

## Electronic Supplementary Information

# Synthesis and Biological Evaluation of Amphotericin B based on Organic Salts and Ionic Liquids against *Leishmania Infantum*

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## Synthesis of OSILs-AmB

In order to minimize the impact from Grob fragmentation and ester hydrolysis, the following OSILs-API based on amphotericin B were prepared using dried solvents (water-free conditions at the beginning of the reaction):

1. [Aliquat][AmB]
2. [Ch][AmB]
3. [C<sub>2</sub>OHMIM][AmB]
4. [C<sub>3</sub>OMIM][AmB]
5. [C<sub>16</sub>Pyr][AmB]
6. [P<sub>6,6,6,14</sub>][AmB]

# 1. [Aliquat][AmB]

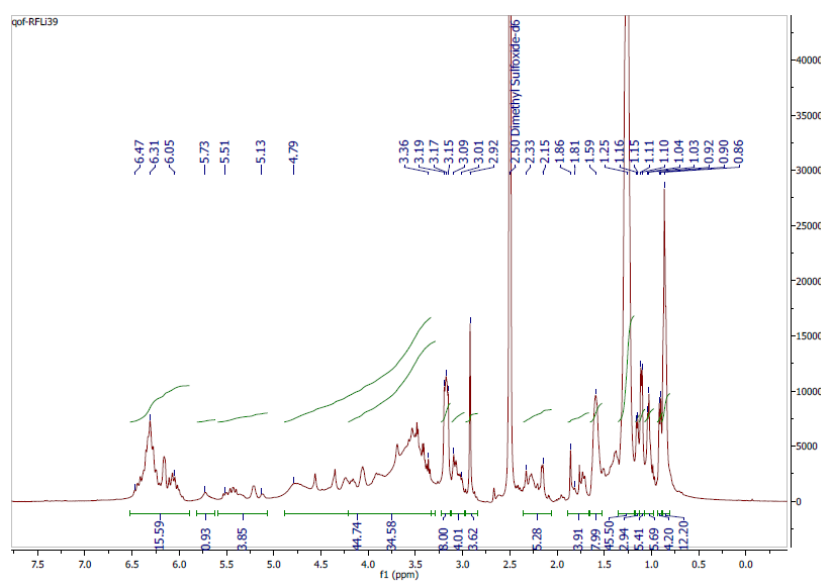


Figure S1: [Aliquat][AmB] <sup>1</sup>H-NMR spectrum in (CD<sub>3</sub>)<sub>2</sub>SO

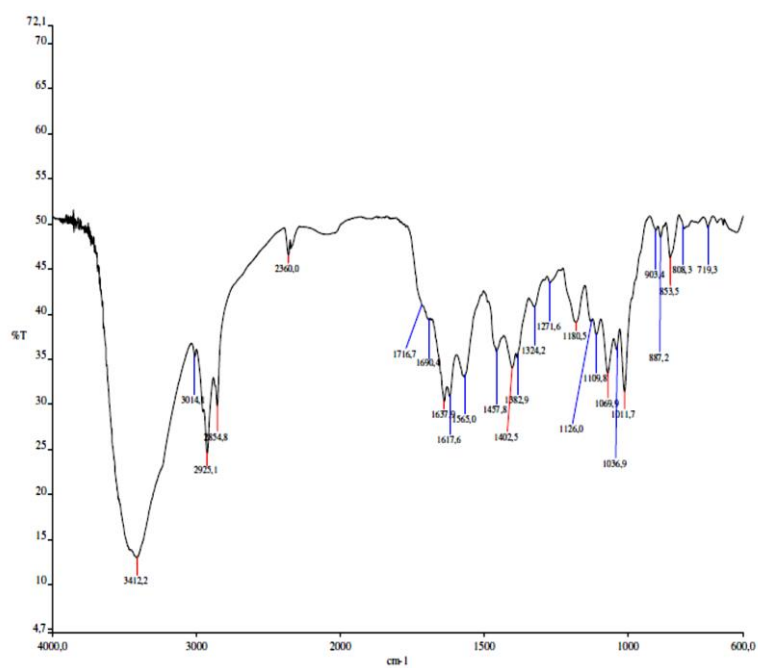
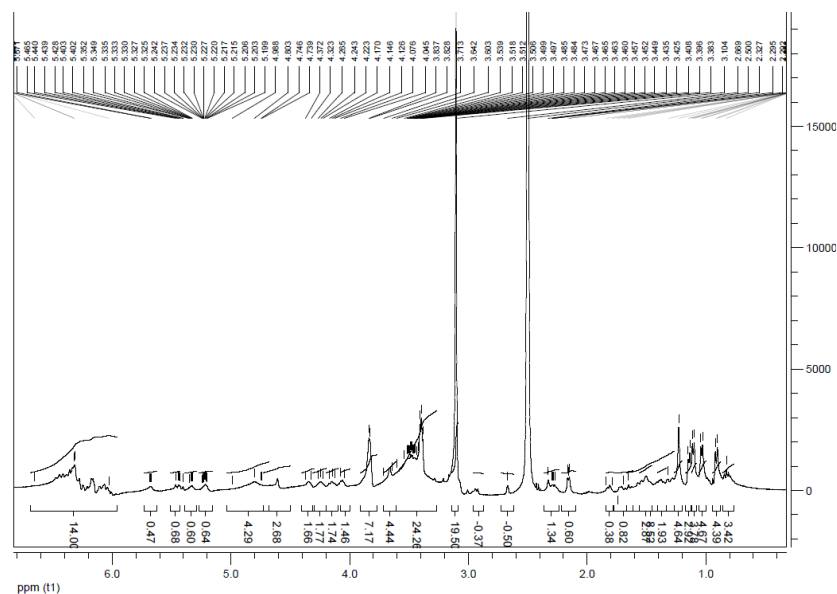
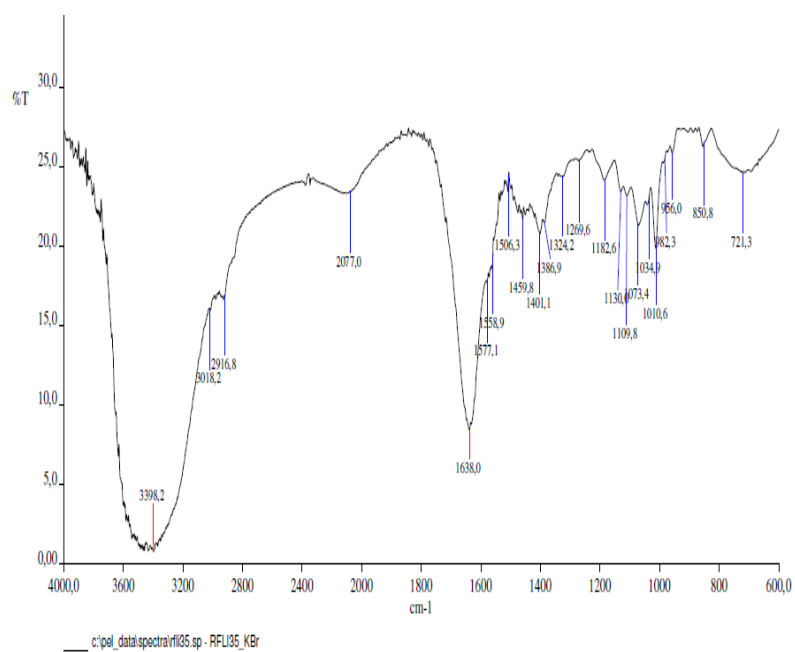


Figure S2: [Aliquat][AmB] FTIR spectrum in KBr

## 2. [Ch][AmB]

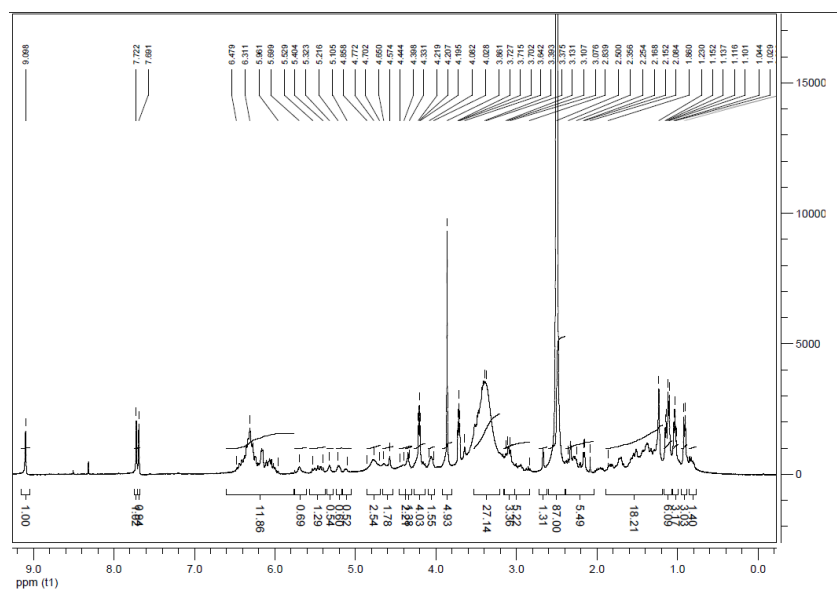


**Figure S3:** [Ch][AmB]  $^1\text{H}$ -NMR spectrum in  $(\text{CD}_3)_2\text{SO}$

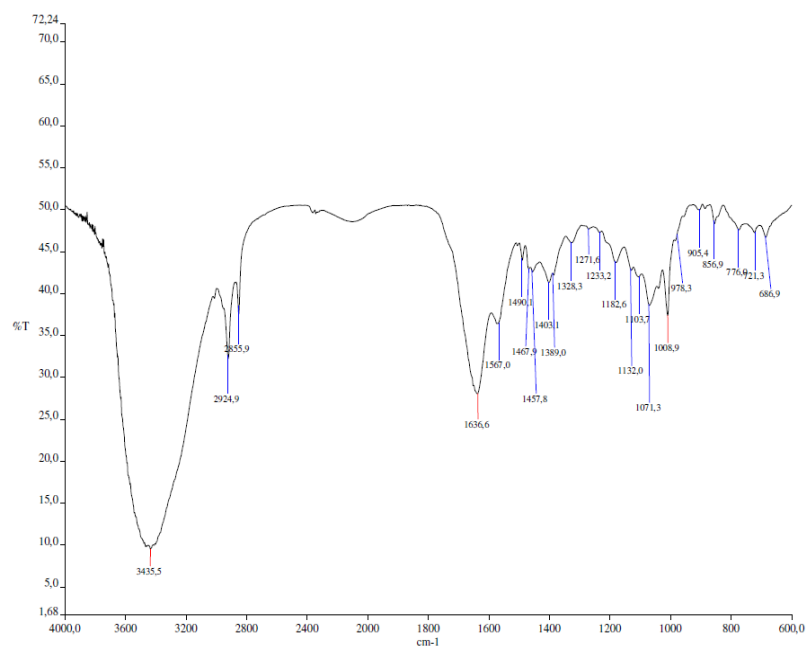


**Figure S4:** [Ch][AmB] FTIR spectrum in KBr

### 3. [C<sub>2</sub>OHMIM][AmB]



**Figure S5:** [C<sub>2</sub>OHMIM][AmB] <sup>1</sup>H-NMR spectrum in (CD<sub>3</sub>)<sub>2</sub>SO



**Figure S6:** [C<sub>2</sub>OHMIM][AmB] FTIR spectrum in KBr

#### 4. [C<sub>3</sub>OMIM][AmB]

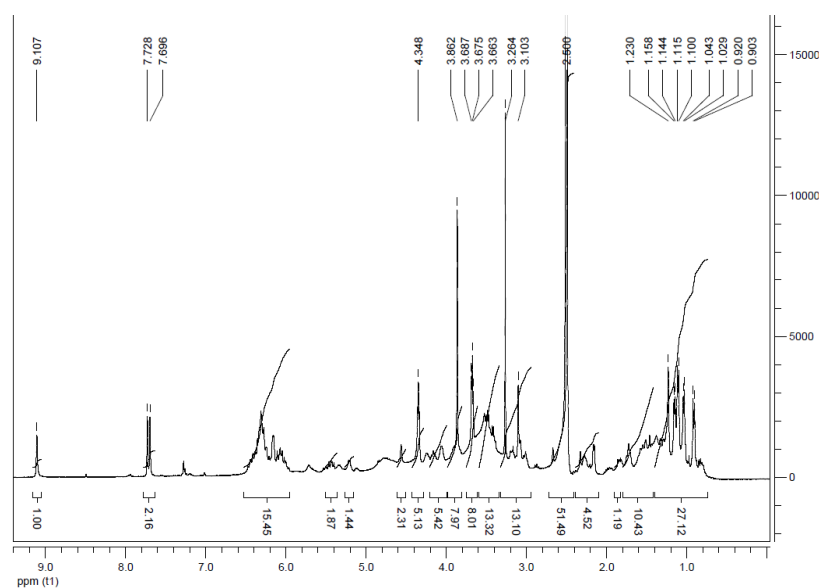


Figure S7: [C<sub>3</sub>OMIM][AmB] <sup>1</sup>H-NMR spectrum in (CD<sub>3</sub>)<sub>2</sub>SO

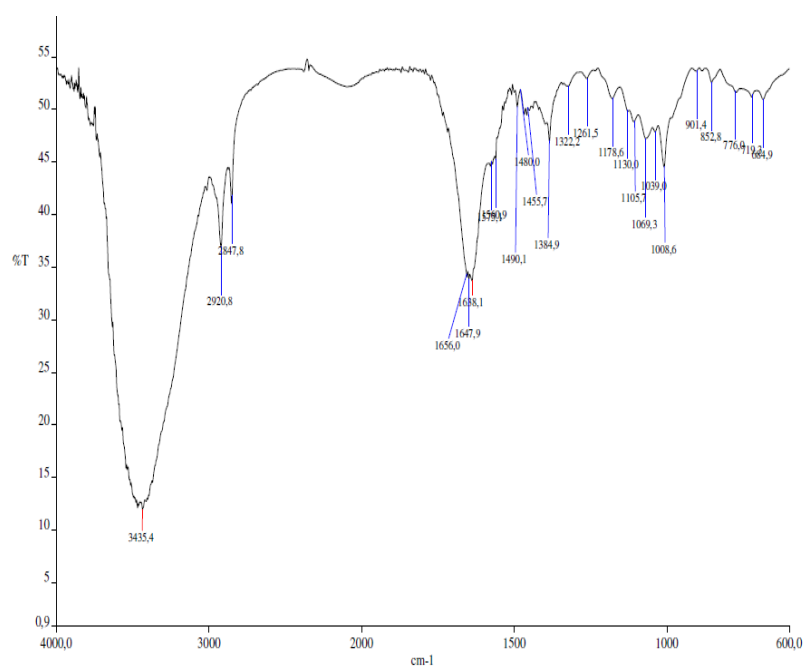
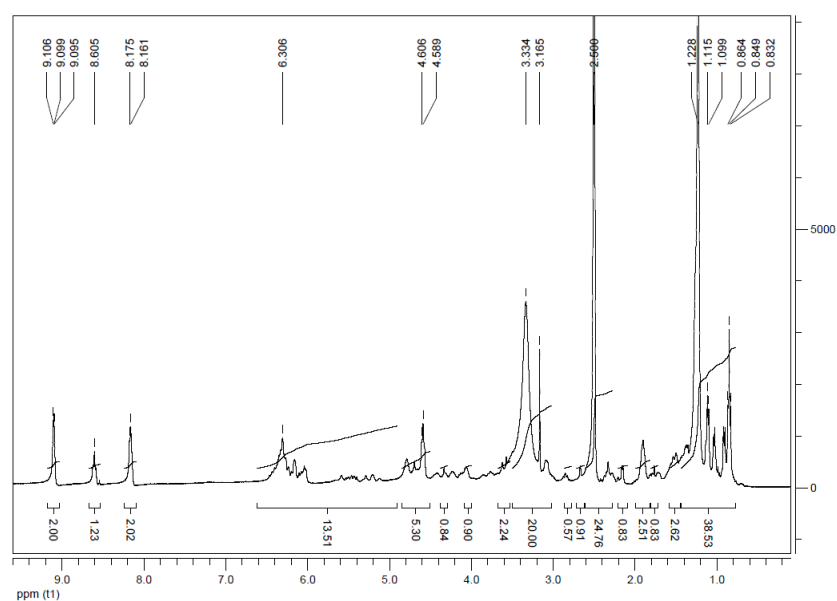
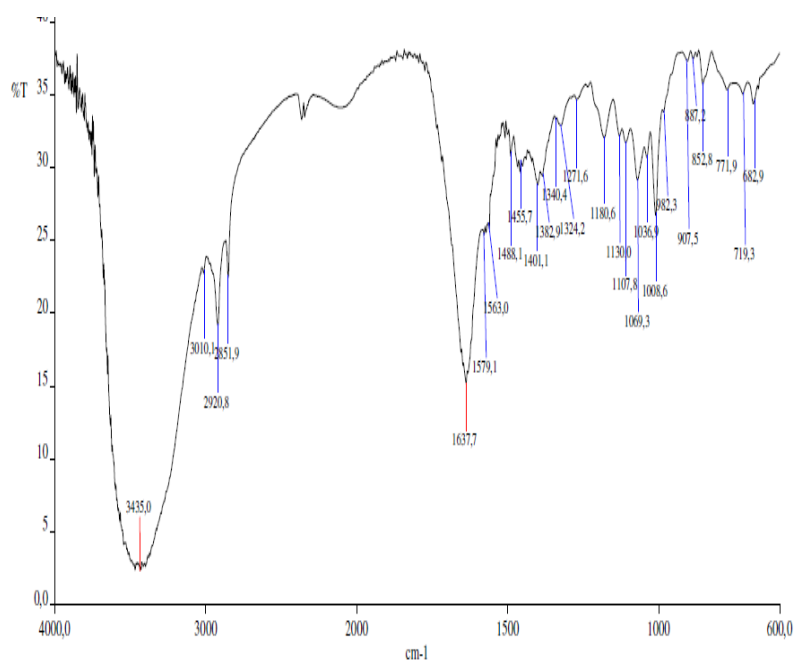


Figure S8: [C<sub>3</sub>OMIM][AmB] FTIR spectrum in KBr

## 5. [C<sub>16</sub>Pyr][AmB]



**Figure S9:** [C<sub>16</sub>Pyr][AmB] <sup>1</sup>H-NMR spectrum in (CD<sub>3</sub>)<sub>2</sub>SO



**Figure S10:** [C<sub>16</sub>Pyr][AmB] FTIR spectrum in KBr

## 6. [P<sub>6,6,6,14</sub>][AmB]

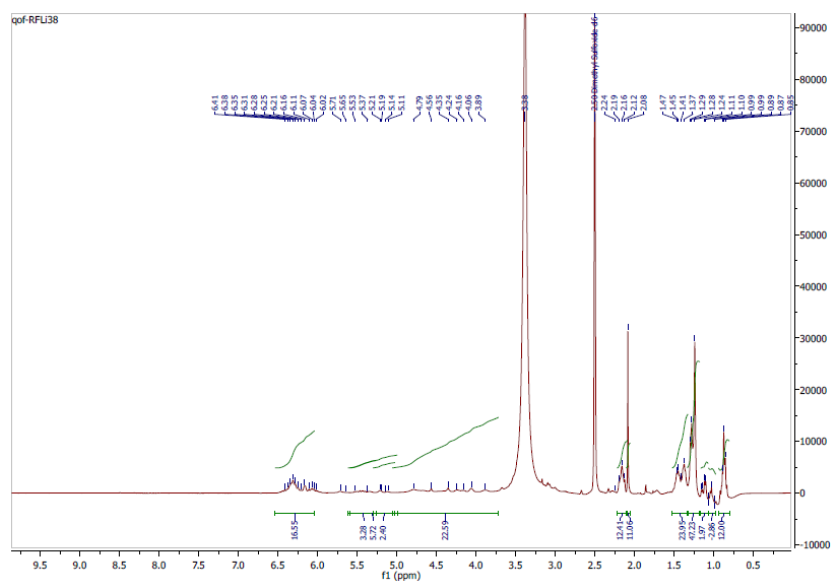


Figure S11: [P<sub>6,6,6,14</sub>][AmB] <sup>1</sup>H-NMR spectrum in (CD<sub>3</sub>)<sub>2</sub>SO

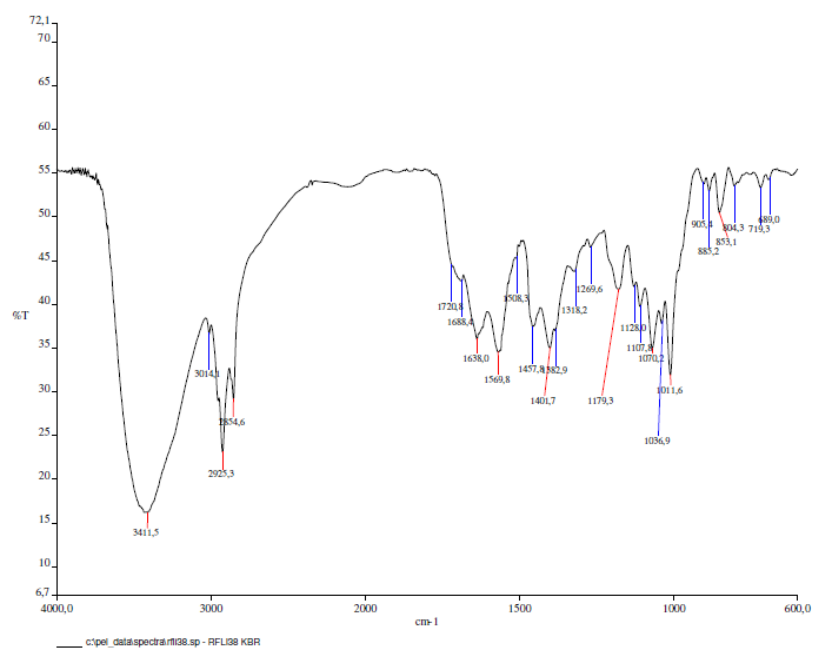
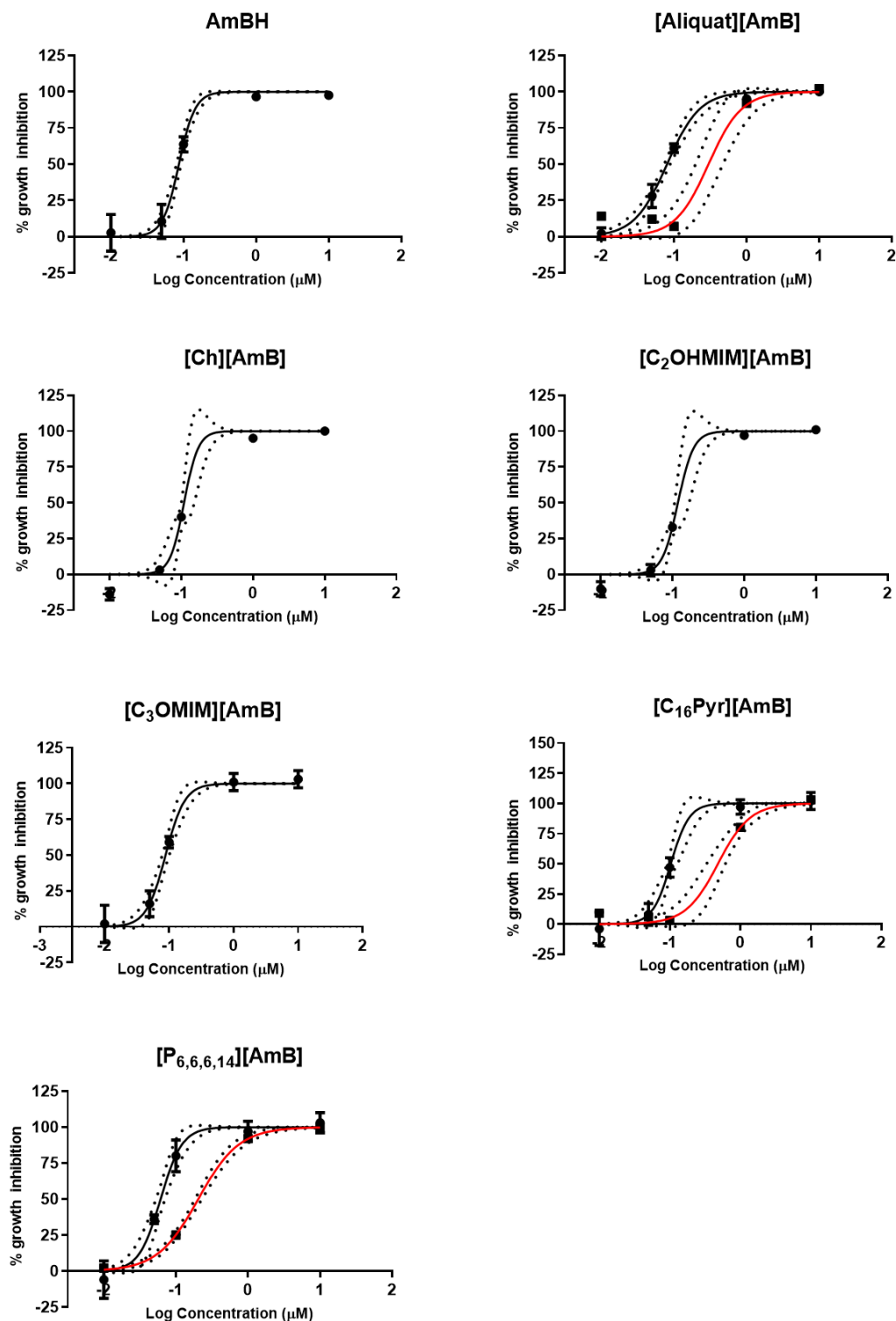


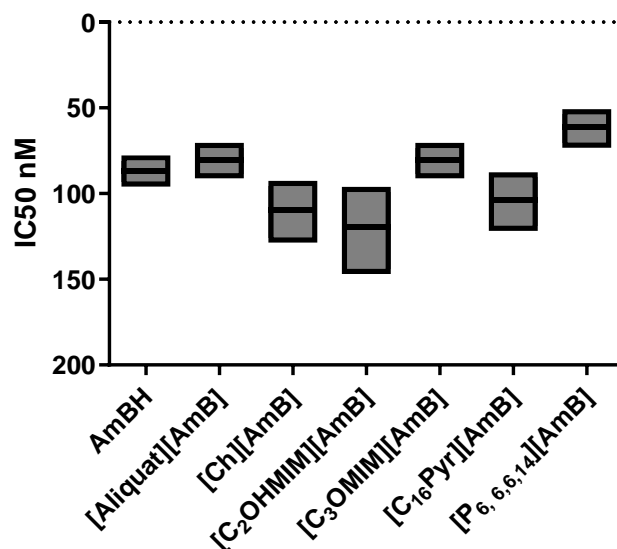
Figure S12: [P<sub>6,6,6,14</sub>][AmB] FTIR spectrum in KBr

## Biological Studies of OSILs-AmB

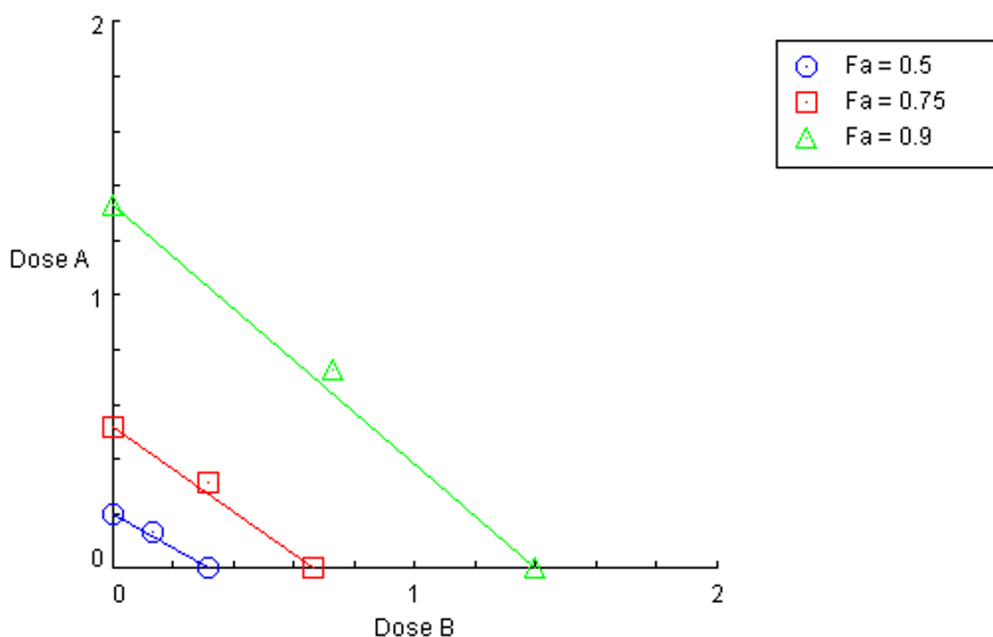


**Figure S13:** Antiparasitic activity of AmBH and each OSIL-AmB. Each point denotes the average growth inhibition and standard deviation for a defined concentration of AmphBH and OSILs-AmphB ( $\bullet$ ) or the respective organic cation in their chloride forms ( $\blacksquare$ ). The solid black line and the solid red line represent the non-linear regression associated with AmBH and OSILs-AmB or the respective organic cation in their chloride forms, respectively. The dashed lines are associated with the non-linear regression, showing 95% confidence bands





**Figure S14:** Graphical representation depicting the average IC<sub>50</sub> with 95% confidence interval for AmbH and the prepared OSILs-AmbB.



**Figure S15:** Isobologram and combination indexes (CIs) to compare the dose-effect of [P<sub>6,6,6,14</sub>][Amb] with their individual moieties: [Amb]<sup>-</sup> (compound A) and [P<sub>6,6,6,14</sub>]<sup>+</sup> (compound B). The red, blue and green lines connect the predicted values of EC<sub>50</sub> (blue), EC<sub>75</sub> (red) and EC<sub>90</sub> (green) for [P<sub>6,6,6,14</sub>]<sup>+</sup> and [Amb]<sup>-</sup>. The predicted CIs, calculated for EC<sub>50</sub>, EC<sub>75</sub> and EC<sub>90</sub> values of the ionic liquid [P<sub>6,6,6,14</sub>][Amb], are 1.10, 1.08 and 1.06, respectively.