List of Publications

1. Cyclodextrins (Article)
   Kiran Y. Anklekar and Manohar V. Kulkarni

2. 4-[2'-Benzylideneanilino aryloxymethyl] coumarins E and Z isomers.
   C.D. Lakkannavar, V.D. Patil, K.Y. Anklekar and M.V. Kulkarni

   Kiran Y. Anklekar and Manohar V. Kulkarni

4. Application of additive increment methods for estimating olefinic proton chemical shifts. An effective approximation for the carbonyl increments in some heterocyclic compounds.
   M.V. Kulkarni, K.Y. Anklekar and G.M. Kulkarni

5. Fused Bicyclic Benzimidazolin-2-thione as a model for a stable tetrahedral intermediate.
   Kiran Y. Anklekar and Manohar V. Kulkarni

Papers presented at conferences

1. Synthesis and Reactivity of some new 3-biheterocyclic Coumarins.
   Kiran Y. Anklekar and Manohar V. Kulkarni

2. Synthesis of some Isomeric Psoralenyl Coumarins.
   Kiran Y. Anklekar and Manohar V. Kulkarni
N-Hydroxymethylbenzimidazoles as formaldehyde release markers

Extrusion of formaldehyde from different N-hydroxymethylbenzimidazoles has been observed and confirmed by chemical and thermogravimetric techniques. The applicability of this behaviour of benzimidazole N-methylols in textile industry is highlighted.

N-Hydroxymethyl compounds have been found to release formaldehyde in the curing process of textile fibres which influences the durable press properties of the cotton fibres1,2.

During an attempted reaction of 1,3-bishydroxymethylbenzimidazolin-2-one3 (1) (m.p. 164-65°C) with diethyl adipate at high temperature, benzimidazolin-2-one (2) (m.p. 311°C) was obtained instead of the expected trans esterification product. This was confirmed by heating (1) in an oil-bath in the temperature range 150-280°C. Similar results were obtained with 1,3-bishydroxymethylbenzimidazoline-2-thione4 (3) (m.p. 160-61°C) and N-hydroxymethylbenzimidazolene5 (5) (m.p. 140-41°C) which afford benzimidazoline-2-thione (4) (m.p. 308°C) and benzimidazolones6 (6) (m.p. 171-72°C), respectively (Scheme I). But in the case of (5), o-dichlorobenzene was used as solvent, since direct heating led to slight decomposition. Extrusion of formaldehyde was confirmed by passing the volatiles in an ethanolic solution of dimedone to obtain the dimethone derivative (m.p. 89°C) and comparing that with an authentic sample7 obtained from formaldehyde, and its UV spectra, (208 and 256 nm). Formation of products 2, 4 and 6 was confirmed by independent synthesis, IR and UV spectra, and mixed melting point determination.

Thermogravimetric analysis of these compounds indicate that the loss of formaldehyde from (3) takes place in a single-step whereas in the case of (1) it resembles a two-step process wherein the loss occurs over two different temperature ranges (Table 1). Differential scanning calorimetry studies have indicated that release of formaldehyde is an endothermic process and in the case of (3), \( \Delta H = 2076 \) J/g.

Table 1—Thermogravimetric analyses of compounds 1 and 2

<table>
<thead>
<tr>
<th>Comp</th>
<th>Temp. range (°C)</th>
<th>% Wt loss</th>
<th>Nature of DTA peak</th>
<th>Proposed chemical change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>150-215</td>
<td>15.10</td>
<td>Endothermic</td>
<td>-HCHO</td>
</tr>
<tr>
<td>2</td>
<td>250-295</td>
<td>18.57</td>
<td>Endothermic</td>
<td>-HCHO</td>
</tr>
<tr>
<td>1</td>
<td>150-195</td>
<td>28.57</td>
<td>Endothermic</td>
<td>2H(CHO)</td>
</tr>
<tr>
<td>2</td>
<td>150-195</td>
<td>28.57</td>
<td>Endothermic</td>
<td>2H(CHO)</td>
</tr>
</tbody>
</table>

Thermal decomposition of N, N'-bishydroxymethylureas and amidazolines depends upon the substituents on nitrogen and ring carbons3. Due to the fusion of benzene ring to the amidazolone moiety, the resulting heteroaromatic systems becomes a rigid molecular framework which makes this process endothermic, and hence extrusion of formaldehyde occurs at a higher temperature. Further, the driving force for the extrusion of formaldehyde could also be due to the enhanced thermal stability of the products (2) and (6). This is also supported by TGA data of our compounds, and is in agreement with DSC results of N, N'-bishydroxymethyl-4, 5-dihydroximidazolin-2-one1.

In view of the observation that (1) and (3) are obtained by the reaction of formalin with (2) and (4) respectively, the latter compounds can be used as carriers of formaldehyde. Compounds (1) and (3) can be employed as markers for release of formaldehyde at temperature > 150°C with the recovery of benzimidazolin-2-one and benzimidazolene-2-thione respectively as these compounds are stable even at 300°C.

UV spectra were recorded on a HITACHI 150-20 spectrophotometer. TG-DTA results were recorded on a Rigaku TAS 100 instrument.

\[ \text{Scheme I} \]
Acknowledgement
The authors thank Prof. K S Jagadish, Head, Polymer Science & Technology Division, S J Engg. College, Mysore for providing DSC results, Prof. M R Udupa of IIT, Madras for TGA data and Prof. V B Mahale & Mr Ullas Shetti of Chemistry Department, KUD for useful discussions.

References
4 Monti L & Venturi M, Gazz Chim Ital, 76 (1946) 365-8; Chem Abstr, 42 (1948) 1261c.

Kiran Y Anklekar &
Manohar V Kulkarni
Department of Chemistry, Karnatak University, Dharwad 580 003
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Table-1
IR and UV spectral data

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>Route</th>
<th>IR(cm⁻¹) C=O</th>
<th>UV (Ethanol) λ_max nm (ε)</th>
<th>Config.</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>H</td>
<td>A</td>
<td>1722</td>
<td>324(7131), 248(18597), 221(31614)</td>
<td>Z</td>
</tr>
<tr>
<td>III</td>
<td>H</td>
<td>A</td>
<td>1700</td>
<td>445(157), 387(194), 317(4539), 255(7066), 218(18874)</td>
<td>E</td>
</tr>
<tr>
<td>III</td>
<td>-4-OC₃H₅</td>
<td>A</td>
<td>1712</td>
<td>317(13978), 254(22716), 217(39434)</td>
<td>E</td>
</tr>
<tr>
<td>III</td>
<td>-4-OC₅H₅</td>
<td>B</td>
<td>1700</td>
<td>317(13918), 255(22880), 217(40900)</td>
<td>Z</td>
</tr>
<tr>
<td>IV</td>
<td>H</td>
<td>-</td>
<td>-</td>
<td>434(177), 335(12224), 266(13120), 225(22700)</td>
<td>E</td>
</tr>
<tr>
<td>IV</td>
<td>-OCH₃</td>
<td>-</td>
<td>-</td>
<td>436(278), 347(16894), 269(12184), 230(17155), 211(16951)</td>
<td>E</td>
</tr>
<tr>
<td>IV</td>
<td>-OC₂H₅</td>
<td>-</td>
<td>-</td>
<td>436(295), 349(17358), 269(11447), 227(17774), 212(17689)</td>
<td>E</td>
</tr>
</tbody>
</table>
* Methanol: 432(280), 338(13400), 270(14000), 225(22700) λ_max nm (ε); Literature values³ are in good agreement with the observed values for compound IV.

Table-2
Analytical data of synthesised compounds

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>Confign</th>
<th>M.P. °C</th>
<th>Mol. formula</th>
<th>Analysis % Found (Calcd)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>III</td>
<td>H</td>
<td>Z</td>
<td>183-4°</td>
<td>C₂₈H₂₈NO₃</td>
<td>78.19(78.04)</td>
</tr>
<tr>
<td>III</td>
<td>H</td>
<td>E</td>
<td>183-4°</td>
<td>C₂₈H₂₈NO₃</td>
<td>78.19(78.04)</td>
</tr>
<tr>
<td>III</td>
<td>-4-OCH₃</td>
<td>E</td>
<td>251-2°</td>
<td>C₂₈H₂₈NO₃</td>
<td>75.26(75.18)</td>
</tr>
<tr>
<td>III</td>
<td>-4-OC₂H₅</td>
<td>E</td>
<td>261-2°</td>
<td>C₂₈H₂₈NO₃</td>
<td>75.42(75.54)</td>
</tr>
<tr>
<td>III</td>
<td>-OC₂H₅</td>
<td>Z</td>
<td>241-2°</td>
<td>C₂₈H₂₈NO₃</td>
<td>75.41(75.54)</td>
</tr>
</tbody>
</table>

* Solvents for crystallisation; b = benzene, c = chloroform.

stirred for about half an hr in dry acetone (20 ml). To this I was added and the stirring was continued for 24 hr. The mixture was filtered and the filtrate was conc and diluted with water. Solid separated was filtered and washed with water and 10% ethanol (50 ml) to remove excess of salicylideneaniline and the residue was crystalline from a suitable solvent.

Synthesis of IIIB

To a solution of II' (0.008 mol) and an arylamine (0.008 mol) in ethanol (25 ml), 10-15 drops of sulphuric acid were added. The mixture was refluxed on a water bath for an hour. After cooling to room temp the separated solid was filtered and washed with ethanol to remove excess of arylamine and crystallised from a suitable solvent (Table-1 & 2)

References
Cyclodextrins

KIRAN Y. ANKLEKAR and MANOHAR V. KULKARNI
Department of Chemistry, Karnataka University, Pavate Nagar, Dharwad - 580 003.

Abstract

Cyclodextrins are a group of homologous oligosacharides which are comprised of α-1,4-linked D-glucopyranosyl residues in a cyclic constitution. Several organic reactions when carried in presence of cyclodextrins have shown remarkable specificity which is presented in this article.

Cyclodextrins are cyclic sugars and are also known as Cycloamyloses. These are made up of six to D-glucose units with glycosidic linkages between d C. Earlier they were used to prepare inclusion complexes with iodine, phenols, organic acids and a variety of other guest molecules. In recent years, reactions modelling the enzymatic transformation brought about by Pyridoxal and kinetic studies on the catalysis of serine protease have been extensively studied by the use of cyclodextrins. Further, they have been found to be useful as organized a in stereoselective solid state photochemical diastereomisation of coumarins. Several well known organic reactions have shown a great deal of specificity when carried out in the presence of cyclodextrins. Hence, it thought of interest to illustrate their remarkable specificity with some organic reactions taught at the graduate level.

ces and preparation of cyclodextrins

The enzyme that has been produced by Bacillus strains degrade starch and produce cyclodextrins. The compounds have been isolated by precipitation with such as toluene and trichloroethylene. Cyclodextrins were one of the earliest oligosacharides to crystallise from water or aqueous propanol.

structure

An important structural feature of cyclodextrins is presence of a large amount of empty space or cavity. Depending upon the diameter of the cavity and number of glucose units these have been classified as α (6,6A°), β (7,8A°) and γ (8,10-11A°)-cyclodextrins. The glucose units are arranged in chair form the conformation for β-cyclodextrin (with 7-glucose units) is shown in Figure 1. This arrangement results in a basket or a bucket type structure with the C2-C3 - hydroxyl groups along the rim and the CH2OH groups form the bottom portion. This results in a polar hydrophilic periphery and apolar hydrophobic cavity (Fig.2). Hence, cyclodextrins can accommodate different guest molecules.

Fig. 1 : β-CYD

Fig. 2 : Bucket type structure of CYD

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rent types of organic molecules and can modify their activities.

**Chlorination of Anisole**

Breslow et al.\(^5\) found that anisole(I) undergoes chlorination with hypochlorous acid giving a mixture of para(II) and ortho chloro anisoles(III) in the ratio .48. In presence of α-cyclodextrin, this ratio was und to increase as the proportion of α-cyclodextrin as increased (Scheme 1). Regioselectivity of chlorination was observed with p/o ratio rising to 41.0 and 6% para-chlorination was observed.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{OH} + \text{HOCl} & \xrightarrow{\alpha-\text{CD}} \text{C}_6\text{H}_4\text{Cl} \quad \text{Cl}^+ \\
\text{C}_6\text{H}_5\text{Cl} & \quad \text{C}_6\text{H}_4\text{Cl}_2O
\end{align*}
\]

(Scheme 1)

The anisole molecule gets entrapped in the cavity of α-cyclodextrin and the C\(_5\)-CH\(_2\)OH reacts with OCl to give CH\(_2\)O-Cl which is a good source of Cl\(^+\)s shown in Figure 3.

**Carboxylation of Phenols**

The reaction of phenols with carbon dioxide at 120-140°C under pressure gives salicylic acid. The reaction shows a high preference for ortho carboxylation, (Kolbe’s reaction). Carboxylation of phenols has been achieved in presence of β-cyclodextrin by reaction with carbon tetrachloride and copper powder in alkaline medium at 80°C (Scheme 2). Komiyama and Hirai\(^7\) proposed that copper powder generates \(\text{CCl}_3^+\) cations which forms ternary molecular complexes with the cyclodextrin bound phenols resulting in exclusive para attack and the products get hydrolysed to the corresponding acids. This is in line with the observation that poor selectivity is observed in the case of m-cresol which follows similar trend in case of p-cresol. In the case of phenol (R=H)(I) was formed in (fifty-nine percent) yield with (ninety-nine percent) selectivity in the presence of cycloexetrins. Similarly (ninety-seven percent) selectivity for (I) was observed in the case of o-cresol (R = 2-CH\(_3\)). In the absence of cycloexetrins (50%) selectivity was observed in both the cases. The proposed mechanism is shown in Figure 4.

**3. Reimer-Tiemann reaction**

Salicylaldehyde (II) can be synthesised by the reaction of phenols (I) with chloroform and alkali. However, in the presence of β-cyclodextrin the chief product is 4-hydroxybenzaldehyde (III). This is further shown by the observation that p-substituted phenols give 4-substituted 4-dichloromethyl cyclohexadienones in very high yields, as illustrated in the case of p-cresol(IA) (Scheme 3). Komiyama and Hirai\(^8\) proposed the mechanism for the selective synthesis of 4-hydroxybenzaldehyde and 4-(dichloromethyl)-2,5-cyclohexadienone which involves the attack of the dichlorocarbene at the para position of the cyclodextrin bound p-cresol (Figure 5).

\[\text{C}_6\text{H}_4\text{Cl} + \text{CCl}_3^+ \rightarrow \text{C}_6\text{H}_4\text{Cl}_2\text{O} + \text{Cl}^+\]

(Figure 3)

\[\text{C}_6\text{H}_5\text{OH} + \text{CO}_2 \rightarrow \text{C}_6\text{H}_4\text{COOH}\]

(Figure 4)

\[\begin{align*}
\text{C}_6\text{H}_5\text{Cl} + \text{CCl}_3^+ & \rightarrow \text{C}_6\text{H}_4\text{Cl}_2\text{O} + \text{Cl}^+ \\
\text{C}_6\text{H}_4\text{Cl}_2\text{O} & \rightarrow \text{C}_6\text{H}_4\text{Cl}_2\text{O} + \text{Cl}^+ \\
\text{C}_6\text{H}_4\text{Cl}_2\text{O} & \rightarrow \text{C}_6\text{H}_4\text{Cl}_2\text{O} + \text{Cl}^+ \\
\text{C}_6\text{H}_4\text{Cl}_2\text{O} & \rightarrow \text{C}_6\text{H}_4\text{Cl}_2\text{O} + \text{Cl}^+
\end{align*}\]

(Figure 5)
derer-Manasse reaction

Hydroxymethylation of phenol(I) can be carried out acting phenols with formaldehyde in presence of i or dilute acid at room temperature. In this case, para (II) and ortho (III) hydroxybenzyl alcohols obtained. But, the p-isomer(II)(p-hydroxymethyl nol) is the chief product formed in the presence hydroxypropyl β-cyclodextrins (HP β-CYD) heme 4). Komiyama9 synthesised modified cy­

cxtrins and introduced hydroxypropyl group at tion 6 in cyclodextrins. This lengthening of the bon chain at C-2 was found to be necessary and ful.

The proposed mechanism for the selective synthesis s that phenolate approaches the formaldehyde, mmodated in the cavity of HP-β-CYD from the involving the p-carbon atom (Figure 6). Here the hydroxypropyl groups situated on the C5-CH2OH side of the cavity form hydrogen bonds with formaldehyde and enhances its inclusion. These hydrogen bonds strictly regulate the position of the formaldehyde in the cavity and make the p-position more dominant.

5. Photochemical reaction

β-CYD influences significantly the course of pho­tochemical Fries rearrangements (Scheme 5). Ohara and Watanabe10 reported that the conversion of phenyl acetate to o-hydroxy acetophenone can be increased to 3.5 folds when irradiated jointly with β-CYD Product III was formed in 69% yield in the presence of cyclodextrin whereas it was formed in 25% yield in its absence which shows its enhanced regioselectivity for p-position. Similarly photochemical rearrangement of acetanilide, benzanilide and ethyl phenyl carbonate in presence of β-CYD has been studied by Chenevert and Plante.
Table 1. Lederer-Manasse reaction (Scheme-4)

<table>
<thead>
<tr>
<th>Additive</th>
<th>HP-CYD</th>
<th>Conc./M</th>
<th>Para: Ortho</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(II) (III)</td>
</tr>
<tr>
<td>HP-β-CYD</td>
<td>0.05</td>
<td>5 : 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.30</td>
<td>10 : 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.60</td>
<td>15 : 7</td>
<td></td>
</tr>
<tr>
<td>HP-α-CYD</td>
<td>0.30</td>
<td>4 : 3</td>
<td></td>
</tr>
<tr>
<td>HP-γ-CYD</td>
<td>0.30</td>
<td>3 : 3</td>
<td></td>
</tr>
<tr>
<td>β-CYD</td>
<td>0.30</td>
<td>2 : 8</td>
<td></td>
</tr>
<tr>
<td>γ-CYD</td>
<td>0.30</td>
<td>1 : 9</td>
<td></td>
</tr>
<tr>
<td>D-Glucose</td>
<td>2.50</td>
<td>1 : 6</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td>2 : 1</td>
<td></td>
</tr>
</tbody>
</table>

6. Cleavage of Phosphate Esters

Hydrolysis of diarylpyrophosphates in the presence of calcium is catalysed by cyclodextrins. Amongst the three cyclodextrins β-cyclodextrin has been found to be the best and the reaction proceeds via the neighbouring group mechanisms. This has also been applied in the regioselective cleavage (P-O 2') bond in 2',3'-cyclic monophosphates of some ribonucleosides.

Kinetic Studies

Cyclodextrins have been used as models to study the behaviour of hydrolytic enzymes like chymotrypsin. Cyclodextrins have been found to accelerate the cleavage of esters, anilides and bromination of phenols. Komiyama and Bender have found that α-CYD catalyzes the hydrolysis of p-nitrotrifluoroacetanilide, which is 16 folds faster than its alkaline hydrolysis at pH 6.

Applications

Utilizing the observed regioselectivity for p-attack in phenols Komiyama has developed methods for the synthesis for the following industrially important organic compounds. 4-Allyl 2,4,6-trimethyl 2, 5-cyclohexadienone which is a starting material for the total synthesis of Erythromycin, 2,4-dihydroxybenzaldehyde and 4-hydroxy benzaldehyde which are synthons for a variety of drugs, dyes and insecticides. 4-hydroxychalcone has been a useful intermediate in the production of nematic liquid crystals and photosensitive polymers. 4-hydroxy-3-(2-nitrovinyl) benzoic acid which is an important antifungal drug. Indole-3-aldehyde has been found to be a valuable intermediate in the synthesis of antiviral drugs.

Conclusion

It can be seen that cyclodextrins form inclusion complexes with substrates and modify the course of organic reactions on the substrate. Cyclodextrins have served as useful models in the study of enzymatic reactions. Certain useful organic intermediates can be made in much better yields in the presence of cyclodextrins.

References