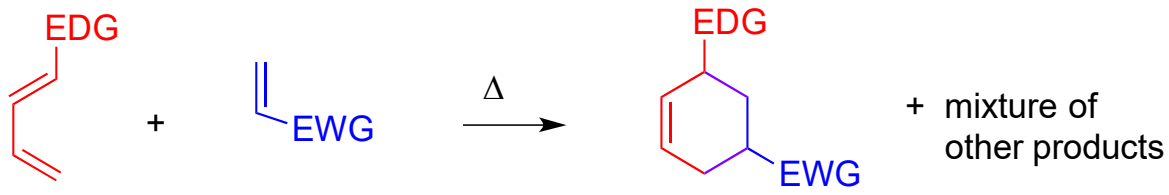
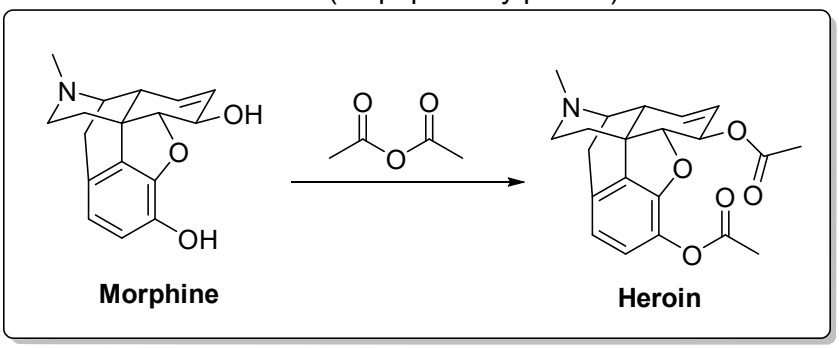
CHEM 110L, Experiment 6 – Diels Alder [4+2] Cycloaddition Reaction in Water



What's so cool about DA reactions?

- This 'cycloaddition' reaction requires no metal catalyst, just heat
- Ring formation is hard, especially forming two C-C bonds at once
- Potential to form 4 chiral centers!
- Initial discovery of this reaction – synthesis of morphine

How to make heroin (on paper only please)



Morphium – Greek god of dreams

Poppy – *Papaver somniferum* – "flower of joy"

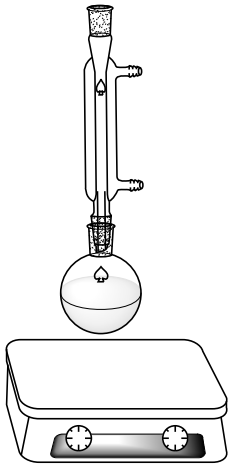
- Sap from seed pod = crude opium (schedule II drug)

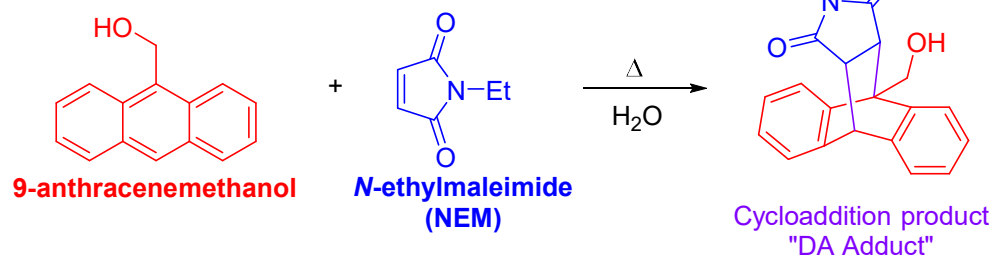
- Grows in central Asia and Latin America – Columbia & Mexico

- Quite different from CA poppy - *Escholzia californica*

1803 – Extraction of Morphine, 10x more powerful – "miracle drug" - analgesic	**1820's** – commercial production (Merck)	**1874** – Heroin synthesis from morphine	**1898 – 1924** medicinal use of heroin

Reaction Set-up





9-anthracenemethanol + ***N*-ethylmaleimide (NEM)** → Cycloaddition product "DA Adduct"

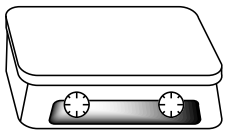
During 1 hr Reflux: **IR & UV-vis spectra of starting materials**

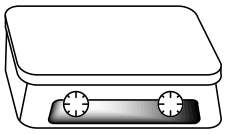
Reaction Work-up = **Vacuum filtration**, wash w/ cold water

Save some crude sample to take **Melting Point** later

<u>Mixed Solvent Recrystallization</u>

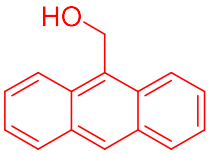
Dissolve in minimum amount of hot **toluene**



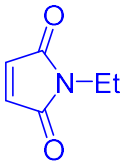


Add **Et_2O** drop-wise until slightly cloudy solution after stirring

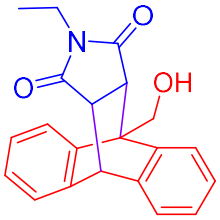
IR Spectroscopy – the search for functional groups



9-anthracenemethanol



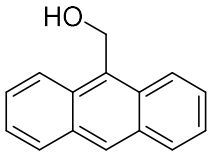
***N*-ethylmaleimide**
(NEM)



Cycloaddition product
"DA Adduct"

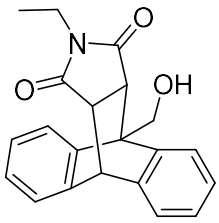
UV-Vis Spectroscopy – The General Idea

More conjugation = lower energy = higher absorbance wavelength (λ_{max})



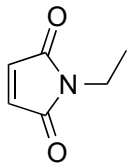
9-anthracenemethanol

vs.



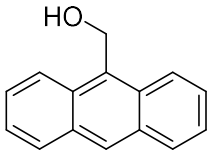
Diels-Alder **Adduct**

Sketch Expected ^{1}H NMR Spectra – *reference with online NMR predictor tool, nmrdb.org*



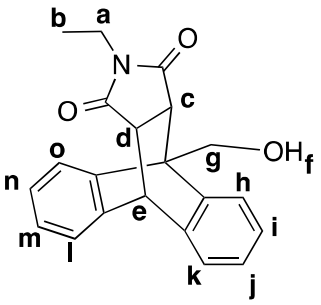
N-ethylmaleimide

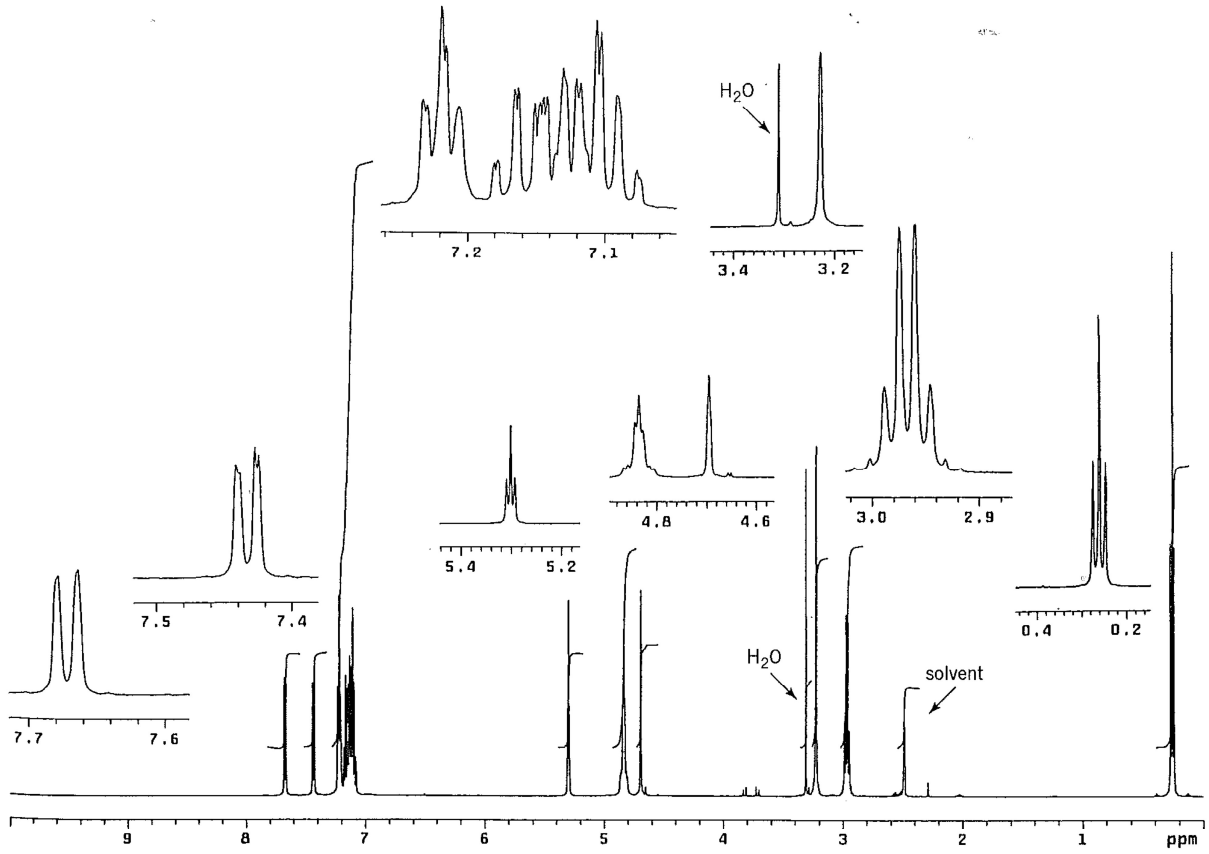
12	Chemical Shift (ppm)	0



9-anthracenemethanol

12	Chemical Shift (ppm)	0





ure 19.13 500-MHz ^{1}H-NMR spectrum of 9-anthracenemethanol-NEM adduct in DMSO-d_6.

Signal (a-o)	Integration	Splitting	Expected Chemical Shift	Observed Chemical Shift
				0.4
				3.0
				3.2
				4.7
				4.8
				5.3
	5H (overlap)			7.1
				7.2
				7.4
				7.7

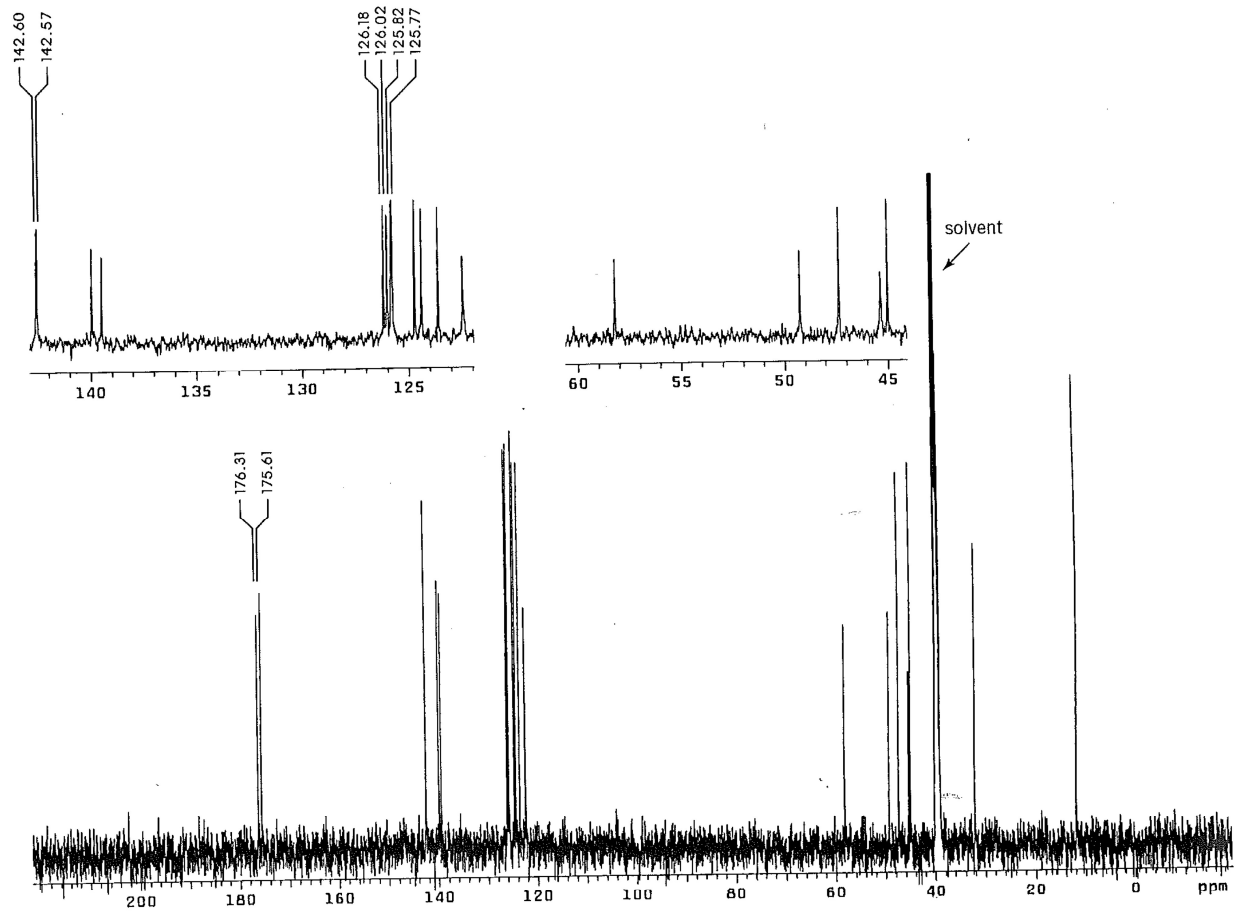
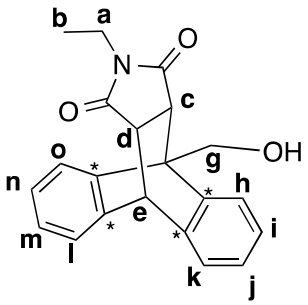


Figure 19.14 125.7-MHz ^{13}C-NMR spectrum of 9-anthracenemethanol-NEM adduct in DMSO-d_6.



Use these designations for unlabeled carbons...
* = aromatic C's without H's
Amide C=O
4º (between c-g)

Signal	Observed Shift	Expected Shift
	10	
	32	
	46	
	45 & 47	
	50	
	57	
	123-125 (4 signals)	
	125-126 (4 signals)	
	139-142 (4 signals)	
	175 & 176	

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