

## SUPPORTING INFORMATION

### Effect of imidazolium room-temperature ionic liquids on aggregation of amphotericin B: a circular dichroism study

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## Materials and methods

All reagents and solvents were purchased from commercial sources (Sigma-Aldrich, Acros, Alfa, Aesar) and were used as received. Ionic liquids were synthesized and purified according to literature procedures; see below for details.<sup>1</sup> NMR spectra were recorded on a Varian (300 MHz) spectrometer. <sup>1</sup>H NMR chemical shifts are reported in ppm ( $\delta$ ) downfield from residual DMSO in DMSO-d<sub>6</sub> or residual acetone in acetone-d<sub>6</sub>; <sup>19</sup>F resonances are reported relative to trifluoroacetic acid ( $\delta = -76.5$  ppm).

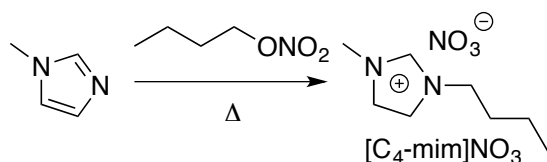
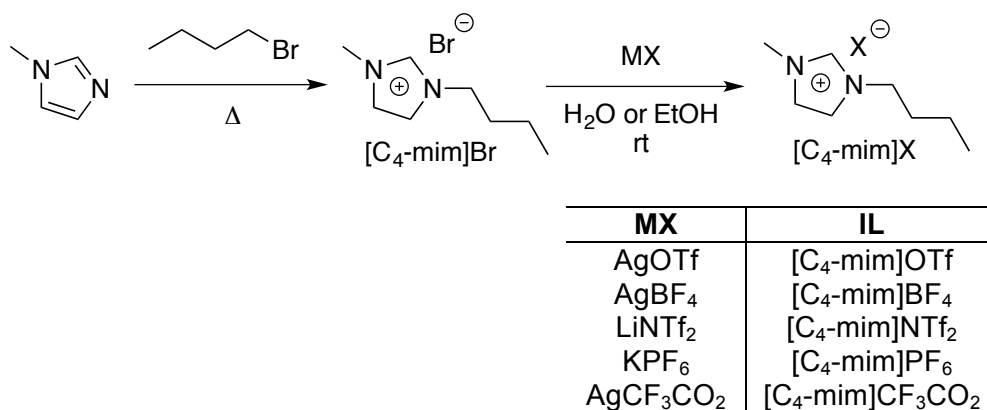
AmB (80% preparation from *Streptomyces*, Sigma Aldrich) was dissolved in DMSO (50 mM), and was subsequently sonicated for 15-20 seconds and centrifuged at room temperature. The supernatant was withdrawn, portioned into 30-50  $\mu$ L fractions and used as AmB stock. The AmB stock solution was prepared fresh before each experiment and used within 8 hours. AmB stock solution was added to the ionic liquid or molecular solvent to achieve 500  $\mu$ M solution of AmB (with 1 % DMSO, v/v), followed by vortexing for 20-30 sec, prior to acquisition of the CD and UV-vis spectra. The handling of AmB, that is, sample preparation and spectroscopic measurements, was done in a red light environment with minimal exposure of the solution to ambient light.

CD spectra were acquired on a Jasco J-815. CD transitions of AmB (300 – 450 nm) were recorded using a 0.01 cm demountable quartz cell. Spectra were recorded at room temperature and 1 nm resolution with a scan rate of 100 nm/min; two scans were acquired and averaged for each sample. Raw data were manipulated by subtraction of appropriate background spectra, and low intensity CD spectra were smoothed using manufacturer provided software. All CD spectra were normalized to the most intense positive peak.

Absorbance measurements were performed on Agilent UV-visible instrument using a 0.01 cm demountable quartz cell with a resolution of 1 nm. All UV-vis spectra were normalized to the most intense peak.

## Synthesis and characterization of ionic liquids

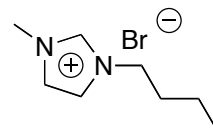
All ionic liquids were prepared according to literature procedures<sup>1</sup> following the general sequences (Scheme 1). All ionic liquids were purified as follows: ionic liquids were dissolved in CH<sub>2</sub>Cl<sub>2</sub>, followed by filtration to remove inorganic impurities. Next, ionic liquids were repeatedly treated with charcoal in EtOH at elevated temperatures followed by filtration and removal of EtOH in vacuo (for azeotropic removal of residual water). Finally, the ionic liquids were dried under vacuum for 8-12 hours. All sample preparations and spectroscopic measurements were conducted immediately after removing the ionic liquids from the vacuum with care to minimize exposure to moisture.



Scheme 1. Syntheses of ionic liquids.

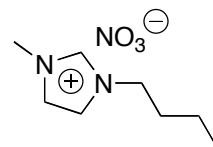
### [C<sub>4</sub>-mim]Br:<sup>2</sup>

<sup>1</sup>H NMR (300 MHz, acetone-d<sub>6</sub>): δ = 10.21 (1H, s), 7.88 (1H, s), 7.80 (1H, s), 4.44 (2H, t, *J* = 7.5 Hz), 4.10 (s, 3H), 1.93 (2H, pent, *J* = 7.5 Hz), 1.37 (2H, sept, *J* = 7.5 Hz), 0.94 (3H, t, *J* = 7.5 Hz).



### [C<sub>4</sub>-mim]NO<sub>3</sub>:<sup>3</sup>

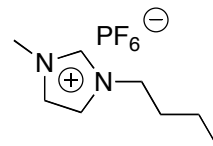
<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>): δ = 9.18 (s, 1H), 7.78 (s, 1H), 7.70 (s, 1H), 4.15 (t, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.74 (pent, *J* = 7.4 Hz, 2H), 1.23 (sext, *J* = 7.4 Hz, 2H), 0.87 (t, *J* = 6.9 Hz, 3H).



**[C<sub>4</sub>-mim]PF<sub>6</sub>**<sup>4</sup>

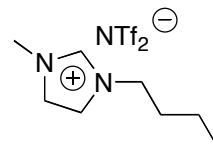
<sup>1</sup>H NMR (300 MHz acetone-d<sub>6</sub>): δ = 8.94 (s, 1H), 7.73 (s, 1H), 7.68 (s, 1H), 4.35 (t, *J* = 7.2 Hz, 2H), 4.07 (s, 3H), 1.92 (pent, *J* = 7.5 Hz, 2H), 1.38 (sext, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 6.9 Hz, 3H);

<sup>19</sup>F NMR (282 MHz acetone-d<sub>6</sub>): δ = -72.9 (d, *J* = 706.0 Hz).

**[C<sub>4</sub>-mim]NTf<sub>2</sub> (also known as [C<sub>4</sub>-mim]N(SO<sub>3</sub>CF<sub>3</sub>)<sub>2</sub>)**<sup>4</sup>

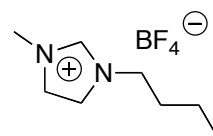
<sup>1</sup>H NMR (300 MHz DMSO-d<sub>6</sub>): δ = 9.02 (s, 1H), 7.76 (s, 1H), 7.71 (s, 1H), 4.37 (t, *J* = 7.2 Hz, 2H), 4.06 (s, 3H), 1.93 (pent, *J* = 7.5 Hz, 2H), 1.38 (sext, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 6.9 Hz, 3H);

<sup>19</sup>F NMR (282 MHz DMSO-d<sub>6</sub>): δ = -80.4 (s).

**[C<sub>4</sub>-mim]BF<sub>4</sub>**<sup>5</sup>

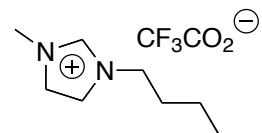
<sup>1</sup>H NMR (300 MHz, acetone- d<sub>6</sub>): δ = 8.91 (1H, s), 7.72 (t, *J* = 1.7 Hz, 1H), 7.66 (t, *J* = 1.7 Hz, 1H), 4.31 (t, *J* = 7.4 Hz, 2H), 4.0 (s, 3H), 1.89 (pent, *J* = 7.5 Hz, 2H) 1.37 (sext, *J* = 7.5 Hz, 4H), 0.92 (3H, t, *J* = 7.4 Hz);

<sup>19</sup>F NMR (282 MHz, acetone- d<sub>6</sub>): δ = -150.96 (m).

**[C<sub>4</sub>-mim]CF<sub>3</sub>CO<sub>2</sub>**<sup>6</sup>

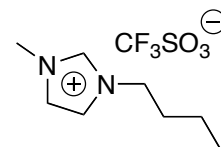
<sup>1</sup>H NMR (300 MHz, acetone-d<sub>6</sub>) δ = 9.93 (s, 1H), 7.89 (t, *J* = 1.65 Hz, 1H), 7.82 (t, *J* = 1.8 Hz, 1H), 4.37 (t, *J* = 7.2 Hz, 2H), 4.05 (s, 3H), 1.89 (pent, *J* = 7.35, 2H), 1.36 (sext, *J* = 7.44, 2H), 0.92 (t, *J* = 7.35, 3H);

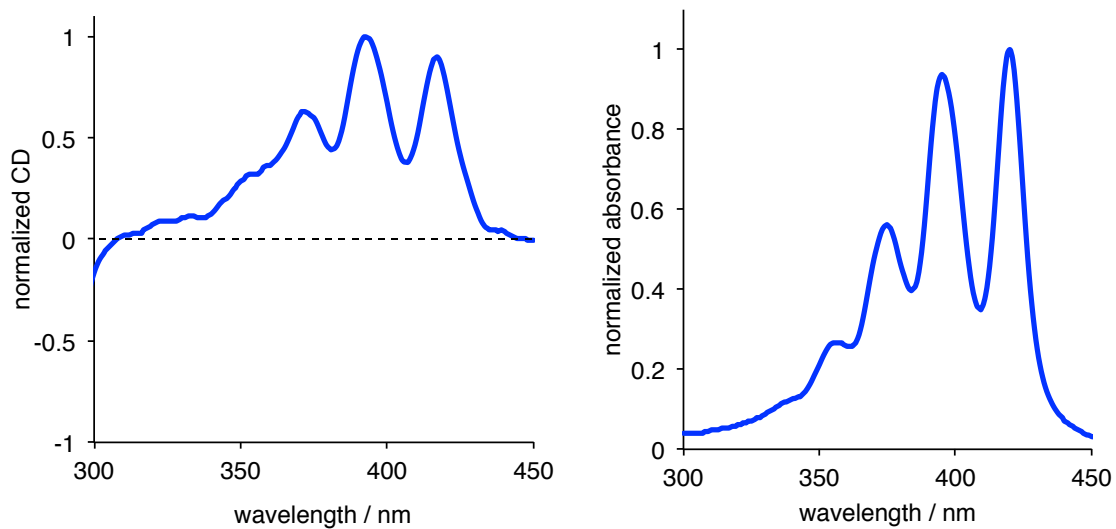
<sup>19</sup>F NMR (282 MHz, acetone-d<sub>6</sub>) δ = -75.53 (s);

**[C<sub>4</sub>-mim]OTf (also known as [C<sub>4</sub>-mim]CF<sub>3</sub>SO<sub>3</sub>)**<sup>6</sup>

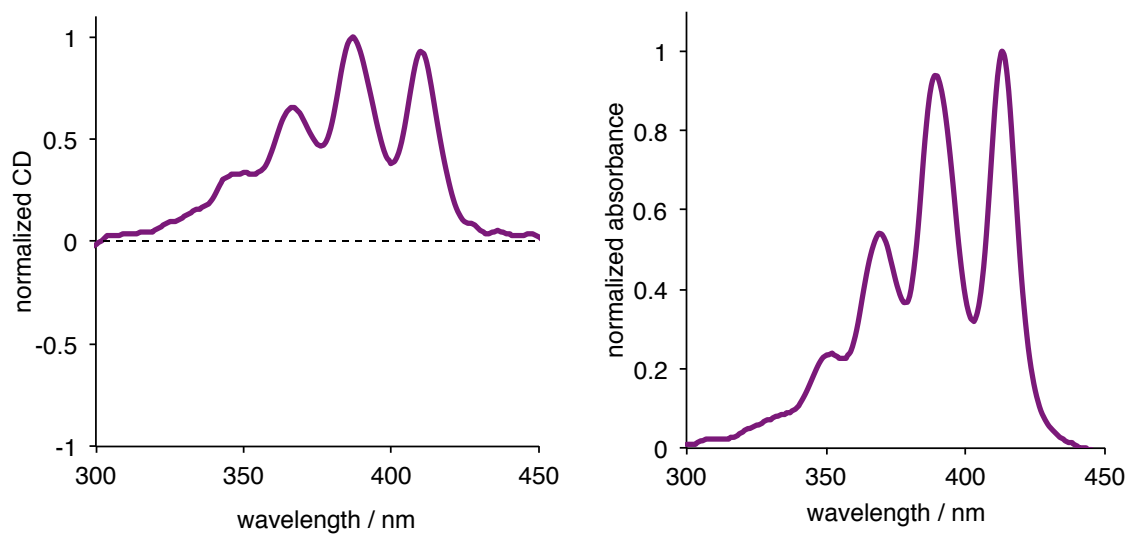
<sup>1</sup>H NMR (300 MHz DMSO-d<sub>6</sub>): δ = 9.08 (s, 1H), 7.75 (s, 1H), 7.68 (s, 1H), 4.13 (t, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 1.73 (p, *J* = 7.5 Hz, 2H), 1.22 (sept, *J* = 7.5 Hz, 2H), 0.88 (t, *J* = 6.9 Hz, 3H);

<sup>19</sup>F NMR (282 MHz DMSO-d<sub>6</sub>): δ = - 78.2 (s).<sup>4</sup>

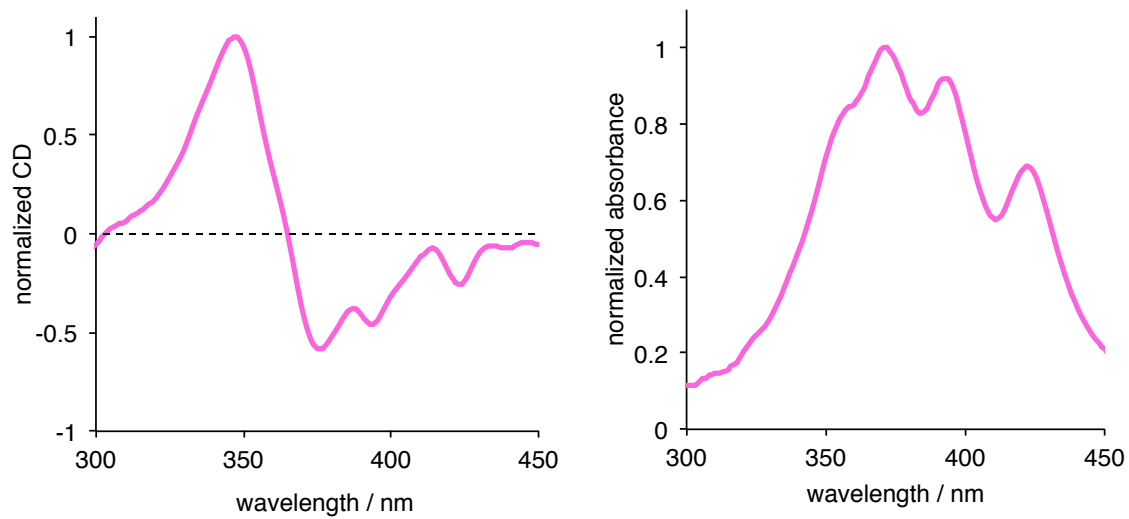




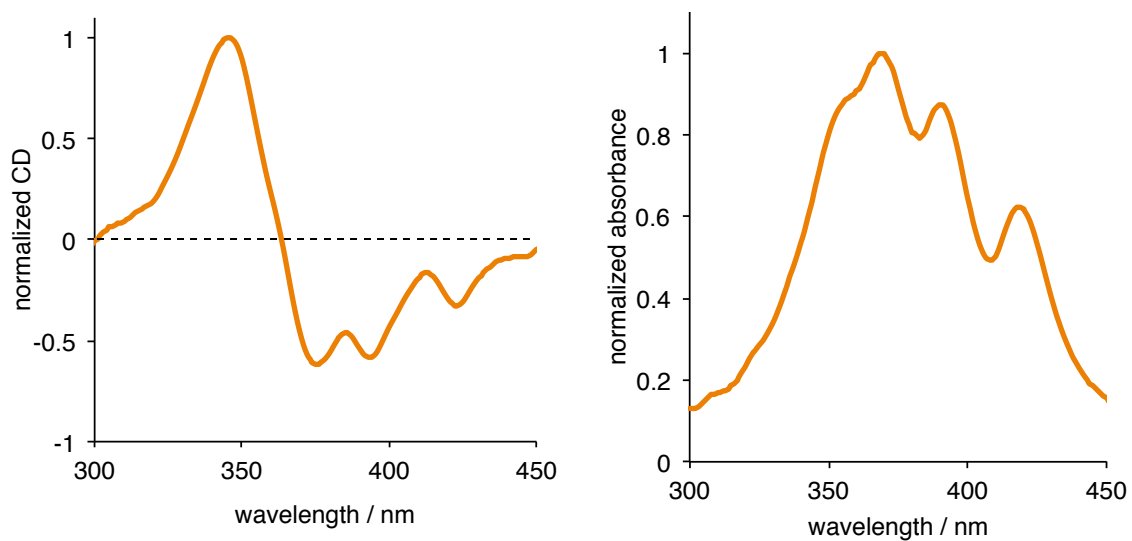
**Figure S1.** CD (left) and UV-vis (right) spectra of AmB in [C<sub>4</sub>-mim]Br.



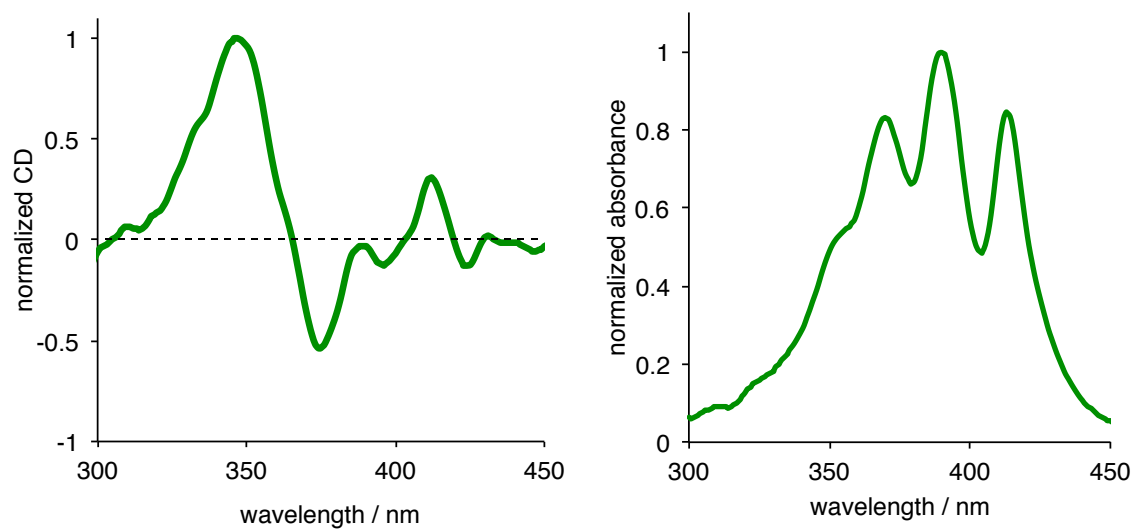
**Figure S2.** CD (left) and UV-vis (right) spectra of AmB in [C<sub>4</sub>-mim]CF<sub>3</sub>CO<sub>2</sub>.



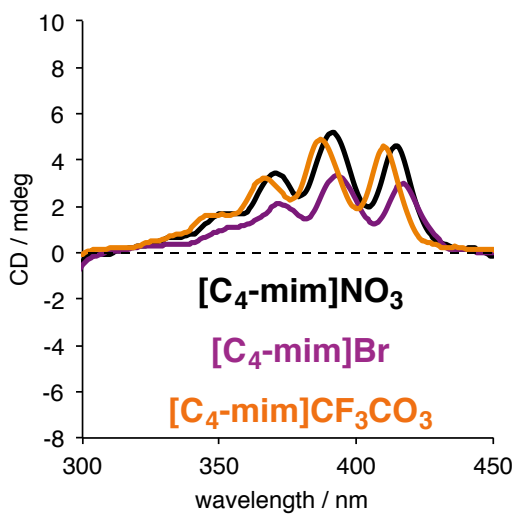
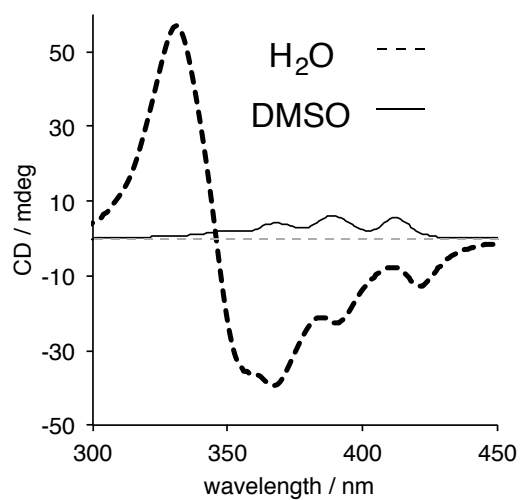
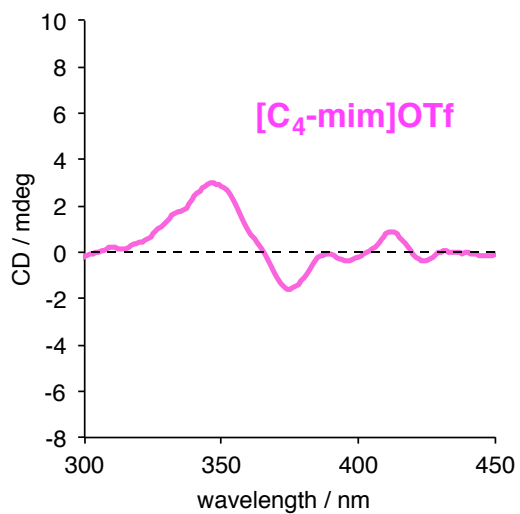
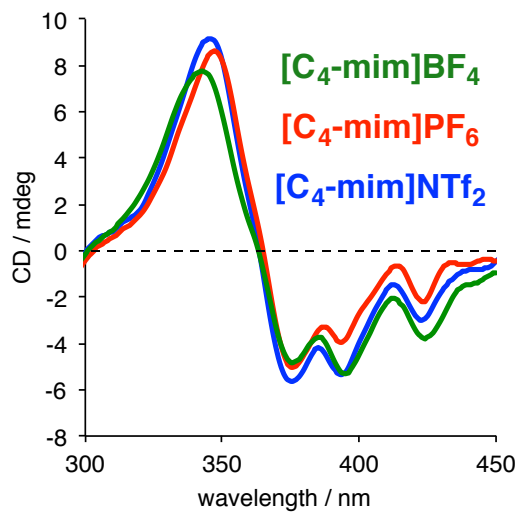
**Figure S3.** CD (left) and UV-vis (right) spectra of AmB in  $[C_4\text{-mim}]PF_6$ .



**Figure S4.** CD (left) and UV-vis (right) spectra of AmB in  $[C_4\text{-mim}]NTf_2$ .



**Figure S5.** CD (left) and UV-vis (right) spectra of AmB in [C<sub>4</sub>-mim]OTf.



**Figure S6.** CD spectra of AmB (500  $\mu$ M) in ionic liquids and molecular solvents



## References

1. (a) J. G. Huddleston, H. D. Willauer, R. P. Swatloski, A. E. Visser, R. D. Rogers, *Chem. Commun.*, **1998**, 1765; (b) S. V. Dzyuba, R. A. Bartsch, *J. Heterocyclic Chem.*, **2001**, 38, 265; (c) S. V. Dzyuba, K. D. Kollar, S. S. Sabnis, *J. Chem. Ed.*, **2009**, 86, 856.
2. A. Xu, J. Wang, H. Wang, *Green Chem.*, **2010**, 12, 268.
3. N. W. Smith, S. P. Gourisankar, J.-L. Montchamp, S. V. Dzyuba, *New J. Chem.*, **2011**, 35, 909.
4. S. V. Dzyuba, R. A. Bartsch, *ChemPhysChem*, **2002**, 3, 161.
5. J. D. Holbrey, K. R. Seddon, *J. Chem. Soc. Dalton Trans.*, **1999**, 2133.
6. P. Bonhôte, A.-P. Dias, N. Papageorgiou, K. Kalyanasundaram, M. Grätzel, *Inorg. Chem.*, **1996**, 35, 1168