





Photocalorimetry: Validation Methods

Andy Morris, Medway Sciences,
University of Greenwich at Medway

Outline of Talk

- Background to Photocalorimetry Project
- Instrument Design
- Validation Techniques & Actinometry
 - 2-NB
 - Ferrioxalate
 - Spectroradiometry
- Conclusions & Future Work
- Applications to solids

Photocalorimetry

- A new area of interest - small amount of previous work (virtually nothing written about the solid state)
- Many benefits:
 - Rapid analysis - conventional storage testing takes many weeks, calorimetric technique can be done in hours
 - Conventional testing is costly
 - Sensitive analysis - heat changes in the μW range detected
- Apparatus enables testing in both the solid and solution phases
- Can apply data to calorimetric equations for analysis
- Simple experimental setup...

Photocalorimetry – apparatus



Photocalorimetry - Validation

- Apparatus has been developed previously (Lehto *et al.*)
- First need to establish a validation method (*cf* triacetin reaction)
i.e. a system that can be used as a chemical actinometer
- Systems well-known in the literature
 - Solids: nifedipine
 - Solutions: ferrioxalate (conventional)
2-nitrobenzaldehyde (2-NB) (novel)
- Initial work in solution phase - simpler systems, in principle
- More complex validation systems will come later (e.g. solids)

Photocalorimetry - Actinometry

Chemical Actinometers

- A solution containing a chemical compound that undergoes a specific chemical reaction as a result of photon absorption
- Reaction Rate related to the rate at which photons are absorbed by the actinometer
- The actinometer solution is illuminated under the same conditions as the drug samples
- The reaction is followed as a function of illumination time
→ Photon Flux → Photon Flux (Wm^{-2})
- Allows results to be compared quantitatively if a value of H is known....

Photocalorimetry - Actinometry

3 Systems to Compare:

- **2-nitrobenzaldehyde - novel**
- **Potassium Ferrioxalate - established**
- **Spectroradiometry (absolute method)**

Photocalorimetric Calculations

$$I_0 = k_0 / \phi$$

where

I_0 is the irradiance

k_0 is the reaction rate constant

ϕ is the quantum yield

and

$$F_0 = I_0 \cdot V \cdot N_A \cdot E_\lambda / A$$

F_0 is the photon flux

V is the volume of solution

N_A is Avogadro's Number

E_λ is the average light wavelength

A is the area of exposed solution

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Photocalorimetry - Calculations

For a zero order reaction: $\Phi = k_0 HV$

- a value of k_0 which can be applied to $I_0 = k_0/\phi$
- a value of I_0 which can be applied to $F_0 = I_0 \cdot V \cdot N_A \cdot E_\lambda / A$
- a quantitative value (in W / m^2) for the photon flux of a light source

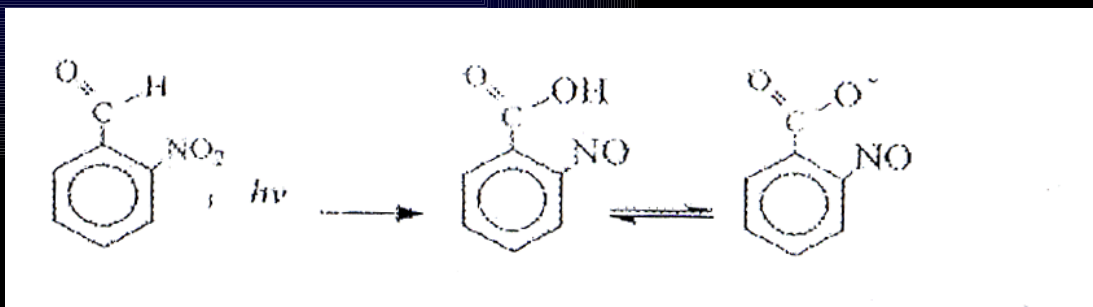
Photocalorimetry - Calculations

For a zero order reaction: $\Phi = k_0 HV$ (D) (from the TAM)

- a value of k_0 which can be applied to $I_0 = k_0/\phi$
- a value of I_0 which can be applied to $F_0 = I_0 \cdot V \cdot N_A \cdot E_\lambda / A$
- a quantitative value for the photon flux of a light source

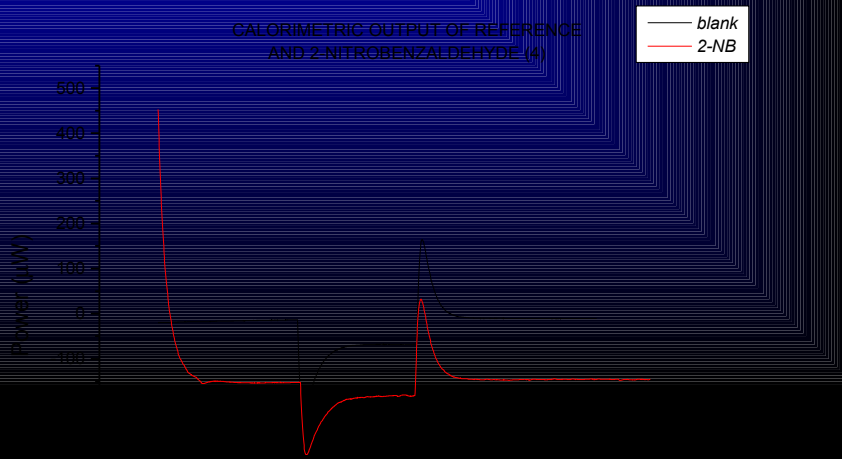
Photocalorimetry - Studies with 2-NB

- Photochemical rearrangement of 2-nitrobenzaldehyde to 2-nitrosobenzoic acid and dissociation of the product yielding H^+



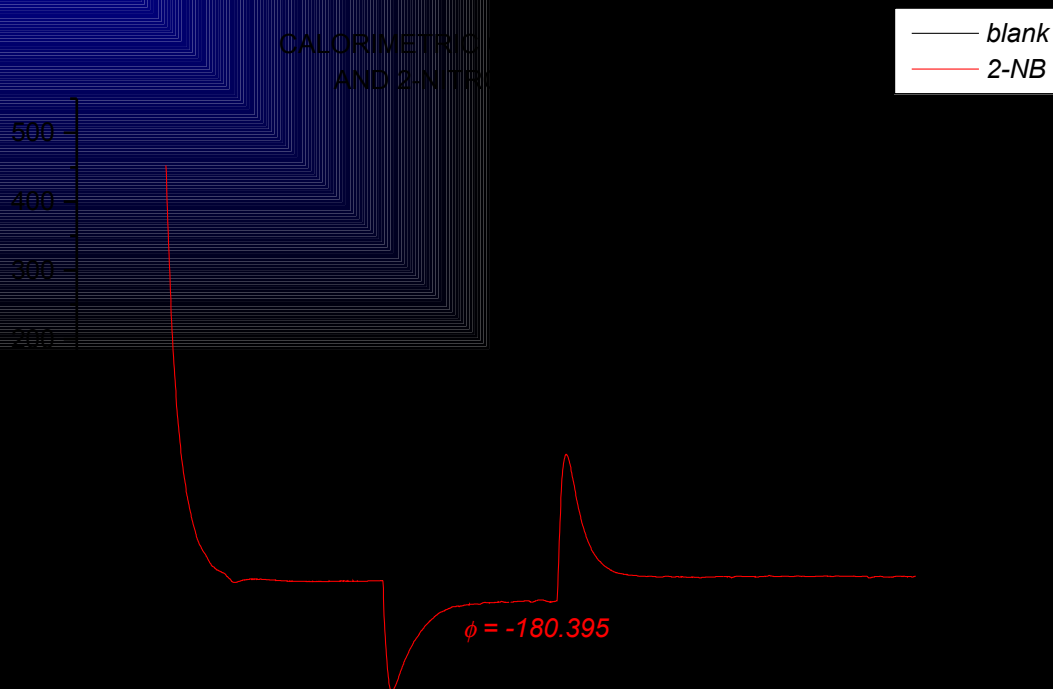
- The quantum yield is 0.5
- Reaction is zero-order (ie linear loss of 2-NB as a function of irradiation time)
- Enthalpy H can be easily determined (202.4 kJmol^{-1})

Photocalorimetry - Studies with 2-NB



- Take measurement after same time has elapsed after light on for each experiment
- Experimental output *should* be a flat line at this point
- Subtract blank from signal to get a value for *phi*

Photocalorimetry - Studies with 2-NB



Photocalorimetry - Studies with 2-NB

Experiment Number	Φ (MW)	H (Jmol ⁻¹)	V (dm ³)	k (mol dm ⁻³ s ⁻¹)
1	-	-	-	
2	110	202464	0.004	1.36 x 10 ⁻⁷
3	116	202464	0.004	1.46 x 10 ⁻⁷
4	114	202464	0.004	1.41 x 10 ⁻⁷
5	114	202464	0.004	1.41 x 10 ⁻⁷

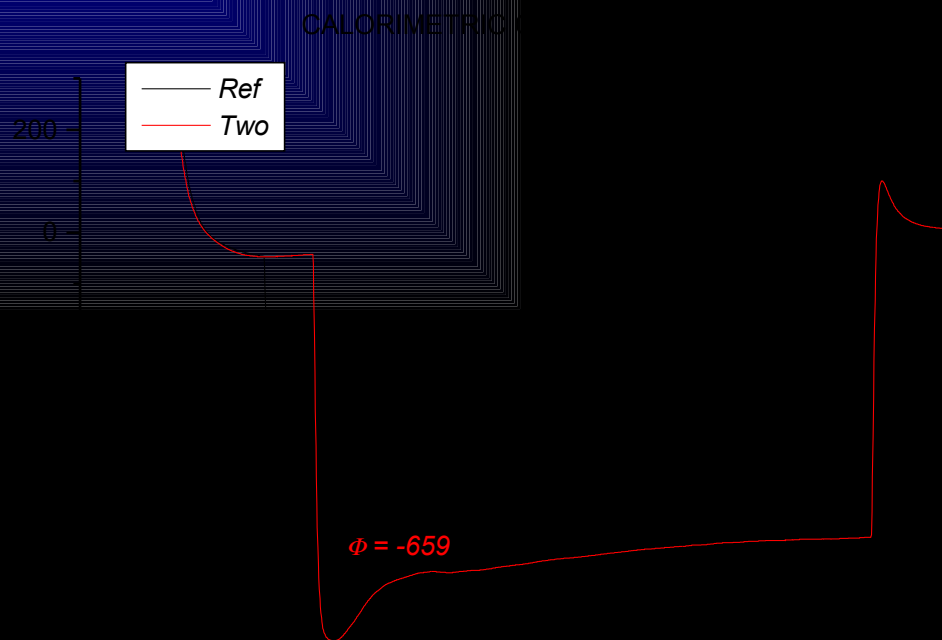
F_0 : 1.1 Wm⁻²

I_0 : 4.2 x 10⁻⁷ einstein dm⁻³ s⁻¹

Photocalorimetry - Studies with Ferrioxalate

- Traditional chemical actinometer
- $2[\text{Fe}(\text{C}_2\text{O}_4)_3]^{3-} \rightarrow 2\text{Fe}(\text{C}_2\text{O}_4)^{2-} + 2\text{CO}_2$
- Many advantages over 2-NB:
 1. Sensitivity
 2. Wavelength Coverage
 3. Photolyte stability and Photolysis Products
 4. Simplicity of operation
 5. Has a known enthalpy
- Highly regarded and widely used
- Adopt the same principles for calculation as before....

Photocalorimetry - Studies with Ferrioxalate



Photocalorimetry - Studies with 2-NB

Experiment Number	Φ (MW)	H (Jmol ⁻¹)	V (dm ³)	k (mol dm ⁻³ s ⁻¹)
1	315	52600	0.004	1.44 x 10 ⁻⁶
2	408	52600	0.004	1.36 x 10 ⁻⁶
3	294	52600	0.004	1.40 x 10 ⁻⁶
4	286	52600	0.004	1.94 x 10 ⁻⁶
5	303	52600	0.004	1.50 x 10 ⁻⁶

F_0 : 4.8 Wm⁻²

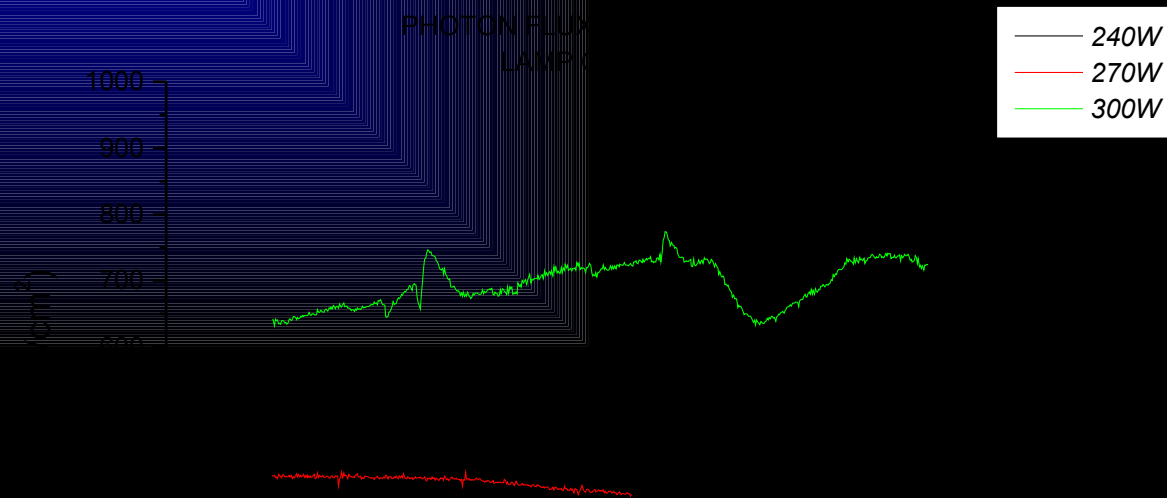
I_0 : 1.9 x 10⁻⁶ einstein dm⁻³ s⁻¹

Photocalorimetry - Spectroradiometry

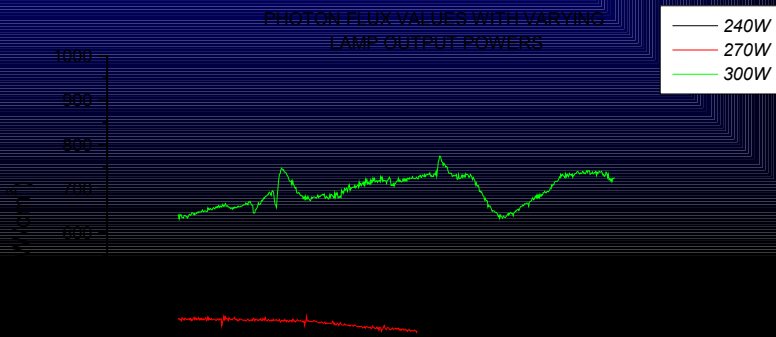
- Spectroradiometers can record irradiance data in real-time
- Available software allows measurement to be carried out directly in Wm^{-2}
- Can connect to the third trifurcated cable on the apparatus
- No chemical method required



Photocalorimetry - Spectroradiometry



Photocalorimetry - Spectroradiometry



Lamp Output (W)	Photon Flux (W/m ²)
240	2.4
270	4.0
300	7.0

Comparing actinometric methods

Method	Mean Photon Flux, F_0 (W/m^2)
2-NB (240W)	1.100
Spectroradiometry (240W)	2.365
<i>Potassium ferrioxalate</i> (300W)	4.800
Spectroradiometry (300W)	6.954

Book value of $F_0 = 1.3 W/m^2$

Comparing actinometric methods

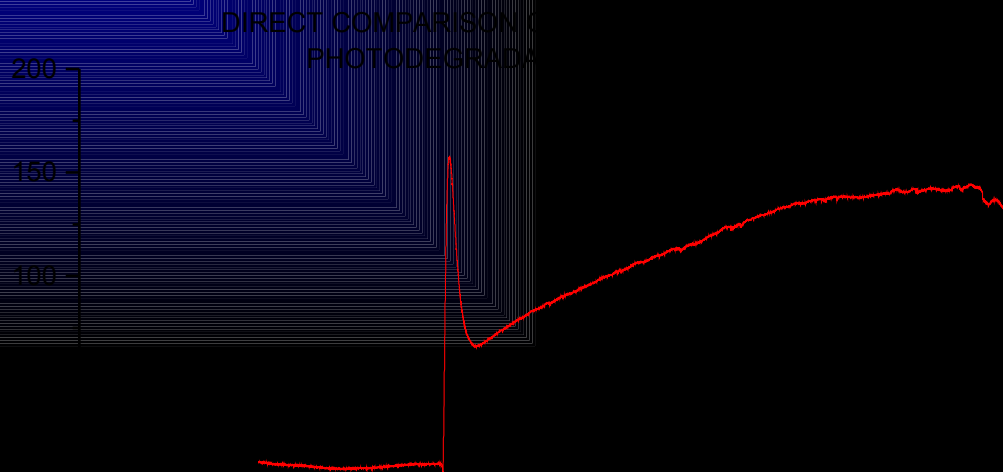
- The values obtained by the two chemical methods compare more favorably than the spectroradiometric method
- 2-NB is more favorable than *potassium ferrioxalate*
 - Steadier calorimetric output (i.e. flat line produced)
 - Easier to prepare and has a longer shelf life
- Interesting that *potassium ferrioxalate* is the IUPAC recommended method
- Investigations into why spectroradiometry is inaccurate need to be carried out

3. Application to Solids

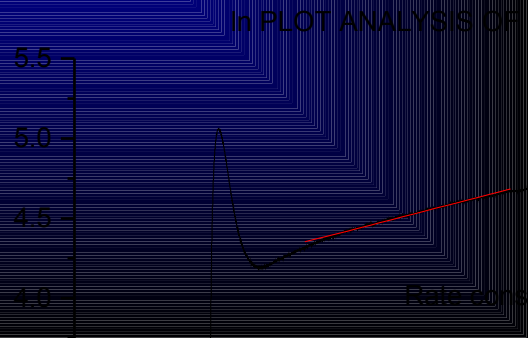
Nifedipine under white light

- No quantitative data recorded for solid state photocalorimetric experiments
- Use *nifedipine* since it is well-known in the literature
- Apparent first-order kinetics - should be easy to spot experimentally
- Acts as a good “test” reaction before moving onto studies involving individual wavelengths of light
- Apply the same rules of analysis as used for *2-NB* and *Potassium Ferrioxalate*
- Talc is used as the reference material

3. Application to Solids: *Nifedipine*



3. Application to Solids: *Nifedipine*



3. Application to Solids: *Nifedipine*

Experiment No	Literature Rate Constant (s ⁻¹)	Experimental Rate Constant (s ⁻¹)
1	7.47 x 10 ⁻⁵	5.79 x 10 ⁻⁵
2	7.28 x 10 ⁻⁵	9.15 x 10 ⁻⁵
3	7.19 x 10 ⁻⁵	9.14 x 10 ⁻⁵
4	7.27 x 10 ⁻⁵	4.50 x 10 ⁻⁵

% error = 2.2 for the first 4000 seconds of reaction

Important since nifedipine photodegradation is complex

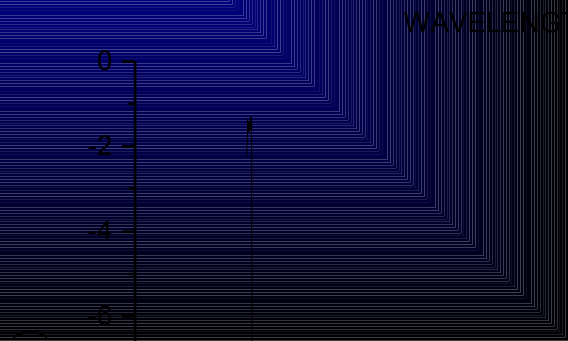


3. Application to Solids

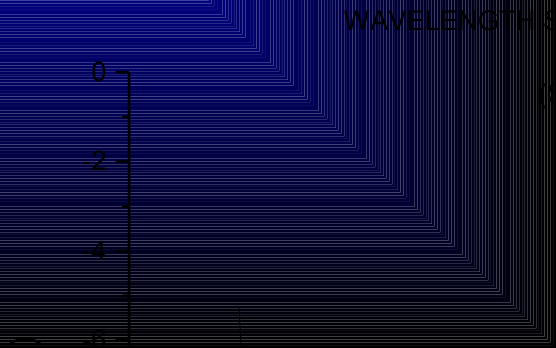
Nifedipine under monochromatic light

- Limited data recorded for solid state photocalorimetric experiments
- Compare with work done by Lehto *et al.*
 - *Reported nifedipine sensitivity at 510nm to 280nm with a maximum at 390nm*
- Use *nifedipine* since it is well-known in the literature
- Wavelength range from 520nm to 300nm
- Scan rate of 10nm / hour
- Use talc as reference material

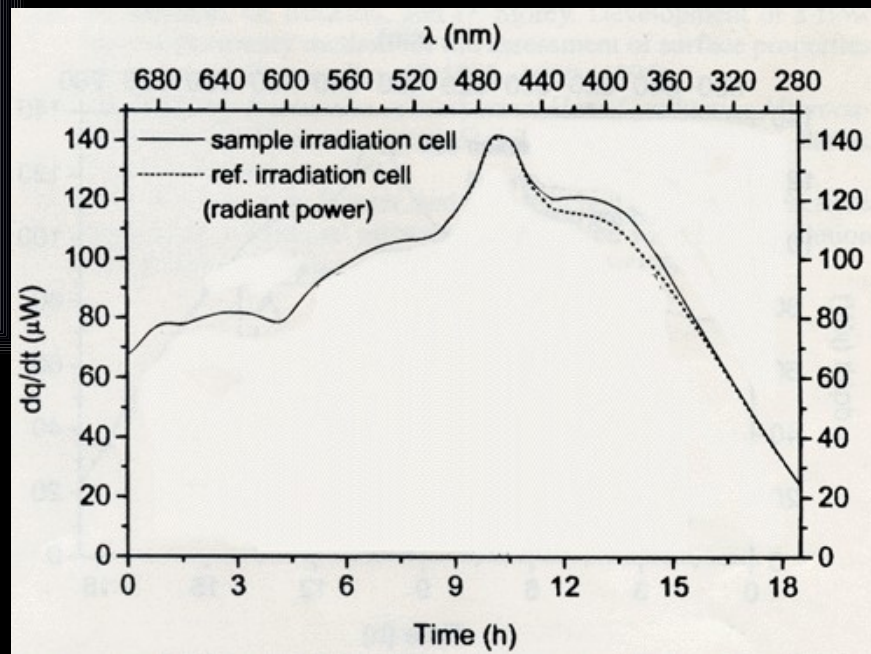
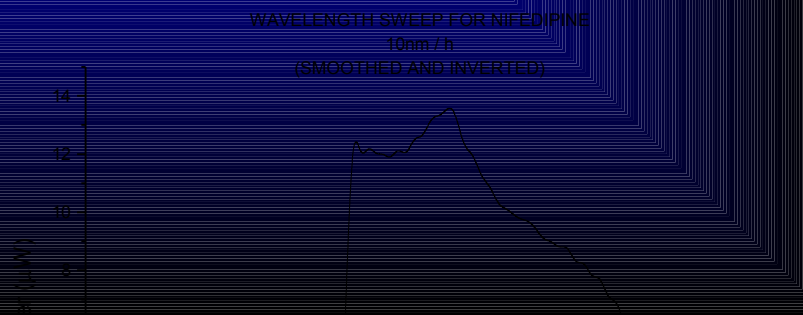
3. Application to Solids: *Nifedipine*



3. Application to Solids: *Nifedipine*



3. Application to Solids: *Nifedipine*



Conclusions and Future Work

- Photocalorimeter designed and built successfully
- 2 main options exist for actinometer selection in solution phase
 - *2-NB v Potassium Ferrioxalate*
 - 2-NB is more stable; easier to prepare and has a simple calorimetric output
- *Nifedipine* is a suitable validation material - first quantitative measurements presented here
 - Complexity is a problem after 4000 s - Use of Chemometrics
- Investigations into effect of wavelength on nifedipine were successful. Further work will investigate the effect of moisture, temperature etc on calorimetric output at different wavelengths

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