Stereochemical aspects and Reactivity of Carbonyl group, An overview
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ABSTRACT
The most important aspect of organic chemical reactivity is the chemistry of carbonyl group (>C=O). It directly undergoes nucleophilic attack by different substrates and yields a series of compounds. The prostereogenic carbon gets converted to prostereogenic carbonyl by a nucleophilic attack on either side of the plane of carbonyl group. Different organic compounds containing >C=O group undergo photocyclisation or photoreduction reactions and result a variety of compounds of both chemical and mechanistic interest. β-diketones an important class of carbonyl compounds afford stable ylides and Aldol adducts when interacted with different reagents under varying conditions.

Introduction
In this article I have highlighted the polar nature of carbonyl group which directly undergoes nucleophilic addition reactions with different substrates and yields a series of products of both pharmaceutical and chemical interest. Its UV-visible and IR spectra have been precisely explained. Interaction of 1,2 and 1,3-diketo compounds with different reagents/substrates leads to the formation of a variety of mechanistically interesting products. Stereochemical aspects with special reference to Cravats and Prelog’s Rules have also been discussed in this article.

The chemistry of carbonyl group is probably the most important feature of organic chemical reactivity. The C-O double bond of carbonyl group is similar in many ways to the C-C double bond of alkenes. The carbonyl carbon atom is sp² hybridised and forms three sigma bonds. The fourth valence electron remains in a carbon p-orbital and forms a pi-bond to oxygen by overlap with an oxygen p-orbital. The oxygen atom has also two non-bonding pairs of electrons which occupy its remaining two orbitals.

The carbon-oxygen double bond is both shorter (122pm verses 143pm) and stronger (175 kcal/mol verses 92 kcal/mol) than C-O single bond.

1) Carbonyl compounds have two principle transitions, the allowed π-π* transition and the forbidden n-π* transition.

Of the two, only n-π* transition, although week (forbidden), is commonly observed above the usual cut-off points of solvents.

The carbonyl group absorbs strongly in the range of 1850-1650 cm⁻¹ because of large change in its dipole moment. The C=O frequency of a ketone is usually considered the reference point for comparison for the other base values of C=O group. The normal base values for the carbonyl stretching vibrations for carbonyl group are:

- Aldehydes = 1725 cm⁻¹
- Ketones = 1715 cm⁻¹
- Esters = 1735 cm⁻¹
- Acid chlorides = 1800 cm⁻¹
- Anhydrides = 1810 cm⁻¹

However, conjugation, α, β-unsaturation, resonance factors etc. alter the fundamental stretching vibrations.

Carbon-Oxygen double bonds are polarized and their polar character is practically demonstrated by the measurements of dipole moments e.g. Aldehyde (acetaldehyde) = 2.72D, Ketone (Me₂C=O) = 2.88D, Carboxylic acid (CH₃COOH) = 1.74D etc. Due to this bipolar nature, the carbonyl carbon becomes electron deficient, so it can easily be attacked by a nucleophile, or can act as a proton donor (Scheme-1)
Nucleophile can approach on either side of the plane. One is re-face and the other is si-face (using EZ&RS systems).

The re- and si faces have an equal probability of being attacked. Consequently, the two enantiomers formed will be of equal amounts.

Cram’s Rule: If a carbonyl group is adjacent to a stereogenic center, it will be easier to attack one side of the carbonyl group than the other. Consequently, more of the one addition product will be formed than the other. The preferred product can be determined by using Cram’s Rule, which states that a Ketone will react in that conformation in which the oxygen of the carbonyl group is anti to the largest of the three substituents on the α-carbon.

Preferential nucleophilic attack (e.g., RMgX) will then take place from the least hindered side of the carbonyl carbon i.e., (a)
Power energy due to less steric C-p C-p a + H C C P R R O e number of aliphatic and bonyl group reactions initiated by R N R C R R 2 6 R u C C M H 40749 alkyl radical to give an alkane. to give CO and alkyl radical, the latter reacting with another disproportionation, Decarboxylation or loss of CO can occur. cleavage of the Carbonyl carbon bond to give an acyl and triplet excited states.

Conformation (i) is of lower energy due to less steric interaction between the nucleophile and the smallest group “S” to give (iii) as a major product.

**Nucleophilic Addition to -Keto Esters The Prelog’s Rule**

Scheme-4

Prelog’s Rule: Nucleophilic attack on the carbonyl group takes place from the side of the medium sized methyl group (backside) in preference to attack from the side of the larger octyl group. Scheme-5

**Intramolecular reactions of carbonyl group. (Photochemical reactions)**

There are many Carbonyl group reactions initiated by n-π* excitation and reaction can occur from both the singlet and triplet excited states.

Some examples of intramolecular reactions are;
1. Saturated acyclic compounds: These are dominated by three reaction processes known as Norrish type –1, Norrish type –11 and Photo reductions.

**NORRISH TYPE-1:** This reaction is initiated by initial cleavage of the Carbonyl carbon bond to give an acyl and alkyl radical. It applies mainly to ketones in gaseous phase.

\[
\text{R}_2\text{C}=\text{CHR}_2 \xrightarrow{hv} \text{R}_2\text{C} + \text{CHR}_2
\]

**n-π* transition**

These free radicals then react subsequently by disproportionation, Decarboxylation or loss of CO can occur followed by dimerisation, e.g., Decarboxylation of acyl radical to give CO and alkyl radical, the latter reacting with another alkyl radical to give an alkane.

**Scheme-5**

Photoreduction e.g.

\[
2\text{CH}_3\text{C}-\text{CH}_3 \xrightarrow{hv} \text{CH}_3\text{CHOHCH}_3 \xrightarrow{3} \left(\text{CH}_3\right)_2\text{C}(-\text{CH}_3)_2
\]

It can be performed with a large number of aliphatic and aromatic ketones.

**The Petrieno Buchi Reaction**

Carbonyl compounds yield oxetanes in the presence of olefins in this photocyclo addition reaction.

**Scheme-6**

1,2-diketo compounds is an important class of carbonyl compounds e.g., Benzillic acid rearrangement.

\[
\text{C}_6\text{H}_5\text{C}=\text{C}\xrightarrow{\text{KOH/C}_2\text{H}_5\text{OH}} \text{C}_6\text{H}_5\text{C}-\text{C}-\text{OH}
\]

Some other examples are

**1,3-di-keto compounds.**

An important class of carbonyl compounds is β-diketones(1,3-diketo compounds). Those bearing α-hydrogen
such as CH$_3$COCH$_2$COCH$_3$ or CH$_3$CH$_2$COOC$_2$H$_5$ are much more acidic than monocarbonyl compounds such as CH$_3$COCH$_3$, and as such are easily converted to the corresponding resonance stabilized carbanions. Scheme-7.

Scheme-7

In presence of α-hydrogen, like other carbonyl compounds, β-diketones also exhibit keto-enol tautomerism and the equilibrium shifts towards enol form which is stabilized through intramolecular hydrogen bonding.

These systems show the IR stretching vibrational band at 1540-1640 cm$^{-1}$ instead of normal carbonyl vibrational band at 1715 cm$^{-1}$.

One of the characteristic reaction of β-diketones is base catalysed addition-elimination reaction in the formation of a ketone and salt of a carboxylic acid. Scheme-8.

β-dicarbonyl compounds form stable ylides when allowed to interact with DMSO/Ac$_2$O reagent. Scheme-9.

Succinimide, Phthalimide, 1,3-indandione etc. are some important members of class of 1,3-diketo-compounds. They yield a wide range of compounds of both chemical and mechanistic interest with different reagents.

N-hydroxy phthalimide (1) has been synthesised by refluxing phthalimide with formaldehyde$^4$.

1,3-indandione is an important member of class of 1,3-diketo compounds, yields a wide range of products with different substrates.$^{2,6}$.

Aldol condensation between 1,3-indandione and chloral gives 2-(α-hydroxy-β,β,β-trichloroethyl)-1,3-indandione (1) which suffers acid catalysed dehydration to give 2-(trichloro ethylidene)-1,3-indandione (ii).

Scheme-10

Aldol condensation has also been observed between 1,3-indandione with aromatic aldehydes under basic conditions.$^7$ Scheme-10.

In a similar way 1,3-indandione reacts with cyclic ketones such as cyclo-pentanone and cyclo-hexanone to give the corresponding 2-cycloalkylidene-1,3-indandiones.

Intramolecular Aldol reactions

Certain dicarbonyl compounds when treated with a base form a cyclic product through intramolecular Aldol reaction. Scheme-11.

Robinson Annulation; A process in which Michael reaction and Aldol addition reaction are put together is called the Robinson annulations. Annulation reaction is a ring forming reaction. In the first stage of Robinson annulations a Michael reaction forms a 1,5-diketone. In the second stage 1,5-diketone upon treatment with a base undergoes an intramolecular aldol addition forming a 2-cyclohexenone ring. Scheme-12.
N.D. Zargar and K.Z. Khan / Elixir Appl. Chem. 95 (2016) 40747-40751

Scheme-12
Some biological nucleophilic addition reactions.

Nucleophilic addition to carbonyl group play a critical role in the biological synthesis of many vital molecules e.g. The bacterium Bacillus subtilis synthesises the amino acid alanine by the nucleophilic addition of an amine to the carbonyl group of pyruvic acid. Scheme-13

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References
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