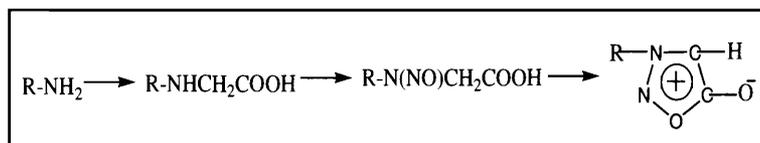
Of all the mesoionic compounds known, Sydnone ring is the most extensively studied because of ease of its synthesis from primary amines and also it is the only mesoionic ring which undergoes a wide variety of chemical reactions of synthetic utility.

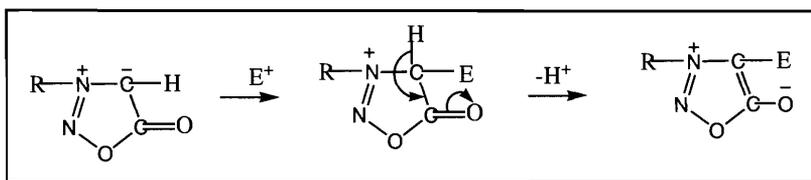
This lactone, which is a 1,2,3-oxadiazole-5-one heterocycle was named as Sydnone in honour of University of Sydney (Sydney + lactone) where it was prepared for the first time by Earl and Mackney in 1935.

Substitution Reaction of Sydnone

The aromatic character and the dipolar nature of sydnone are reflected in its chemical properties. Sydnone unsubstituted at

Scheme 1. Synthetic route to sydnone.





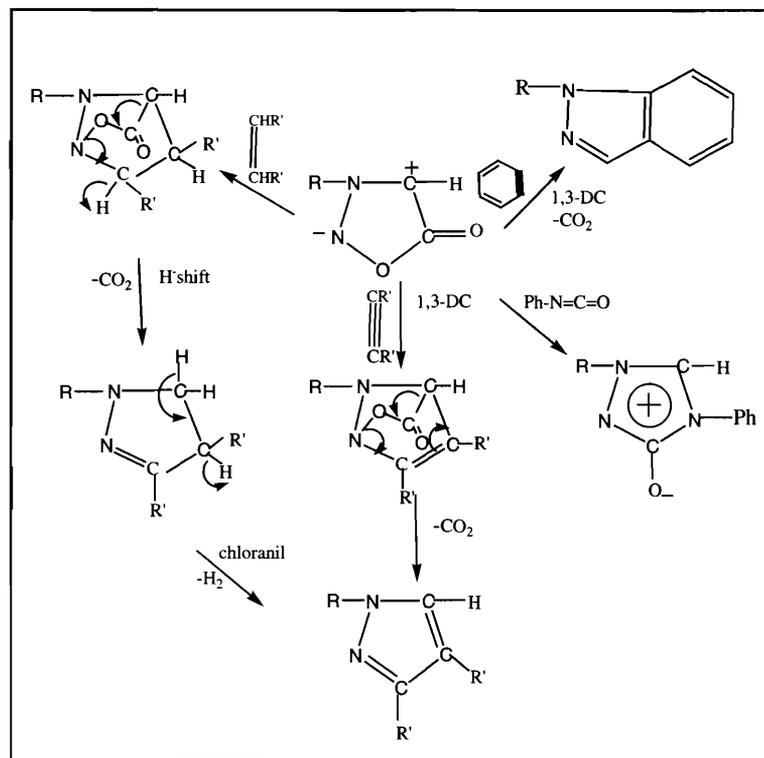
4-position undergoes substitution with a wide variety of electrophiles, with retention of the ring, typical of aromatic substrates.

Scheme 2. Substitution reaction of sydnone.

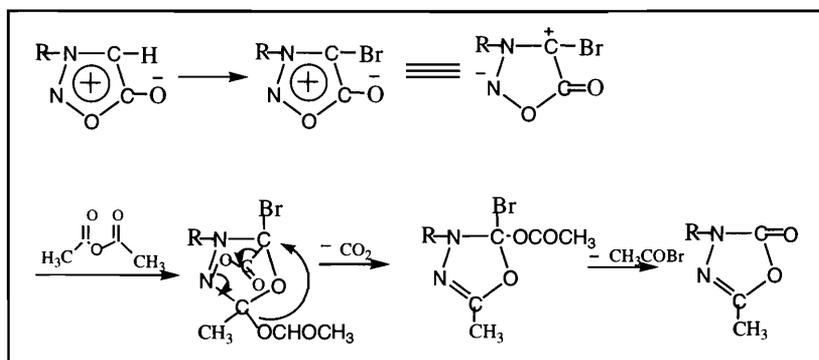
Tandem Reactions of Sydnone

Though aromatic, sydnone ring is readily cleaved by hydrochloric acid, and as dipolarophile undergoes 1,3-dipolar cycloaddition reaction with unsaturated systems. This supports the azomethine imine structure (1d) and suggests that the degree of aromaticity of sydnone ring is about the same order as that of furan. These two reactions are highly useful in heterocyclic synthesis as they involve one-pot ring conversions to the 5-membered 1,2-diazaheterocycles. Sydnone ring transformation

Though aromatic, sydnone ring is readily cleaved by hydrochloric acid, it undergoes 1,3-dipolar cycloaddition reaction with unsaturated systems.



Scheme 3. 1,3-dipolar addition-elimination reactions of sydnone.



Scheme 4. Oxadiazolinone synthesis.

to pyrazoles with acetylenic compounds involves tandem cycloaddition-elimination (CO₂) reaction while this conversion with alkenes in presence of chloranil is a tandem cycloaddition-elimination (CO₂)-oxidation (-H₂) reaction. Pyrazolines are isolated in the absence of chloranil. Similar type of reactions with benzyne and phenylisocyanate give the indazole and mesoionic triazoles respectively.

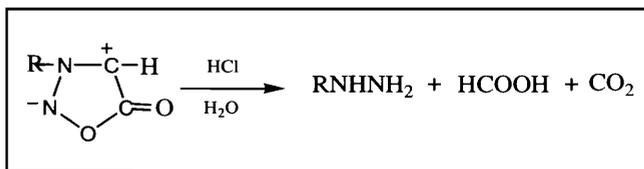
Tandem sydnone ring transformation to 1,3,4-oxadiazolinones in excellent yields (~90 %) with bromine in acetic anhydride involves electrophilic substitution (bromination)-1,3-dipolar cycloaddition (C=O) - elimination (-CO₂ and -CH₃COOH) - nucleophilic attack (CH₃COO⁻) - elimination (-RCOBr) reactions.

Only two lengthy procedures for the synthesis of these compounds (in isomeric forms) from phenylhydrazine in ~ 30 % yield, are reported in the literature. Ring conversion of some sydnone derivatives to the so far unknown 1,3,4-oxadiazolinones have been reported from our laboratory. Cycloaddition is now considered among the best approaches to the five-membered ring heterocycles and probably the most useful reactions.

Hydrazines from Sydnones

Another synthetically useful reaction of sydnone ring is its facile ring cleavage to monosubstituted hydrazines in almost quantitative yields.





Scheme 5. Synthesis of hydrazines.

This method has been recommended by Fugger *et al* as a general and convenient method of converting primary amines to the corresponding hydrazines, especially when the hydrazines are otherwise accessible with difficulty (*Figure 8*).

This acid hydrolysis of 3-arylsydnone has been used in an approach to one-pot synthesis of pyrazoles, indoles and tetrahydrocarbazoles (90 % yield). Sydnone ring can be utilised as masked hydrazine, and it is perhaps the only aromatic heterocycle which can be used as a source of hydrazine.

Publications from our laboratory¹, over the past three decades, have documented the use of sydnone in the synthesis of a wide variety of heterocyclic derivatives, which in turn have been utilized as precursors for many complex molecules.

Advantages of Sydnone as Synthons

The importance and usefulness of these reactions is enhanced by the following facts:

- The sydnone ring, a versatile 1,3-dipolarophile, is obtained with ease from the readily accessible primary amines and inexpensive reagents, using simple reactions.
- Sydnone ring undergoes tandem reactions which are powerful avenues for convergent synthetic routes.

¹The work on sydnone was started in 1968 by Prof G S Puranik, now retired, at the Department of Chemistry, Karnatak University, Dharwad, which has made useful contribution to the area of synthesis and synthetic application of sydnone.

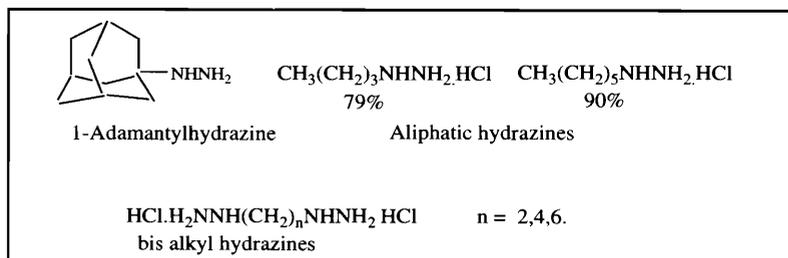
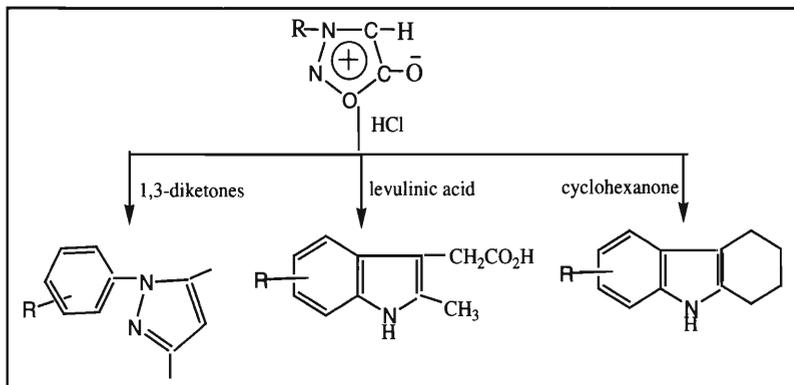


Figure 8. Hydrazines prepared from sydnone.



Scheme 6. Synthesis of heterocycles.



Heterocycles have enormous potential as the most promising molecules as lead structures for the design of new drugs. The synthetic strategies mediated by sydnone as synthons offer alternate efficient routes, for the synthesis of a wide variety of 1,5-diaza five-membered heterocycles from primary amines.

Suggested Reading

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