# Supporting information

**Novel organic salts based on mefloquine: synthesis, solubility, permeability and *in vitro activity* against the *Mycobacterium tuberculosis***

## *NMR and FTIR Spectra*

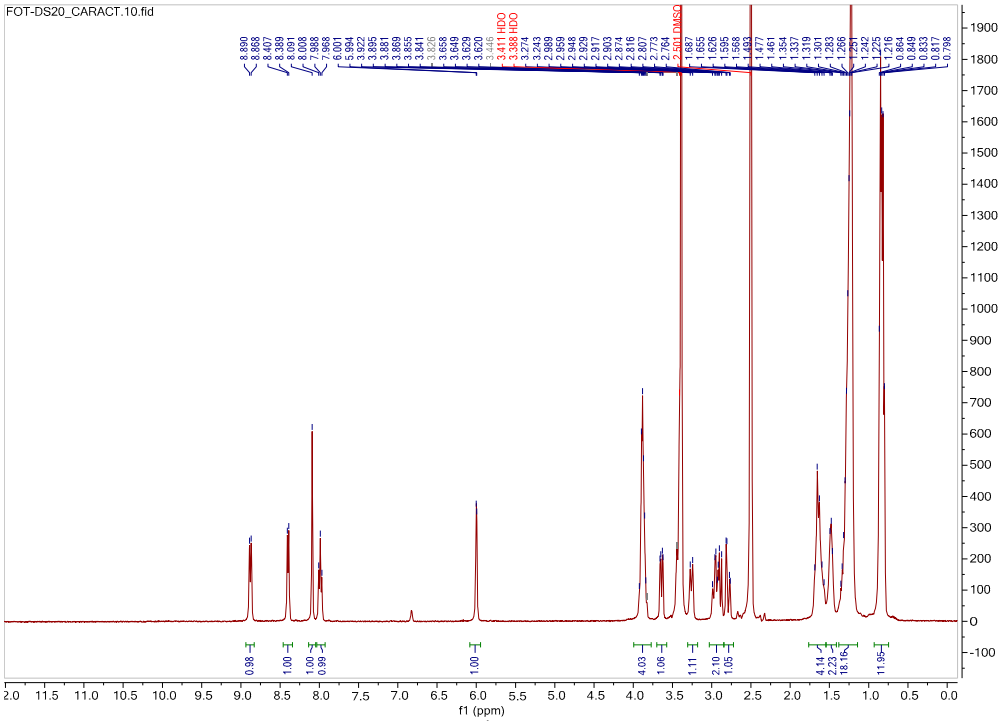


**Figure S1.** [MFLH][AOT] $^{1}$H NMR spectrum in DMSO-*d*$_6$.

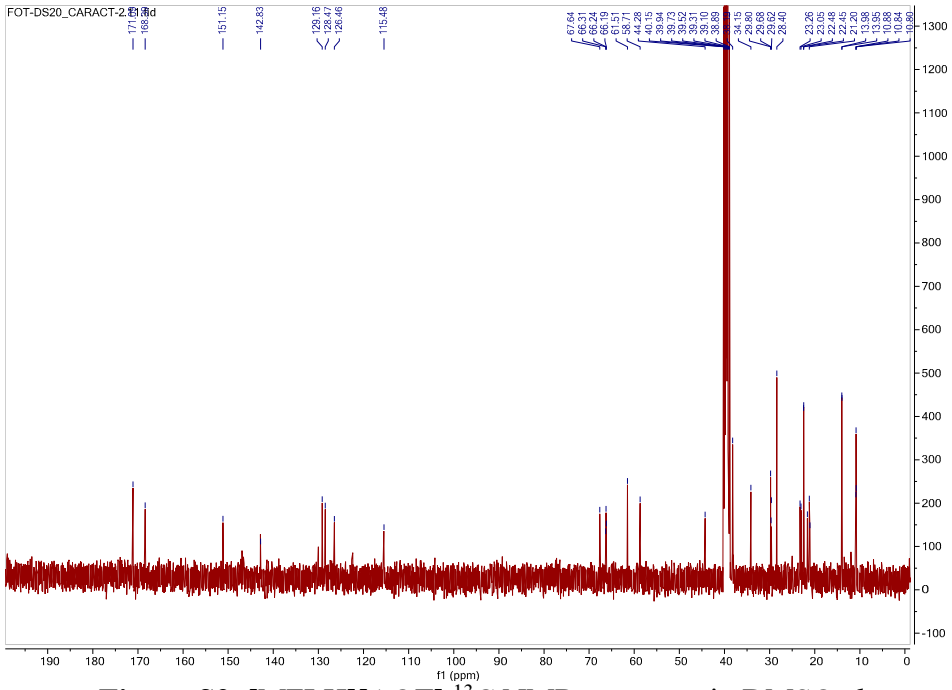


**Figure S2.** [MFLH][AOT] $^{13}$C NMR spectrum in DMSO-*d*$_6$.

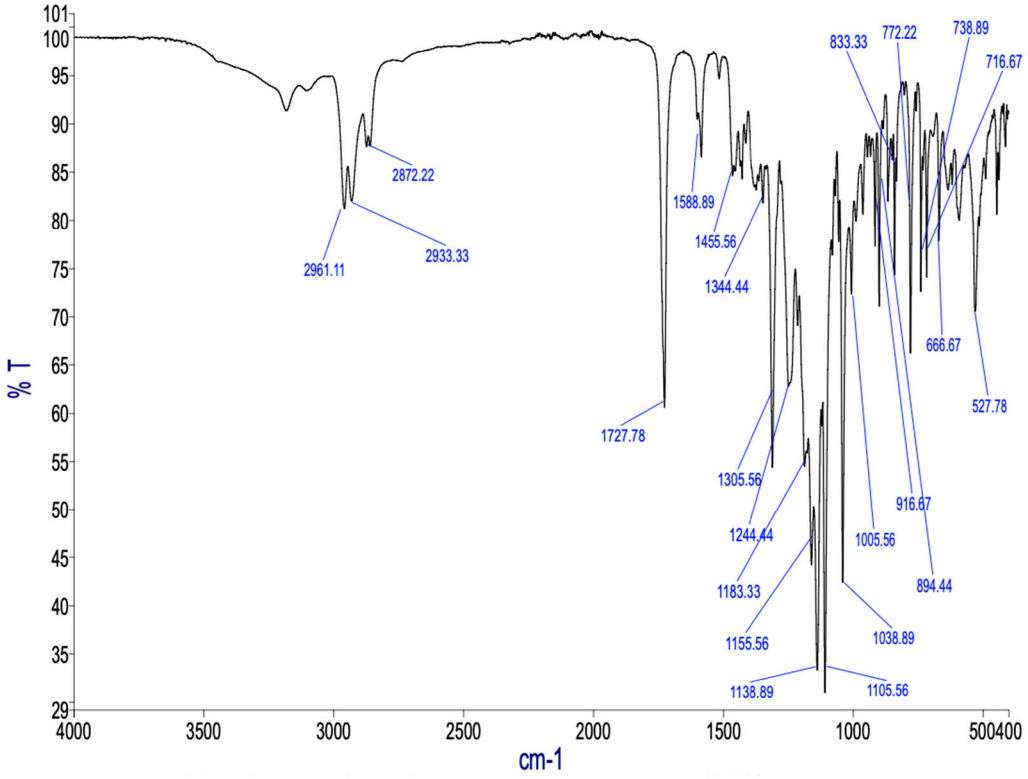


**Figure S3.** [MFLH][AOT] FTIR-ATR spectrum.

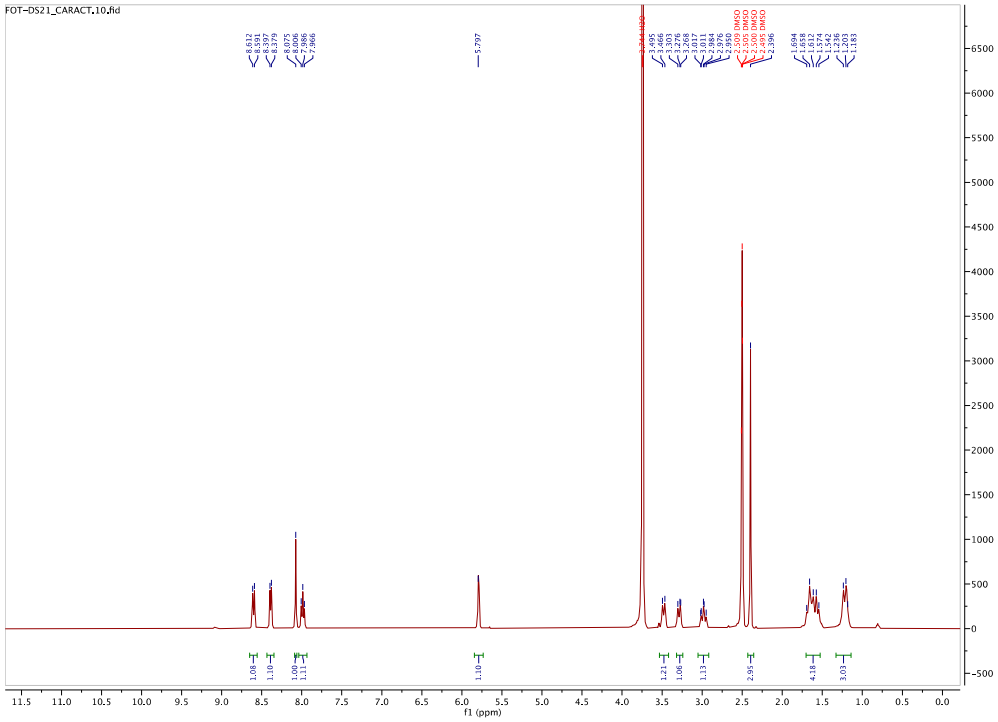


**Figure S4.** [MFLH][MsO] $^{1}$H NMR spectrum in DMSO-$d_6$.

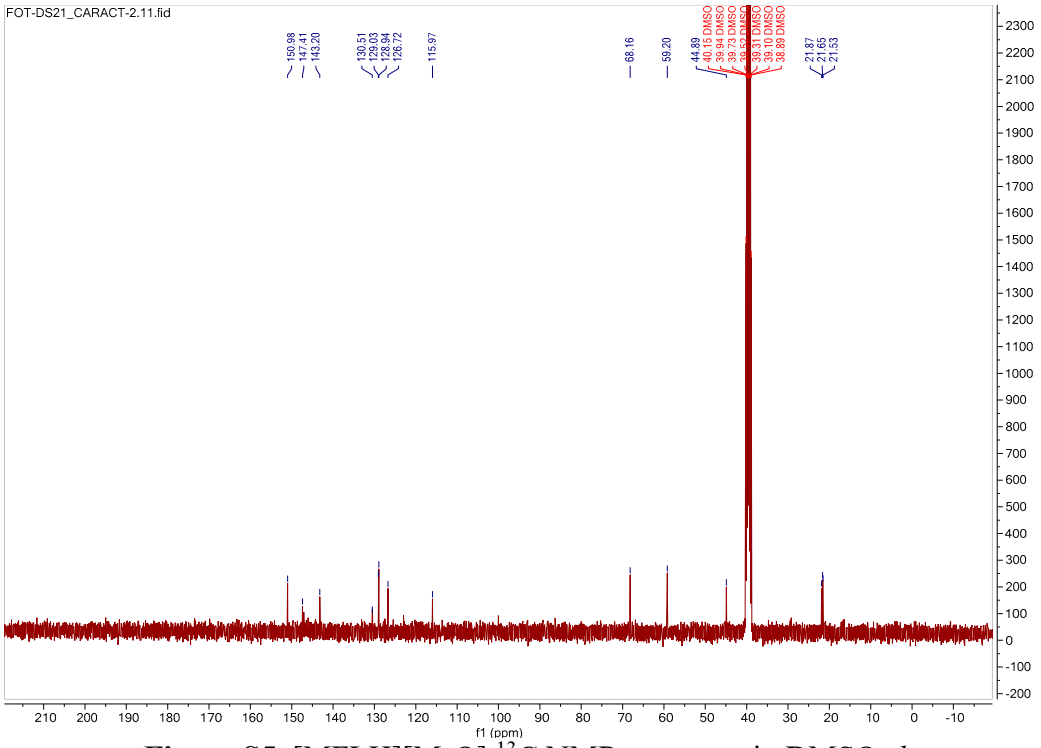


**Figure S5.** [MFLH][MsO] $^{13}$C NMR spectrum in DMSO-*d*$_6$.

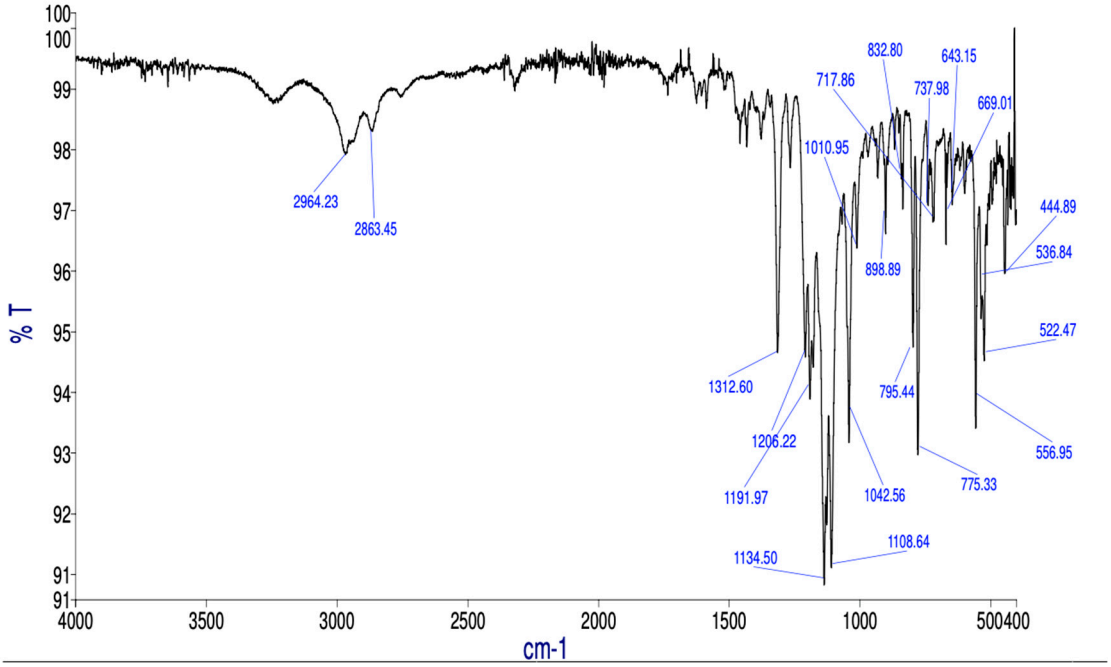


**Figure S6.** [MFLH][MsO] FTIR-ATR spectrum.

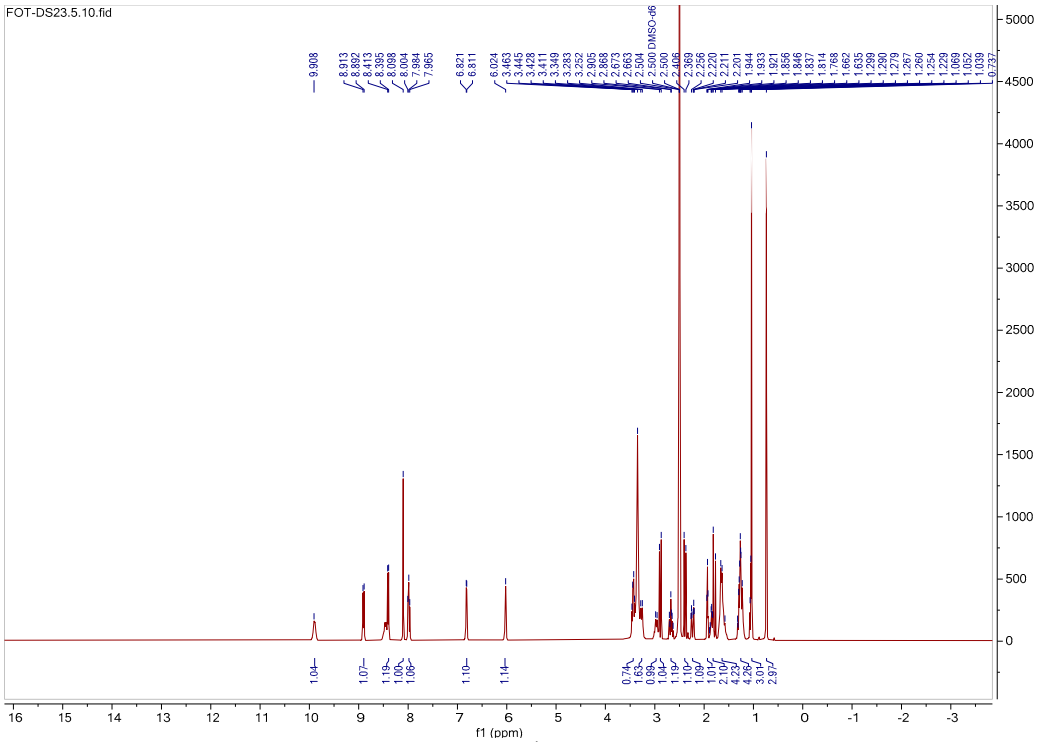


**Figure S7.** [MFLH][(1*S*)-CSA] $^{1}$H NMR spectrum in DMSO-*d*$_6$.

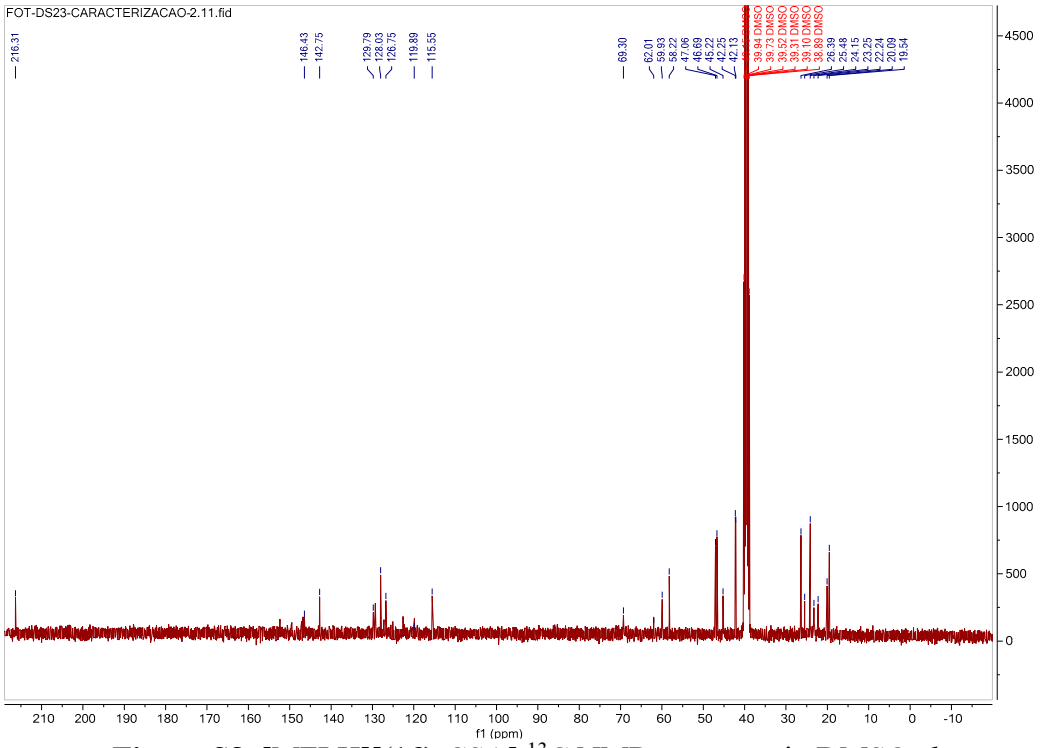


**Figure S8.** [MFLH][(1*S*)-CSA] $^{13}$C NMR spectrum in DMSO-*d*$_6$.

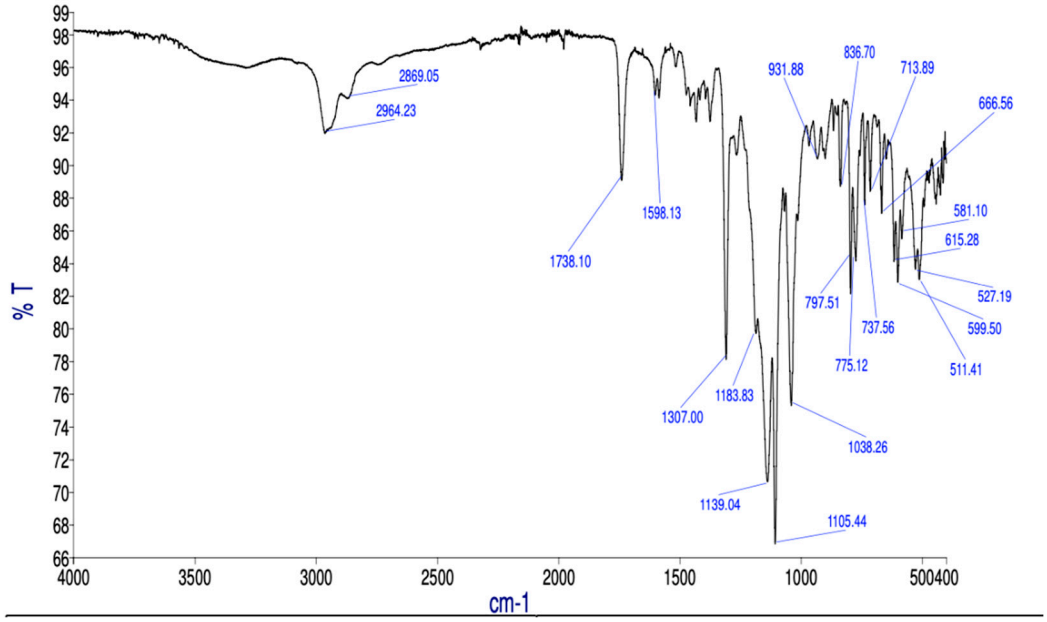


**Figure S9.** [MFLH][(1*S*)-CSA] FTIR-ATR spectrum.

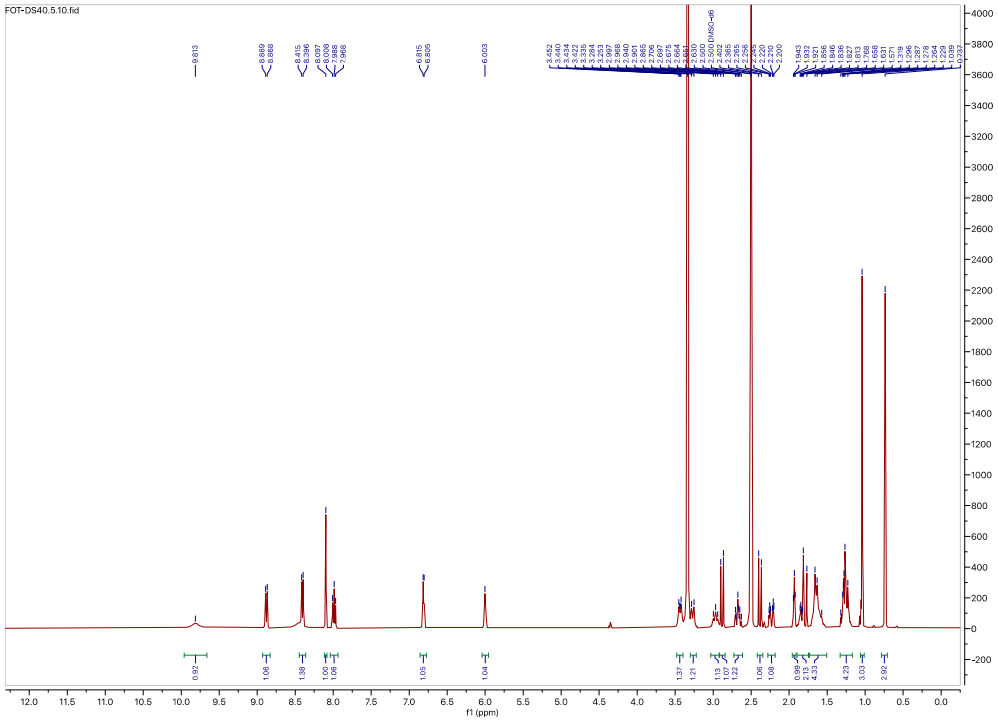


**Figure S10.** [MFLH][(1*R*)-CSA] $^{1}$H NMR spectrum in DMSO-$d_6$.

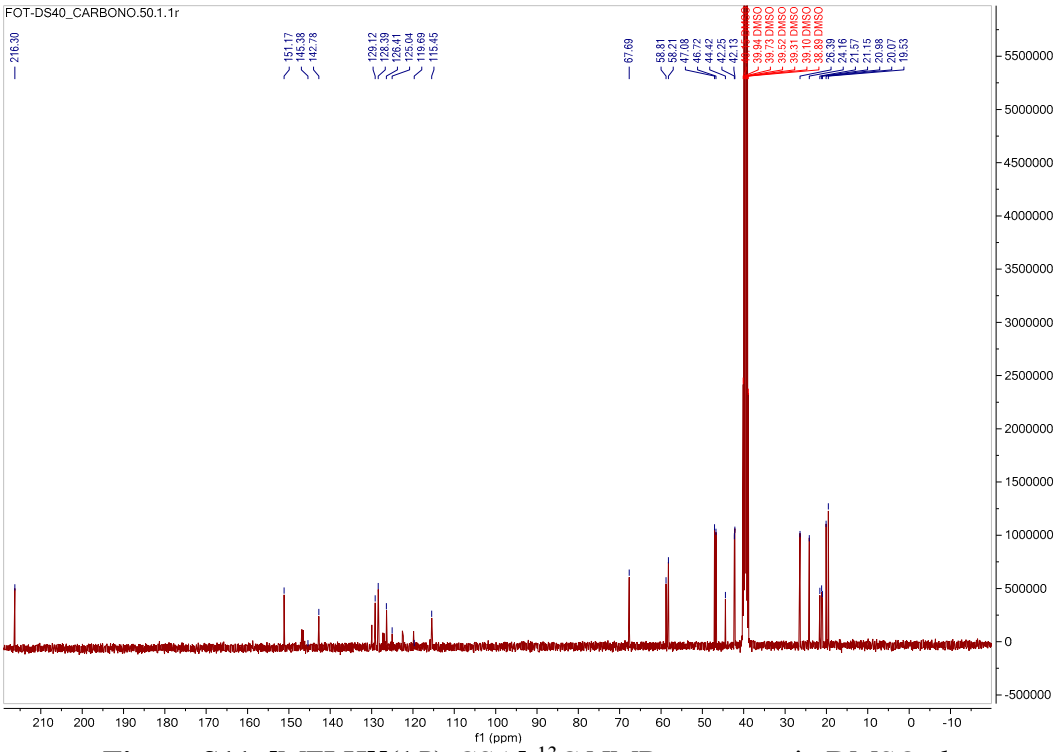


**Figure S11.** [MFLH][(1*R*)-CSA] $^{13}$C NMR spectrum in DMSO-$d_6$.

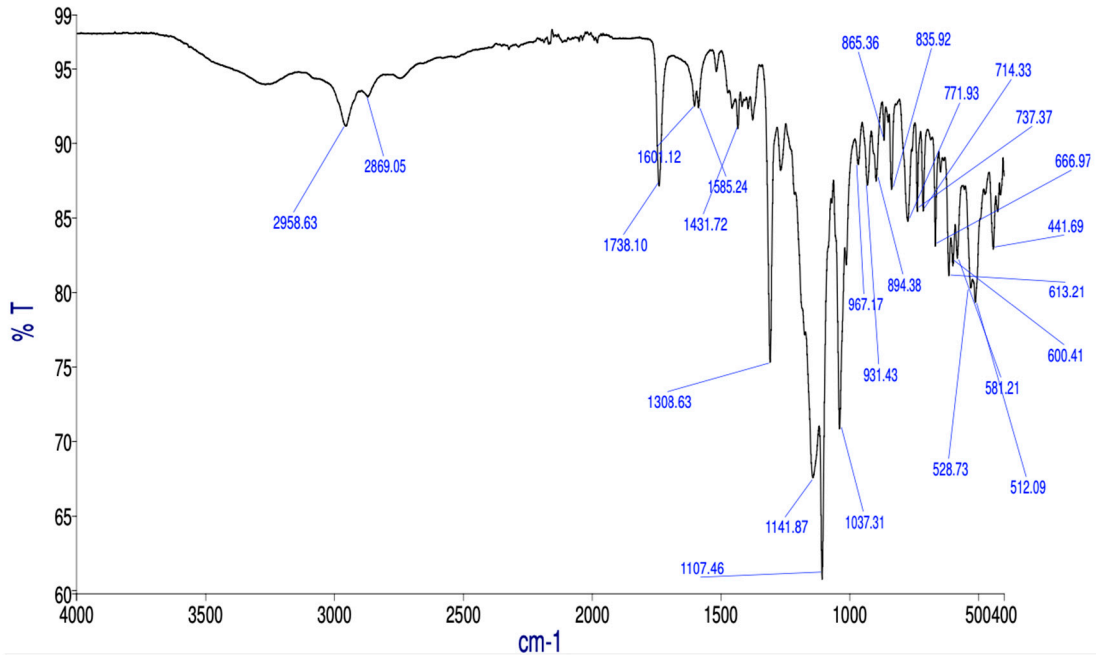


**Figure S12.** [MFLH][(1*R*)-CSA] FTIR-ATR spectrum.

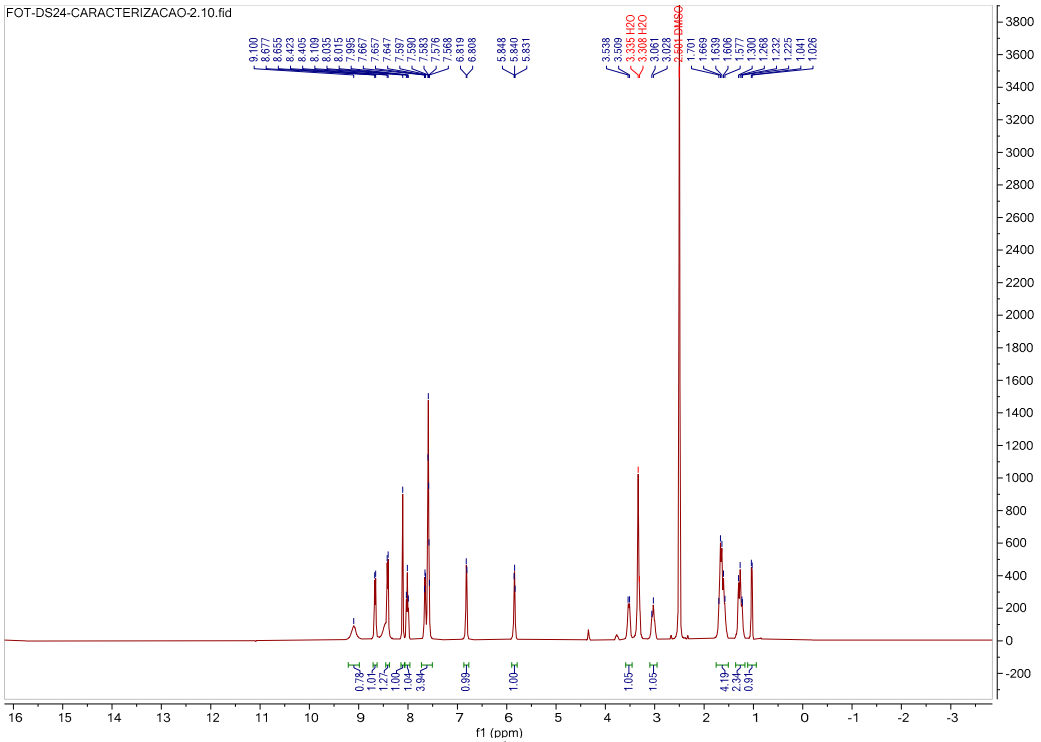


**Figure S13.** [MFLH][Sac] $^{1}$H NMR spectrum in DMSO-*d*$_6$.

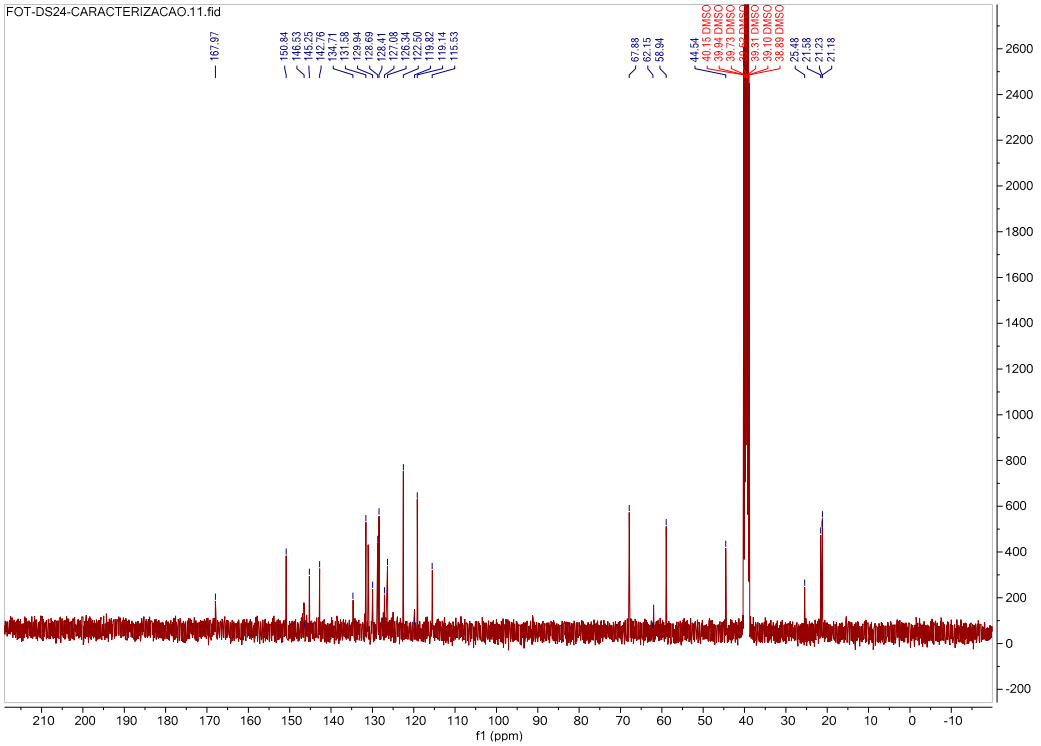


**Figure S14.** [MFLH][Sac] $^{13}$C NMR spectrum in DMSO-*d*$_6$.

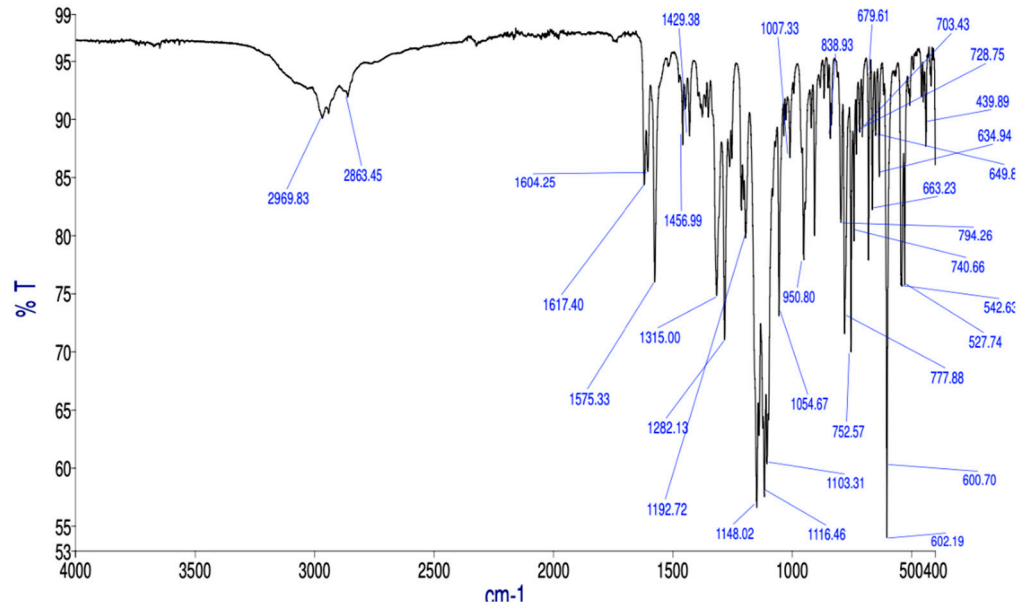


**Figure S15.** [MFLH][Sac] FTIR-ATR spectrum.

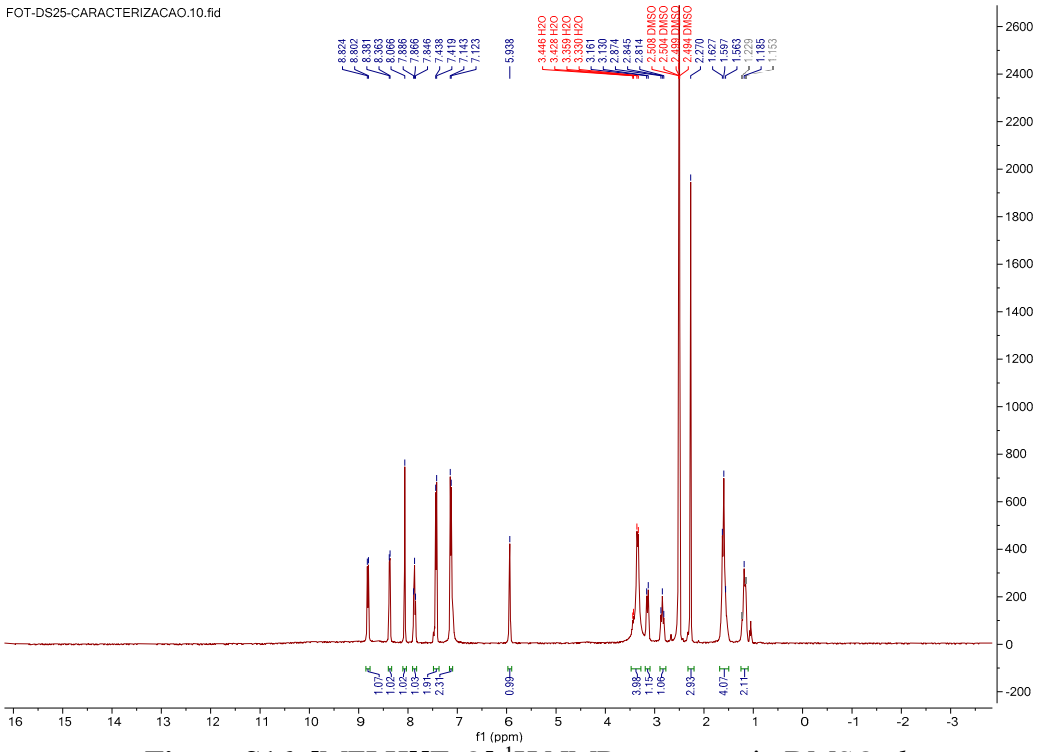


**Figure S16.** [MFLH][TsO] $^{1}$H NMR spectrum in DMSO-*d*$_6$.

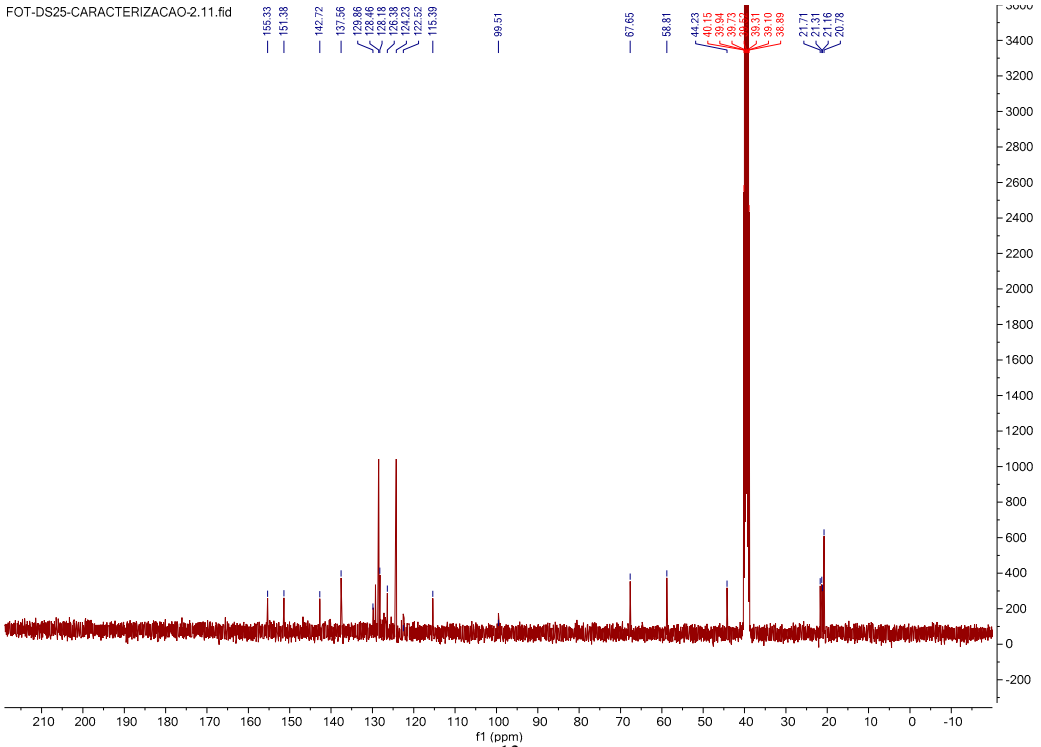


**Figure S17.** [MFLH][TsO] $^{13}$C NMR spectrum in DMSO-$d_6$.

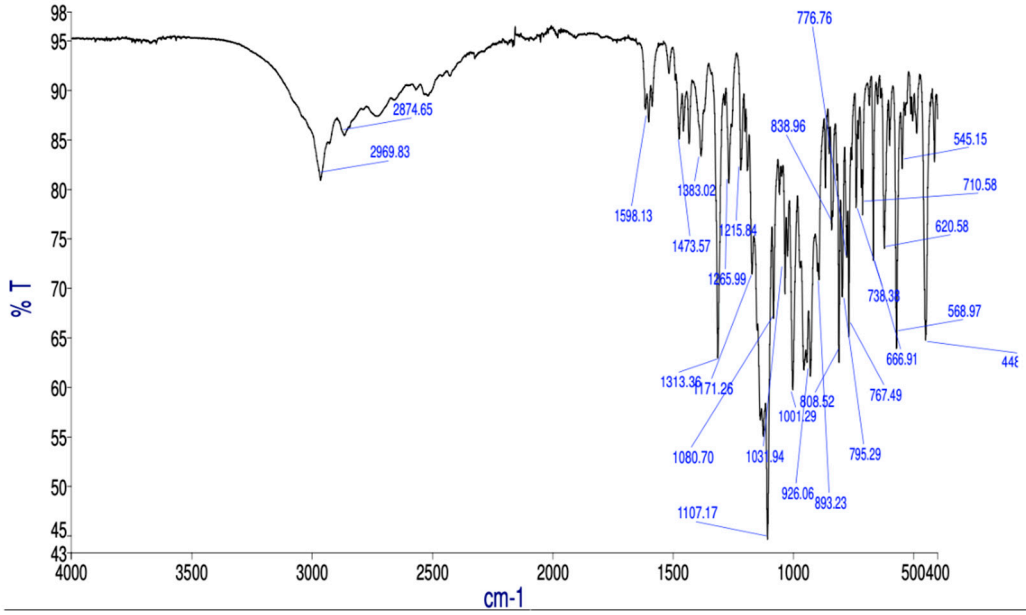


**Figure S18.** [MFLH][TsO] FTIR-ATR spectrum.

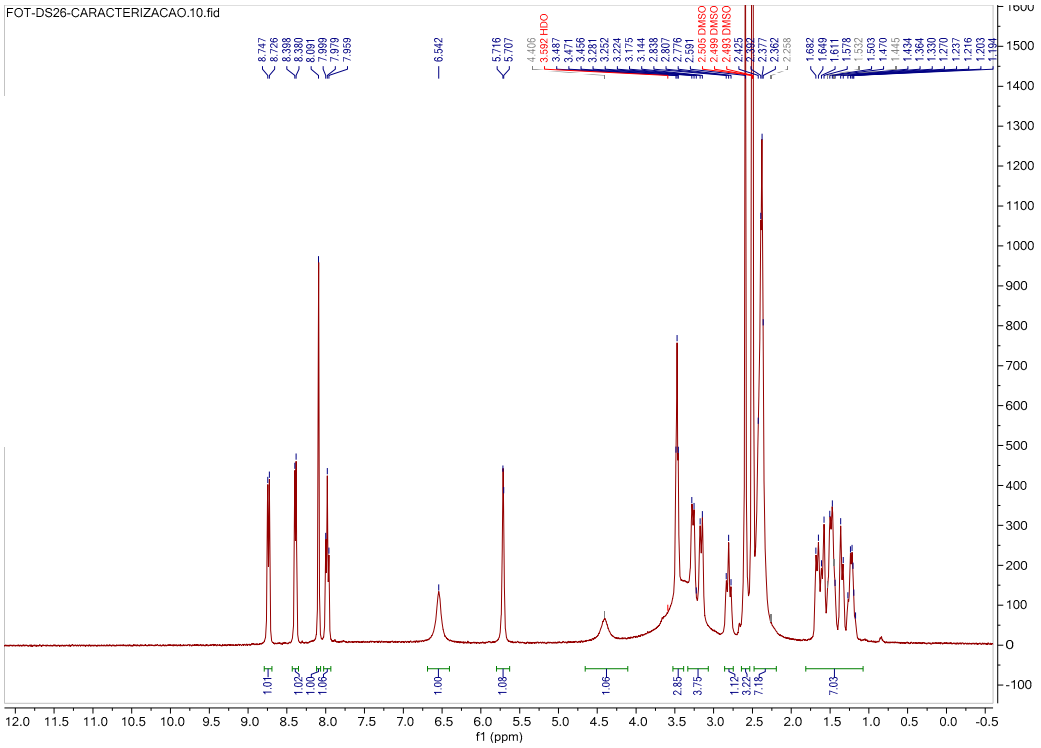


**Figure S19.** [MFLH][HEPES] $^{1}$H NMR spectrum in DMSO-*d*$_6$.

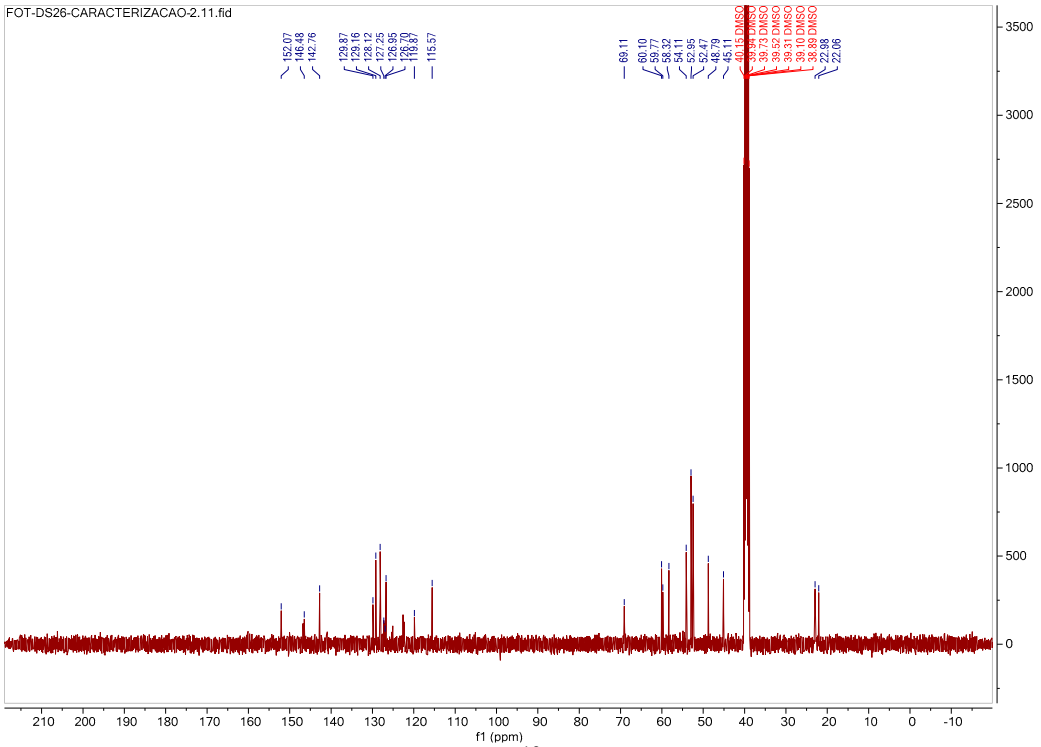


**Figure S20.** [MFLH][HEPES] $^{13}$C NMR spectrum in DMSO-*d*$_6$.

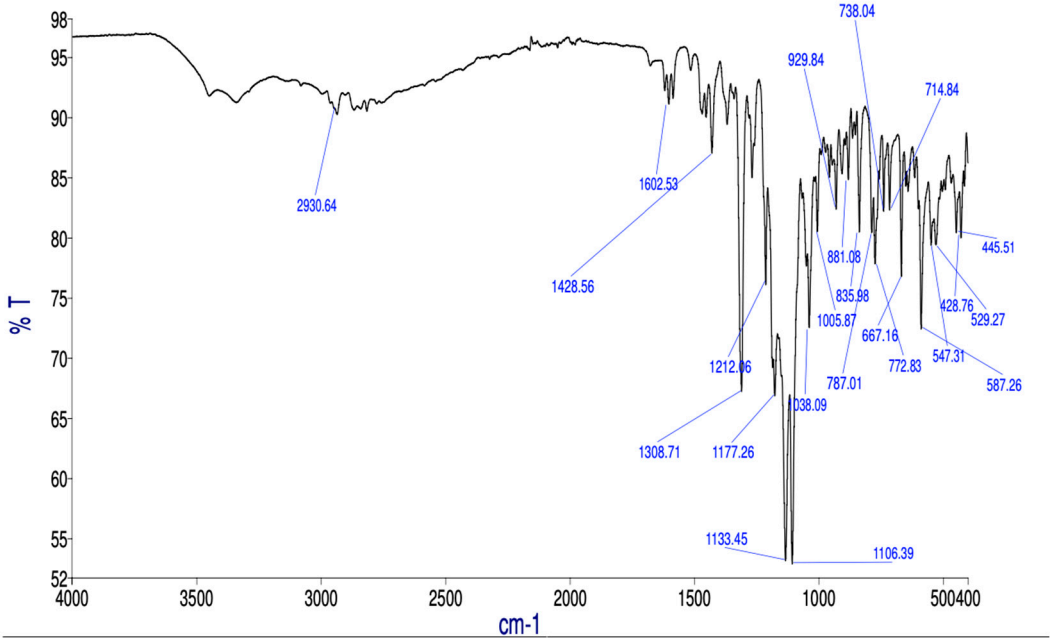


**Figure S21.** [MFLH][HEPES] FTIR-ATR spectrum.

*DSC thermograms*

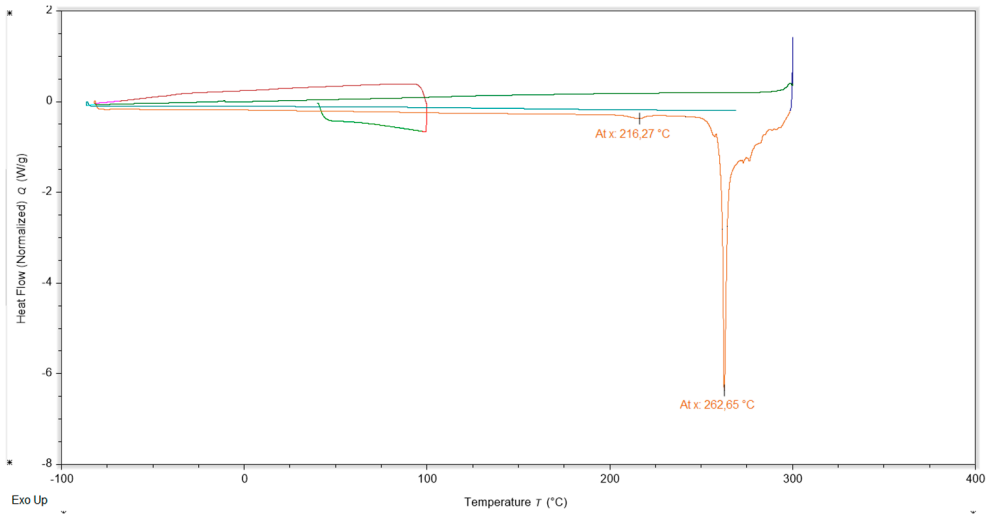


Figure S22. DSC thermogram of [MFLH][Cl].

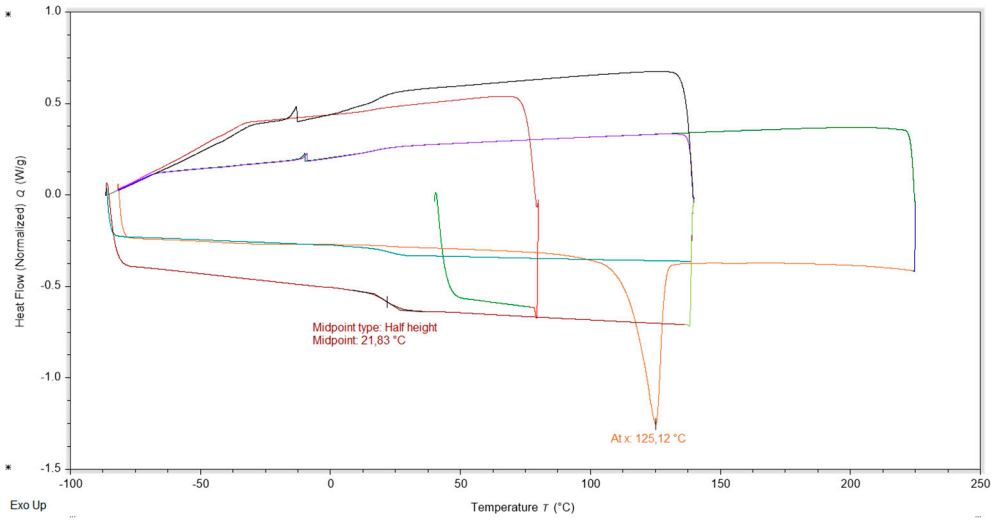


Figure S23. DSC thermogram of [MFLH][AOT].

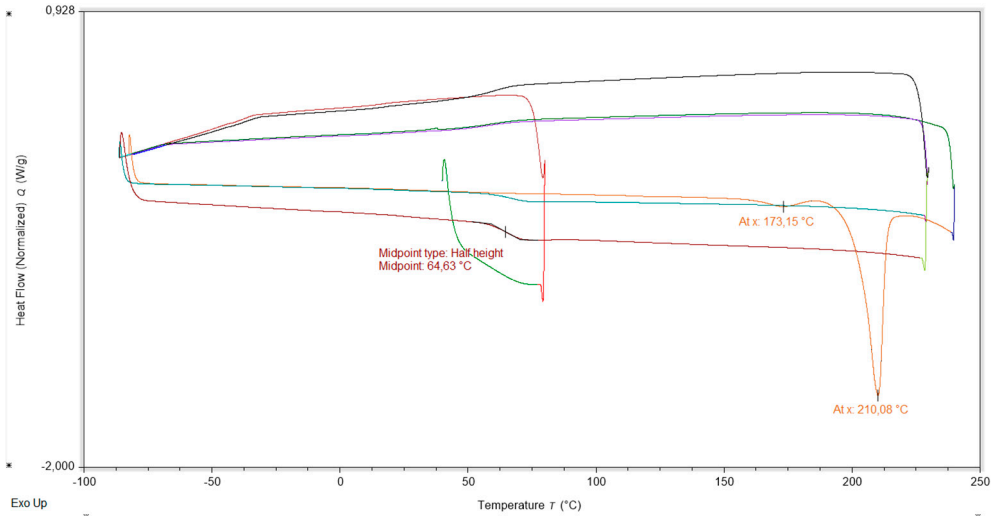


Figure S24. DSC thermogram of [MFLH][MsO].

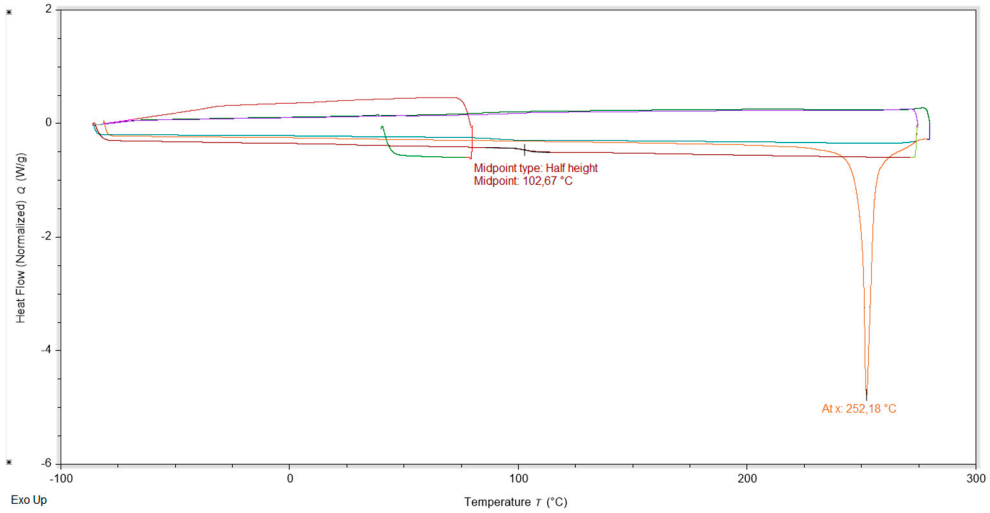


Figure S25. DSC thermogram of [MFLH][Sac].

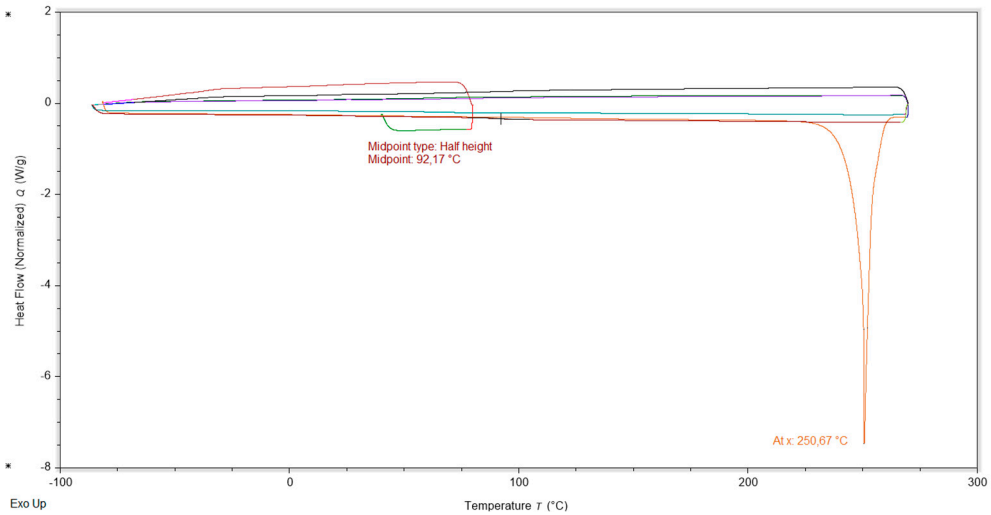


Figure S26. DSC thermogram of [MFLH][TsO].

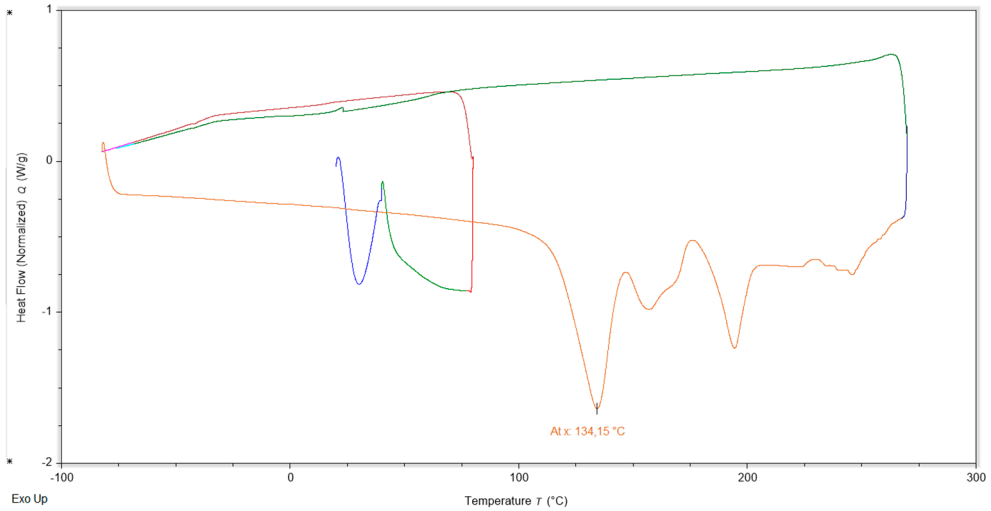


Figure S27. DSC thermogram of [MFLH][HEPES].

*Water solubility studies*

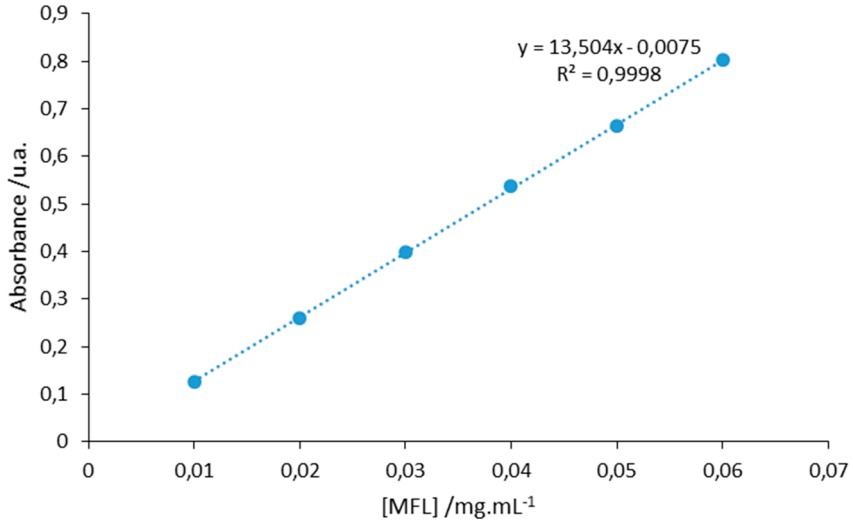


**Figure S28.** Calibration curve of Mefloquine in water.

*Permeability (P), diffusion (D) and partition coefficient ($K_d$) studies*

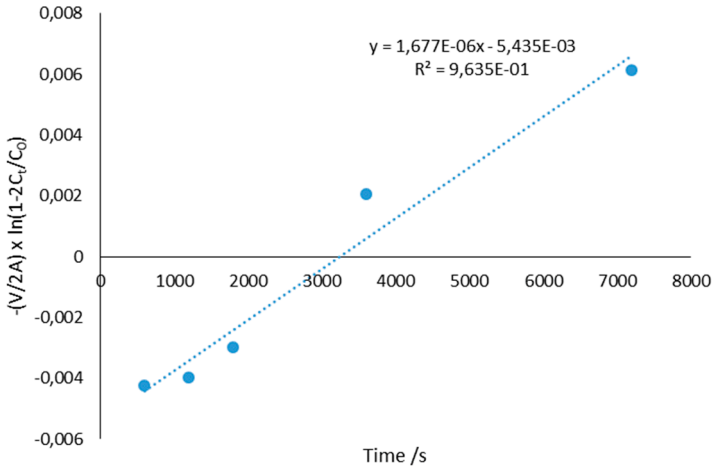


**Figure S29.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][Cl].

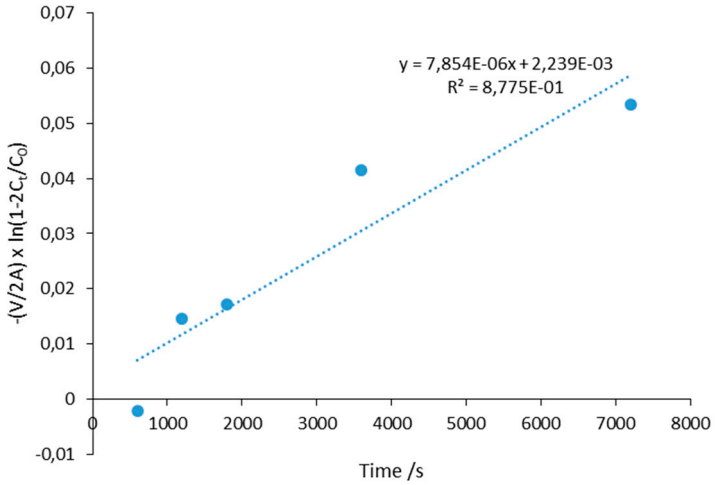


**Figure S30.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][MsO].

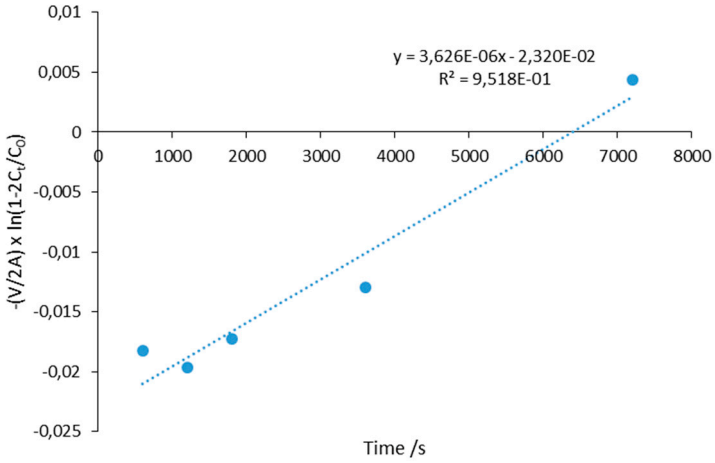


**Figure S31.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][(1*S*)-CSA].

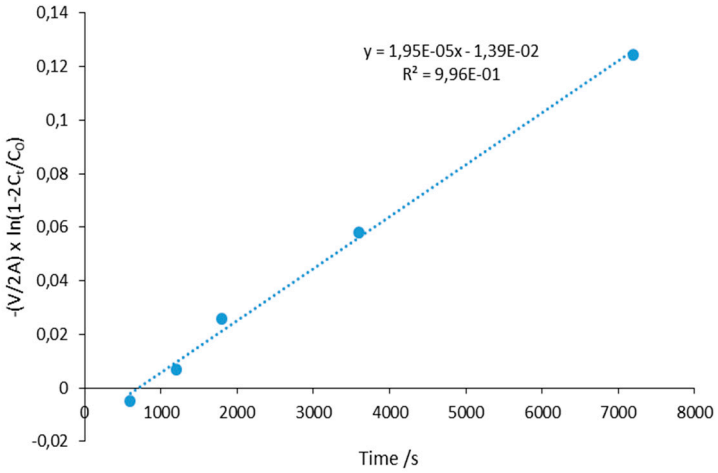


**Figure S32.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][(1*R*)-CSA].

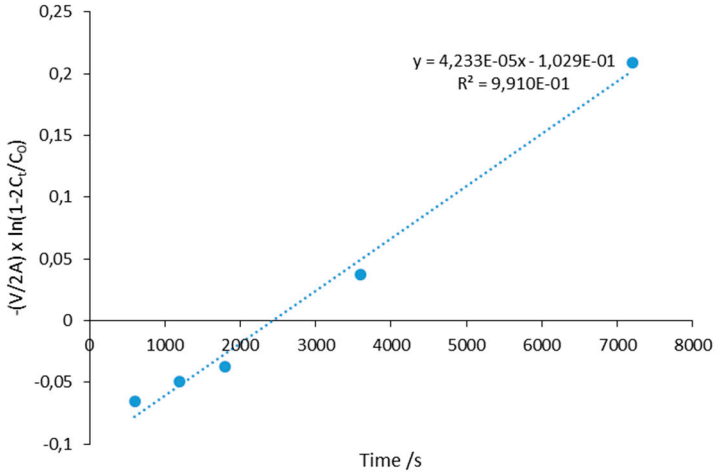


**Figure S33.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][TsO].

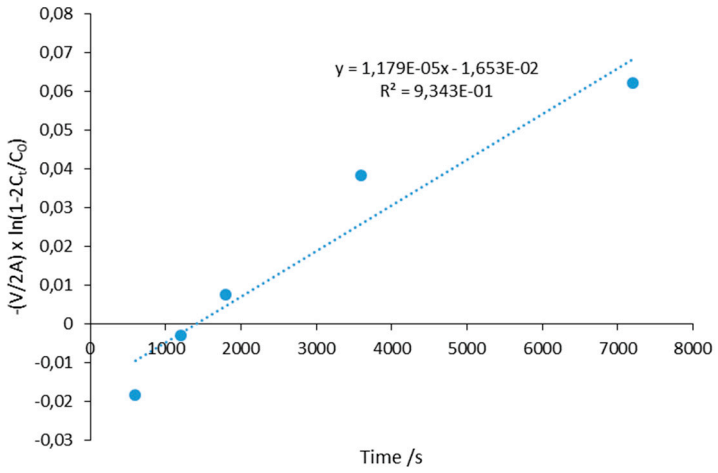


**Figure S34.** Plot of -(V/2A) × ln(1-2$C_t$/$C_0$) versus time (s) of [MFLH][Sac].

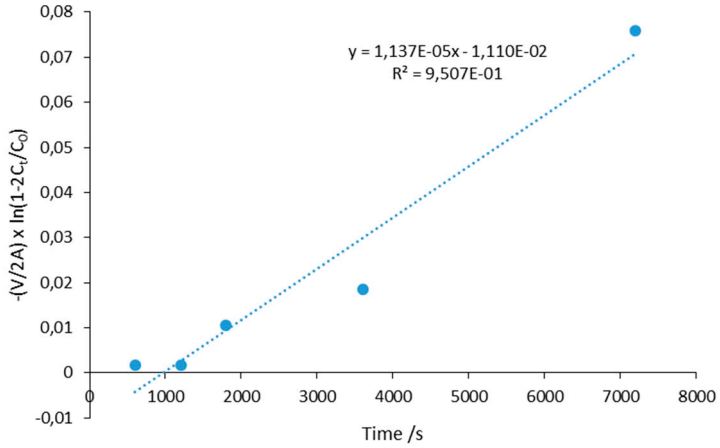


**Figure S35.** Plot of $-(V/2A) \times \ln(1-2C_t/C_0)$ versus time (s) of [MFLH][HEPES].

*Antimycobacterial activity studies*

**Table S1.** Minimum inhibitory concentrations (MIC) of the anions as sodium salts.

| **Salts** | **MIC (μM)** |
|---|---|
| Na[AOT] | > 350 |
| Na[MsO] | > 350 |
| Na[1*R*-CSA] | > 350 |
| Na[1*S*-CSA] | > 350 |
| Na[Sac] | > 350 |
| Na[TsO] | > 350 |
| Na[HEPES] | > 350 |

*Cytotoxicity assays*

Table S2. Data of the cellular viability of macrophage Raw 264.7 cells by the MTT assay of [MFLH][Cl], MFL salts and corresponding sodium salts.

| **Compounds** | **% Cell Viability (CV)/Dose (µM)** | | |
|---|---|---|---|
| | **15** | **30** | **60** |
| [MFLH][Cl] | 100 | 100 | 100 |
| [MFLH][AOT] | 100 | 74.7 | 50.6 |
| [MFLH][MsO] | 70.0 | 38.7 | 13.2 |
| [MFLH][(1*R*)-CSA] | 97.1 | 34.9 | 32.2 |
| [MFLH][(1*S*)-CSA] | 100 | 88.1 | 58.0 |
| [MFLH][Sac] | 100 | 36.5 | 17.1 |
| [MFLH][TsO] | 100 | 98.2 | 68.3 |
| [MFLH][HEPES] | 44.4 | 34.5 | 24.9 |
| Na[AOT] | 100 | 100 | 100 |
| Na[MsO] | 100 | 100 | 100 |
| Na[(1*R*)-CSA] | 100 | 100 | 100 |
| Na[(1*S*)-CSA] | 100 | 100 | 100 |
| Na[Sac] | 100 | 95.9 | 34.8 |
| Na[TsO] | 100 | 100 | 92.5 |
| Na[HEPES] | 100 | 100 | 100 |