Supplementary Material (ESI) for Photochemical & Photobiological Sciences

An antenna triplet sensitizer for 1-acyl-7-nitroindolines improves the efficiency of carboxylic acid photorelease

George Papageorgiou,[a] Matthew Lukeman,[b] Peter Wan[b] and John E.T. Corrie*[,a]

[a]*National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, U.K. and* [b]*Department of Chemistry, Box 3065, University of Victoria, Victoria, British Columbia, Canada V8W 3V6*

Electronic Supplementary Information

4-(2-Bromoethoxy)benzaldehyde

This preparation was a modification of the method of Reunitz et al.[1] 1,2-Dibromoethane (188 g, 1 mol) was added in one portion to a solution of 4-hydroxybenzaldehyde (12.21 g, 100 mmol) and KOH (5.61 g, 100 mmol) in a mixture of boiling *n*-butanol (200 mL) and DMF (50 mL) and the mixture was heated under reflux for 18 h. After cooling to room temperature, the precipitated solid was filtered off, washed with DMF and the filtrate was concentrated under vacuum. The residue was dissolved in Et_2O (200 mL) and washed with 1 M aq. NaOH and brine, dried and evaporated to give a brown oil (12.51 g) which crystallised on standing in the fridge. Recrystallisation from Et_2O–petroleum ether followed by flash chromatography [EtOAc–petroleum ether (1:9)] of the mother liquor to recover additional product gave the title compound as white crystals (8.57 g, 37%) mp 49-50 °C (from Et_2O–petroleum ether) (lit.[2] mp 52 °C); ^{1}H NMR: (90 MHz) δ 9.88 (s, 1H), 7.83 (2H, d, J = 8 Hz), 7.02 (2H, d, J = 8 Hz), 4.37 (2H, t, J = 6 Hz) and 3.66 (2H, t, J = 6 Hz).

4-[(*tert*-Butyldimethylsilyl)oxy]-1-bromobenzene 7

This was adapted from an outline procedure of Angle and Louie.[3] To a solution of 4-bromophenol (10.38 g, 60 mmol) and imidazole (6.13 g, 90 mmol) in dry CH_2Cl_2 (150 mL) was added dropwise a solution of *tert*-butyldimethylsilyl chloride (10.85 g, 72 mmol) in dry CH_2Cl_2 (50 mL) and the mixture was stirred under nitrogen at room temperature for 18 h. The cloudy solution was diluted with CH_2Cl_2 (100 mL) and washed successively with 0.5 M aq. HCl, 0.5 aq. NaOH and brine. The organic phase was dried and evaporated to give a colourless liquid which was fractionally distilled under reduced pressure to give **7** as a colourless oil (16.50 g, 96%), bp 76-78 °C, 0.25 mm Hg, (lit.[3] bp 120-125 °C, 1 mmHg); ^{1}H NMR: (90 MHz) δ 7.32 (2H, d, J = 8 Hz), 6.70 (2H, d, J = 8 Hz), 0.97 (9H, s) and 0.18 (6H, s).

4-(2-Bromoethoxy)-4'-[(*tert*-butyldimethylsilyl)oxy]benzhydrol 8

A solution of the TBDMS ether **7** (6.32 g, 22 mmol) in dry THF (44 mL), cooled under N_2 to -78 °C, was treated dropwise with *tert*-BuLi (1.7 M solution in pentane; 13.2 mL, 22.5 mmol), keeping the temperature below -76 °C. The solution was stirred for 2 h at -78 °C and a solution of 4-(2-bromoethoxy)benzaldehyde (4.58 g, 20 mmol) in dry THF (60 mL) was added dropwise, keeping the same temperature control. The solution was then allowed to warm to 0 °C and stirred for a further 2 h, diluted with ether (200 mL) and washed with saturated aq. $NaHCO_3$ and brine. The organic phase was dried, evaporated and flash chromatographed [petroleum ether, then EtOAc–petroleum ether(1:4)] to give **8** as a pale oil (6.98 g, 80%) which was used in the next step without further purification. ^{1}H NMR: (90 MHz) δ 7.08-7.36 (4H, m), 6.68-6.96 (4H, m), 5.70

(1H, d, *J* = 3.6 Hz), 4.24 (2H, t, *J* = 6 Hz), 3.58 (2H, t, *J* = 6 Hz), 2.32 (1H, d, *J* = 3.6 Hz), 0.97 (9H, s) and 0.18 (6H, s).

4-(2-Bromoethoxy)-4'-hydroxybenzophenone 9

A solution of the benzhydrol **8** (6.44 g, 14. 7 mmol) in CH_2Cl_2 (250 mL) was treated with manganese(IV) oxide (14.7 g) and the mixture was stirred at room temperature for 3.5 h, then filtered through Celite. The filtrate was evaporated to leave the TBDMS ether of **9** as a pale oil (6.40 g, 100%) which was used in the next step without further purification. ^{1}H NMR: (90 MHz) δ 7.60-7.88 (4H, m), 6.80-7.08 (4H, m), 4.36 (2H, t, *J* = 6 Hz), 3.66 (2H, t, *J* = 6 Hz), 1.00 (9H, s) and 0.25 (6H, s).

A solution of the above TBDMS ether (13.76 g, 32 mmol) in THF (250 mL) was cooled to 0 °C and treated with glacial acetic acid (1.92 g, 32 mmol) and 1 M TBAF (32 mL, 32 mmol) for 20 min. The solution was concentrated to ~80 mL, diluted with water (250 mL) and extracted with Et_2O (3 × 120 mL). The combined organic phases were washed with brine, dried and flash chromatographed [EtOAc–petroleum ether (3:7)] to give **9** as pale crystals (7.57 g,74%), mp 139-140 °C (from EtOAc–petroleum ether), (lit.[4] 139-142 °C).

Progressive photolysis of 4

A solution of **4** (0.32 mM in 25 mM Na phosphate, pH 7.0) was irradiated in a 1-mm path length cell for increasing times in the range 0-70 s. The extent of photolysis was monitored by UV spectroscopy. Conversion was ~50% after 20 s and no further change was observed after 50 s (Fig. 2). As a control experiment, a solution of methyl 1-[5-(dihydroxyphosphoryloxy)pentanoyl]-7-nitroindoline-5-acetate **22** (0.27 mM) was

irradiated for increasing times up to 8 min under the same conditions. Conversion was ~50% after ~2 min and near-complete photolysis required irradiation for >6 min.

Relative photolysis efficiencies of 4 and 22

Separate solutions of **4** and **22** (each 0.28 mM in 25 mM Na phosphate, pH 7.0 with 5 mM dithiothreitol) were simultaneously irradiated in 1-mm path length cells. The solutions were analysed by reverse-phase HPLC with mobile phase 25 mM Na phosphate, pH 6.0–MeCN (10:4 v/v) for **4**, t_R 4.2 min and 25 mM Na phosphate, pH 6.0–MeCN (4:1 v/v) for **22**, t_R 5.0 min. The extent of photolysis of each solution was determined by comparison of peak areas with those of non-irradiated controls and quantification was by measurement of peak heights. After 8 s irradiation, conversions for **4** and **22** were 41% and 2.7% respectively. A 39% conversion of **3** was reached after 120 s irradiation, indicating that **4** photolysed about 16-fold more efficiently than **22**.

References

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(3) S.R. Angle and M.S. Louie, *J. Org. Chem.*, 1991, **56**, 2853.

(4) J.A. Katzenellenbogen, T. Tatee and D.W. Robertson, *J. Labelled Compd. Radiopharm*., 1981, **18**, 865.

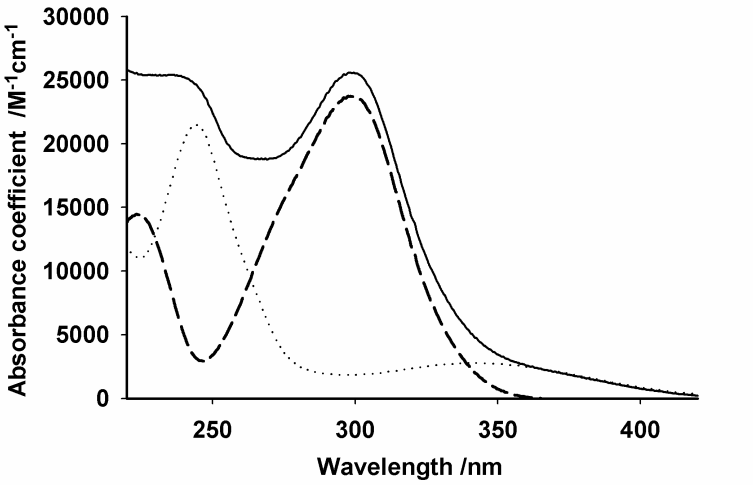

Fig. 1. Measured absorption spectra for aqueous solutions of **1** (·····) and **11** (-----) and the sum of these two spectra, i.e. calculated spectrum of **4** (——).

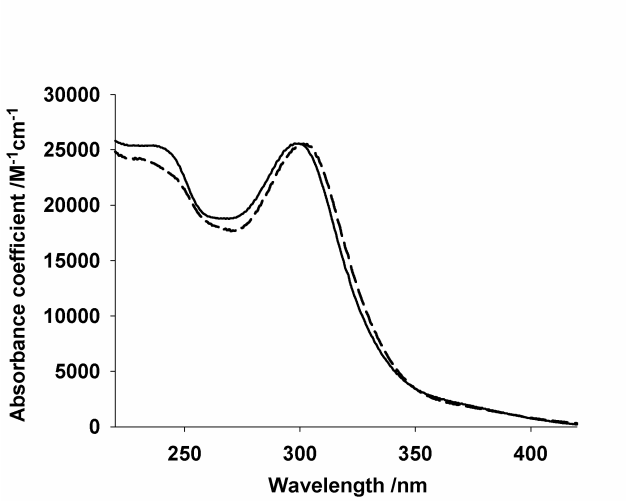

Fig. 2. Comparison of the calculated (——) and experimental (-------) UV-Vis spectra for **4**. The experimental spectrum is normalised to the calculated spectrum at the calculated absorbance maximum (300 nm).

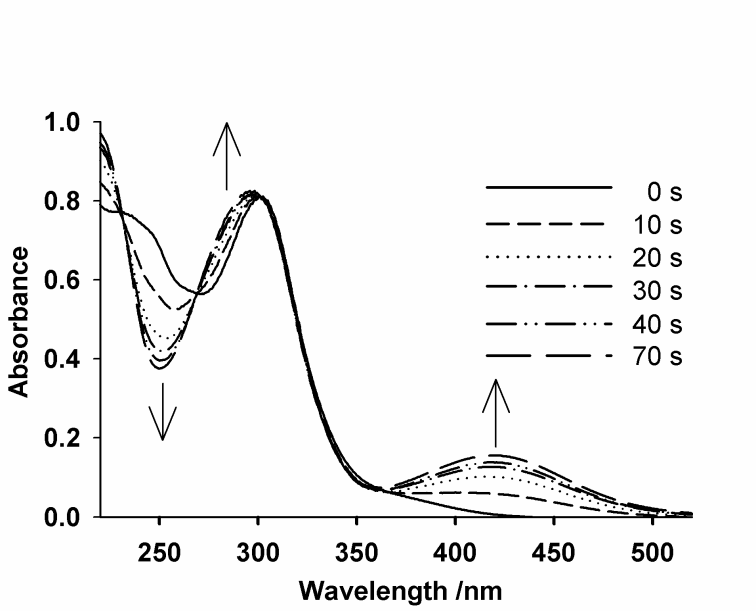

Fig. 3. UV-Vis absorption spectra for an aqueous solution of **4** after 300 nm irradiation for the cumulative time periods indicated. Arrows indicate the direction of absorbance changes with increasing irradiation time.

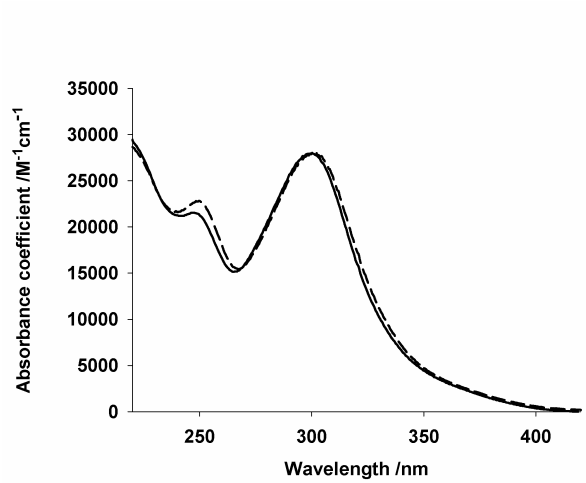

Fig. 4. Comparison of the calculated (——) and experimental (-------) UV-Vis spectra for **5**. The experimental spectrum is normalised to the calculated spectrum at the calculated absorbance maximum (300 nm).