Supporting Information

pH-degradable imidazolium oligomers as antimicrobial materials with tuneable loss of activity

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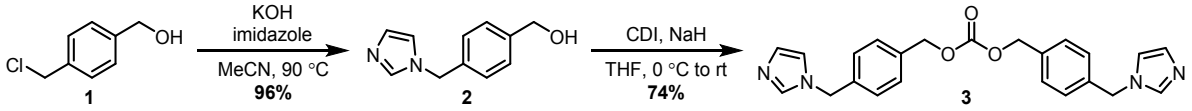
1. General information

All anhydrous solvents were purchased from Sigma-Aldrich, and used without further purification. All other reagents were used as received, except where otherwise noted.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F-254 silica gel plates with visualization by ultraviolet light (254 nm) and/or heating the plate after staining with a solution of 20% $KMnO_4$ w/v in H_2O. Flash column chromatography was conducted on Silica gel 60 (0.040–0.063 mm) supplied by Merck under positive pressure.

^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on Bruker AV-400 (400 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million (ppm) with the residual solvent peak of tetramethylsilane used as the internal standard at 0.00 ppm. ^1H NMR data were reported in the following order: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constants (*J*, Hz), integration and assignment. High-resolution mass spectra (HRMS) were recorded on a Bruker MicroTOF-Q system. The samples were directly injected into the chamber at 20 μL min^{-1}. Typical instrument parameters were capillary voltage: 4 kV, nebulizer: 0.4 bar; dry gas: 2 L min^{-1} at 120 °C, and *m/z* range: 40–3000.

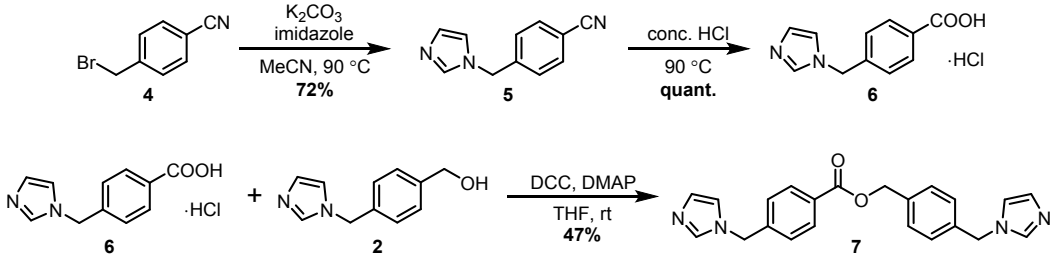
2. Synthesis of degradable linkers



[4-(1H-Imidazol-1-yl)methylphenyl]methanol (2). A two-neck round-bottom flask fitted with a dropping funnel and reflux condenser was filled with imidazole (871 mg, 12.8 mmol) and powder KOH (1.16 g, 16.6 mmol). Acetonitrile (70 mL) was added to the flask, and the mixture was stirred at 25 °C over 1 h. The dropping funnel was then charged with a solution of benzyl chloride **1** (2.00 g, 12.8 mmol) in acetonitrile (57 mL) that was added dropwise to the stirring mixture. Upon complete

addition, the reaction mixture was stirred at reflux over 16 h, then cooled to room temperature and concentrated under reduced pressure. The resultant solids were dissolved in chloroform (20 mL) and washed with water (20 mL). The aqueous layer was then extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain benzyl alcohol **2** as a yellow oil (2.31 g, 12.3 mmol, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (s, 1H, ImH), 7.33 (d, *J* = 8.0 Hz, 2H, PhH), 7.08 (d, *J* = 8.0 Hz, 2H, PhH), 6.97 (t, *J* = 1.0 Hz, 1H, ImH), 6.85 (d, *J* = 1.0 Hz, 1H, ImH), 5.04 (s, 2H, NCH_2), 4.66 (s, 2H, OCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.4, 137.4, 135.3, 129.7, 127.5, 119.3, 64.6, 50.6.

Bis[4-(1H-Imidazol-1-yl)methylbenzyl] carbonate (3). 1,1'-Carbonyldiimidazole (CDI, 1.03 g, 6.35 mmol) was added to a solution of benzyl alcohol **2** (1.20 g, 6.35 mmol) in anhydrous THF (20 mL) at 0 °C in one portion. The solution was stirred and warmed to room temperature over 2 h. In the meantime, a second solution of benzyl alcohol **2** (1.20 g, 6.35 mmol) in anhydrous THF (20 mL) was cooled to 0 °C. NaH (60% dispersion in mineral oil, 254 mg, 6.35 mmol) was added to the second solution, and the mixture was stirred at 0 °C for 30 min. The solution of benzyl carbamate was then added slowly to the solution of deprotonated benzyl alcohol at 0 °C, and the resulting mixture was warmed to room temperature over 1 h. The reaction mixture was diluted with ethyl acetate (10 mL), and quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude material was purified by column chromatography (1% MeOH in $CHCl_3$) to obtain carbonate **3** as an off-white solid (1.90 g, 4.72 mmol, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (s, 2H, ImH), 7.36 (d, *J* = 8.0 Hz, 4H, PhH), 7.14 (d, *J* = 8.0 Hz, 4H, PhH), 7.09 (s, 2H, ImH), 6.89 (s, 2H, ImH), 5.15 (s, 4H, OCH_2), 5.12 (s, 4H, NCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.9, 137.4, 136.6, 135.2, 129.9, 128.9, 127.5, 119.3, 69.2, 50.4.

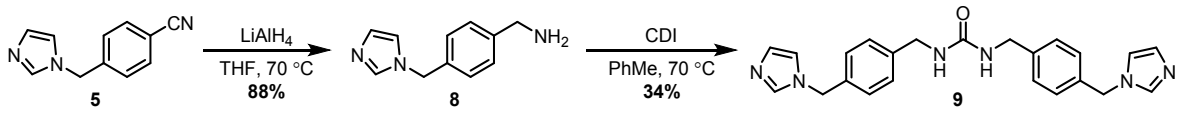


4-[(1H-Imidazol-1-yl)methyl]benzonitrile (5). To a solution of benzyl bromide **4** (3.00 g, 15.3 mmol) in acetonitrile (50 mL) in a two-neck round-bottom flask fitted with a reflux condenser was added imidazole (3.10 g, 45.9 mmol), followed by K_2CO_3 (10.6 g, 76.5 mmol). The reaction mixture was stirred under reflux over 16 h, and then cooled to room temperature and filtered through cotton wool. The filtrate was concentrated, and the resultant solids were re-dissolved in dichloromethane (50 mL). The organic solution was washed with saturated aqueous sodium carbonate solution (2 × 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain benzonitrile **5** as a yellow powder (2.01 g, 11.0 mmol, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H, PhH), 7.57 (s, 1H, ImH), 7.22 (d, *J* = 8.5 Hz, 2H, PhH), 7.14 (s, 1H, ImH), 6.91 (s, 1H, ImH), 5.21 (s, 2H, NCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.6, 137.6, 132.9, 130.5, 127.6, 119.3, 118.3, 112.4, 50.2.

4-[(1H-Imidazol-1-yl)methyl]benzoic acid (6). Benzonitrile **5** (100 mg, 0.546 mmol) was dissolved in 37% concentrated hydrochloric acid (1.5 mL) and stirred at reflux for 3 h. The solution was cooled to room temperature, then concentrated under reduced pressure to obtain carboxylic acid **6** as a white solid (130 mg, 0.546 mmol, quant.). **^{1}H NMR** (400 MHz, d_4-MeOD) δ 7.86 (d, *J* = 8.5 Hz, 2H, PhH), 7.78 (s, 1H, ImH), 7.32 (d, *J* = 8.5 Hz, 2H, PhH), 7.14 (s, 1H, ImH), 7.01 (s, 1H, ImH), 5.31 (s, 2H, NCH_2); **^{13}C NMR** (101 MHz, d_4-MeOD) δ 171.8, 142.3, 138.8, 134.7, 129.5, 129.3, 128.5, 121.0, 51.1.

4-[(1H-Imidazol-1-yl)methyl]benzyl 4-[(1H-imidazol-1-yl)methyl]benzoate (7). To a solution of carboxylic acid **6** (193 mg, 0.808 mmol) and DMAP (85 mg, 0.699 mmol) in anhydrous THF (35 mL) was added a solution of benzyl alcohol **2** (101 mg, 0.538 mmol) and DCC (111 mg, 0.538 mmol) in

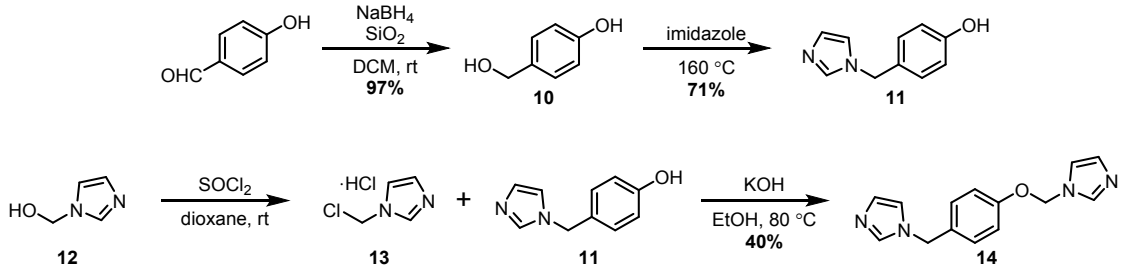
anhydrous THF (35 mL). The resulting mixture was stirred at room temperature over 12 h, and filtered through cotton wool. The filtrate was concentrated and the resulting solids were dissolved in ethyl acetate (10 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 10 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude material was purified by column chromatography (0 → 5% MeOH in $CHCl_3$) to obtain ester **7** as a white solid (94 mg, 0.252 mmol, 47%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 2H, PhH), 7.55 (s, 1H, ImH), 7.54 (s, 1H, ImH), 7.42 (d, *J* = 8.0 Hz, 2H, PhH), 7.20–7.16 (m, 4H, PhH), 7.10 (s, 1H, ImH), 7.08 (s, 1H, ImH), 6.89 (s, 2H, ImH), 5.34 (s, 2H, OCH_2), 5.18 (s, 2H, NCH_2), 5.12 (s, 2H, NCH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.7, 141.5, 137.5, 137.4, 136.3, 136.0, 130.4, 130.0, 129.9, 129.8, 128.8, 127.5, 127.1, 119.3, 66.3, 50.4, 50.3.



4-(1H-Imidazol-1-yl)methylphenylmethanamine (8). To a three-neck round-bottom flask fitted with a dropping funnel and reflux condenser was added solid $LiAlH_4$ (1.70 g, 43.9 mmol), followed by anhydrous THF (12 mL). The suspension was heated at a gentle reflux. The dropping funnel was then charged with a solution of benzonitrile **5** (2.01 g, 11.0 mmol) in anhydrous THF (35 mL), which was added dropwise to the refluxing mixture over the course of 1 h. The resulting thick brown slurry was stirred at reflux over 16 h, then cooled to 0 °C and quenched carefully with water (10 mL) until it formed a thick white slurry. The pH of the slurry was adjusted to 12 with 3 M aqueous NaOH, and the resulting mixture was filtered through Celite® that was rinsed with dichloromethane. The organic layer from the filtrate was collected, and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain benzylamine **8** as a yellow oil (1.81 g, 9.67 mmol, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (s, 1H, ImH), 7.31 (d, *J* = 8.0 Hz, 2H, PhH), 7.13 (d, *J* = 8.0 Hz, 2H, PhH), 7.08

(s, 1H, ImH), 6.90 (s, 1H, ImH), 5.11 (s, 2H, NCH_2), 3.87 (s, 2H, CH_2NH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.4, 137.4, 134.6, 129.8, 127.7, 127.6, 119.2, 50.6, 46.0.

1,3-Bis[4-(1H-imidazol-1-yl)methylbenzyl]urea (9). A solution of benzyl amine **8** (1.80 g, 9.82 mmol) and CDI (1.17 g, 5.93 mmol) in anhydrous toluene (21 mL) was stirred at 70 °C over 16 h. The resulting mixture was cooled to room temperature and concentrated. The solids obtained were dissolved in dichloromethane (50 mL) and washed with saturated aqueous Na_2CO_3 (20 mL). The aqueous layer was extracted with DCM (2 × 10 mL), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude material was purified by column chromatography (6 → 10% MeOH in dichloromethane) to obtain urea **9** as a white solid (662 mg, 1.65 mmol, 34%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (s, 2H, ImH), 7.17 (d, *J* = 8.0 Hz, 4H, PhH), 7.00 (d, *J* = 8.0 Hz, 4H, PhH), 6.98 (s, 2H, ImH), 6.84 (s, 2H, ImH), 6.01 (t, *J* = 5.5 Hz, 2H, NH), 5.01 (s, 4H, NCH_2), 4.27 (d, *J* = 5.5 Hz, 4H, CH_2NH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.7, 140.1, 137.2, 134.8, 129.4, 127.8, 127.5, 119.4, 50.5, 43.6.



4-(1H-Imidazol-1-yl)methylphenol (11). Benzyl alcohol **10**[1] (1.92 g, 15.5 mmol) and imidazole (3.17 g, 46.5 mmol) were combined in vial vented by a needle and heated at 160 °C over 30 min. The hot mixture was poured into boiling water (100 mL), and the hot suspension was filtered through a Büchner funnel. The residue was rinsed with hot water (2 × 10 mL) and dried *in vacuo* (50 °C, 10 mbar) to obtain phenol **11** as a white powder (1.92 g, 11.0 mmol, 71%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.50 (br s, 1H, OH), 7.69 (s, 1H, ImH), 7.13 (t, *J* = 1.0 Hz, 1H, ImH), 7.10 (d, *J* = 8.5 Hz,

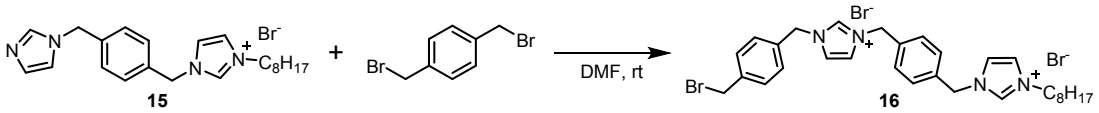
2H, PhH), 6.87 (t, J = 1.0 Hz, 1H, ImH), 6.72 (d, J = 8.5 Hz, 2H, PhH), 5.03 (s, 2H, NCH_2). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 157.0, 137.1, 129.1, 128.6, 128.0, 119.3, 115.3, 49.1.

The spectroscopic data were found to be in agreement with that reported by McNulty and co-workers.[1]

1-(Chloromethyl)-1H-imidazole (13). To a solution of 1H-imidazole-1-methanol **12**[2] (80% w/w, 1.00 g, 8.15 mmol) in anhydrous dioxane (16 mL) was added $SOCl_2$ (1.8 mL, 24.5 mmol). The reaction mixture was stirred at room temperature over 2 h, then concentrated under reduced pressure to obtain chloride **13** as an off-white syrup (1.79 g). Analysis of the material by ^{1}H NMR spectroscopy (d_6-DMSO) revealed chloride **13** present as its HCl salt along with imidazole hydrochloride in a 3:2 ratio (69% w/w).

1-[4-(1H-Imidazol-1-yl)methoxybenzyl]-1H-imidazole (14). To a solution of chloride **13** (69% w/w, 1.35 g, 6.09 mmol) in EtOH (12 mL) were added phenol **11** (1.06 g, 6.09 mmol) and KOH pellets (1.03 g, 18.3 mmol). The solution was stirred under reflux for 16 h, cooled to room temperature, and filtered through cotton wool. The filtrate was concentrated and the resulting solids were re-dissolved in dichloromethane (10 mL). The organic solution was washed with water (10 mL), followed by 1 M aqueous NaOH (3 × 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain hemiaminal **14** as a yellow oil (616 mg, 2.42 mmol, 40%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.87 (s, 1H, ImH), 7.73 (s, 1H, ImH), 7.34 (t, J = 1.5 Hz, 1H, ImH), 7.23 (d, J = 8.5 Hz, 2H, PhH), 7.16 (t, J = 1.5 Hz, 1H, ImH), 7.04 (d, J = 8.5 Hz, 2H, PhH), 6.92 (t, J = 1.0 Hz, 1H, ImH), 6.88 (t, J = 1.0 Hz, 1H, ImH), 5.98 (s, 2H, OCH_2), 5.11 (s, 2H, NCH_2). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 155.4, 138.3, 137.3, 131.6, 129.2, 129.0, 128.7, 119.9, 119.5, 116.1, 72.9, 48.9.

3. Synthesis of imidazolium oligomers

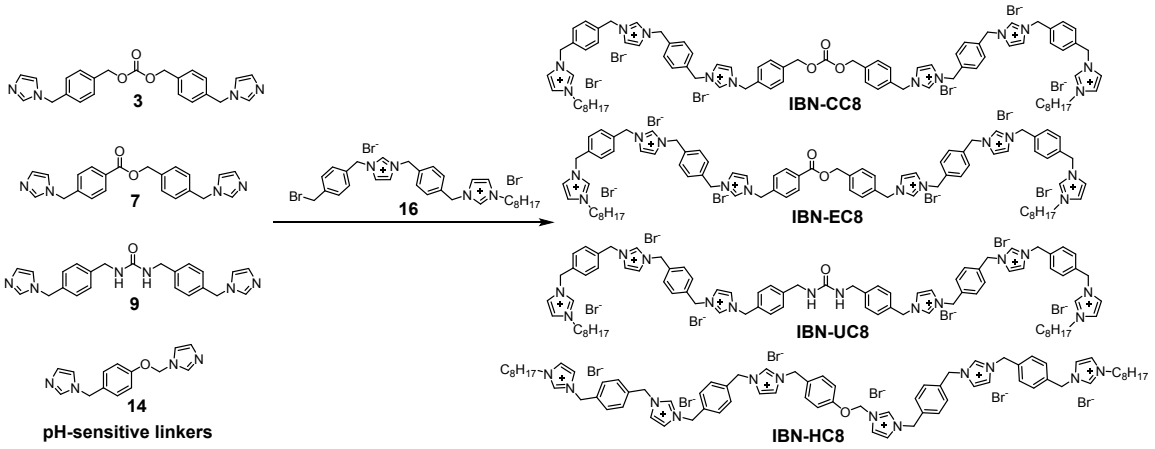


A solution of **15**[3] (2.63 g, 6.23 mmol) in DMF (62 mL) was added dropwise to a solution of 1,4-dibromo-*p*-xylylene (16.4 g, 62.3 mmol) and the resulting mixture was stirred at 25 °C over 48 h. The reaction mixture was concentrated *in vacuo*, and the product was precipitated with ether. The solids were spun down in a Falcon® tube in a centrifuge (5000 rpm), and the supernatant was decanted. The solids were washed with ether followed by acetone. The resulting solids were dried in a vacuum oven (50 °C, 10 mbar) over 16 h to obtain bisimidazolium salt **16** as white solids (2.88 g, 4.44 mmol, 71%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.49 (s, 1H, ImH), 9.39 (s, 1H, ImH), 7.86–7.82 (m, 4H, ImH),7.51–7.40 (m, 8H, PhH), 5.45 (s, 6H, 3 x NCH_2), 4.71 (s, 2H, CH_2Br), 4.17 (t, J = 7.4 Hz, 2H, CH_2N), 1.80–1.76 (m, 2H, NCH_2CH_2), 1.31–1.15 (m, 10H, C_5H_{10}), 0.85 (t, J = 6.5 Hz, 6H, 2 x CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 138.7, 136.4, 136.2, 135.5, 135.3, 134.9, 129.9, 129.1, 128.9, 128.7, 123.0, 122.9, 122.6, 51.6, 51.5, 51.4, 49.0, 31.2, 29.3, 28.5, 28.3, 25.5, 22.1, 14.0. Unreacted α,α'-dibromo-*p*-xylene (~ 8 equiv.) was recovered by concentrating the combined ether washings.

General procedure for the synthesis of imidazolium oligomers (Scheme 2)**.** Linker (1.0 eq) and bisimidazolium salt **16** (2.4 eq) were dissolved in anhydrous DMF (0.05 M), and stirred at room temperature over 24–48 h. The reaction mixture was concentrated *in vacuo* to ~ 5–10 mL, and the product was precipitated with acetone. The solids were spun down in a Falcon® tube in a centrifuge (5000 rpm), and the supernatant was decanted. They were washed twice more by first dissolving in a minimum amount of methanol, and then precipitated with acetone (total volume of 40–50 mL). The resulting solids were dried in a vacuum oven (50 °C, 10 mbar) over 16 h to obtain the imidazolium oligomers as white powders.

Where DMF was detected in NMR spectroscopic analysis of the compounds, it could be azeotropically removed with toluene. This was achieved by first dissolving the powder in a minimum amount of methanol, adding 3–4 times the volume of toluene, and removing the solvents *in vacuo*.

Repeating this step twice was usually sufficient to remove traces of DMF from the samples for biological testing.



IBN-Carbonate-C8 (**IBN-CC8**) was prepared by the general procedure from carbonate linker **3** and isolated as a white powder (438 mg, 0.244 mmol, 47%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.56–9.54 (m, 4H, ImH), 9.42 (s, 2H, ImH), 7.86–7.84 (m, 12H, ImH), 7.51–7.43 (m, 24H, PhH), 5.47 (s, 20H, 10 × NCH_2), 5.16 (s, 4H, 2 × OCH_2), 4.17 (t, J = 7.0 Hz, 4H, 2 × NCH_2CH_2), 1.80–1.77 (m, 4H, 2 × NCH_2CH_2), 1.24–1.23 (m, 20H, 2 × C_5H_{10}), 0.85 (t, J = 6.5 Hz, 6H, 2 × CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 154.4, 136.4, 136.2, 136.1, 135.6, 135.4, 135.4, 135.3, 135.0, 129.1, 129.0, 128.8, 128.7, 123.0, 122.9, 122.6, 68.7, 51.7, 51.6, 51.5, 49.0, 31.2, 29.3, 28.5, 28.4, 25.6, 22.1, 14.0. **HRMS** (ESI+) calc. for $C_{83}H_{100}Br_4N_{12}O_3$ $[M–2Br]^{2+}$ 816.2361; found 816.1995. **Anal.** calcd for $C_{83}H_{100}Br_6N_{12}O_3$: C, 55.59; H, 5.62; N, 9.37; found: C, 55.23; H, 5.58; N, 9.60.

IBN-Ester-C8 (IBN-EC8) was prepared by the general procedure from ester linker **7** and isolated as a white powder (102 mg, 0.060 mmol, 34%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.56–9.42 (m, 6H, ImH), 8.05–8.02 (m, 2H, PhH), 7.90–7.80 (m, 12H, ImH), 7.61–7.37 (m, 22H, PhH), 5.58–5.36 (m, 22H, OCH_2 + 10 × NCH_2), 4.18 (t, J = 7.0 Hz, 4H, 2 × NCH_2CH_2), 1.82–1.75 (m, 4H, 2 × NCH_2CH_2), 1.31–1.17 (m, 20H, 2 × C_5H_{10}), 0.85 (t, J = 6.5 Hz, 6H, 2 × CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 165.2, 140.1, 136.7, 136.4, 136.2, 135.5, 135.4, 135.3, 129.9, 129.1, 129.0, 128.7, 128.5, 122.9, 122.6, 65.9, 51.6, 51.4, 49.0, 31.2, 29.3, 28.5, 28.3, 25.5, 22.1, 14.0. **HRMS** (ESI+)

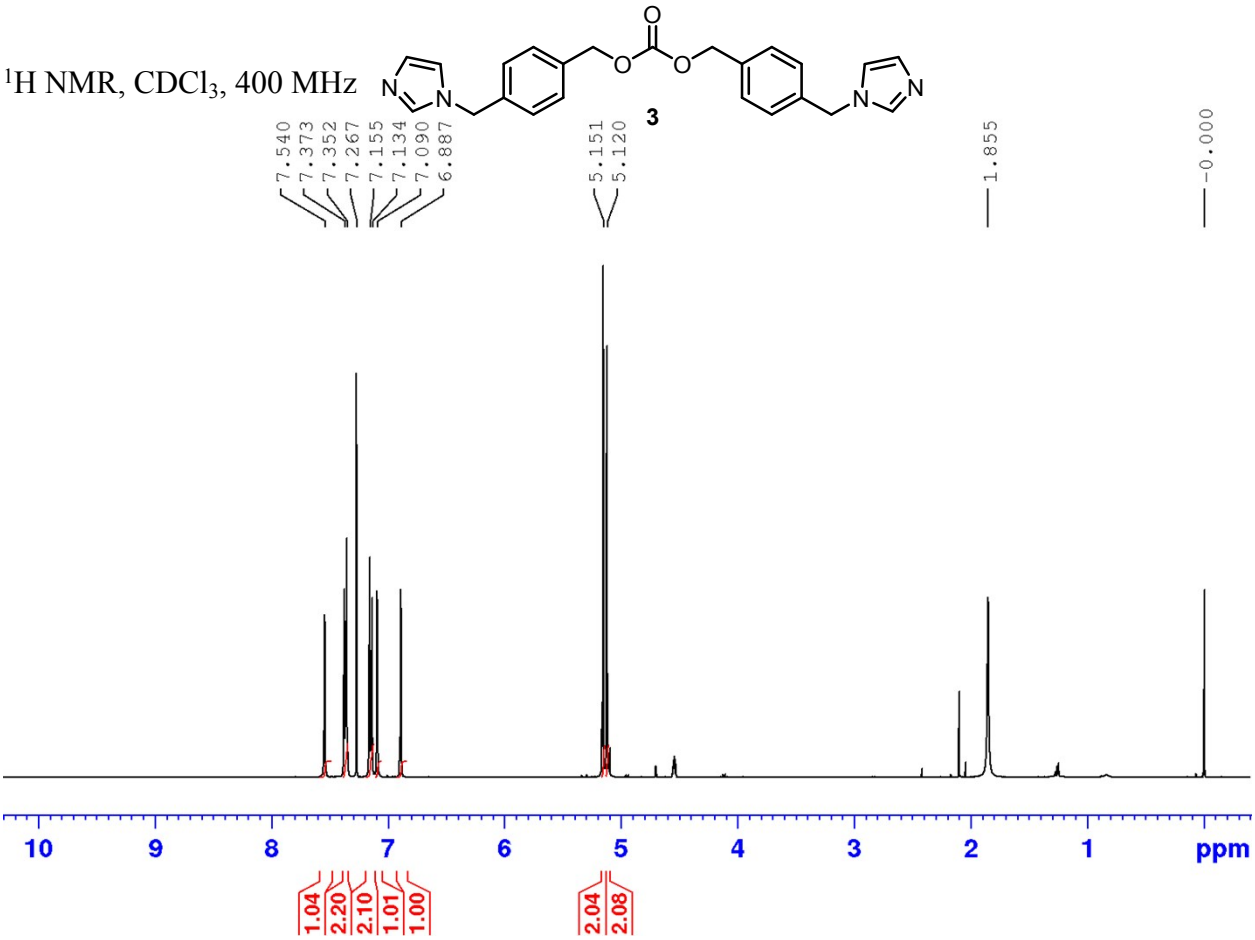
calc. for $C_{82}H_{98}Br_4N_{12}O_2$ $[M–2Br]^{2+}$ 801.2309; found 801.1903. **Anal.** calcd for $C_{82}H_{108}Br_6N_{12}O_7$ $[M+5H_2O]$: C, 53.14; H, 5.87; N, 9.07; found: C, 52.76; H, 5.52; N, 8.99.

IBN-Urea-C8 (IBN-UC8) was prepared by the general procedure from urea linker **9** and isolated as white powder (745 mg, 0.416 mmol, 75%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.57–9.38 (m, 6H, ImH), 7.86–7.82 (m, 12H, ImH), 7.51–7.21 (m, 24H, PhH), 6.65–6.57 (m, 2H, 2 × NH), 5.49–5.26 (m, 20H, 10 × NCH_2), 4.23–4.16 (m, 8H, 2 × $NHCH_2$ + 2 × NCH_2CH_2), 1.82–1.76 (m, 4H, 2 × NCH_2CH_2), 1.31–1.78 (m, 20H, 2 × C_5H_{10}), 0.85 (t, J = 6.5 Hz, 6H, 2 × CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 158.1, 141.8, 136.4, 136.3, 135.5, 135.3, 133.0, 129.1, 129.0, 128.4, 128.5, 127.6, 127.7, 127.5, 127.4, 122.8, 122.9, 122.6, 51.9, 51.6, 51.4, 49.0, 42.3, 31.2, 29.3, 28.5, 28.3, 25.5, 22.1, 14.0. **HRMS** (ESI+) calc. for $C_{83}H_{102}Br_4N_{14}O$ $[M–2Br]^{2+}$ 815.2521; found 815.2153.

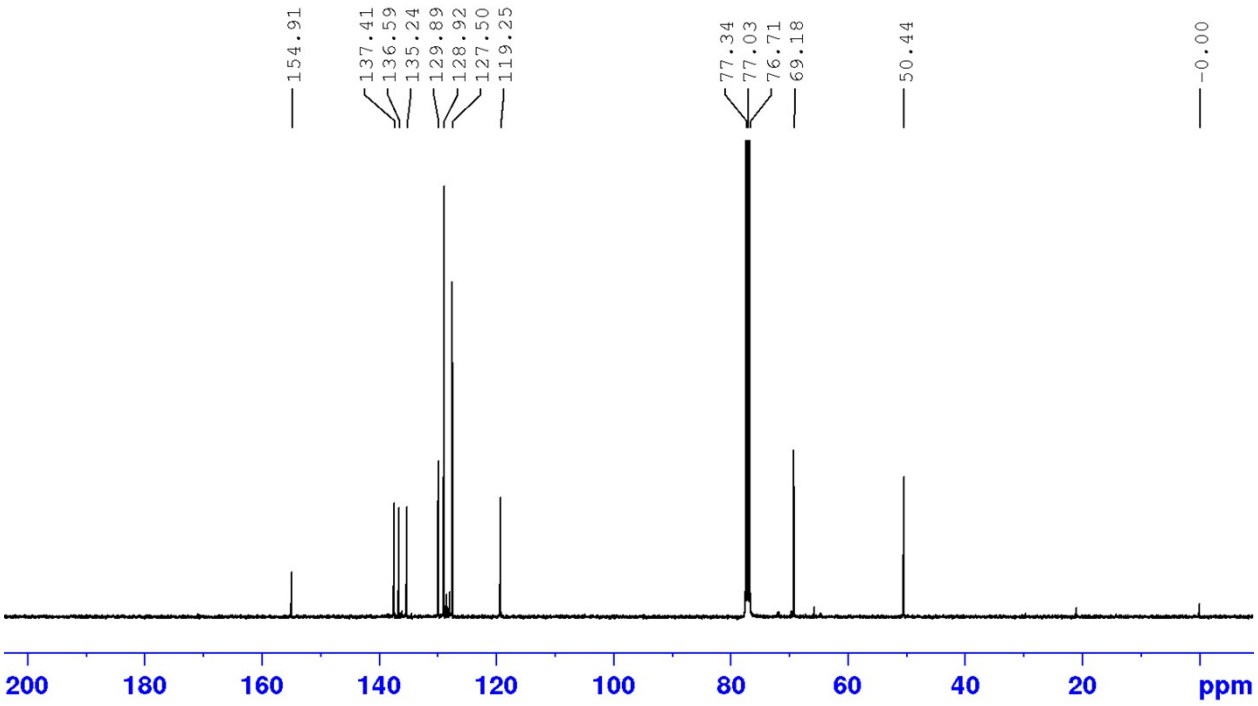
IBN-Hemiaminal-C8 (IBN-HC8) was prepared by the general procedure from hemiaminal linker **14** and isolated as a white powder (625 mg, 0.427 mmol, 50%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.74–9.35 (m, 6H, ImH), 8.00–7.77 (m, 12H, ImH), 7.52–7.45 (m, 18H, PhH), 7.19–7.12 (m, 2H, PhH), 6.26 (s, 2H, OCH_2N), 5.51–5.36 (m, 18H, NCH_2), 4.16 (t, J = 7.0 Hz, 4H, 2 × NCH_2CH_2), 1.81–1.74 (m, 4H, 2 × NCH_2CH_2), 1.31–1.16 (m, 20H, 2 × C_5H_{10}), 0.84 (t, J = 6.5 Hz, 6H, 2 × CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 155.6, 136.5, 136.3, 135.6, 135.5, 135.4, 130.7, 130.4, 129.3, 129.2, 129.1, 123.0, 122.6, 116.5, 116.4, 75.2, 51.8, 51.7, 51.5, 51.4, 49.1, 31.2, 29.4, 28.6, 28.4, 25.6, 22.2, 14.1.

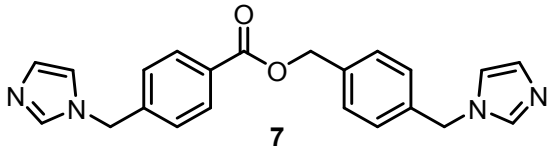
^{1}H and ^{13}C NMR spectra of linkers and oligomers

^{1}H NMR, $CDCl_3$, 400 MHz



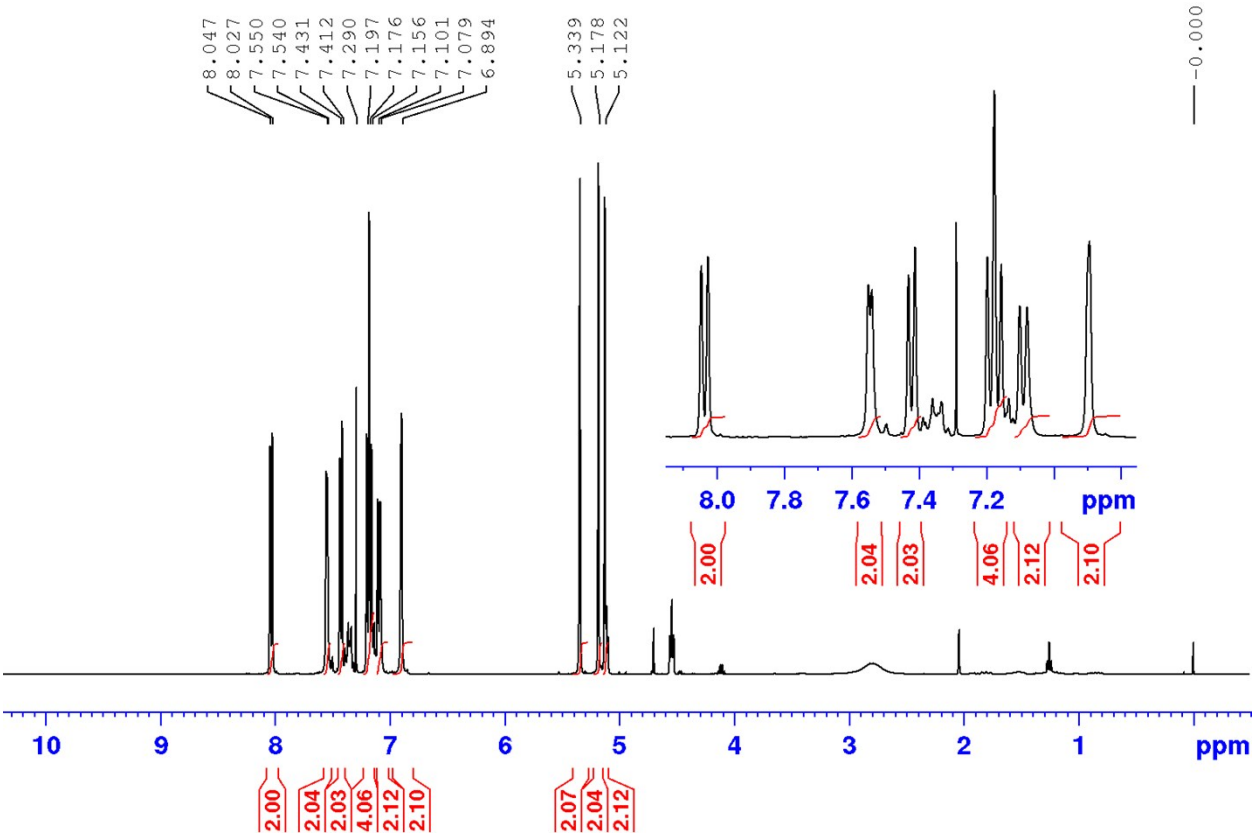
^{13}C NMR, $CDCl_3$, 101 MHz



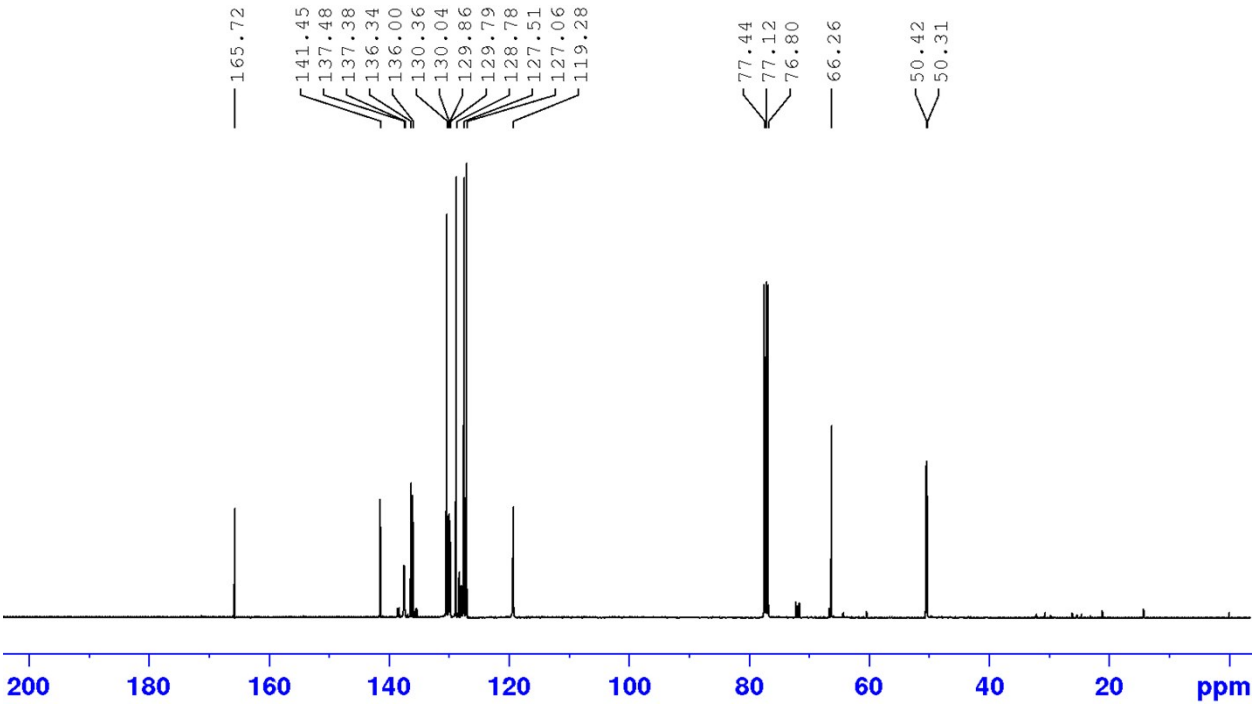


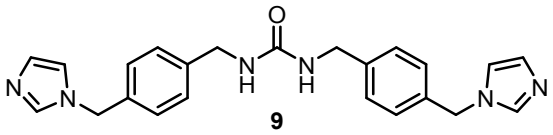
7

^{1}H NMR, $CDCl_3$, 400 MHz



^{13}C NMR, $CDCl_3$, 101 MHz





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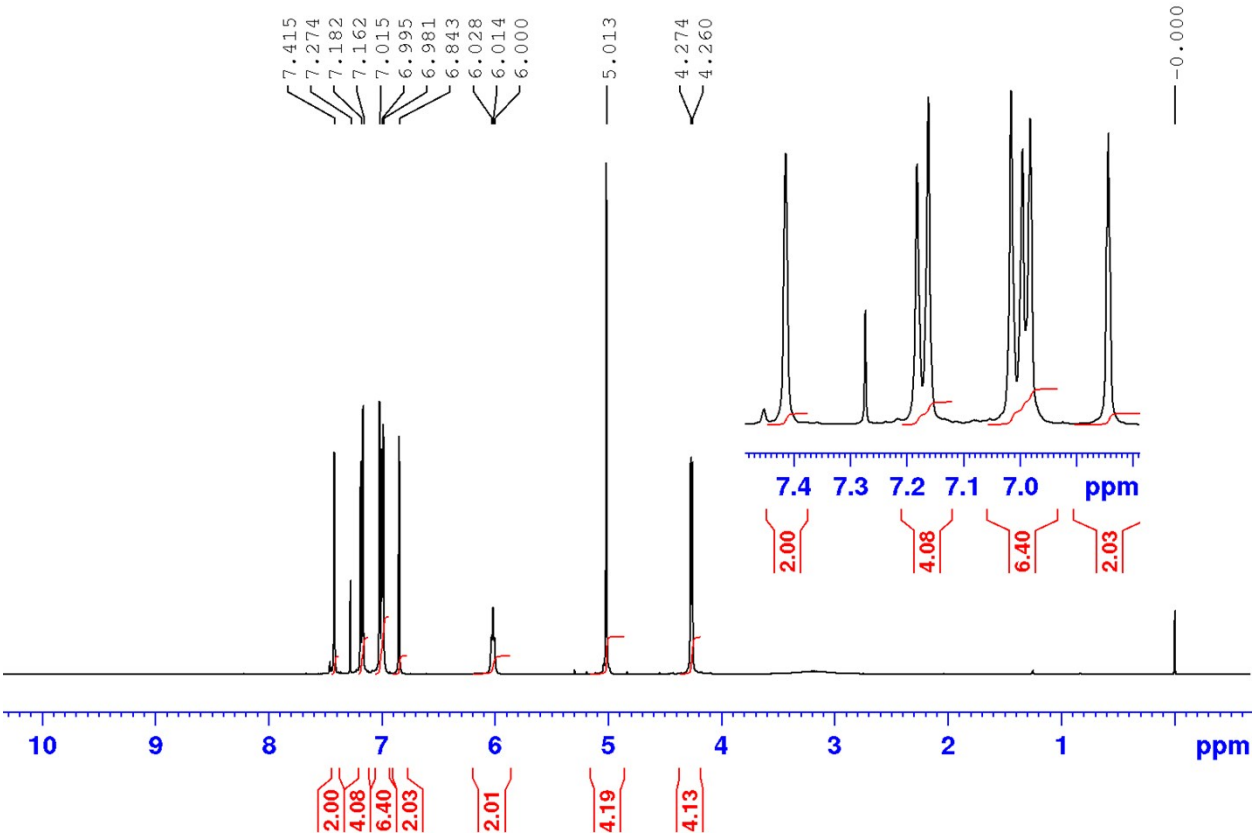
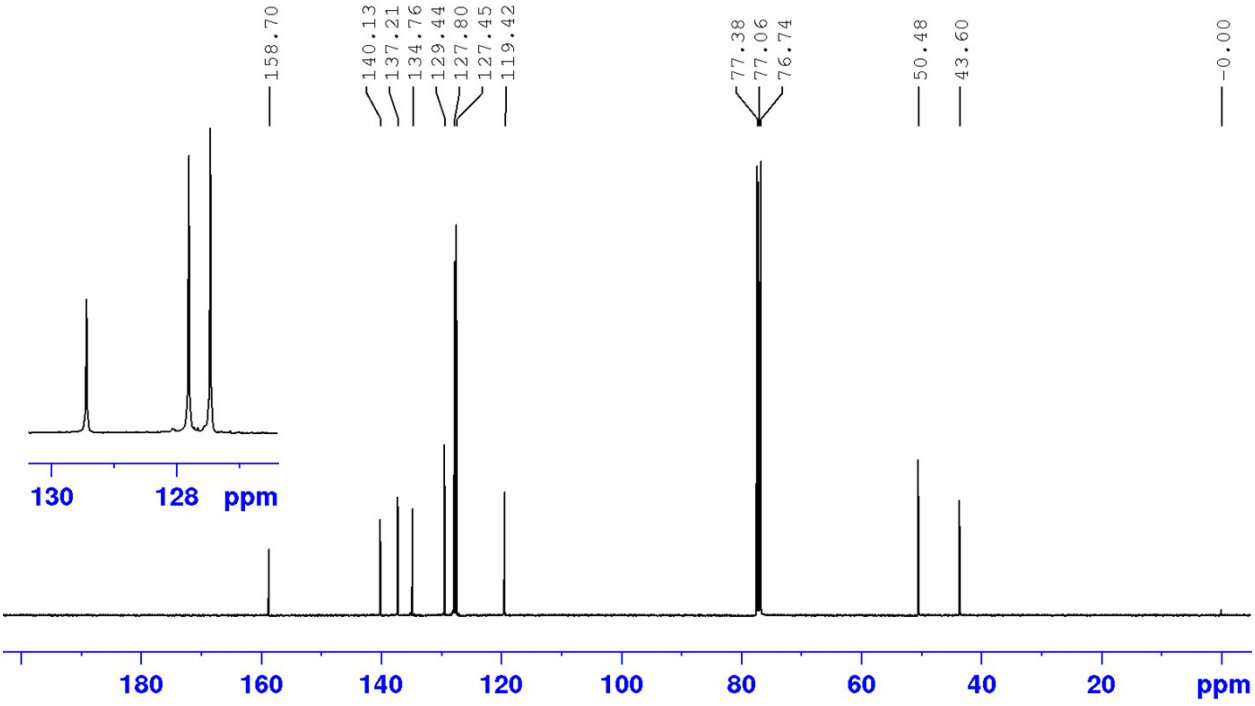
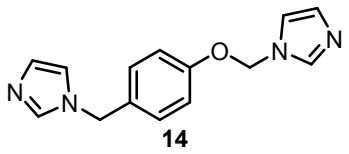
^{1}H NMR, $CDCl_3$, 400 MHz



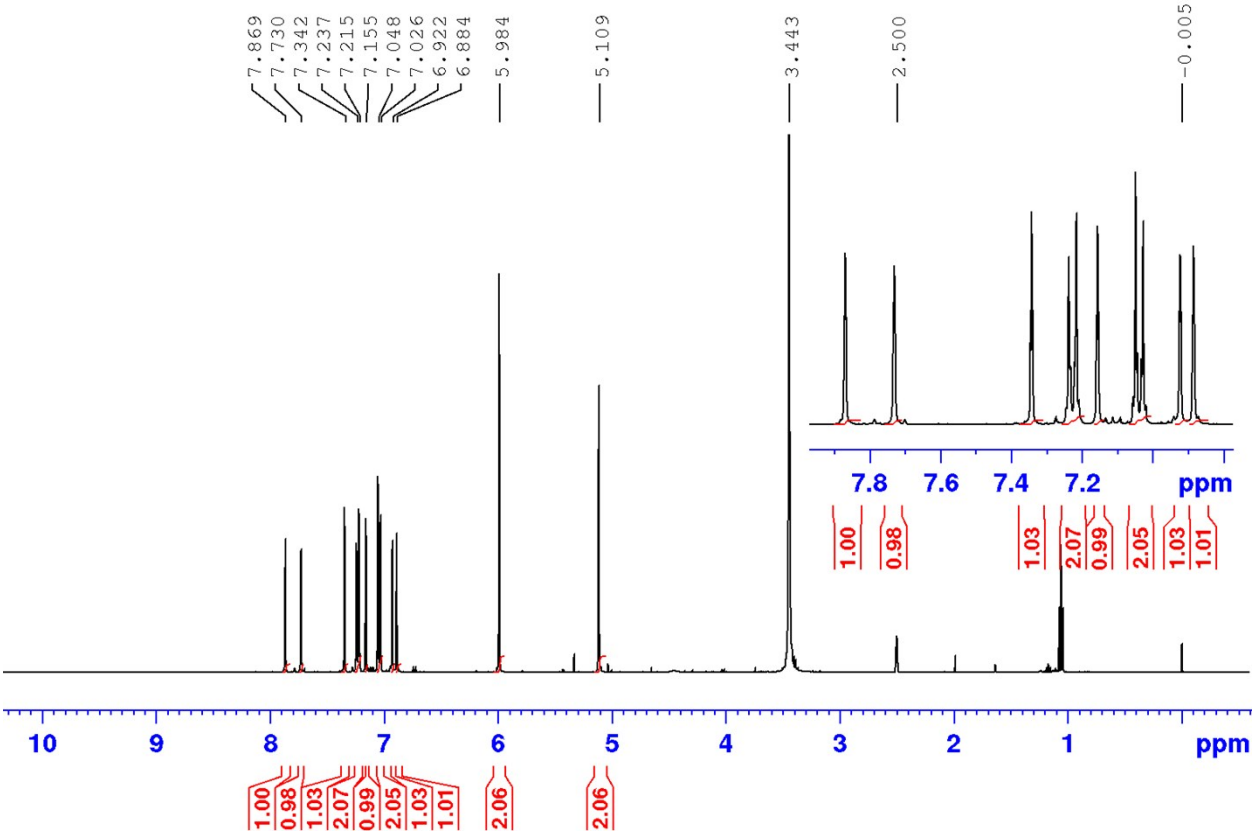
^{13}C NMR, $CDCl_3$, 101 MHz



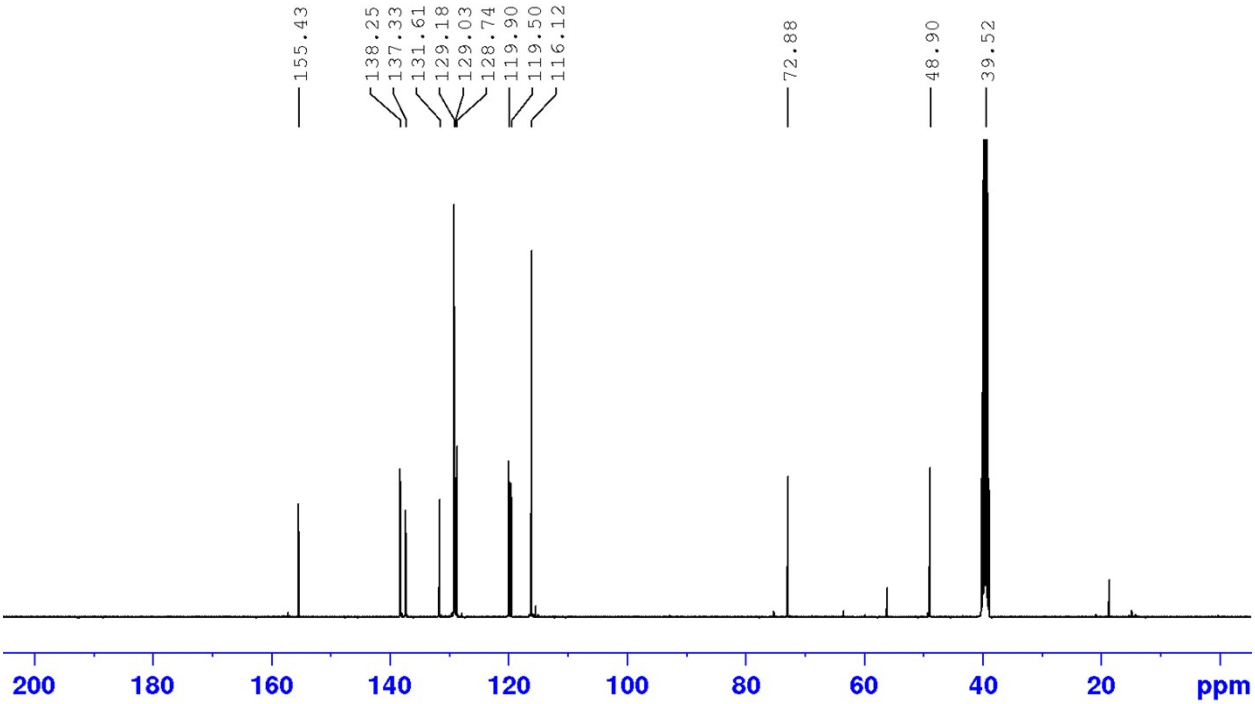


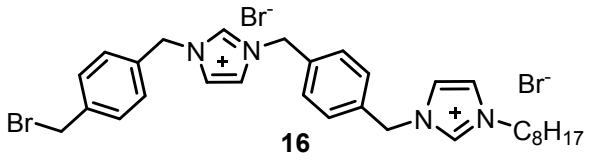
14

^{1}H NMR, d_6-DMSO, 400 MHz



^{13}C NMR, d_6-DMSO, 101 MHz





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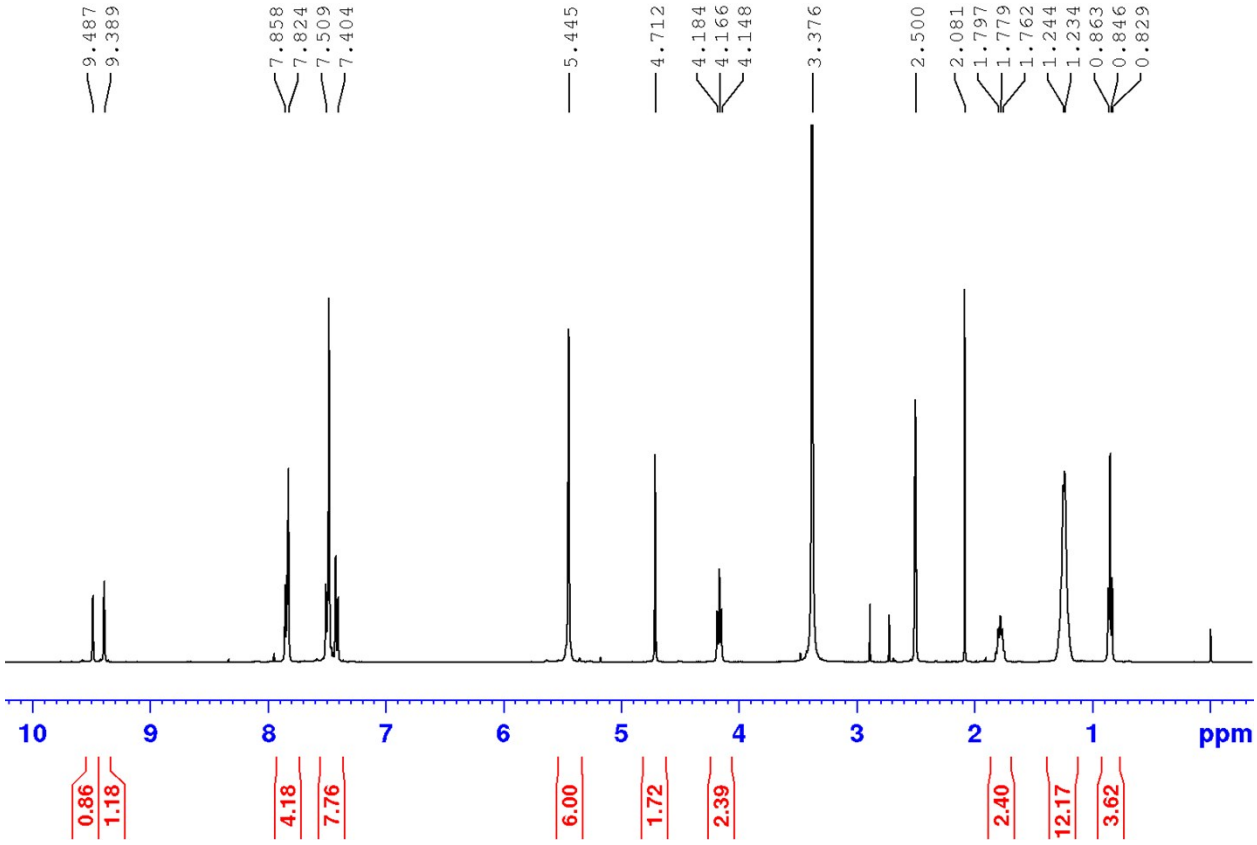
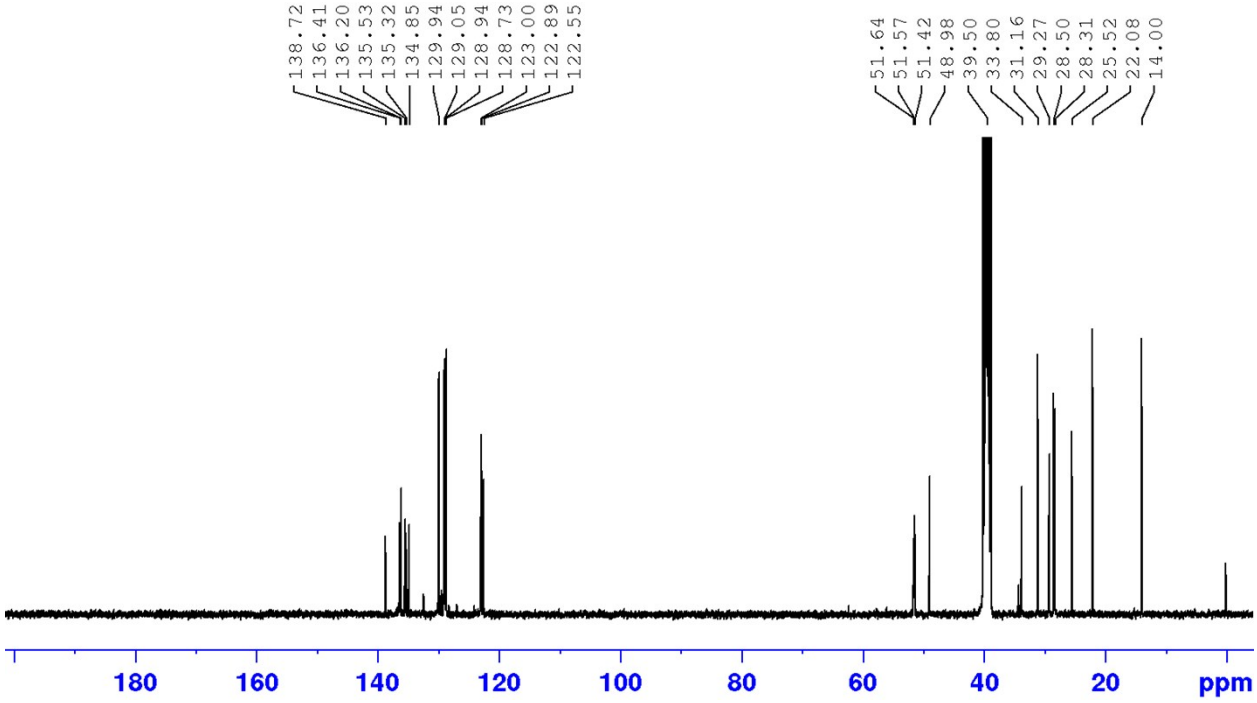
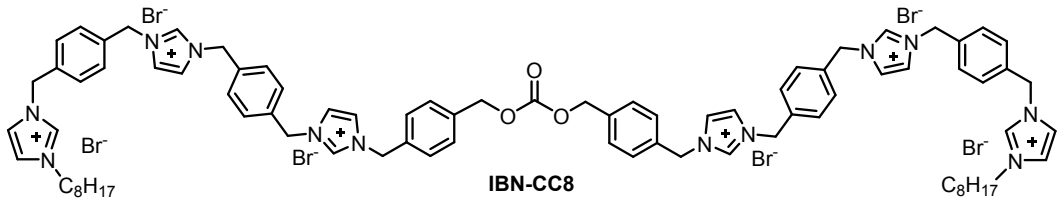
^{1}H NMR, d_6-DMSO, 400 MHz

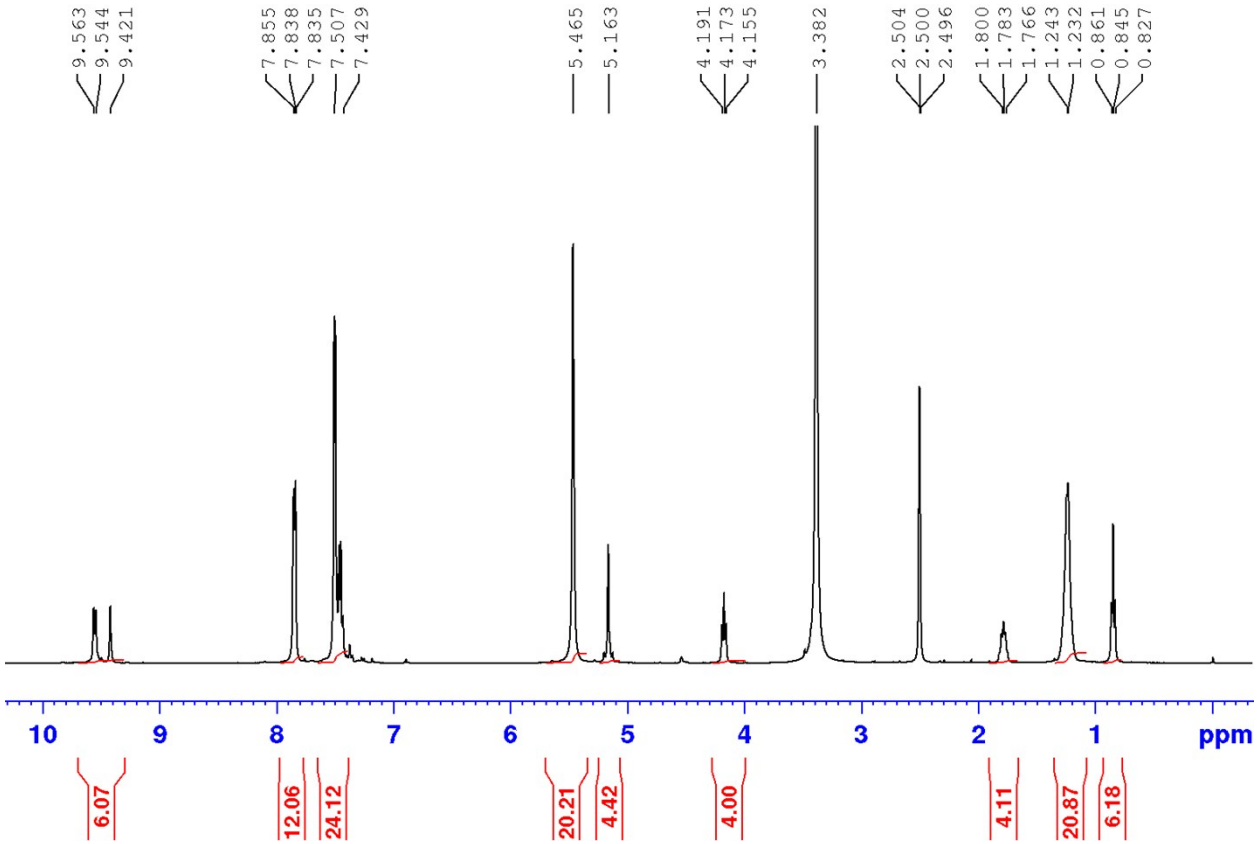


^{13}C NMR, d_6-DMSO, 101 MHz

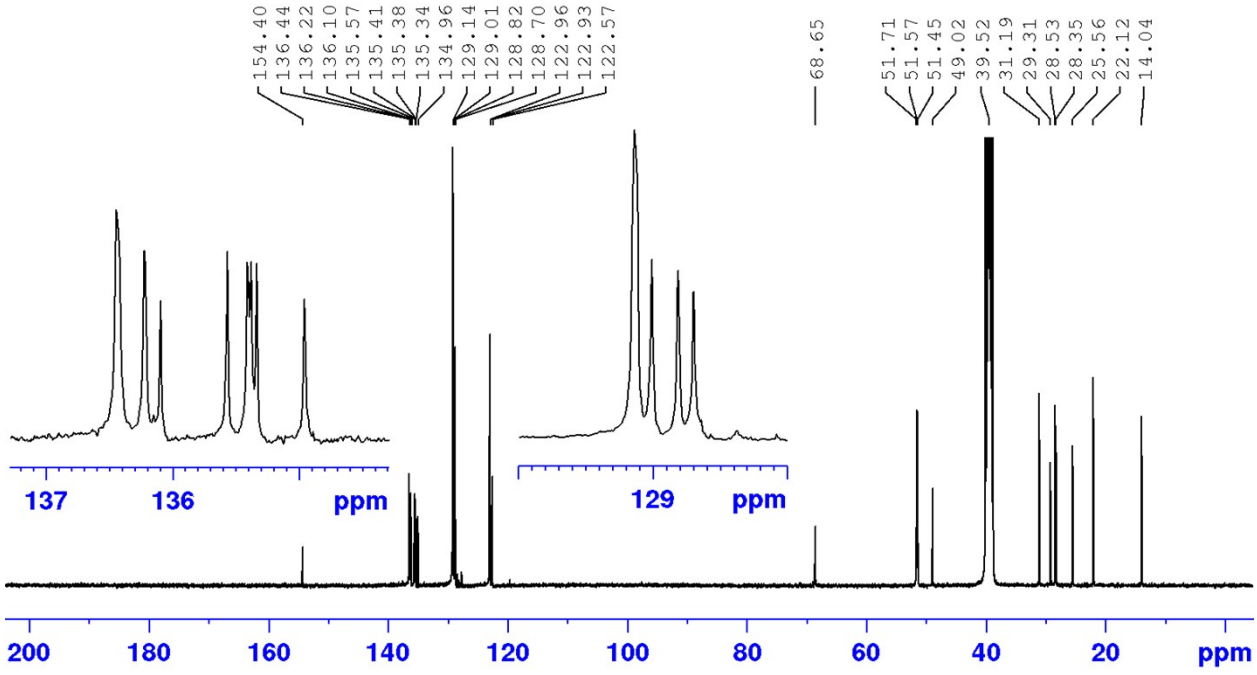


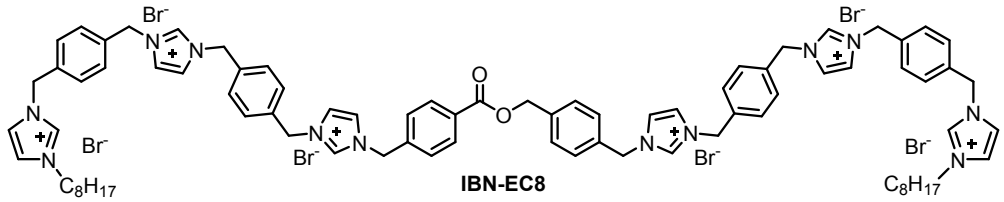


^{1}H NMR, d_6-DMSO, 400 MHz

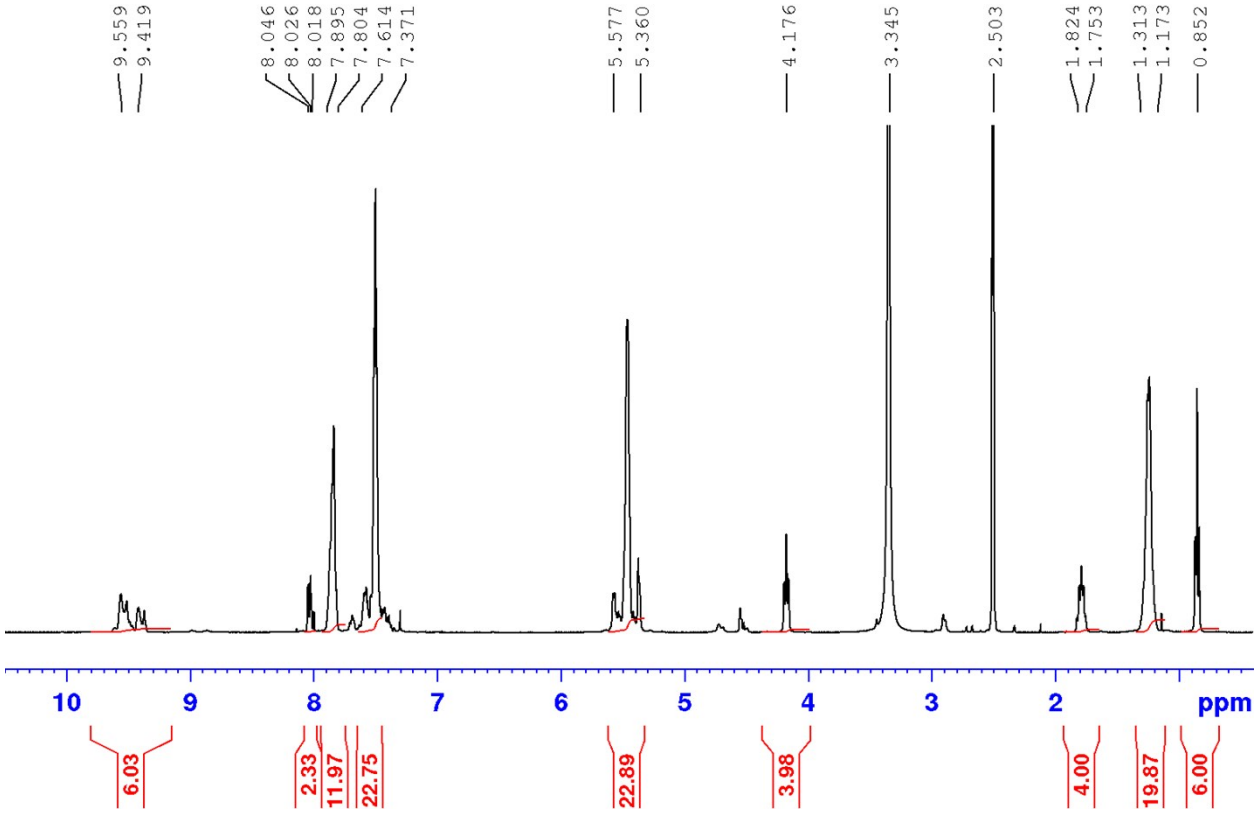


^{13}C NMR, d_6-DMSO, 101 MHz

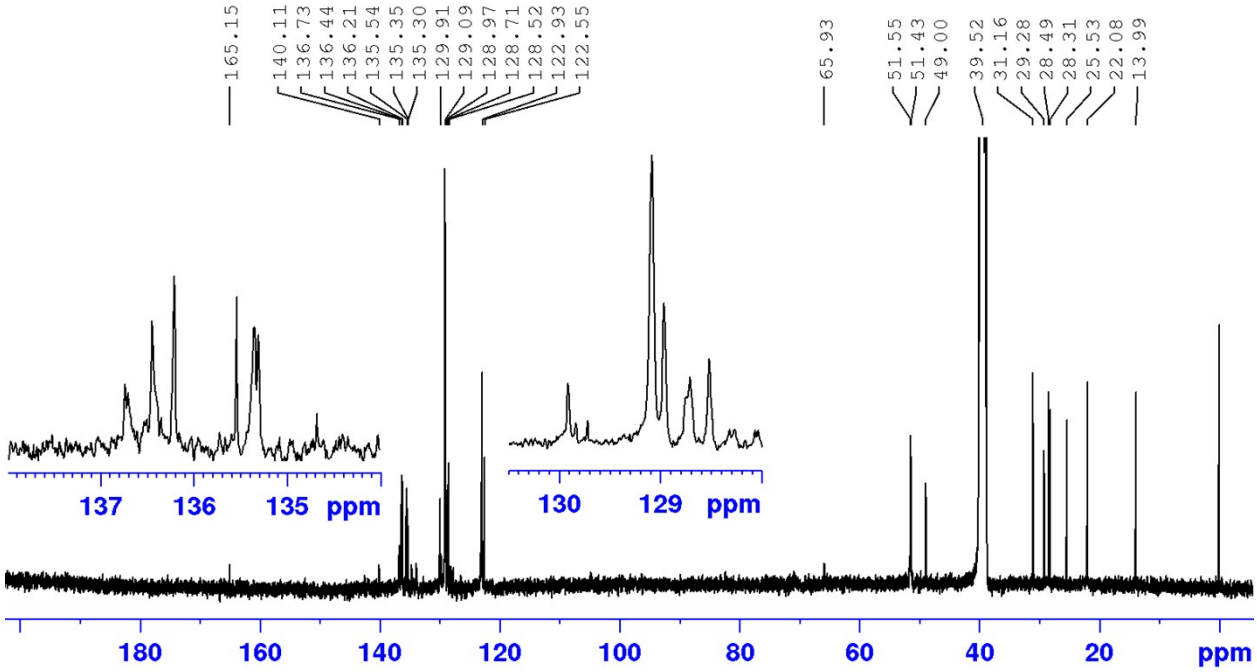


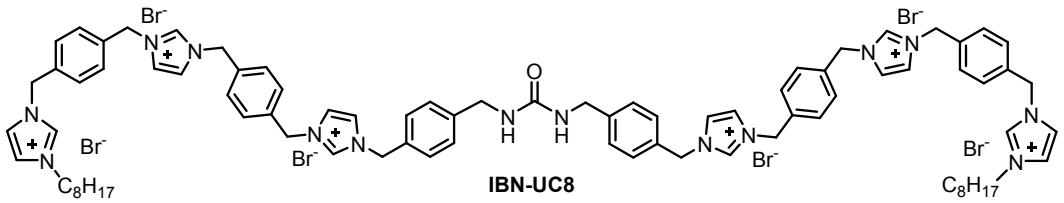


^{1}H NMR, d_6-DMSO, 400 MHz

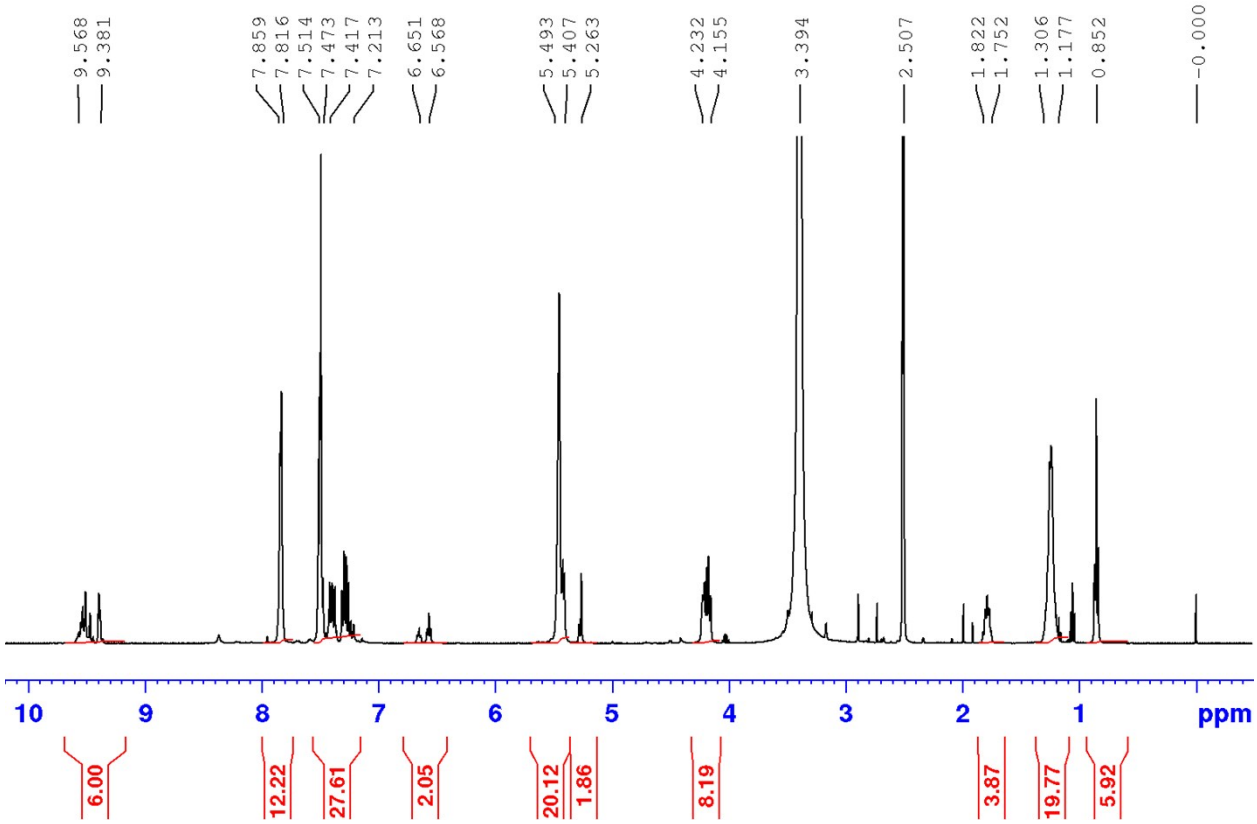


^{13}C NMR, d_6-DMSO, 101 MHz

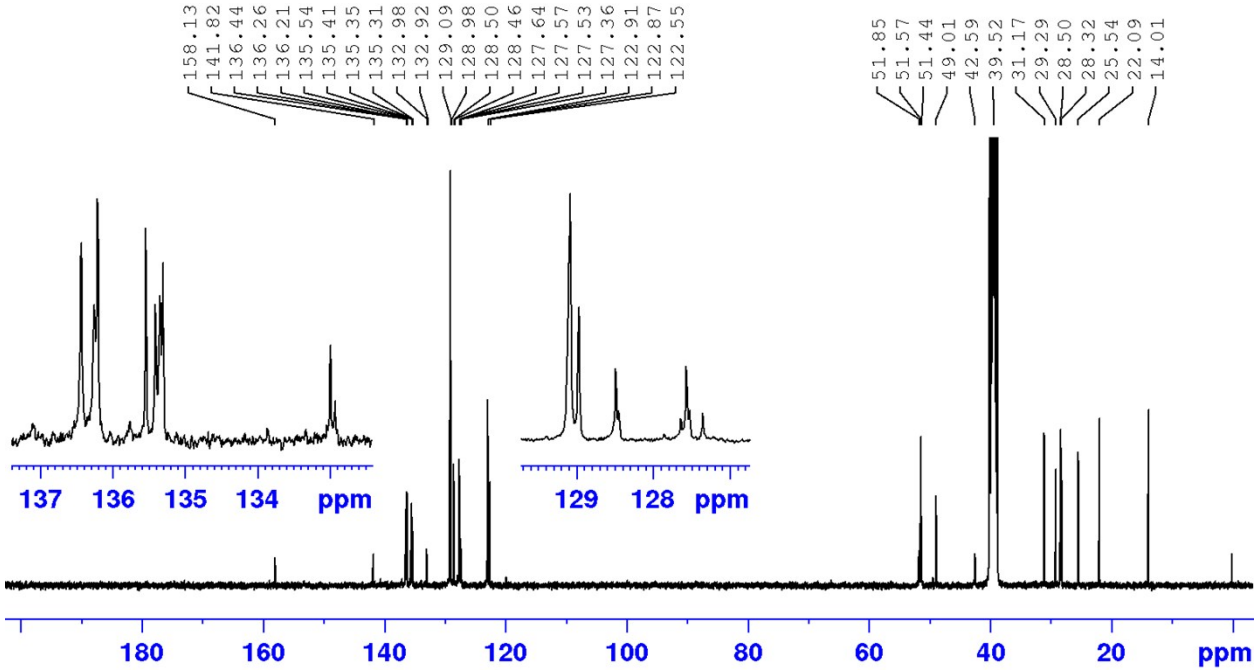


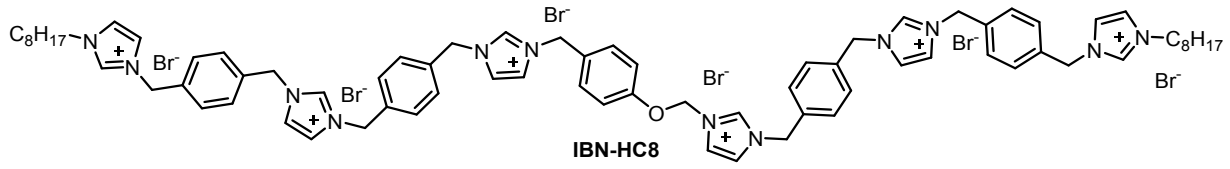


^{1}H NMR, d_6-DMSO, 400 MHz



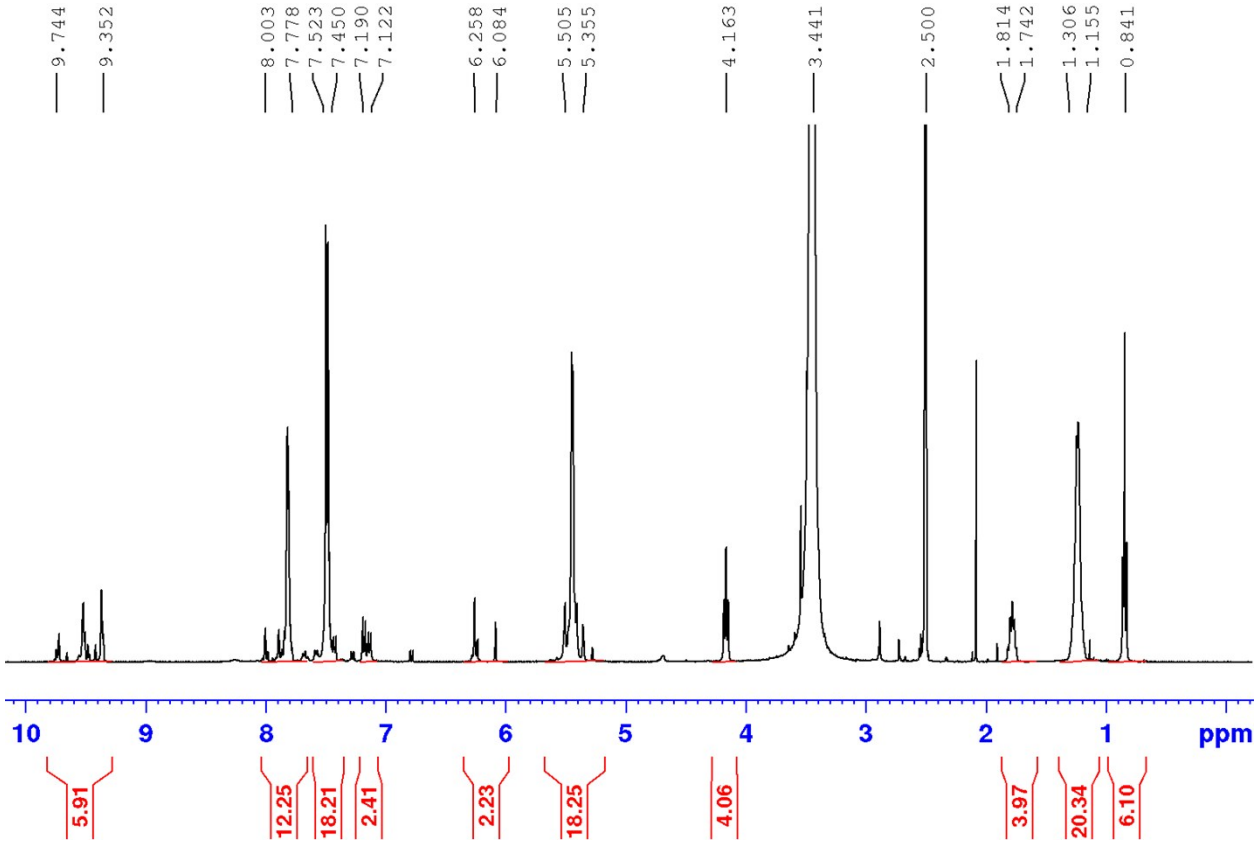
^{13}C NMR, d_6-DMSO, 101 MHz



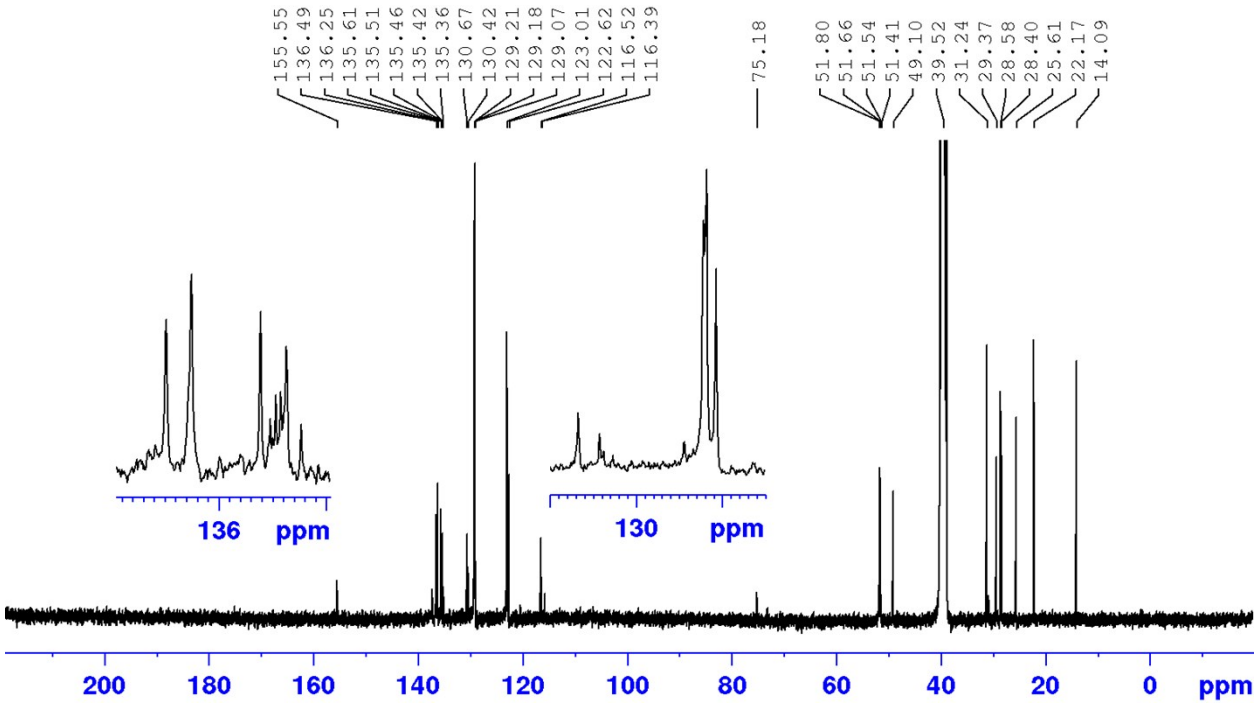


IBN-HC8

^{1}H NMR, d_6-DMSO, 400 MHz

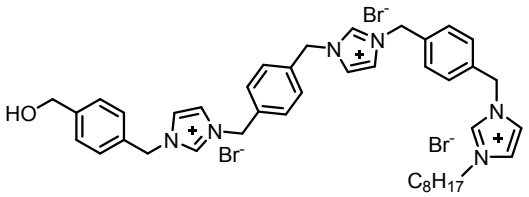


^{13}C NMR, d_6-DMSO, 101 MHz

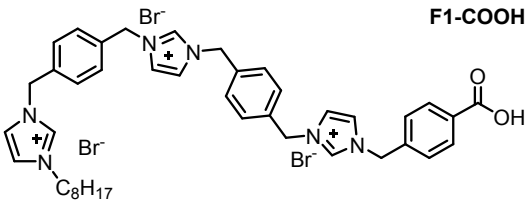


Synthesis of degradation products

General procedure for the synthesis of degradation products. Benzyl imidazole **2**, **6**, **8** or **11** (1.0 eq) and bisimidazolium salt **16** (1.2 eq) were dissolved in anhydrous DMF (0.05 M), and stirred at room temperature over 24–48 h. The reaction mixture was concentrated *in vacuo* to ~ 5–10 mL, and the product was precipitated with THF. The solids were spun down in a Falcon® tube in a centrifuge (5000 rpm), and the supernatant was decanted. They were washed twice more by first dissolving in a minimum amount of methanol, and then precipitated with THF (total volume of 40–50 mL). The resulting solids were dried in a vacuum oven (50 °C, 10 mbar) over 16 h to obtain the degradation products.

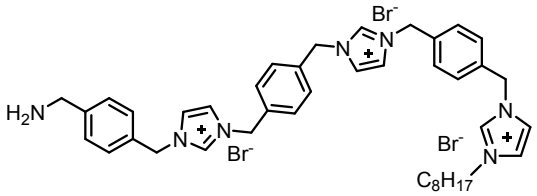


F1-CH$_2$OH was prepared by the general procedure from benzyl alcohol **2** and isolated as a white powder (182 mg, 0.218 mmol, 41%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.54 (s, 1H, ImH), 9.50 (s, 1H, ImH), 9.41 (s, 1H, ImH), 7.85–7.83 (m, 6H, ImH), 7.51–7.49 (m, 8H, PhH), 7.41–7.34 (m, 4H, PhH), 5.45–5.42 (m, 10H, 5 × NCH_2), 5.28 (t, J = 5.0 Hz, 1H, OH), 4.49 (d, J = 5.0 Hz, 2H, OCH_2), 4.17 (t, J = 7.0 Hz, 2H, NCH_2CH_2), 1.82–1.75 (m, 2H, NCH_2CH_2), 1.28–1.18 (m, 10H, C_5H_{10}), 0.85 (t, J = 6.5 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 143.4, 136.5, 136.3, 136.2, 135.6, 135.5, 135.4, 135.3, 133.0, 129.2, 129.1, 129.0, 128.4, 127.0, 123.0, 122.9, 122.6, 62.5, 52.0, 51.7, 51.5, 49.1, 31.2, 29.4, 28.6, 28.4, 25.6, 22.2, 14.1.

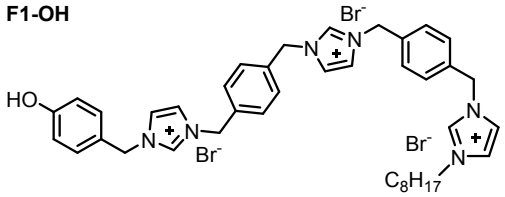


F1-COOH was prepared by the general procedure from benzonitrile **5**. The resulting tris-imidazolium salt was hydrolyzed in concentrated HCl and isolated as a white powder (64 mg, 0.069 mmol, 45%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.48 (s, 1H, ImH), 9.46 (s, 1H, ImH), 9.35 (s, 1H, ImH), 7.99 (d, J = 8.0 Hz, 2H, PhH), 7.86–7.80 (m, 6H, ImH), 7.53–7.44 (m, 10H, PhH), 5.54–5.44 (m, 10H, 5 × NCH_2), 4.17 (t, J = 7.0 Hz, 2H, NCH_2CH_2), 1.82–1.75 (m, 2H, NCH_2CH_2), 1.28–1.15 (m, 10H, C_5H_{10}), 0.85 (t, J = 6.5 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 178.7, 136.26,

135.6, 135.4, 135.3, 130.0, 129.1, 129.0, 128.5, 128.2, 123.0, 122.6, 51.7, 51.6, 51.5, 49.1, 31.2, 29.3, 28.6, 28.4, 25.6, 22.2, 14.1.

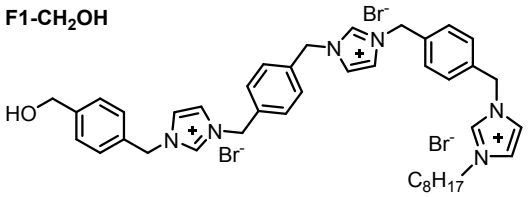


F1-CH_2NH_2 was prepared by the general procedure from benzyl amine **8** and isolated as a white powder (180 mg, 0.192 mmol, 63%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.56–9.32 (m, 3H, ImH), 8.21–7.81 (m, 6H, ImH), 7.59–7.37 (m, 8H, PhH), 7.28–7.23 (m, 2H, PhH), 7.18–7.12 (m, 2H, PhH), 5.52–5.24 (m, 8H, 4 × NCH_2), 4.18–4.04 (m, 4H, CH_2NH_2 + NCH_2CH_2), 1.81–1.75 (m, 2H, NCH_2CH_2), 1.28–1.18 (m, 10H, C_5H_{10}), 0.85 (t, J = 6.5 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 136.4, 136.3, 136.2, 135.5, 135.4, 135.3, 130.7, 130.5, 129.1, 129.0, 128.9, 128.6, 128.1, 122.9, 122.6, 51.8, 51.6, 51.5, 51.4, 49.0, 31.2, 29.3, 28.5, 28.3, 25.5, 22.1, 14.0.

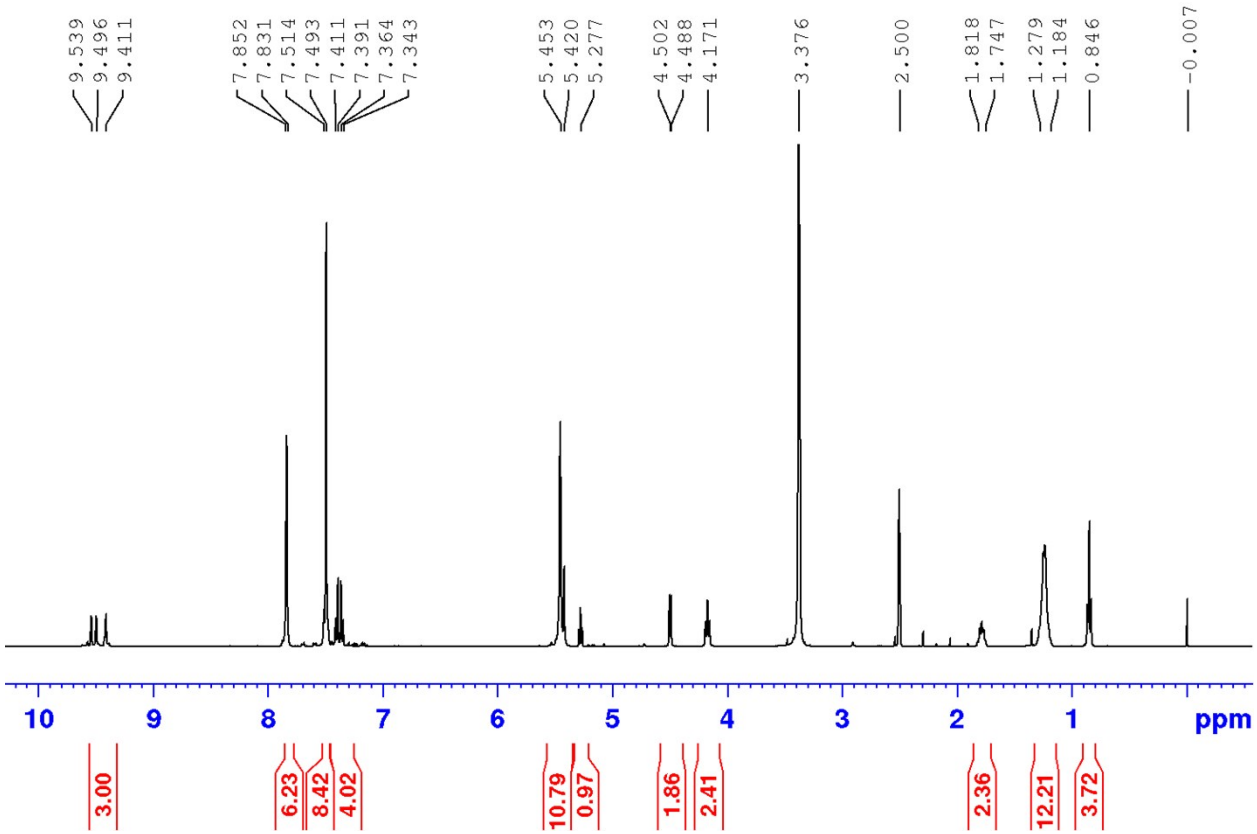


F1-OH was prepared by the general procedure from phenol **11** and isolated as a white powder (190 mg, 0.219 mmol, 76%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 9.78 (s, 1H, OH), 9.58 (s, 1H, ImH), 9.46 (s, 1H, ImH), 9.44 (s, 1H, ImH), 7.83–7.80 (m, 6H, ImH), 7.51–7.47 (m, 8H, PhH), 7.28 (d, J = 8.5 Hz, 2H, PhH), 6.80 (d, J = 8.5 Hz, 2H, PhH), 5.46–5.41 (m, 10H, 5 × NCH_2), 4.17 (t, J = 7.0 Hz, 2H, NCH_2CH_2), 1.82–1.75 (m, 2H, NCH_2CH_2), 1.28–1.17 (m, 10H, C_5H_{10}), 0.85 (t, J = 6.5 Hz, 3H, CH_3). **^{13}C NMR** (101 MHz, d_6-DMSO) δ 158.0, 136.5, 136.3, 136.0, 135.6, 135.5, 135.4, 135.3, 130.3, 129.1, 129.0, 128.9, 124.8, 123.0, 122.9, 122.9, 122.8, 122.6, 115.7, 51.9, 51.6, 51.5, 51.4, 49.0, 31.2, 29.3, 28.5, 28.3, 25.6, 22.1, 14.0.

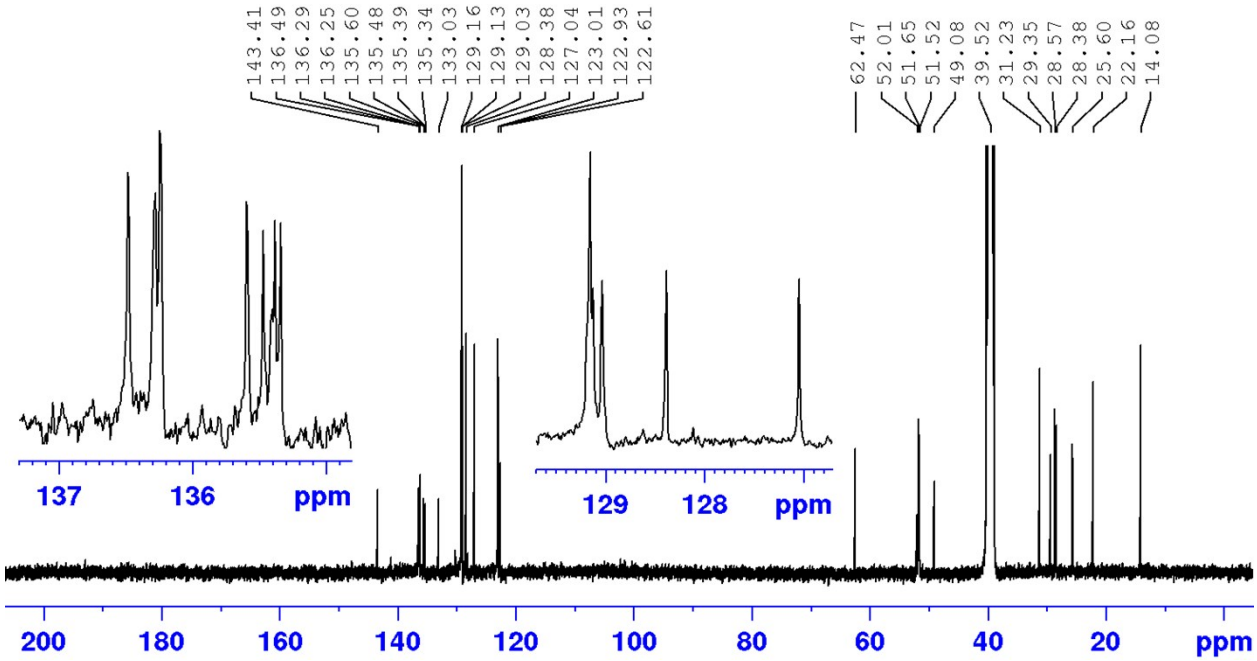
F1-CH$_2$OH

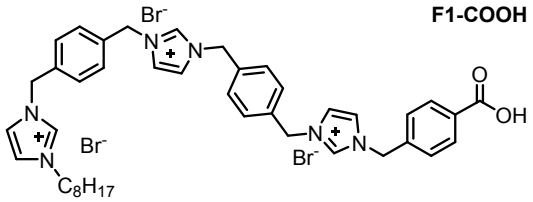


^{1}H NMR, d_6-DMSO, 400 MHz

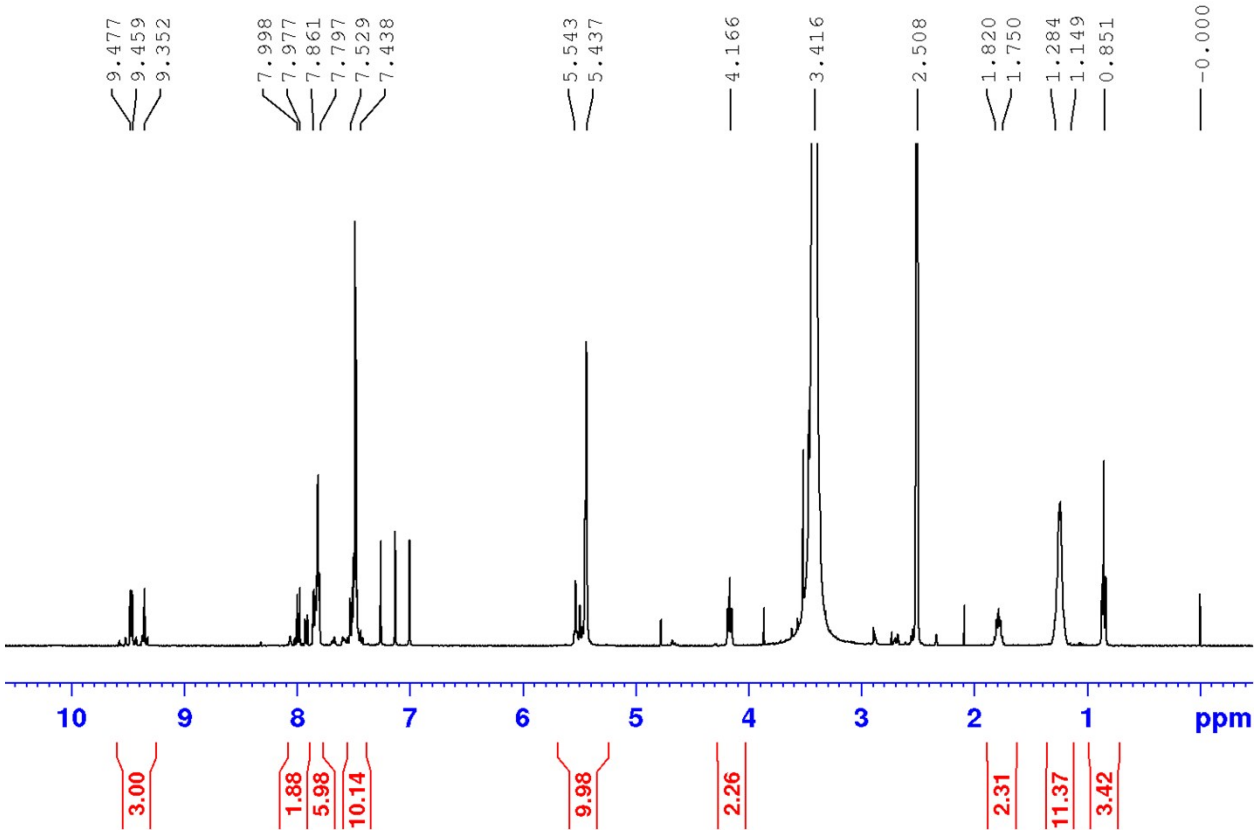


^{13}C NMR, d_6-DMSO, 101 MHz

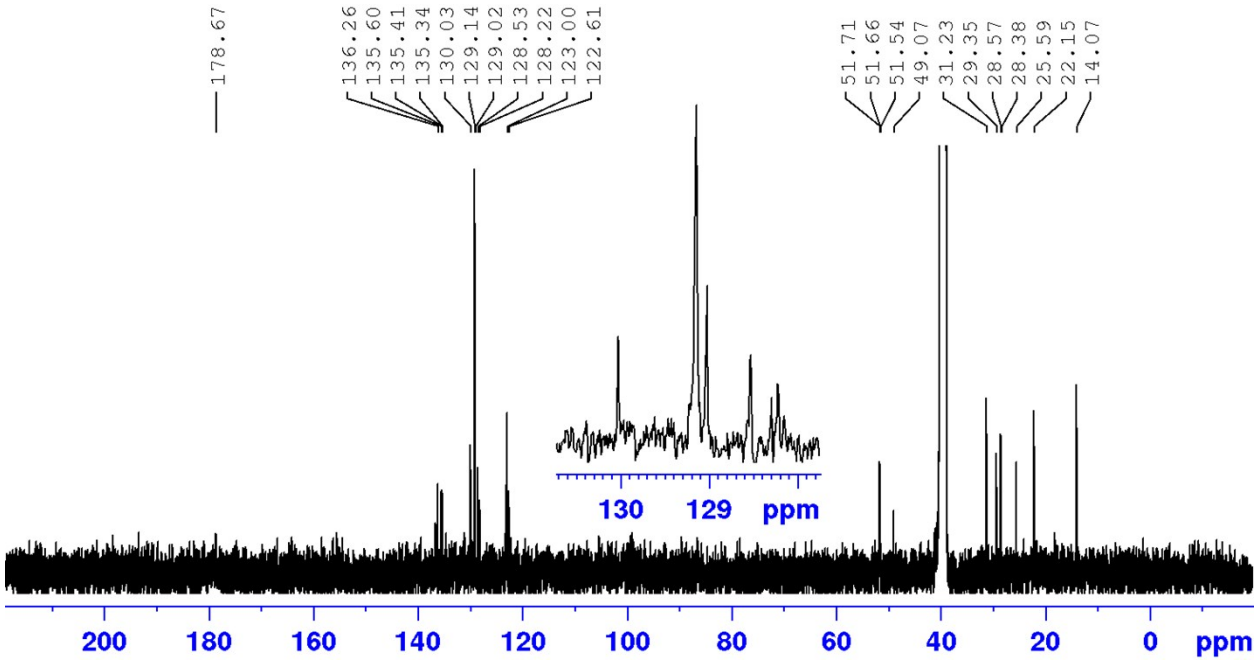




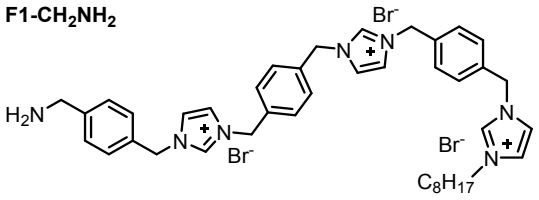
^{1}H NMR, d_6-DMSO, 400 MHz



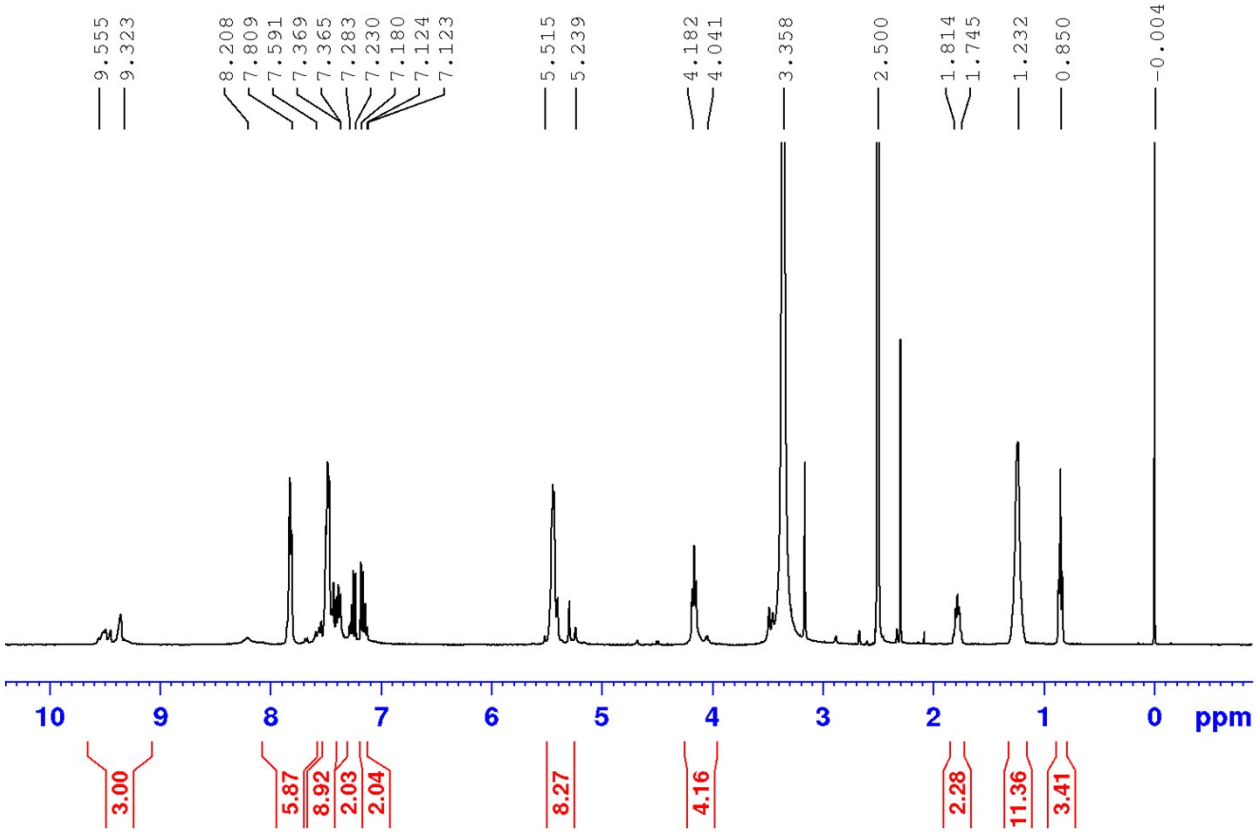
^{13}C NMR, d_6-DMSO, 101 MHz



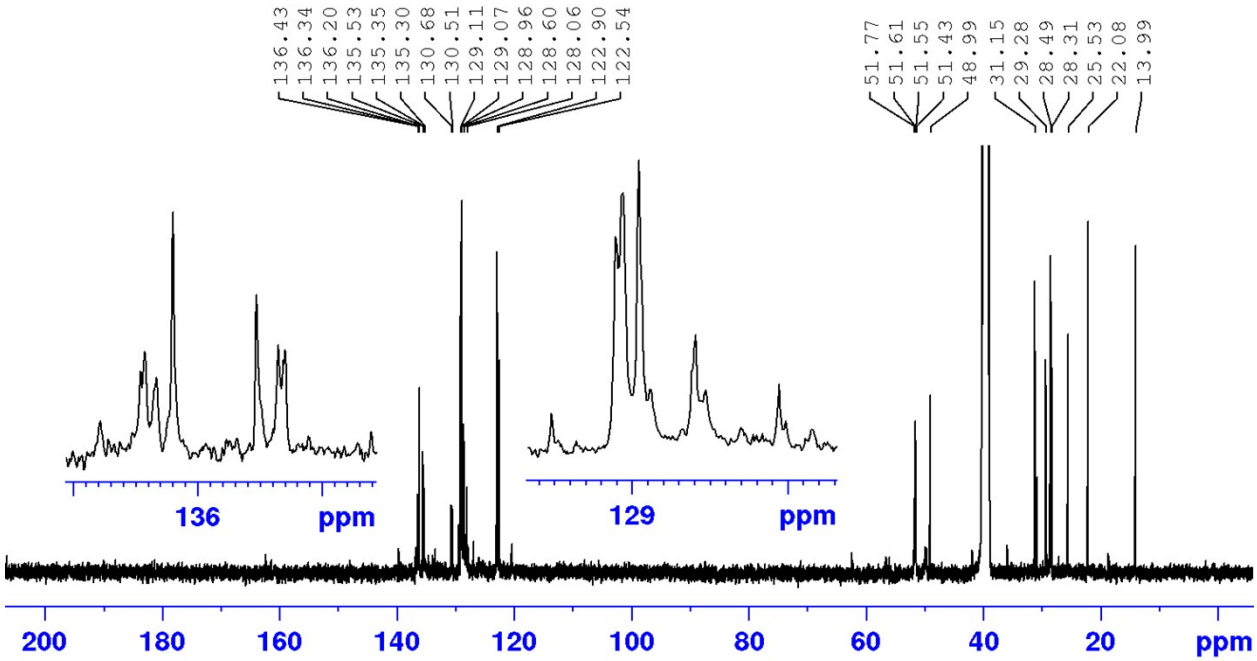
F1-CH_2NH_2



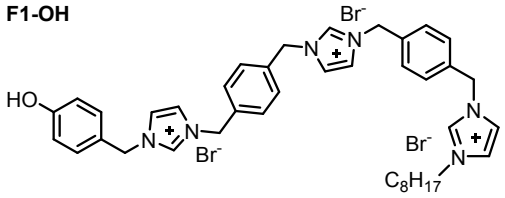
^{1}H NMR, d_6-DMSO, 400 MHz



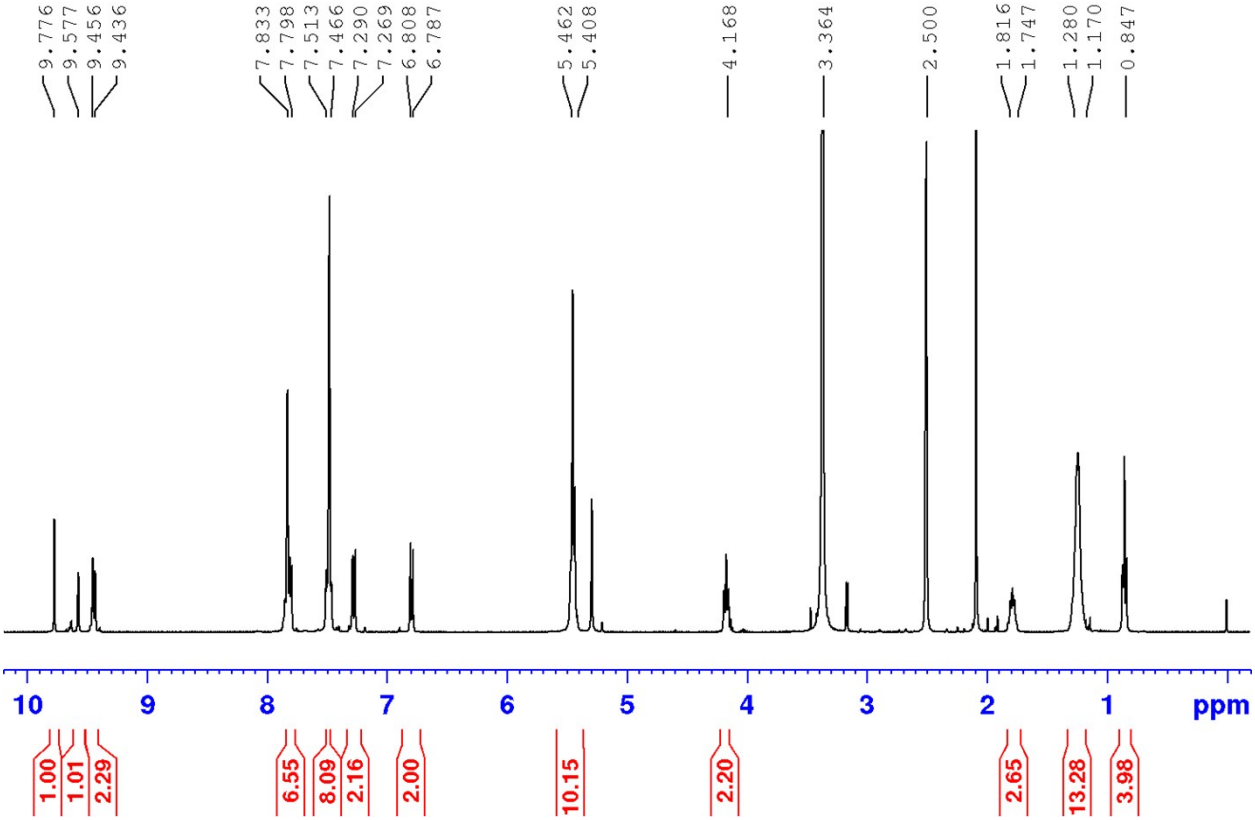
^{13}C NMR, d_6-DMSO, 101 MHz



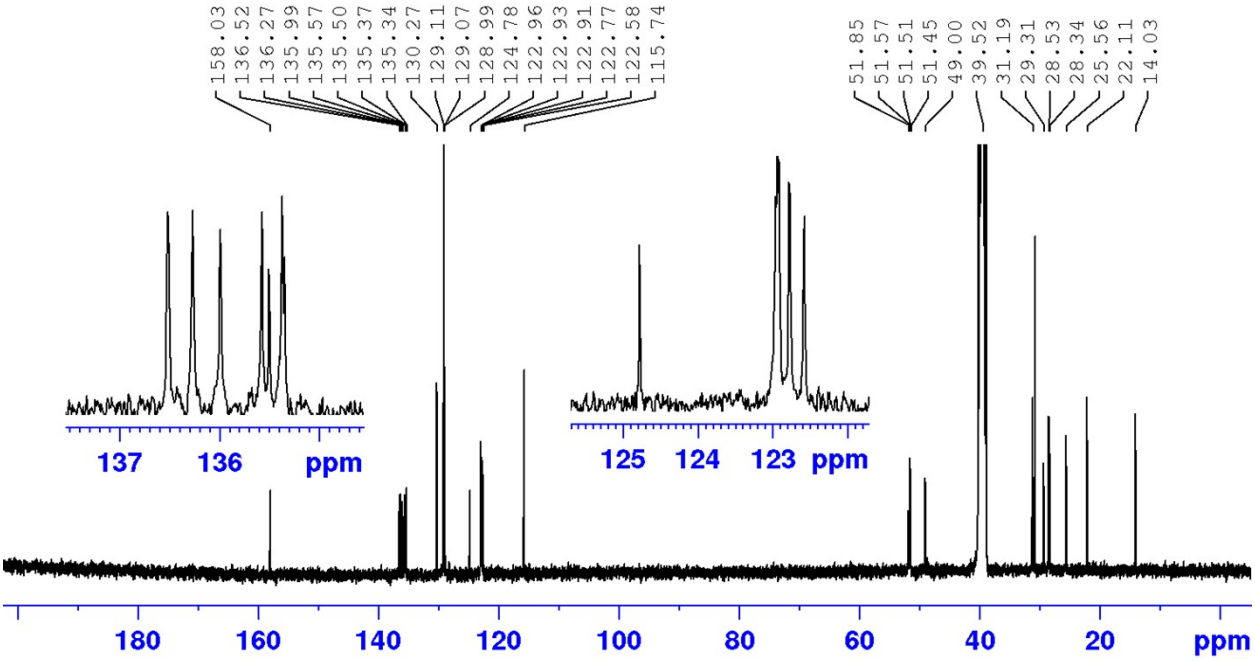
F1-OH



^{1}H NMR, d_6-DMSO, 400 MHz



^{13}C NMR, d_6-DMSO, 101 MHz



Characterization of gels

Table S1. Critical gelation concentrations (wt%) of the degradable oligomers in alcohols.

	ethanol	*n*-propanol	*n*-butanol
IBN-CC8	2.0	2.0	–
IBN-EC8	2.0	1.5	1.5
IBN-HC8	1.5	0.5	1.0

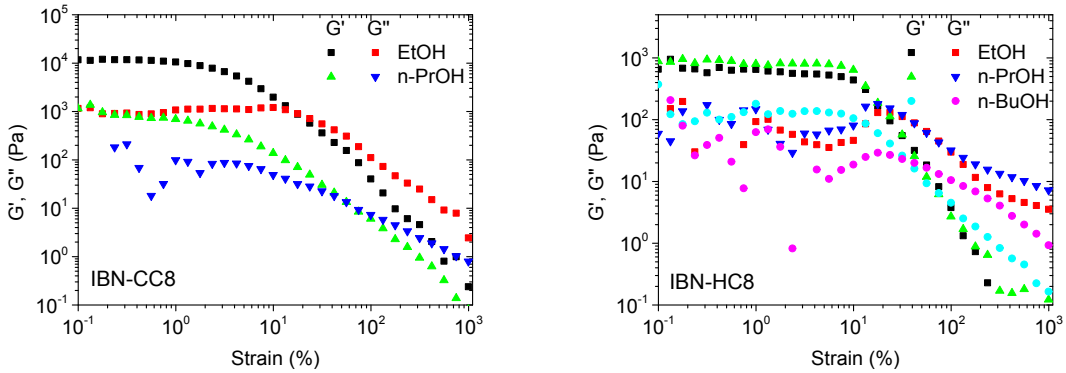


Figure S1. Storage and loss moduli of **IBN-CC8** (4.0 wt% in alcohols) and **IBN-HC8** (2.0 wt% in alcohols) obtained with a strain-amplitude sweep at 10 rad s^{-1}.

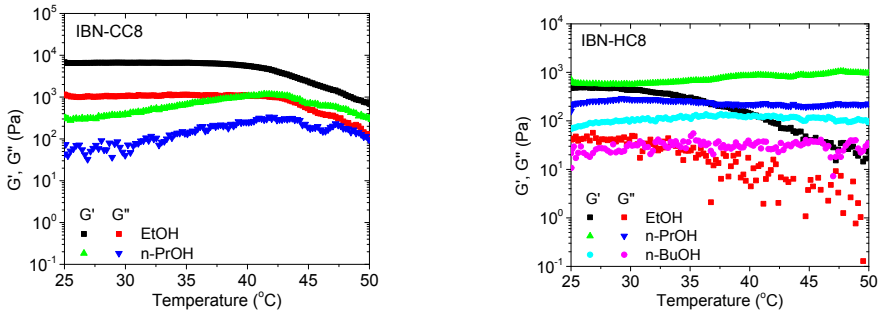


Figure S2. Storage and loss moduli of **IBN-CC8** (4.0 wt% in alcohols) and **IBN-HC8** (2.0 wt% in alcohols) obtained with a ramp of 2°C min^{-1} at 2% and 5% strain, respectively.

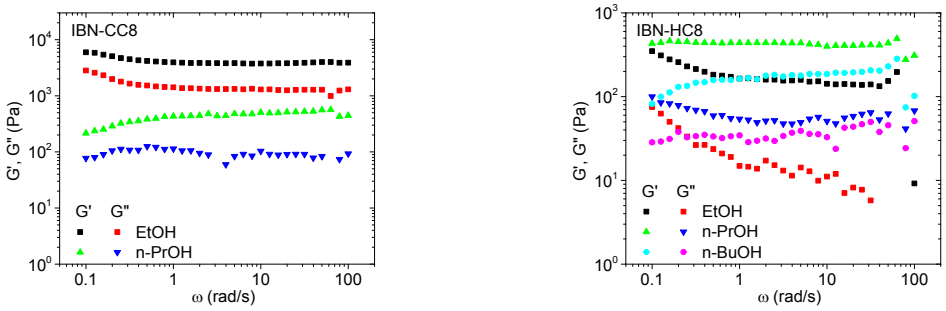


Figure S3. Storage and loss moduli of **IBN-CC8** (4.0 wt% in alcohols) and **IBN-HC8** (2.0 wt% in alcohols) obtained with an angular frequency sweep at 2% and 5% strain, respectively.

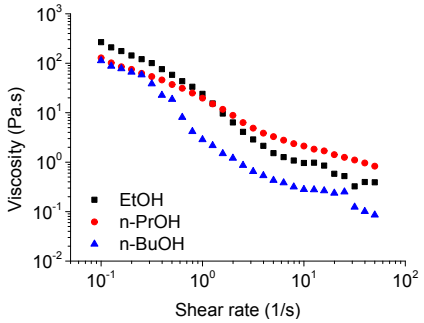


Figure S4. Viscosity as a function of the shear rate for gels of **IBN-HC8** (2.0 wt% in alcohols).

Measuring oligomer degradation by ^{1}H NMR spectroscopy

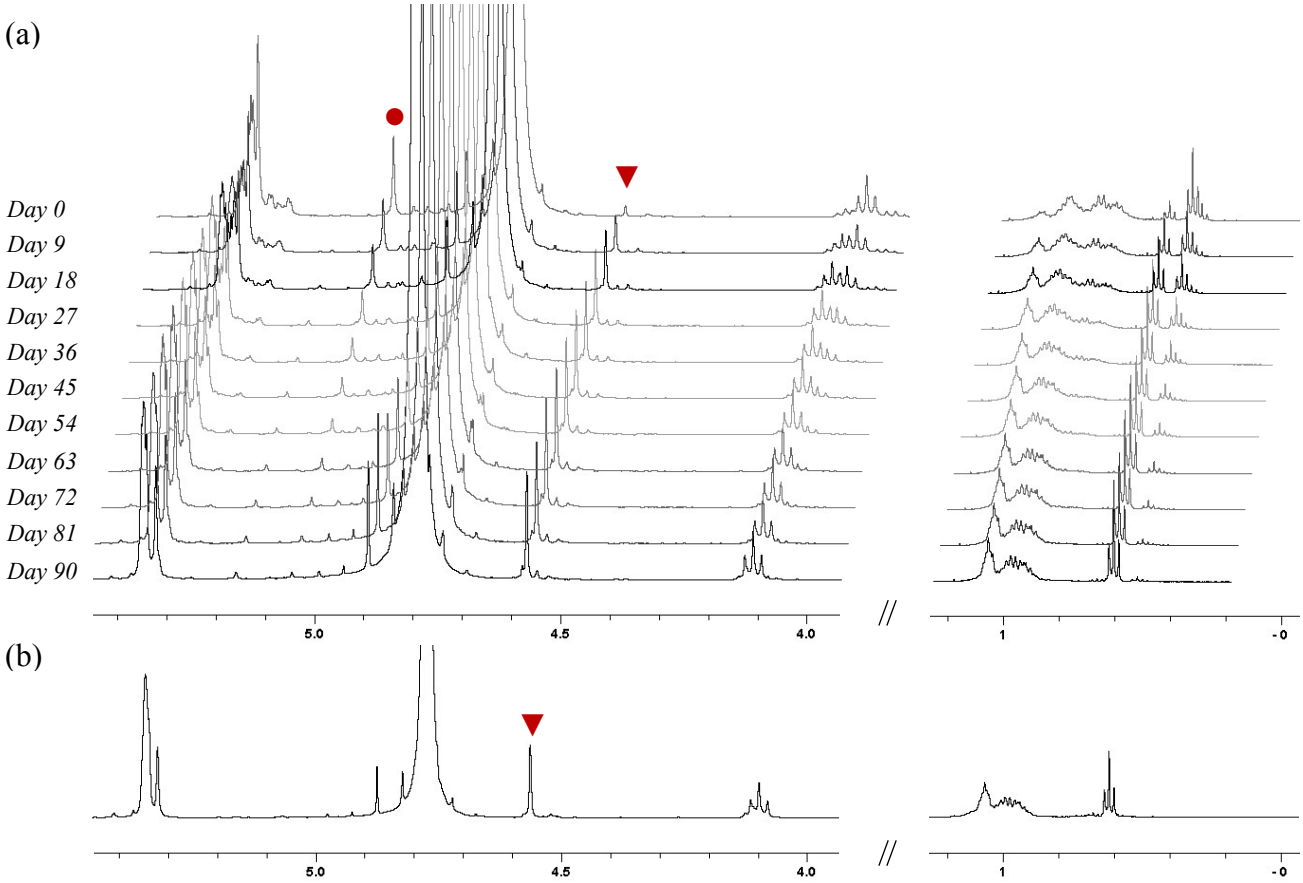


Figure S5. (a) ^{1}H NMR spectra of **IBN-CC8** (4 mg mL^{-1}) over the course of 90 days. NMR solvent was Sorenson's phosphate buffer (pH 8, 100 mM) in D_2O. **(b)** ^{1}H NMR spectra of **F1-CH$_2$OH** in D_2O. ● = OCH_2 in **IBN-CC8**, ▼ = OCH_2 in **F1-CH$_2$OH**.

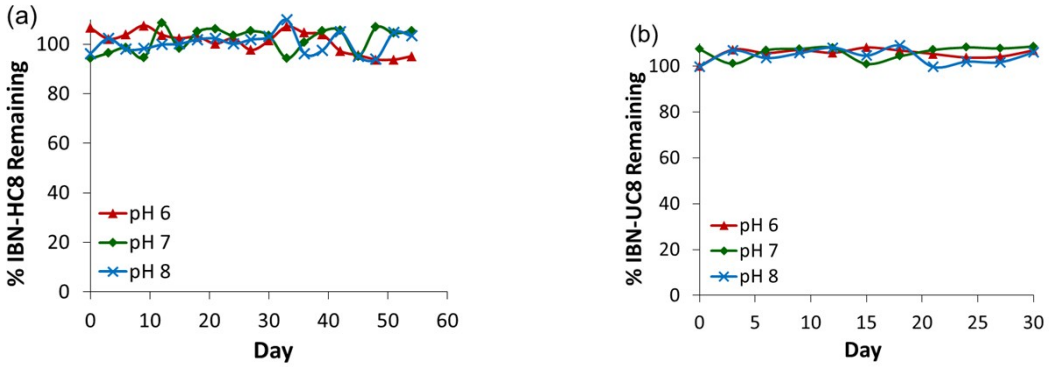


Figure S6. Degradation of (a) **IBN-HC8** and (b) **IBN-UC8** (4 mg mL^{-1} in Sorenson's phosphate buffer (pH 6, 7, 8; 100 mM)).

Monitoring the changes in antimicrobial activity during degradation

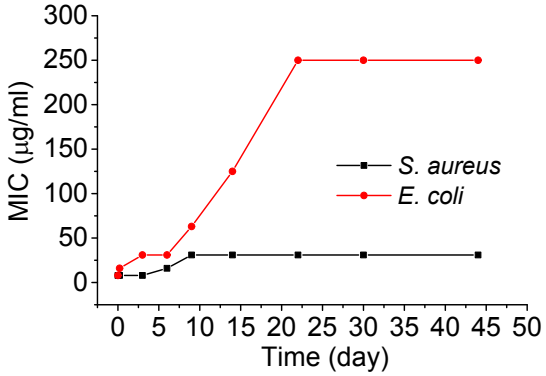


Figure S7. Changes in MIC for **IBN-CC8** stored in tris buffer (pH 8; 100 mM) against *E. coli* and *S. aureus*.

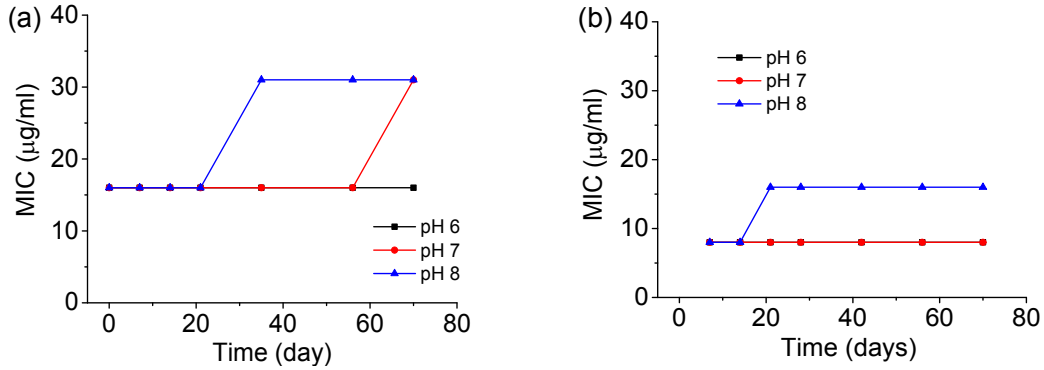


Figure S8. Changes in MIC for **IBN-EC8** stored in **(a)** Sorenson's phosphate buffer (pH 6, 7 and 8) against *E. coli*, and **(b)** Sorenson's phosphate buffer (pH 6, 7 and 8) against *S. aureus*.

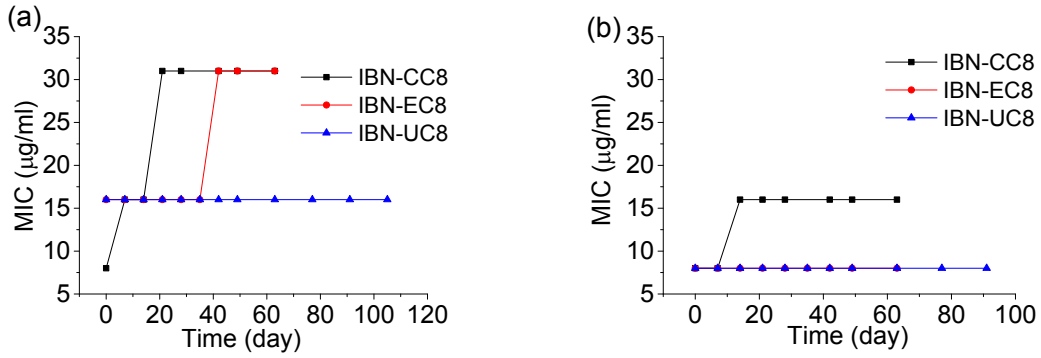


Figure S9. Changes in MIC for **IBN-CC8**, **IBN-EC8** and **IBN-UC8** in saline solution (0.9% NaCl) against **(a)** *E. coli* and **(b)** *S. aureus*.

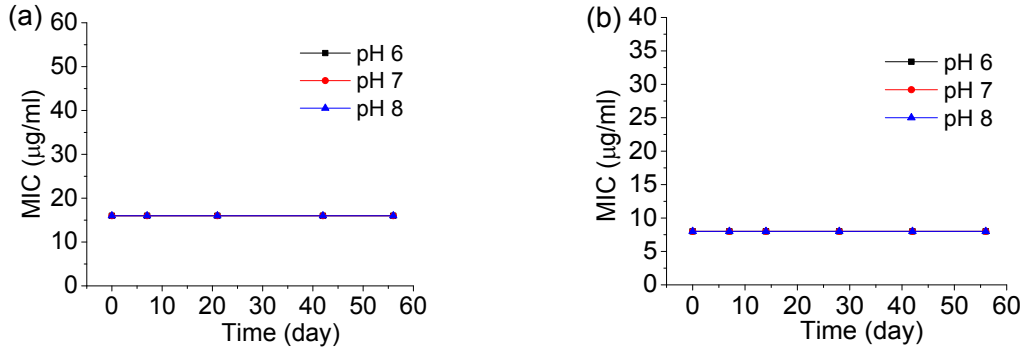


Figure S10. Changes in MIC for **IBN-UC8** in in Sorenson's phosphate buffer (pH 6, 7 and 8) against **(a)** *E. coli* and **(b)** *S. aureus*.

Drug resistance development study

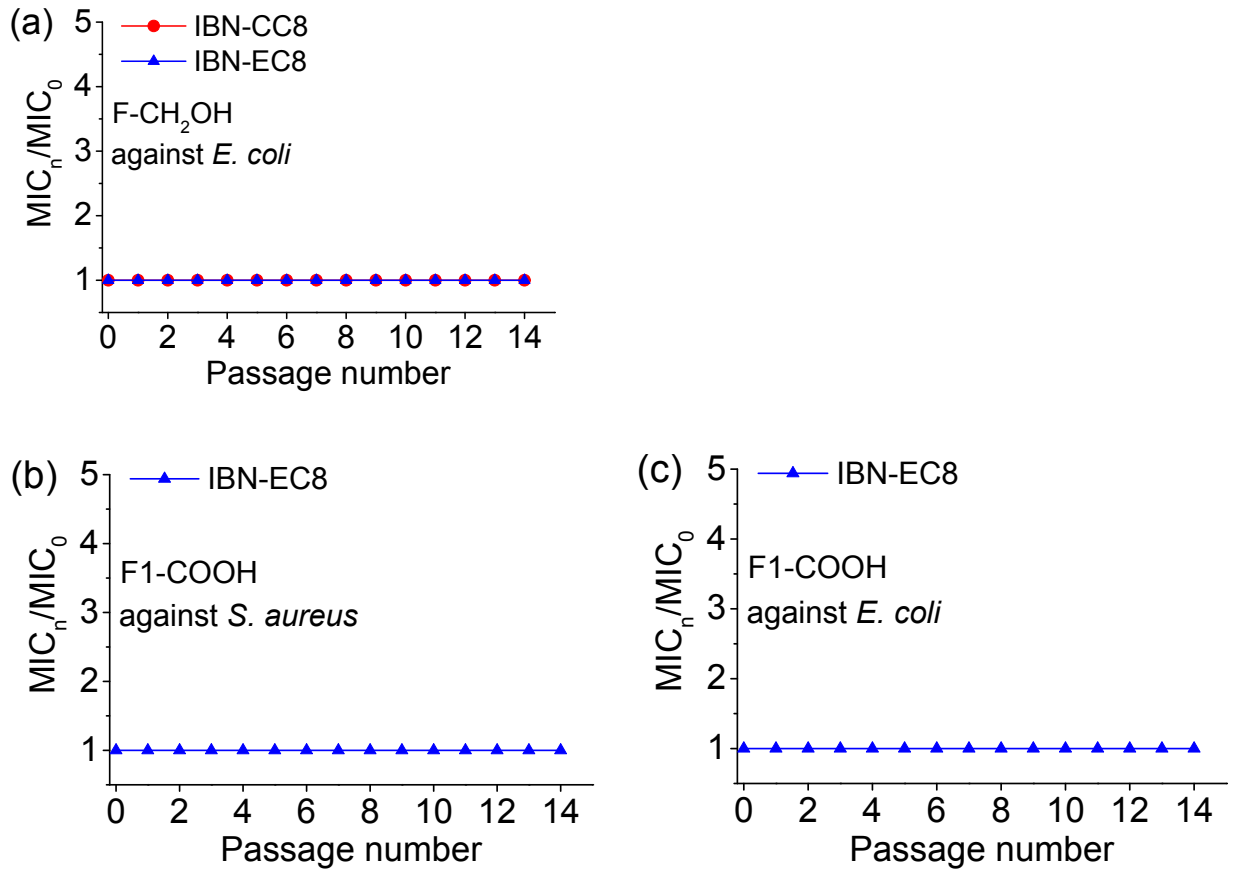


Figure S11. (a) Changes in MICs for **IBN-CC8** and **IBN-EC8** against *E. coli* in the presence of degradation product **F1-CH$_2$OH** (20 μg mL^{-1}). Changes in MICs for **IBN-EC8** against **(b)** *S. aureus* and **(c)** *E. coli* in the presence of degradation product **F1-COOH** (20 μg mL^{-1}).

Hemolysis assay

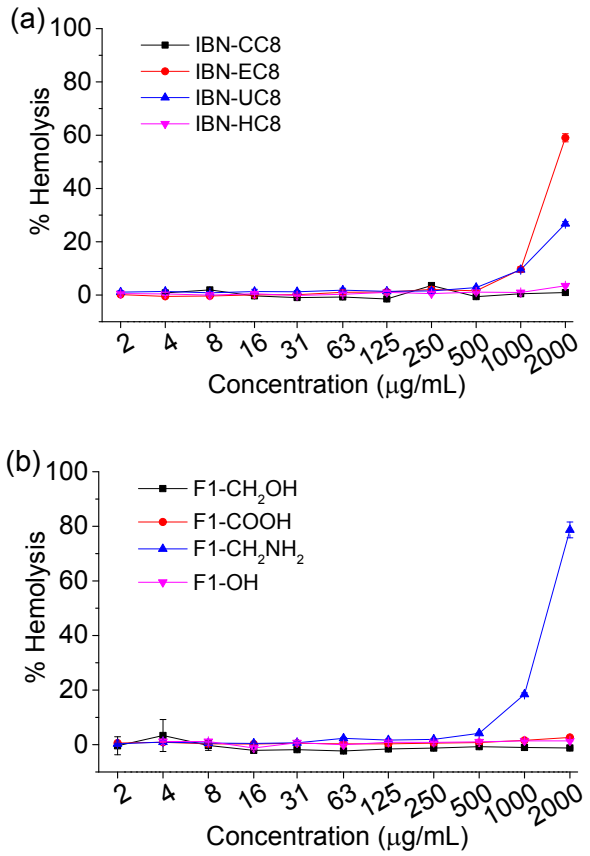


Figure S12. Haemolytic activities of (a) degradable oligomers **IBN-CC8**, **IBN-EC8**, **IBN-UC8** and **IBN-HC8** and (b) the degradation products **F1-CH$_2$OH**, **F1-COOH**, **F1-CH$_2$NH$_2$** and **F1-OH** at various concentrations. The data are expressed as mean ± S.D. of quadruplicates.

In vitro cytotoxicity study

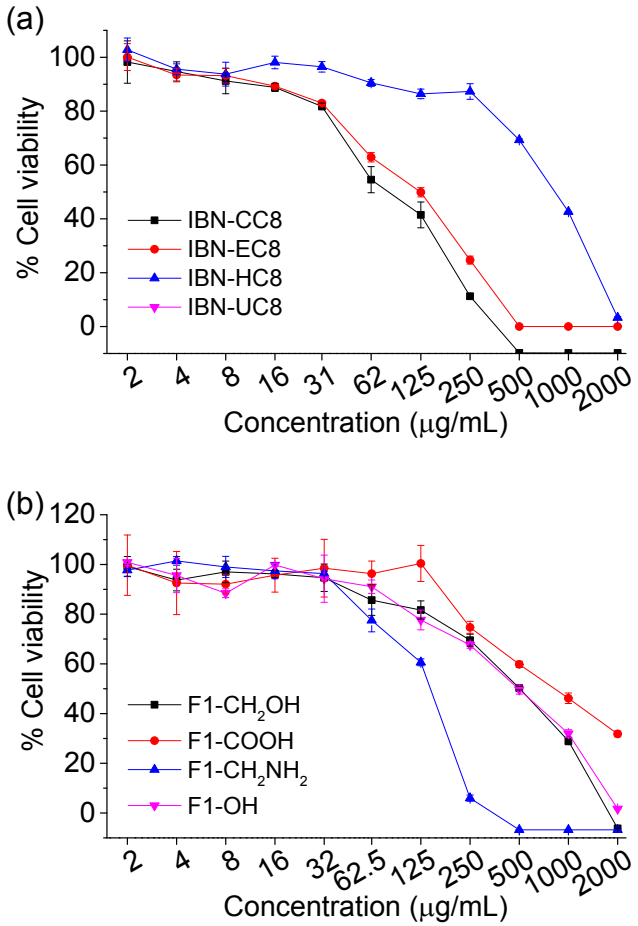


Figure S13. Viability of human primary dermal fibroblasts after treatment with (a) degradable oligomers **IBN-CC8**, **IBN-EC8**, **IBN-UC8** and **IBN-HC8**, and (b) the degradation products **F1-CH_2OH**, **F1-COOH**, **F1-CH_2NH_2** and **F1-OH** at various concentrations for 24 h via MTT test. The data are expressed as mean ± S.D. of triplicates.

References

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