

Pharmacy 570 Lecture #5

UV Spectra of Conjugated Polyenes and α,β Ketones

The Woodward Feiser Rules

R.B. Woodward (Robert Burns Woodward) - Thought by many to be the greatest chemist who ever lived. Made seminal contributions to organic chemistry, medicinal chemistry, biochemistry and UV spectroscopy.

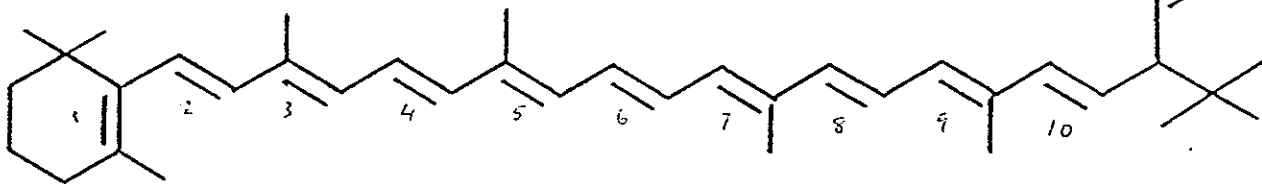
In the 1930's UV spectroscopy was emerging as a technique of choice for characterizing and quantifying many different compounds. Feiser, a noted Harvard chemist, was among the first to make use of UV absorption spectroscopy in characterizing organic molecules. R.B. Woodward arrived in his lab in 1937 as a Post-doc and was interested in characterizing and synthesizing steroid-like molecules. Woodward had a hunch that UV spectroscopy would be useful for characterizing substitution patterns in steroids. At the time, there was no simple way of characterizing what steroid derivatives were being made.

Woodward worked mostly at night and proceeded to collect huge quantities of UV data from Feiser's high-tech instrument, but no one knew exactly what he was doing. After several months, Feiser pointedly asked Woodward what he was doing and why he was wasting valuable instrument time and expensive chemical resources. The next day (as legend has it), Woodward demonstrated to Feiser that he could precisely calculate the maximum absorption (λ_{\max}) of a large variety of conjugated polyenes and conjugated α,β unsaturated ketones and aldehydes (i.e. derivatives of steroids). This was the first instance where it was shown to be possible to accurately predict UV λ_{\max} of organic compounds. The set of rules that Woodward came up with are now called the Woodward-Feiser Rules and are particularly useful for characterizing the substitution patterns on steroids as well as many other related compounds.

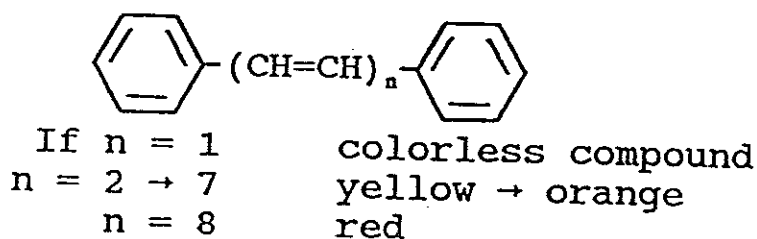
UV Spectra of Conjugated Polyenes, Ketones and Aldehydes

Early on in Woodward's studies of conjugated systems, he noticed the following phenomena:

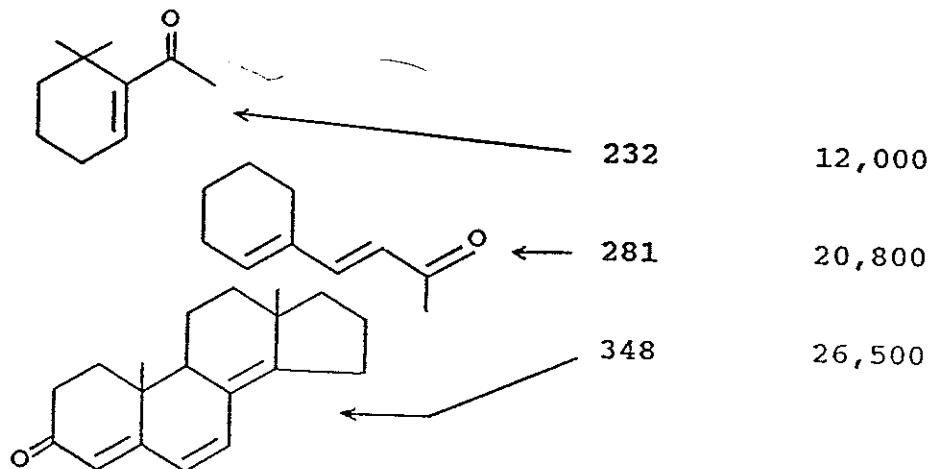
<u>Chromophore</u>	λ_{\max} (nm)	ϵ_{\max}
$\text{CH}_2=\text{CH}_2$	165	15,000
$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$ —	217	21,000
$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$	260	50,000
$\text{CH}_2=\text{CH}-(\text{CH}=\text{CH})_2-\text{CH}=\text{CH}_2$	304	80,000
$\text{CH}_2=\text{CH}-(\text{CH}=\text{CH})_3-\text{CH}=\text{CH}_2$	334	118,000
$\text{CH}_3\text{CH}=\text{CH}-(\text{CH}=\text{CH})_4-\text{CH}=\text{CHCH}_3$	380	146,500
$\text{CH}_3\text{CH}=\text{CH}-(\text{CH}=\text{CH})_6-\text{CH}=\text{CHCH}_3$	411	156,000
α -Carotene (10 conj. d.bs.)	485	162,000



The effect of extended conjugation is also observed in the diphenyl polyene series:

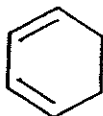


Woodward also observed the same situation existed in conjugated systems with unlike chromophores (i.e. α,β unsaturated ketones and aldehydes):



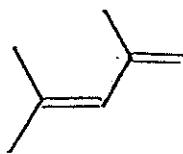
Additional work by Woodward on the polyene series indicated that it was possible to use diene UV spectra (and perturbations thereof) to build up and predict the spectra of larger conjugated systems. However, in order to do so it was important to distinguish between two very general types of conjugated dienes: (1) cyclic polyenes with two double bonds within the same ring; and (2) all others.

Cyclic conjugated dienes in which the two double bonds are contained in the same ring (usually a 6-membered ring) are called homoannular dienes. These compounds and their derivatives have a distinctly higher λ_{max} (254 nm) and higher ϵ_{max} than other conjugated dienes.

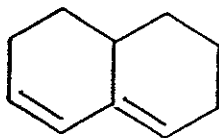


Other groups of conjugated dienes (which have a λ_{max} of ~215 nm) include:

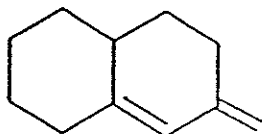
1) The acyclic conjugated dienes (butadiene being the simplest).



2) Cyclic conjugated dienes in which the two alkene double bonds are contained within separate but fused ring systems (usually 6-membered rings). These are called heteroannular dienes. Note the double bonds are not in the same ring.



3) Cyclic conjugated dienes in which one of the two alkene double bonds is within a ring and the other is attached to, but outside that ring. Note the double bonds are ~~not~~ in the same ring.



Based on these observations, Woodward was able to put together the following general rules for calculating the λ_{\max} of conjugated polyenes:

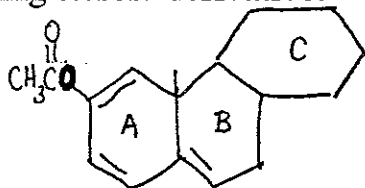
Woodward-Feiser Rules for Homoannular Rings

Assume the compound has a nominal λ_{\max} baseline of 254 nm (the smallest and simplest cyclic conjugated homoannular ring is cyclohexadiene) then for:

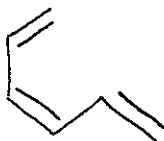
- 1) Each alkyl group adds 5 nm to λ_{\max}
- 2) Each exocyclic double bond adds 5 nm to λ_{\max}
- 3) Each double bond that extends conjugation adds 30 nm to λ_{\max}
- 4) Each RCO (acetyl group) adds 0 nm to λ_{\max}
- 5) Each RO (ether group) adds 6 nm to λ_{\max}
- 6) Each RS (thioether group) adds 30 nm to λ_{\max}
- 7) Each Cl, Br or I adds 17 nm to λ_{\max}
- 8) Each NR_2 adds 60 nm to λ_{\max}

Examples

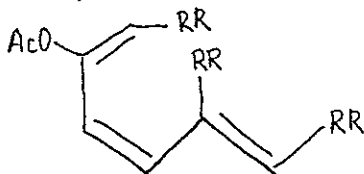
Consider the following steroid derivative:



To calculate the λ_{\max} let's start by redrawing the basic chromophore (i.e. the region of the molecule that contains the conjugated double bonds)



From this structure we can redraw the chromophore to include the substituents (rings and other attachments) as follows:



From inspection we can see that there are 3 attached alkyl (cyclohexyl) groups, 1 attached acetyl group, 1 attached exocyclic double bond and 1 conjugated double bond extension (i.e. there are 3 conjugated double bonds instead of 2). Therefore the predicted λ_{\max} is:

$$\lambda_{\max} = 254 + (3 \times 5) + (1 \times 0) + (1 \times 5) + (1 \times 30) = 304 \text{ nm}$$

The actual λ_{\max} for this compound has been measured to be 306 nm. Pretty Good!

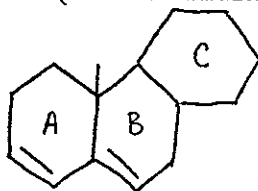
Woodward-Feiser Rules for "Other" Conjugated Dienes

Assume the compound has a nominal λ_{\max} baseline of 214 nm (the smallest and simplest acyclic conjugated polyene is butadiene) then for:

- 1) Each alkyl group adds 5 nm to λ_{\max}
- 2) Each exocyclic double bond adds 5 nm to λ_{\max}
- 3) Each double bond that extends conjugation adds 30 nm to λ_{\max}
- 4) Each RCO (acetyl group) adds 0 nm to λ_{\max}
- 5) Each RO (ether group) adds 6 nm to λ_{\max}
- 6) Each RS (thioether group) adds 30 nm to λ_{\max}
- 7) Each Cl, Br or I adds 17 nm to λ_{\max}
- 8) Each NR₂ adds 60 nm to λ_{\max}

Examples

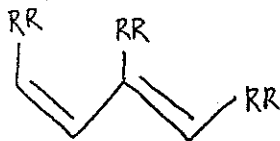
Consider the following cyclic (heteroannular) conjugated diene:



To calculate the λ_{\max} lets start by redrawing the basic chromophore (i.e. the region of the molecule that contains the conjugated double bonds)



From this structure we can redraw the chromophore to include the substituents (rings and other attachments) as follows:



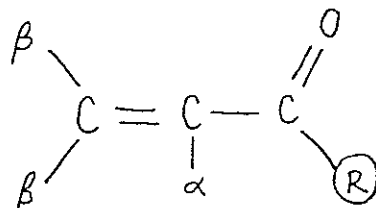
From inspection we can see that there are 3 attached alkyl (cyclohexyl) groups and 1 attached exocyclic double bond. Therefore the predicted λ_{max} is:

$$\lambda_{\text{max}} = 214 + (3 \times 5) + (1 \times 5) = 234 \text{ nm}$$

The actual λ_{max} for this compound has been measured to be 235 nm. Not bad!

Woodward-Feiser Rules for α,β Unsaturated Ketones

A large number of steroids and steroid derivatives are actually α,β unsaturated ketones and aldehydes. Woodward observed a similar substituent based progression in the UV spectra of these compounds, but in order to predict the λ_{\max} more precisely he had to modify the rules for the conjugated dienes to suite the peculiarities of α,β unsaturated ketones and aldehydes. An α,β unsaturated ketone or aldehyde is defined as having the following structure:

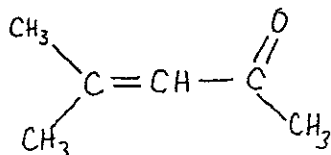


To predict the λ_{\max} of an α,β unsaturated ketone or aldehyde, assume the compound has a nominal λ_{\max} baseline of 215 nm (the absorption of the simplest unsaturated ketone) then:

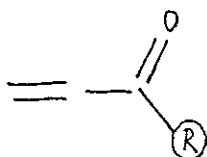
- 1) Each α substituent adds 10 nm to λ_{\max}
- 2) Each β substituent adds 12 nm to λ_{\max}
- 3) Each γ (and above) substituent adds 18 nm to λ_{\max}
- 4) Each exocyclic double bond adds 5 nm to λ_{\max}
- 5) Each double bond that extends conjugation adds 30 nm to λ_{\max}
- 6) Each homodiene ring adds 39 nm to λ_{\max}

Examples

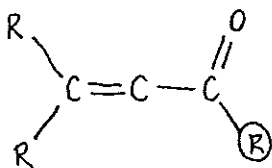
Consider the compound called mesityl oxide:



To calculate the λ_{\max} lets start by redrawing the basic chromophore (i.e. the region of the molecule that contains the conjugated double bonds)



From this structure we can redraw the chromophore to include the substituents (rings and other attachments) as follows:

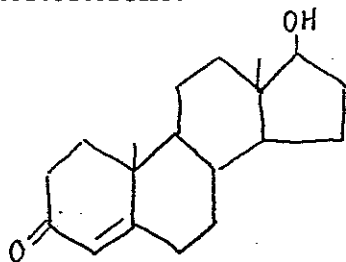


From inspection we can see that there are just 2 attached β substituents. Therefore the predicted λ_{\max} is:

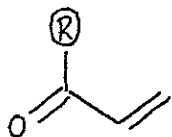
$$\lambda_{\max} = 215 + (2 \times 12) = 239 \text{ nm}$$

The actual λ_{\max} for this compound has been measured to be 237 nm. Pretty Good!

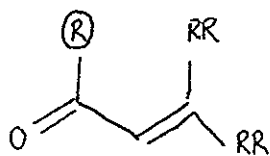
Consider the steroid testosterone:



To calculate the λ_{\max} let's start by redrawing the basic chromophore (i.e. the region of the molecule that contains the conjugated double bonds)



From this structure we can redraw the chromophore to include the substituents (rings and other attachments) as follows:



From inspection we can see that there are 2 attached β substituents and 1 exocyclic double bond Therefore the predicted λ_{\max} is:

$$\lambda_{\max} = 215 + (2 \times 12) + (1 \times 5) = 244 \text{ nm}$$

The actual λ_{\max} for testosterone has been measured to be 243 nm. Not bad!