The Potential of 2-Nitrobenzaldehyde as a Chemical Test and Reference Reaction for Photocalorimetry
- Giauque Travel Award Presentation -

M. Dhuna [S], S. Gaisford[C], M.A.A. O'Neill and A.E. Beezer
The School of Pharmacy, University of London, London, U.K.
simon.gaisford@pharmacy.ac.uk

J.A. Connor
Natural Resources Institute, University of Greenwich, Medway Campus, Chatham Maritime, Kent, U.K.

D. Clapham
GlaxoSmithKline, Harlow, Essex, U.K.

Recent work from our group has reported the development of a photocalorimeter, the specific aim of the project being to develop a robust system capable of quantifying the photostability of pharmaceuticals [1]. The system uses an optical beamsplitter and liquid light guides to direct light from a Xe arc lamp into sample and reference ampoules (20 mL volume). The amount of light entering both cells can be adjusted by a number of focusing and shuttering assemblies; the amount of light entering the sample side can be set to a predefined level while the light entering the reference side is adjusted until a zero baseline signal is achieved. Thus the calorimeter itself is used as a null-adjuster to ensure parity between the sample and reference sides.

The light entering the sample side can be quantified using an actinometer but, as we have discussed previously, it is preferable to be able to validate instrumental parameters using in-situ methods [2]. This led us to consider the use of chemical actinometers for validating photocalorimeters and is the focus of this paper. ICH guideline Q1B (Photostability testing of new active substances and medicinal products) indicates a chemical actinometer based on quinine while IUPAC indicates, among others, the use of potassium ferrioxalate [3]. However, both these systems have drawbacks; the quantum yield of quinine photodegradation has not been determined while potassium ferrioxalate is difficult to handle. For these reasons, we decided to investigate the suitability of an alternative system; the photodegradation of 2-nitrobenzaldehyde (2-NB). The photodegradation of 2-NB is considered to follow zero-order kinetics [4] and, hence, should give a constant deflection from zero in the photocalorimeter. The output would then be described by; $\Phi = k\Delta HV$ where Φ is power, k is the zero-order rate constant, ΔH is the reaction enthalpy and V is volume. The calorimetric data settled to a zero-order deflection after ca. 5 h. However, in order to derive the value of ΔH, the value of k must be known. There is no literature value for k, so we followed the reaction using the change in pH as the photodegradation product, 2-nitrosobenzoic acid, built up. It became clear from these data that an additional oxidation event occurred in addition to photodegradation; when EDTA was added to the system zero-order degradation was observed, giving a rate constant of ca. 2.5×10^{-7} mol dm^{-3} s^{-1}. The oxidation event would clearly impact upon the measured response in the photocalorimeter and was the likely cause of the non zero-order behavior seen during the first 5 h of measurement. Hence, the data show that 2-NB has potential as a chemical actinometer for photocalorimeters but care must be taken during its preparation and use.

[1] Dhuna, et. al., *British Pharmaceutical Conference*, MICC, UK 26th-28th Sept. (2004).
[2] Beezer, et. al., *Thermochimica Acta*, **380**, 13-17 (2001).
[3] Wadso I, et. al., *Pure and App. Chem.* **73**, 1625-1639 (2001).
[4] Allen JM, et. al., *J. Pharm. Biomed. Anal.* **24**, 167-178 (2000).