CHEMISTRY OF SYDNONES
Sydnones are regarded as the representatives of meso-ionic compounds and are the only meso-ionic compounds, which undergo a wide variety of reactions.

**Synthesis**

Inspite of extensive studies of sydnone ring, only one preparative route is available. The method involves treating N-substituted-N-nitroso-α-amino carboxylic acid with acetic anhydride. The reaction is slow at room temperature but proceeds rapidly when heated (Equation 1).\(^8\)

\[
\begin{align*}
R' & \quad \text{(CH}_3\text{CO})_2\text{O} \\
\text{R-N-CH-COOH} & \quad \rightarrow \\
\text{N=O} & \quad \text{R-N}^+ \text{O} \\
\end{align*}
\]

Where \( R = \text{alkyl, aryl, aryl alkyl or heteroaryl} \) and \( R' = \text{H, aryl, alkyl or aryl alkyl} \).

Baker *et al.*\(^{1b}\) reported the probable mechanism of cyclodehydration of N-nitrosoglycine to sydnone as follows (Scheme 1).

\[
\begin{align*}
\text{R} & \quad \text{N=O} \\
\text{R-N-CH-C-OH} & \quad \rightarrow \\
\text{N=O} & \quad \text{R-N}^+ \text{O} \\
\text{N=O} & \quad \text{N=O} \\
\end{align*}
\]

**Scheme 1**
Putter and co-workers\textsuperscript{9} reported the use of various other reagents to bring about cyclisation, which include acid chlorides, phosgene, sulfonylchloride, chloroformates, phosphorous oxychloride and chloroacetyl chloride in the presence of a base. Carbodiimides and phenyl cyanate are also effective for this purpose. A novel method for cyclodehydration involving ultrasonic method has been reported.\textsuperscript{10} The use of N,N-dimethylchlorosulfatemethiaminium chloride as cyclodehydrating agent has been recently reported\textsuperscript{11a}.

An interesting method of preparation of sydnone, which consists of heating N-nitroso sydnone imine in organic solvents, has been reported. This is the only known method permitting the preparation of sydnones from starting materials other than N-nitroso glycines\textsuperscript{11b}.

\begin{center}
\begin{tikzpicture}
\begin{scope}
\node[draw] (a) at (0,0) {\textbf{Nomenclature}};
\end{scope}
\begin{scope}
\node[draw] (a) at (0,0) {Several methods of naming sydnones are currently in use, for instance N-phenyl sydnone (7a) is systematically named as:\textsuperscript{12}};
\end{scope}
\end{tikzpicture}
\end{center}

\textbf{Nomenclature}

Several methods of naming sydnones are currently in use, for instance N-phenyl sydnone (7a) is systematically named as:

\begin{enumerate}
\item \textit{Meso-ionic 1,2,3-oxadiazolium-5-olate,\textsuperscript{12} the ring is referred to as a cation and the exocyclic oxygen as an anion}(7a)
\end{enumerate}
b) Meso-ionic 1,2,3-oxadiazole-5-one,\textsuperscript{12} the double bond character of the exocyclic bond is emphasized.

c) $\Psi$-keto-3-phenyl-3,5-dihydro-1-oxo-2,3-diazole\textsuperscript{7a} based on unknown 1,2,3-oxadiazole (7b). The symbol $\Psi$ refers to the delocalisation of $\pi$-electrons in a meso-ionic system.

d) Anhydro-5-hydroxy-3-phenyl-1-oxa-2,3-diazolium hydroxide\textsuperscript{13} based on betaine structure (7c) which is one of the important contributing structures to the resonance hybrid.

**Aromaticity of sydnones**

The aromaticity of the sydnones can be explained based on the classical sextet theory. There are a total of seven $2p_z$ electrons supplied by the atoms, which make up the five-membered ring and one more on exocyclic atom. A sextet of electrons can be obtained if one of the seven $2p_z$ electrons is paired with the single electron on the oxygen atom. The ring becomes aromatic and positively charged.

\[
\begin{align*}
\text{RR-N=O} & \quad \text{R-N}^+\text{O}^- \\
\end{align*}
\]

The situation is very much similar to tropone. Thus sydnones may be regarded as five-membered heterocyclic analogs of tropone (Equation 2). However, tropone is not a mesoionic compound.

\[
\text{Equation 2}
\]
Physical properties

Ultraviolet spectrum

Alkyl sydnones in general show an absorption maximum around 290nm which is an evidence for aromatic character of the ring.\textsuperscript{7a} Aryl sydnones show a bathochromic shift due to interannular conjugation.\textsuperscript{14}

Infrared spectrum

Sydnones show a strong band in the range 1730-1830cm\textsuperscript{-1} due to ring carbonyl stretching. Usually the carbonyl absorption appears as a doublet with 2240cm\textsuperscript{-1} differences presumably due to Fermi resonance.\textsuperscript{15} Sydnones unsubstituted at position-4 show a medium intensity absorption band around 3150cm\textsuperscript{-1}. This is due to CH stretching frequency.\textsuperscript{16} The bands around 1090cm\textsuperscript{-1} and in the region 861-848cm\textsuperscript{-1} have been assigned to C-O and N-O stretching frequencies respectively.

\textsuperscript{1}H-Nuclear Magnetic Resonance Spectrum

When compared to ring protons of various aromatic five membered heterocycles, the \textsuperscript{1}H-NMR signal of the sydnone ring proton at position-4 appears at relatively high magnetic field at $\delta$ 6.8 ppm.\textsuperscript{17} This is explained by the contributing structure 2f which would place negative charge on the C-4 with consequent shielding of the attached proton.

Turnbull et. al. showed that the deshielding of the sydnone proton takes place if electron-donating group is present on position-3 of phenyl ring. Due to deshielding effect of aromatic ring combined with an electronegative effect of the nitrogen atom of the sydnone ring, the phenyl ring protons appear at $\delta$ 7.7 ppm.
The chemical shift of C-4 in 4-substituted sydnones at $\delta$ 96.77 ppm. is considerably at a higher field than observed for the ring carbon of unsubstituted heterocycles, but is in consistent with the anticipated shielding effect represented by the following structure 2a.

Substitution at C-4 causes a downfield shift indicating the deshielding effect by atoms other than hydrogen (Table 1).

**Table 1:** Substituent effect on $\delta$ values of C-4 and C-5 carbon atoms.

<table>
<thead>
<tr>
<th>$R$</th>
<th>$R'$</th>
<th>C-4 $\delta$ ppm</th>
<th>C-5 $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$</td>
<td>H</td>
<td>96.77</td>
<td>169.2</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>H</td>
<td>94.23</td>
<td>169.7</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>CH$_3$</td>
<td>104.08</td>
<td>168.7</td>
</tr>
<tr>
<td>C$_6$H$_5$CH$_2$</td>
<td>H</td>
<td>94.93</td>
<td>169.3</td>
</tr>
</tbody>
</table>
The chemical shift of C-5 at δ 169.2 ppm, though at higher field than in normal ketones, is similar to that observed for carbonyl carbons of lactones, amides and imides.\(^{18}\)

**Mass Spectrum**

Mass spectra of various alkyl and aryl sydnones have been studied\(^ {19}\). The spectrum for 3-phenylsydnone had intense ions that correspond to M\(^+\), (M-NO)\(^+\) and (M-NO-CO)\(^+\) and the fragmentation pattern is suggested as follows\(^ {17}\).

This initial fragmentation is typical for 4-substituted sydnones also\(^ {46}\).

\[
\begin{align*}
\text{C}_6\text{H}_5-\text{N}=\text{H} & \quad \rightarrow \quad \text{C}_6\text{H}_5-\text{C}=\text{H} \\
\text{C}_6\text{H}_5-\text{NO} & \quad \rightarrow \quad \text{C}_6\text{H}_5-\text{CO}
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \rightarrow \quad \text{C}_6\text{H}_5-\text{HCN}
\end{align*}
\]

**X-Ray Diffraction**

A detailed structural analysis of 3-(p-bromophenyl) sydnone has been reported\(^ {20}\). The phenyl and the sydnone rings, which are individually planar, are twisted at dihedral angle at 27°. It is noteworthy that the length of the exocyclic C-O bond is close to that of a normal carbonyl group.
Chemical properties

Sydnones can be chemically regarded as aromatic because they undergo electrophilic substitution reactions, which are typical of aromatic substances. Though sydnones are aromatic, they also undergo 1,3-dipolar addition reactions and are readily cleaved by acids and alkali, suggesting that the degree of aromaticity of the sydnone ring is about the same as that of the furan ring. These properties can be attributed to their dipolar nature.

The aromatic nature of sydnones can be explained not only by physical studies but also by its chemical properties. Sydnones unsubstituted at position-4 undergo electrophilic substitution reaction with retention of ring, viz., chlorination, bromination, nitration, sulfonation, formylation, acetylation, and chlorosulphonation. The hydrogen atom at the position-4 of 3-phenylsydnone is acidic enough to be replaced by metal. It reacts with alkyl or aryl magnesium bromide, butyl lithium and sodamide, to give corresponding metallic derivatives. Various 4-substituted derivatives of sydnones can be prepared by these metallic derivatives.

1,3-Dipolar cycloaddition reactions

One of the interesting and novel reaction of sydnones, which has received detailed attention, is the 1,3-dipolar-cycloaddition reaction with variety of dipolarophiles to give various heterocycles viz., pyrazoles, pyrazolines and other meso-ionic compounds. This is an addition elimination reaction accompanied by loss of carbon dioxide (Scheme 1). Badami et. al. have reported the utility of this reaction.
from this laboratory by converting 4-halogenosydnones into 5-halogenopyrazoles. It may be mentioned that halogenation of pyrazoles at C-5 is not a facile process.

The formation of dibenzoyl pyrazole by 1,3-dipolar addition of sydnones has been reported from this laboratory. With phenyl isocyanate, 3-phenylsydnone undergoes 1,3-dipolar reaction to afford meso-ionic 1,2,3-triazole derivative. Benzyne also reacts with 3-phenylsydnone in a 1,3-dipolar fashion to form 2-phenylindazole. The addition of acetic anhydride to 4-bromo-3-phenylsydnone to yield the oxadiazole during the bromination of 3-phenylsydnone was explained in terms of 1,3-dipolar cycloaddition reaction by Stansfield.
Badami et al.\textsuperscript{32c} extended this reaction to some more aryl sydnones to obtain the corresponding 3-aryl-5-methyl-2-oxo-$\Delta^1$-1,3,4-oxadiazolines (equation 6). All these reactions demonstrate the use of sydnones as synthons for a variety of heterocycles.

\begin{equation}
\begin{split}
    R-N^+R' & + C-COPh & \rightarrow & R-N^+R'-COPh \\
\end{split}
\end{equation}

\textit{Equation 3}

\begin{equation}
\begin{split}
    R-N^+R' & + Ph-N=C=O & \rightarrow & Ph-N^+R'-COPh \\
\end{split}
\end{equation}

\textit{Equation 4}

\begin{equation}
\begin{split}
    R-N^+R' & + C\text{COOH} & \rightarrow & N-Ph \\
\end{split}
\end{equation}

\textit{Equation 5}

\begin{equation}
\begin{split}
    R-N & \rightarrow & Br_2/AcO \\
\end{split}
\end{equation}

\textit{Equation 6}

**Hydrolysis**

Another reaction of sydnones, which is of great synthetic utility, is the hydrolysis with hydrochloric acid to give substituted hydrazines and a carboxylic acid (Equation 7).

\begin{equation}
\begin{split}
    R-NHNH_2.HCl & + R'COOH^+ & \rightarrow & R-NHNH_2.HCl + R'COOH^+ \\
\end{split}
\end{equation}

\textit{Equation 7}

\( R = \text{H, Br, CH}_3 \)
Fugger\textsuperscript{21a} has recommended this method as a convenient and a general method of converting primary amines to the corresponding hydrazines via sydnones, especially when the hydrazines are accessible with difficulty. For example alkyl hydrazines (9a), alkyl bishydrazines (9b), hydrazine adamantane (9c) etc. from the corresponding sydnones.

\[
\begin{align*}
\text{CH}_3 \\
\text{Ph-CH}_2\text{-C-NHNH}_2\text{HCl} \\
\text{HCl}\cdot\text{H}_2\text{NHN-}\text{(CH}_2\text{)}_n\text{NHNH}_2\text{HCl} \\
\text{CH}_3 \\
9a & \quad 9b & \quad 9c
\end{align*}
\]

Baker and Ollis\textsuperscript{7a} suggested the probable mechanism of the acid hydrolysis (Scheme 2).

\[
\begin{align*}
\text{R-N}^- & \quad \text{H}^+ & \quad \text{R-N}^- & \quad \text{H}_2\text{O} & \quad \text{R-N(NH}_2\text{-COR}^+ \\
\text{R'-COOH} & \quad \text{R-NHNNH}_2 & \quad \text{H}_2\text{O} & \quad \text{R-N(NH}_2\text{-COR}^+
\end{align*}
\]

\textbf{Scheme 2}

The evidence in support of this mechanism has been reported from this laboratory by Puranik et al.\textsuperscript{21b} They isolated α-acyl phenyl hydrazine by hydrolysis of 4-methyl-3-phenyl sydnone in benzene with stoichiometric quantities of water and hydrogen chloride. The synthetic utility of the acid hydrolysis has been demonstrated by one-pot
synthesis of various heterocycles from sydnones using reagents like 1,3-diones, cyclohexanone and levulinic acid (Scheme 3).

Sydnones are the only five membered aromatic heterocycles, which are of great synthetic utility in heterocyclic synthesis. It is also noteworthy to mention that the primary amines can be converted to a wide variety of heterocycles through sydnones by simple reactions avoiding elaborate procedures. The importance of using sydnones as precursors is that most of the heterocycles are obtained with difficulty by other methods.

The purpose of our work was to further the synthetic utility of sydnones in the development of novel heterocyclic systems.