

Spectral Properties of Chalcones II

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SUMMARY

Chalcones (1,3-diaryl-2-propen-1-ones), member of flavonoids family, are important class of natural or synthetic products. They are protector of plants against insects and pathogens and give colour to the flowers of plants. Chalcones have a lot of pharmacologic effects and can be used as intermediates for synthesis of drugs. Spectral properties of chalcones are important to understand formation of chalcones and continue other synthesis steps if they are used as intermediates. In this review, we aimed to provide a comprehensive presentation of spectral properties of chalcone derivatives, to the researchers.

Key Words: Review, chalcones, spectral properties.

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Şalkonların Spektral Özellikleri II

ÖZET

Flavonoid ailesinin bir üyesi olan şalkonlar (1,3-diaril-2-propen-1-on) doğal ve sentetik ürünlerin önemli bir sınıfıdır. Böcek ve patojenlere karşı bitkileri korurlar ve bitkilerin çiçeklerine renk verirler. Şalkonlar pek çok farmakolojik etkiye sahiptir ve ilaçların sentezinde ara ürün olarak da kullanılabilirler. Şalkonların spektral özellikleri, şalkonların oluşumunu anlamak ve eğer ara ürün olarak kullanılacaklarsa diğer sentez basamaklarına devam edebilmek açısından önemlidir. Bu derleme ile araştırmacılara şalkon türevlerinin spektral özelliklerini bir arada topluca sunmayı amaçladık.

Anahtar kelimeler: Derleme, şalkonlar, spektral özellik

INTRODUCTION

Chalcones, α , β -unsaturated ketones consisting of two aromatic rings (ring A and B) (Figure 1), are abundant in edible plants (1). Chalcones can be natural or synthetic. Synthetic chalcones are commonly synthesized with the reaction of acetophenone and benzaldehyde via the Claisen-Schmidt condensation. This reaction is catalyzed by bases and acids under homogeneous conditions (2, 3).

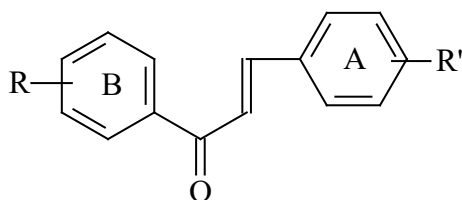


Figure 1. General presentation of chalcone

Chalcones may exist in two isomeric forms, *cis* and *trans*, of which the *trans* form is thermodynamically favourable. In nature, mainly hydroxyl, methoxy and alkenyl functions combine to the aryl substituents of chalcones. However the synthetically derived chalcones may also contain one or more aryl substituents which

contain halogens, alkyl, amino, nitro, nitrile, acetamido and carboxyl groups (4).

Chalcones have numerous biological activities such as antiviral (5-9), antibacterial (10-14), antiinflammatory (15-26) antifungal (27, 28), anticancer (29-38), antioxidant (39-46), analgesic (47), antiulcer (48), antimalarial (49-54) and antihelminthic (55) and thus comprise a class with important therapeutic potential.

Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine, pyrazolines, 1,4-diketones, and flavones. For this reason, growing interest amongst the scientists continues to the chalcones (1). Chalcones may be used as result products or intermediates to synthesize new pharmaceuticals. For using chalcones as a product or as an intermediate, identification of chalcones is important and this is possible by analyzing the spectral properties of chalcones.

UV Spectrum

Generally, it is known that the chalcones absorb light in the UV region and transmit in the remaining region (56-59). The UV spectrum of chalcones consists of two essential absorption band: band I and relatively a minor band, band II. In chalcones, band I usually appears in

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340-390 nm, although a minor inflection or peak often occurs at 300-320 nm. Band II appears in 220-270 nm. Increasing oxygenation generally causes bathochromic shifts, particularly in band I. The addition of an unsubstituted 2'-hydroxyl group to the chalcone causes a marked effect on the spectrum e.g. 2',4',4'-trihydroxychalcone (λ_{\max} 370 nm), 4',4'-dihydroxychalcone (λ_{\max} 348 nm). Glycosylation or methylation of 2'-position leads to 15-20 nm hypsochromic shift (60).

Most of the absorption spectroscopy of organic compounds are based on transitions of n or p electrons to the p^* excited state which takes place in the range 200-700 nm (61). It is clear that the crystal is transparent in the entire visible region and the absorption takes place in the UV range between 214 and 456 nm (57, 58, 61-63). Maximum absorption can be assigned to $n \rightarrow p^*$ transition and may be attributed to the excitation in the aromatic ring and C=O group (56, 58).

2'-OH chalcones have intramolecular bond between the H of the OH group at position 2' and the carbonyl oxygen atom. The intramolecular bond has changed the spectroscopic properties (64) of 2'-OH chalcones. The benzoyl and cinnamoyl groups of 2'-OH chalcones interact with the carbonyl group by σ and π bonds, favoring the delocalization of the π electrons. Due to these interactions, the carbonyl group loses part of its individual character and partially integrates to the adjacent olefinic group. This phenomenon causes a transference of electron deficiency from the CO carbon atom to the C atom at position β so, intramolecular hydrogen bond formation occurs (65).

The UV spectrum of 2'-OH chalcones in ethanol are characterized by two main absorption bands with maxima between 345 and 435 nm (band I, transition $p \rightarrow p^*$) and 220 and 280 nm (band II, transition $p \rightarrow p^*$) due to the benzoyl and cinnamoyl groups, respectively. For example, the UV absorption spectra of 2'-hydroxy-4-methoxy chalcone in ethanol is characterized by two absorption bands with maxima at 365 and 240 nm, and a valley at 296 nm. In 2'-OH-4X-chalcones, the electron-donating substituents favor planarity and π electronic delocalization of the cinnamoyl group and this causes a bathochromic UV spectral shift of band I (65).

Absorption spectrum of *trans*-chalcone reveals two bands, the strongest one in the near-UV at 4 eV, and a second, somewhat less intense band in the UV at 5.5 eV. These localized transitions belong to the Ph-CH=CH- and Ph-CHO entities (66). *Trans* isomer of chalcones have two conformers; *trans*-(*s-trans*)-chalcone and *trans*-(*s-cis*)-chalcone. The presence of these conformers may complicate the interpretation of the UV spectrum of *trans*-chalcone, as the two CO stretch peaks have intensity ratios of only 3:1-5:1 (67).

The photoisomerization of *trans*-(*s-cis*)-chalcone to *cis*-(*scis*) chalcone changes the absorption spectrum. Be-

cause of steric hindrance between the carbonyl oxygen and a phenyl ring, *cis*-(*s-cis*)-chalcone is expected to be non-planar. This was interpreted as evidence that these two absorption bands depend on the associated conjugation between all chromophores and planarity of the entire molecule. In subsequent work, a third higher wavelength absorption was observed at 6.1 eV, and was interpreted as being derived from a modified band of the phenyl groups (66). UV measurements in MeOH-NaOMe cause shifts to longer wavelength for hydroxy chalcones. Because, sodium methoxide is a strong base so, hydroxyl groups on chalcone nucleus are ionized. Chalcones having a 4-hydroxyl group give a 60-100 nm band I bathochromic shift with an increase in intensity. Chalcones possessing a 2 or 4'-hydroxyl give same bathochromic shift with no increase in intensity (68, 69). For this review, spectrum samples is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one. General presentation of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one is shown with Figure 2. A sample of UV spectrum is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one (Figure 3).

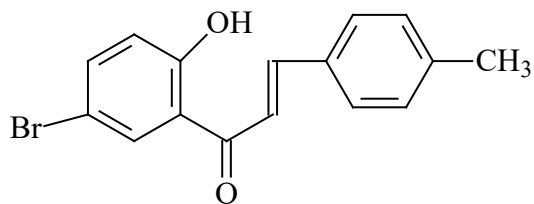


Figure 2. General presentation of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

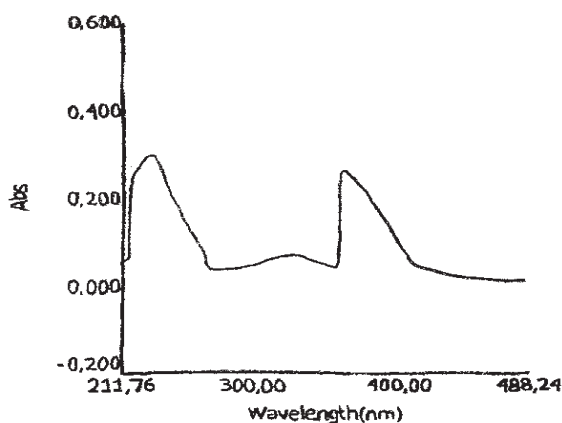


Figure 3. UV spectrum of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

IR Spectrum

In the IR spectra of chalcones asymmetric and symmetric stretching vibrations of the aromatic C-H bonds are seen at 3120-3080 cm^{-1} and 3060-3040 cm^{-1} ranges with two low intensity bands. C-H stretching band of the =C-H group is observed at 3030-3010 cm^{-1} . The

bands at 1610-1570 cm^{-1} are assigned to the vibrations of the aromatic ring. The inplane deformation of the =C-H bond is appeared as broad weak band at 1460-1430 cm^{-1} . When the acceptor character of the arylidene system increases, this band generally shifts to higher values (70).

The carbonyl stretching vibrations for the enones (=C-C=O) can be found between 1650 and 1685 cm^{-1} (70,71) Ketone group that is in conjugation showed a peak at 1640 cm^{-1} , the double bond peak appeared around 1580 cm^{-1} (72).

When 2'-hydroxychalcones made complexes with metals, C=O stretching vibration absorptions at 1638 and 1640 cm^{-1} , aromatic C=C stretching vibration absorptions at 1571, 1572, 1574 cm^{-1} and C-O stretching vibration absorptions at 1339, 1340, 1368, 1369 cm^{-1} were observed. Vibrations in the range of 618-621 cm^{-1}

¹ determined in the metal complexes that indicate the presence of M-O bond (M-metal) in the molecules, which are not present in the original ligand (73).

IR studies show two peaks for the C=O stretching mode which suggest that a second isomer, *trans-(s-trans)*-chalcone, coexists in solution with *trans-(s-cis)*-chalcone (66, 67, 74, 75). These conformers are observed in the range of 1600-1700 cm^{-1} as doublets (76, 77). The C=O stretching mode of *s-trans* conformer is observed at the lower frequency, whereas the C=O stretching mode of *s-cis* conformer is observed at the higher frequency (76, 78-81). In order to avoid the shoulder formation on carbonyl doublets, KBr disc is preferred for recording the infrared spectra (81). The presence of only *trans-(s-cis)*-chalcone in the solid state caused disappearance of the splitting of the carbonyl in the IR spectra (66, 75). A sample of IR spectrum is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one (Figure 4).

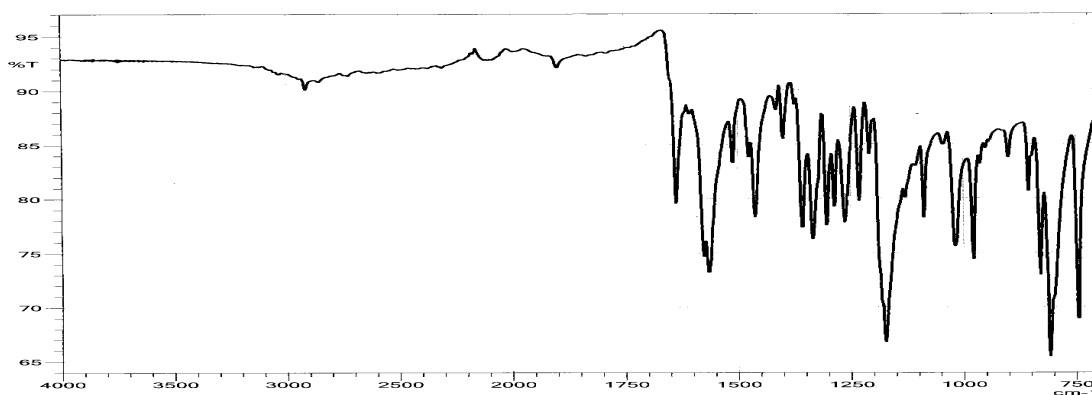


Figure 4. IR spectrum of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

NMR Spectrum

The ¹H-NMR spectrum of double bonds of chalcones were seen at 5.4 and 6.1 ppm. The aromatic regions were observed at 6.9-8.1 ppm (72).

The ethylenic protons nearer the carbonyl group are called as H_a protons and those next to H_a protons are called as H_b protons (Figure 5). H_a protons of chalcones showed chemical shift at higher field than those of H_b protons (82).

This is possibly due to the polarization of the C=C double bond in the system being predominantly caused by the carbonyl group so as to make electron density at a position than at b position (82).

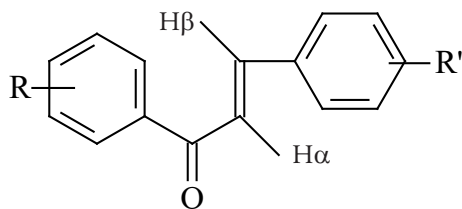


Figure 5. General presentation of chalcone protons which have enone structure.

In the ¹H-NMR spectrum of 2'-hydroxy chalcones, hydroxyl proton appears at 10.41-13.23. The high frequency resonances of these protons are due to the intramolecular hydrogen bond formed with the carbonyl group. The vinylic protons appear as doublets at H_a= 7.15-8.23 ppm and H_b= 7.45-8.07 ppm. If the coupling constants value is J_{H_a-H_b}=8 Hz, that indicates *cis* configuration of vinylic system (83). But if the coupling constants value is J_{H_a-H_b}=15-16.1 Hz, that points out *trans* configuration of vinylic system (75, 84-87). A sample of ¹H NMR spectrum is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one (Figure 6).

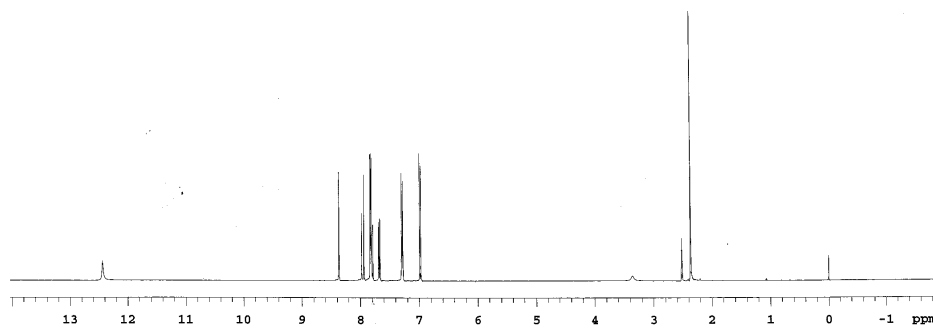


Figure 6. ^1H NMR spectrum of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

In ^{13}C -NMR spectrum of chalcones, the carbonyl carbon usually appears between δ 186.6 and 196.8 (83, 88-92). For 2-pyrrolyl chalcones carbonyl carbon usually appears at 177-179.5 ppm (93). The α - and β - carbon atoms with respect to the carbonyl group give characteristic signals between δ 116.1-128.1 and δ 136.9-145.4

respectively (77, 92, 94) as a six line multiplet in the half resonance decoupled spectrum. Enol tautomer of chalcone gives C- α resonance at δ 90 to 92 (92). A sample of ^{13}C NMR spectrum is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one (Figure 7).

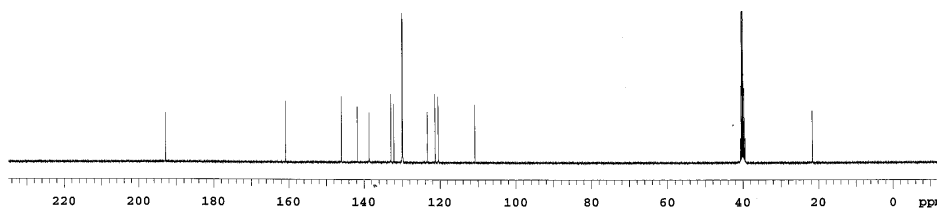
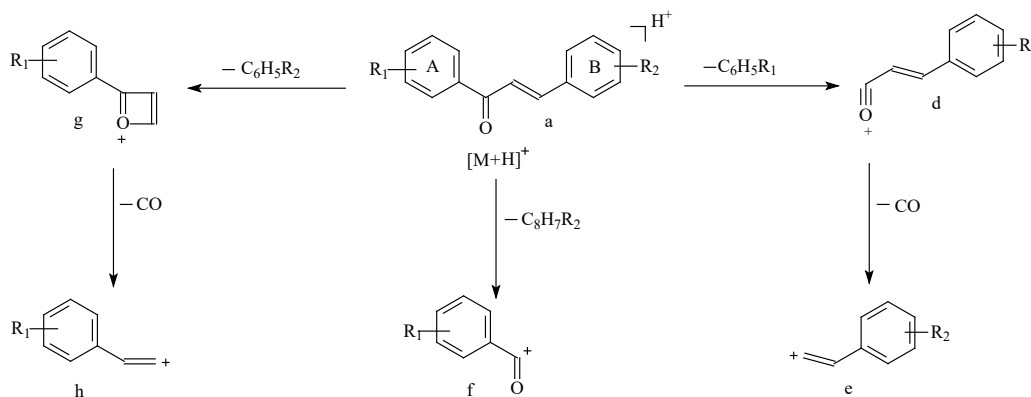


Figure 7. ^{13}C NMR spectrum of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

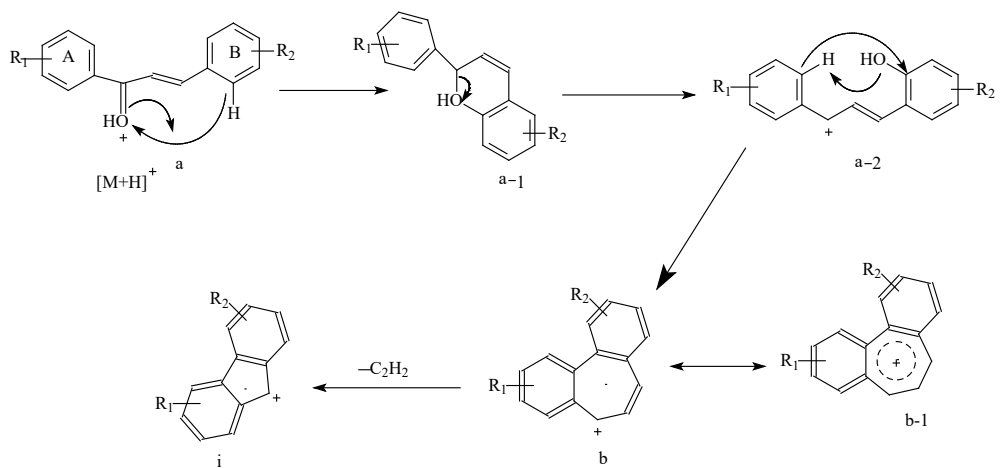
Mass Spectrum

Basic fragmentation pathways of chalcones are obtained by loss of the phenyl group from the A or B ring, and loss of CO (60, 95-98) (Scheme 1). Losses of H_2O and CO from the precursor ions of $[\text{M}+\text{H}]^+$ can occur via rearrangements. Elimination of water from protonated chalcones, a stable ion was composed but it was rarely obtain skeletal fragmentation of a precursor ion

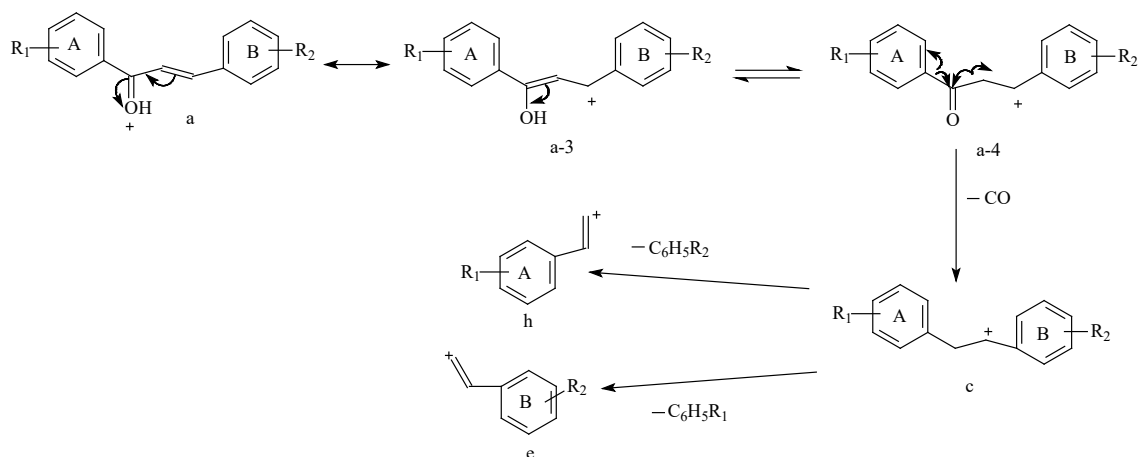
(Scheme 2). Except for the nitrosubstituted chalcones, loss of CO was observed in the MS/MS spectra of all the compounds (Scheme 3). When the $[\text{M}+\text{H}-\text{CO}]^+$ ion was fragmented in the MS/MS experiments, first methyl radical (m/z 15), then ethylene (m/z 28) were lost (Scheme 4). The ion at m/z 130, was found only in the nitro-substituted chalcones and observed commonly in the electron ionization (EI) spectra of chalcones (96-98) (Scheme 5).



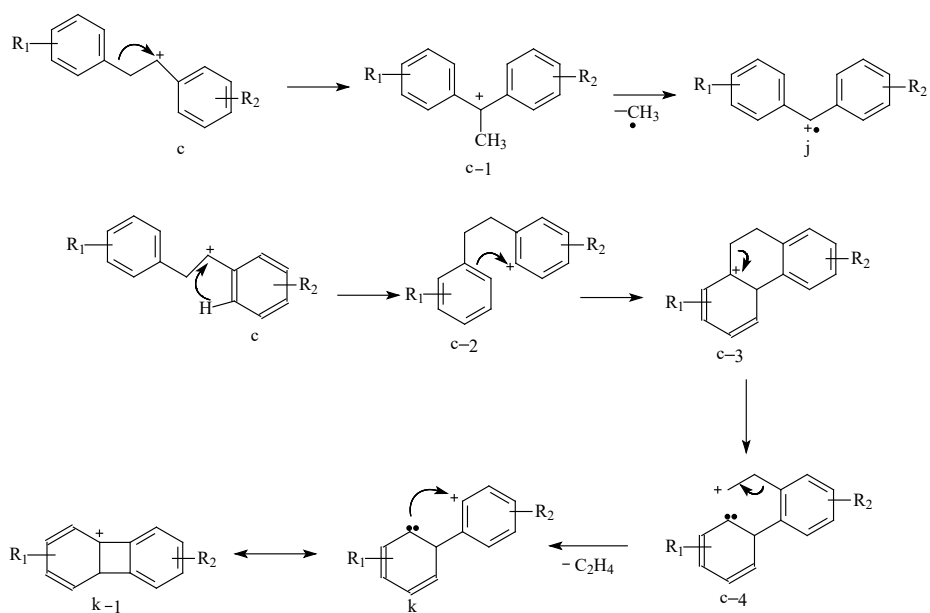
Scheme 1. Proposed MS/MS fragmentation mechanism of protonated chalcones (95-98)



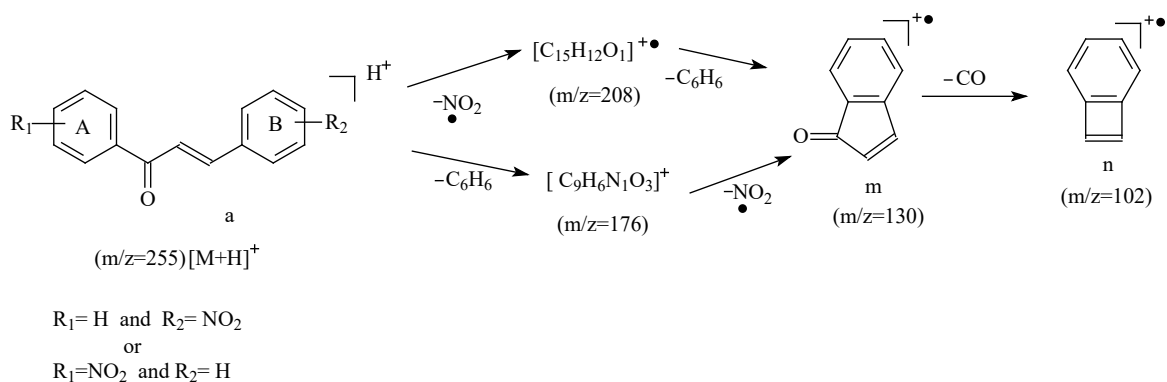
Scheme 2. Proposed fragmentation pathway for loss of water from protonated chalcones (96)



Scheme 3. Proposed fragmentation pathway for loss of CO from protonated chalcones (96, 98).



Scheme 4. Proposed MS³ fragmentation pathways from the precursor ions [M+H-CO] (96).



Scheme 5. Proposed mechanisms for the protonated nitro-substituted chalcone (96-98).

The mass spectra of 2'-hydroxy-chalcones and flavanones (i.e. 2-phenyl-chroman-4-ones) are essentially identical (95). Methoxy chalcones give strong ions for M^+ , $[M-H]^+$, $[M-CH_3]^+$ (60).

A sample of Mass spectrum is given for 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one (Figure 8).

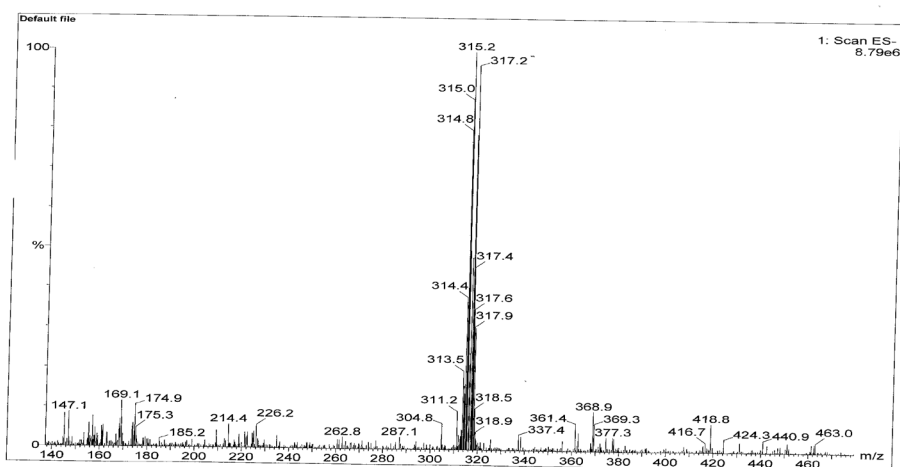
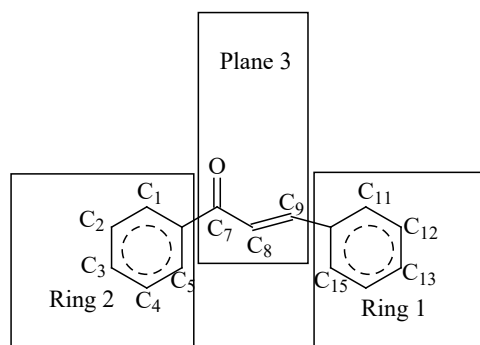


Figure 8. Mass spectrum of 1-(5-Bromo-2-hydroxyphenyl)-3-p-tolylprop-2-en-1-one

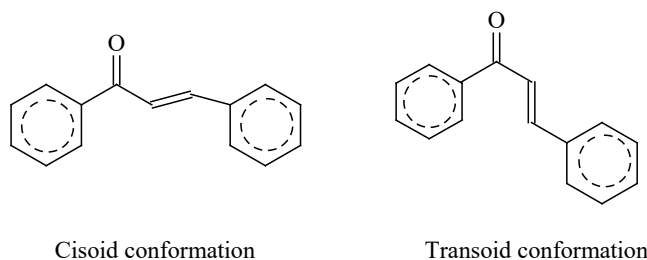
X Ray Spectra of Chalcones

Chalcone molecule has three approximately planar parts. Corresponding to the two conformational types, "cisoid" and "transoid", the dihedral angle between ring 2 and plane 3 changes into one of two ranges $0-35^\circ$ and $85-90^\circ$. (Figure 2) The dihedral angle of ring1/plane3 get involved in the range of $0-16^\circ$. In all instances, these parts of the molecule are almost coplanar. The molecular conformation is determined by the balance of intramolecular forces according to the stabilization due to $n-n$ overlap across the three planar regions of the molecule and destabilisation due to steric repulsion between C(2) and C(6) substituents and H(8) and H(7) and between C(12) and C(16) substituents and O(1) and H(8) (99).

According to Xue and Gong, the trans configuration is more stable than the cis one by 4.8 kcal/mol (67). The cis configuration is unstable due to the strong steric effects between the B-ring and the carbonyl group. Carbonyl stretching mode of IR studies show two peaks which suggests that a second isomer, trans-(s-trans)-chalcone, coexists in solution with trans-(s-cis)-chalcone. According to calculated equilibrium structure, the s-cis conformer seems to be fully planar, whereas steric hindrance between H atoms leads the s-trans conformer to be nonplanar, with a torsion angle O8-C7-C9-C10 of approximately 5° and -152° , respectively (22, 67).



A chalcone molecule has three planar moieties



Cisoid conformation

Transoid conformation

Figure 9. Molecular conformation (99)

When the entire molecule of chalcone is planar, the stabilization due to conjugation is maximized. Nonetheless steric repulsion is also greatest in this conformation. The repulsion experienced by ring 2 when coplanar with the central part is greater than that experienced by ring 1 due to the position of ketone oxygen. After all, repulsive and the stabilising forces between ring 2 and plane 3 are more closely balanced. When methoxy groups are substituted at C(12) and C(16), ring 2 becomes perpendicular, but when hydrogens are present at this positions, ring 2 lies coplanar to the rest of the molecule. When methoxy groups are substituted at C(2) and C(6), ring 1 remains coplanar with plane 3, the lowering in energy provided by the conjugation of ring 1 with the unsaturated ketone (99).

X ray crystal properties changes for each molecule. (2*E*)-3-(4-hydroxyphenyl)-1-phenylprop-2-en-1-one crystallizes orthorhombic system, $P2_12_12_1$ space group with $Z=4$. Dihedral angle between hydroxyphenyl ring and benzene ring is 25° , which indicates the non-planar ge-

ometry of the crystal structure. The hydroxyphenyl ring is connected to the phenyl group through the C6-C7=C8-C9-C10 chain with the C=C bond length being 1.330 (3) Å. Crystalline lattice is held together by weak intermolecular C-H...O hydrogen bond. While the mean plane of hydroxy phenyl ring (C1-C6) is deviated from a plane (H1O1-O1-C3) by an angle of 17.27° , the mean plane of phenyl ring (C10-C15) is deviated from a plane (O2-C9-C10) by an angle of 9.95° . Very weak aromatic stacking interactions stabilised the crystal structure (100).

CONCLUSION

Chalcones are important intermediates for synthesis of compounds such as flavonoids, 2-pyrazolines and hydrazones and they have various biological activities which make them very valuable for treatment. This review including UV, IR, NMR, Mass, X ray spectral data of chalcones will be useful in providing an approach to elucidate chemical structures of chalcones.

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