**SUPPORTING INFORMATION**

# Antimicrobial Polymers Prepared by ROMP with Unprecedented Selectivity: A Molecular Construction Kit Approach

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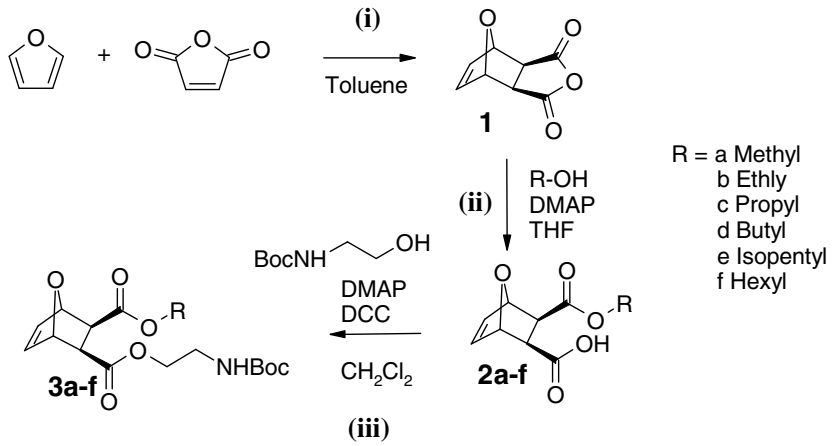
**Experimental:**

**General:** Maleic anhydride, furane, 4-dimethyl aminopyridine (DMAP), 1,3-dicyclohexylcarbodiimide (DCC), methanol, ethanol, 1-propanol, 1-butanol, isopentanol, 1-hexanol, ethylvinyl ether and trifluoroacetic acid (TFA) were obtained as reagent grade from Aldrich, Fluka or Acros and used as received.

3rd generation Grubbs catalyst (Dichloro-di(3-bromopyridino)-N,N'-Dimesitylenoimidazolino-Ru=CHPh; G3) was synthesized as described previously by Grubbs et al.[1]. The HPLC grade solvents N,N-dimethylformamide (DMF), toluene, ethyl acetate and hexane were purchased from Aldrich, Fisher Scientific or Acros and used as received. THF (HPLC grade, Fisher Scientific) was distilled from sodium/benzophenone under nitrogen. Dichloromethane (HPLC grade, Fisher Scientific) was distilled from $CaH_2$ under nitrogen.

Gel permeation chromatography (DMF/0.01 M LiCl, calibrated with polystyrene standards, toluene as flow marker, 50°C) was measured on a PL50 GPC setup (Polymer Laboratories, Amherst, MA) with a PL Gel 5 µm pre-column and two 10 µm analytical Mixed-D columns (Polymer Laboratories, Amherst, MA). NMR spectra were recorded on a Bruker DPX300 spectrometer (Bruker, Madison, WI). High resolution mass spectra were obtained from a JEOL JMS 700 instrument (JEOL, Peabody, MA); Matrix Assisted Laser Desorption and Ionization Time of Flight Mass Spectra (MALDI-TOF MS) were measured on a Bruker Daltonics Reflex III (Bruker, Madison, WI). The biological activity of the polymer samples (the minimal concentration inhibiting 90% of bacterial growth ($MIC_{90}$) for *Escherischia coli* (D31) and *Staphylococcus aureus* (ATCC25923), and the concentration that lyses 50% of red blood cells ($HC_{50}$) were determined as reported previously.[2]

**Monomer Synthesis**:

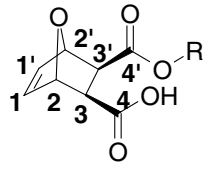



(i) Using a literature procedure, maleic anhydride (100 g, 1.02 mol) was dissolved in 1 L toluene. 150 mL (140.7 g, 2.05 mmol) furan were added. The solution was stirred for 3 days. The product (**1**) was then filtered, washed with toluene and dried under vacuum. A colorless powder was obtained. Yields and spectroscopic data matched those reported previously.[3]

(ii) **1** (5 g, 30.0 mmol) was dissolved in THF. Two equivalents of the respective alcohol (e.g. 5.26 g (60 mmol) isopentanol for R = isopentyl) and 10 mol% DMAP were added. After stirring over night, the solvent was removed by vacuum evaporation at room temperature. The unreacted alcohol was removed by dynamic vacuum ($5 \cdot 10^{-2}$ mbar). Crystallization from dichloromethane/hexane yielded, e.g. for R = isopentyl, 4.7 g (18.5 mmol, 62 %) of the product (**2**).

**2a**: R = Methyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 2.86 (m, 2H, H3 & H3'), 3.71 (s, 3H, C$H_3$), 5.27 & 5.32 (m, 2H, H2 & H2'), 6.47 (m, 2H, H1 & H1').

**2a-f**




**2b**: R = Ethyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 1.25 (t, $J$ = 7.2 Hz, 3H, $CH_2$-C$H_3$), 2.83 (m, 2H, H3 & H3' ), 4.16 (q, $J$ = 7.1 Hz, 2H, C$H_2$-$CH_3$), 5.25 & 5.31 (s, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'), 7.53-8.21 (br s, 1H, OH).

**2c**: R = Propyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 0.92 (t, *J* = 7.3 Hz, 3H, $CH_2$-C*H*$_3$), 1.63 (m, 2H, β-$CH_2$), 2.84 (m, 2H, H3 & H3'), 4.05 (m, 2H, α-$CH_2$), 5.23 & 5.29 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'), 9.12-9.68 (br s, 1H, OH).

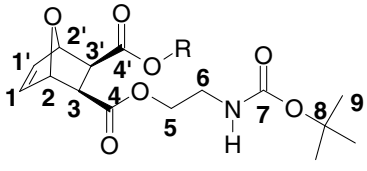
**2d**: R = Butyl: colorless oil, $^1$H-NMR (300 MHz, $CDCl_3$): 0.85 (t, *J* = 7.1 Hz, 3H, $CH_2$-C*H*$_3$), 1.30 (m, 2H, γ-$CH_2$), 1.54 (m, 2H, β-$CH_2$), 2.78 (m, 2H, H3 & H3'), 4.04 (m, 2H, α-$CH_2$) 5.21 & 5.27 (m, 2H, H2 & H2'), 6.39 (m, 2H, H1 & H1').

**2e**: R= iso-Pentyl: colorless oil, $^1$H-NMR (300 MHz, $CDCl_3$): 0.90 (d, *J* = 6.6 Hz, 6H, $CH_2$-C*H*$_3$), 1.53 (m, 1H, C*H*-$CH_3$), 1.68 (m, 2H, β-$CH_2$), 2.84 (m, 2H, H3 & H3'), 4.08 (m, 2H, α-$CH_2$) 5.25 & 5.31 (m, 2H, H2 & H2'), 6.45 (m, 2H, H1 & H1'), 8.70-9.68 (br s, 1H, OH).

**2f**: R = Hexyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 0.88 (t, *J* = 6.4 Hz, 3H, $CH_2$-C*H*$_3$), 1.28 (m, 6H, γ- to ε-$CH_2$), 1.61 (m, 2H, β-$CH_2$), 2.85 (m, 2H, H3 & H3'), 4.13 (m, 2H, α-$CH_2$) 5.25 & 5.29 (m, 2H, H2 & H2'), 6.47 (m, 2H, H1 & H1').

(iii) 1 eq **2a-f** (e.g. 2 g (7.88 mmol) for R = isopentyl) was dissolved in 25 mL dichloromethane. 1 eq (1.27 g, 7.88 mmol) boc-protected 2-amino ethanol and 10 mol% of DMAP were added. The solution was cooled to 0°C. 1 eq (206.3 g, 7.88 mmol) DCC was added, and the suspension was stirred over night. It was then filtered through a short alumina column (5 cm neutral $Al_2O_3$/dichlormethane). The solvent was removed by vacuum evaporation and the crude product was chromatographed (15 cm silica gel, ethyl acetate:hexane 9:1 to 1:1). Evaporation of the solvent yielded the pure monomer. The yield ranged from 70-80%.

**3a**: R = Methyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 1.43 (s, 9H, H9), 2.82 (m, 2H, H3 & H3'), 3.40 (m, 2H, H6), 3.73 (s, 3H, $CH_3$), 4.16 (m, 2H, H5), 5.03 (br s, 1H, NH), 5.25 & 5.29 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR (75 MHz, $CDCl_3$):



**3a-f**

28.4 (C9), 39.5 (C6), 46.9 & 47.1 (C3, C3'), 52.4 (R, $CH_3$), 64.8 (C5), 79.3 (C8), 80.4 & 80.6 (C2, C2'), 136.6 & 136.7 (C1, C1'), 171.6 (C4, C4').

HR-MS (FAB): calc. 341.36, found 342.15.

**3b**: R = Ethyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 1.27 (t, $J$ = 7.2 Hz, 3H, $CH_2$-C$H_3$), 1.44 (s, 9H, H9), 2.81 (m, 2H, H3 & H3'), 3.39 (m, 2H, H6), 4.16 (m, 4H, C$H_2$-$CH_3$ and H5), 5.05 (br s, 1H, NH), 5.25 & 5.31 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR (75 MHz, $CDCl_3$): 14.4 (R, $CH_3$), 28.4 (C9), 39.4 (C6), 46.8 & 47.1 (C3, C3'), 61.3 (R, $CH_2$), 64.8 (C5), 79.3 (C8), 80.4 & 80.7 (C2, C2'), 136.6 & 136.7 (C1, C1'), 155.9 (C7), 171.6 & 171.7 (C4, C4'). HR-MS (FAB): calc. 355.39, found 356.17.

**3c**: R = Propyl: colorless solid, $^1$H-NMR (300 MHz, $CDCl_3$): 1.25 (m, 3H, $CH_2$-C$H_3$), 1.43 (s, 9H, H9), 1.67 (m, 2H, β-$CH_2$), 2.81 (q, 2H, H3 & H3'), 3.40 (m, 2H, H6), 4.12 (m, 4H, α-$CH_2$ and H5), 5.07 (br s, 1H, NH), 5.24 & 5.30 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR (75 MHz, $CDCl_3$): 10.4 (R, $CH_3$), 21.9 (R, β-$CH_2$), 28.4 (C9), 39.5 (C6), 46.8 & 47.2 (C3, C3'), 64.8 (C5), 66.9 (R, α-$CH_2$), 79.3 (C8), 80.4 & 80.7 (C2, C2'), 136.6 & 136.7 (C1, C1'), 155.9 (C7), 171.6 & 171.8 (C4, C4'). HR-MS (FAB): calc. 369.42, found 370.19

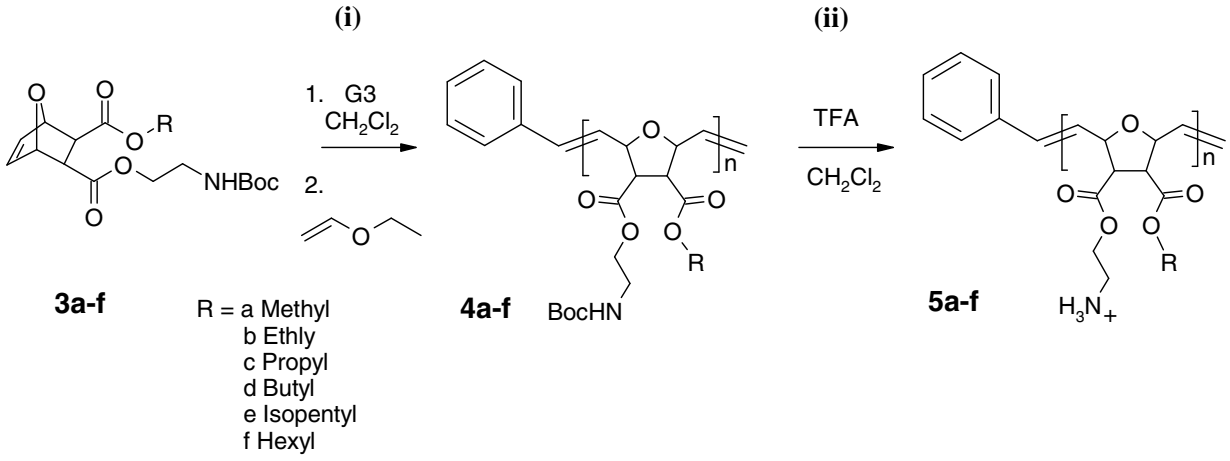
**3d**: R = Butyl: colorless oil, $^1$H-NMR (300 MHz, $CDCl_3$): 0.93 (m, 3H, $CH_2$-C$H_3$), 1.37 (m, 2H, γ-$CH_2$), 1.44 (s, 9H, H9), 1.62 (m, 2H, β-$CH_2$), 2.82 (q, 2H, H3 & H3'), 3.39 (m, 2H, H6), 4.12 (m, 4H, α-$CH_2$ and H5), 5.06 (br s, 1H, NH), 5.23 & 5.29 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR (75 MHz, $CDCl_3$): 13.7 (R, $CH_3$), 19.0 (R, γ-$CH_2$), 28.3 (C9), 30.4 (R, β-$CH_2$), 39.4 (C6), 46.7 & 47.1 (C3, C3'), 64.7 (C5), 65.1 (R, α-$CH_2$), 79.2 (C8), 80.4 & 80.6 (C2, C2'), 136.5 & 136.6 (C1, C1'), 155.9 (C7), 171.5 & 171.8 (C4, C4'). HR-MS (FAB): calc. 383.45, found 384.21.

**3e**: R= iso-Pentyl: colorless oil, $^1$H-NMR (300 MHz, $CDCl_3$): 0.92 (d, $J$ = 6.4 Hz, 6H, CH-C$H_3$), 1.44 (s, 9H, H9), 1.53 (m, 1H, C$H$-$CH_3$), 1.69 (m, 2H, β-$CH_2$), 2.82 (q, 2H, H3 & H3'), 3.41 (m,

2H, H6), 4.18 (m, 4H, α-$CH_2$ and H5), 5.07 (br s, 1H, NH), 5.23 & 5.29 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR: n.d., HR-MS (FAB): n.d.

**3f**: R = Hexyl: colorless oil, $^{1}$H-NMR (300 MHz, $CDCl_3$): 0.88 (t, *J* = 6.6 Hz, 3H, $CH_2$-C*H*$_3$), 1.43 (s, 9H, t-butyl), 1.37 (m, 6H, γ-ε-$CH_2$) 1.62 (m, 2H, β-$CH_2$), 2.82 (m, 2H, H3 & H3'), 3.42 (m, 2H, H6), 4.14 (m, 4H, α-$CH_2$ and H5), 5.07 (br s, 1H, NH), 5.23 & 5.29 (m, 2H, H2 & H2'), 6.46 (m, 2H, H1 & H1'). $^{13}$C-NMR (75 MHz, $CDCl_3$): 10.9 (R, $CH_3$), 22.5 (R, δ-$CH_2$), 15.4 (R, γ-$CH_2$), 28.3 (C9), 28.5 (R, β-$CH_2$), 39.3 (C6), 46.6 & 46.9 (C3, C3'), 64.4 (C5), 65.2 (R, α-$CH_2$), 78.9 (C8), 80.3 & 80.5 (C2, C2'), 136.4 & 136.6 (C1, C1'), 155.8 (C7), 171.5 & 171.7 (C4, C4'). HR-MS (FAB): calc. 411.50, found 412.24.

**Polymer Synthesis:**

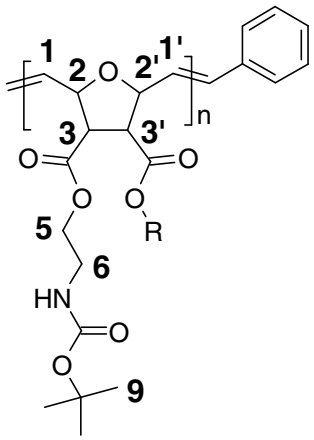



(**i**) The monomer **3a-f** and G3-catalyst amounts (see Table S1 for details) were dissolved in 1 mL dichloromethane each and subject to three freeze-thaw cycles. The catalyst was added in one shot to the vigorously stirring monomer solution at room temperature under argon. After 30 min, the living polymer chain was end-capped with an excess of ethylvinyl ether (1 mL, 754 mg, 10.5 mmol). The solution was allowed to stir over night. After evaporation of the solvent and

drying, an aliquot of each polymer was taken for GPC and NMR analysis. The product was a brown solid. Attempts to remove the catalyst by filtration over alumina, precipitation into ether/hexane, dialysis and ultrafiltration reduced the brown color, however the color could not be removed quantitatively.

Table S1: Experimental parameters for homopolymer synthesis

| Sample | Monomer | $N_{repeat\ units}$ | $M_{n\ Target}$ g mol$^{-1}$ | $M_{Monomer}$ g mol$^{-1}$ | $n_{Monomer}$ mmol | $m_{Monomer}$ mg | $M_{Catalyst}$ g mol$^{-1}$ | $n_{Catalyst}$ mmol | $m_{Catalyst}$ mg |
|---|---|---|---|---|---|---|---|---|---|
| Methyl_3k | Methyl | 9.7 | 3000 | 341 | 0.290 | 100 | 885 | 0.030 | 29.0 |
| Methyl_10k | Methyl | 29 | 10000 | 341 | 0.290 | 100 | 885 | 0.010 | 8.9 |
| Ethyl_3k | Ethyl | 8.6 | 3000 | 355 | 0.563 | 200 | 885 | 0.065 | 57.6 |
| Ethyl_10k | Ethyl | 28 | 10000 | 355 | 0.563 | 200 | 885 | 0.020 | 17.7 |
| Propyl_3k | Propyl | 8.4 | 3000 | 369 | 0.282 | 104 | 885 | 0.034 | 29.7 |
| Propyl_10k | Propyl | 29 | 1000 | 369 | 0.278 | 103 | 885 | 0.010 | 8.50 |
| Butyl_3k | Butyl | 7.2 | 3000 | 383 | 0.525 | 202 | 885 | 0.073 | 64.5 |
| Butyl_10k | Butyl | 27 | 1000 | 383 | 0.565 | 217 | 885 | 0.021 | 18.6 |
| Isopentyl_3k | Isopentyl | 7.9 | 3000 | 397 | 0.515 | 205 | 885 | 0.065 | 57.5 |
| Isopentyl_8k | Isopentyl | 20.1 | 8000 | 397 | 1.926 | 766 | 885 | 0.096 | 85.0 |
| Isopentyl_10k | Isopentyl | 26 | 10000 | 397 | 0.508 | 202 | 885 | 0.020 | 17.5 |
| Hexyl_3k | Hexyl | 7.7 | 3000 | 412 | 0.516 | 212 | 885 | 0.067 | 59.0 |
| Hexyl_10k | Hexyl | 25 | 10000 | 412 | 0.493 | 203 | 885 | 0.020 | 17.7 |




**4a**: R = Methyl: $^{1}$H-NMR (300 MHz, $CDCl_3$): 1.43 (s, 9H, H9), 3.12 (br m, 2H, H3 & H3'), 3.34 (br m, 2H, H6), 3.71 (s, 3H, $CH_3$), 4.16 (br m, 2H, H5), 4.71 (m, 1H, H2 & H2' trans), 5.10 (br s, 1 H, H2 & H2' cis), 5.40 (br s, 1H, NH), 5.58 (br m, 1H, H1 & H1' cis) and 5.88 (br m, 1H, H1 & H1' trans).

**4b**: R = Ethyl: $^{1}$H-NMR (300 MHz, $CDCl_3$): 1.24 (s, 3H, $CH_2$-C$H_3$), 1.42 (s, 9H, H9), 3.09 (br m, 2H, H3 & H3'), 3.34 (br m, 2H, H6), 4.16 (br m, 4H, C$H_2$-$CH_3$ and H5), 4.72 (br m, 1H, H2 & H2' trans), 5.10 (br m, 1H, H2 & H2' cis), 5.30 (br s, 1H, NH), 5.58 (br m, 1H, H1 & H1' cis), 5.88 (br m, 1H, H1 & H1' trans).

**4c**: R = Propyl: $^1$H-NMR (300 MHz, $CDCl_3$): 0.92 (m, 3H, $CH_2$-C*H*$_3$), 1.43 (s, 9H, H9), 1.62 (m, 2H, β-$CH_2$), 3.12 (br m, 2H, H3 & H3'), 3.34 (br m, 2H, H6), 4.10 (m, 4H, α-$CH_2$ and H5), 4.69 (br m, 1H, H2 & H2' trans), 5.12 (br m, 1H, H2 cis & H2'), 5.31 (br m, 1H, H1 & H1' cis), 5.59 (br s, 1H, NH), 5.88 (br m, 1H, H1 & H1' trans).

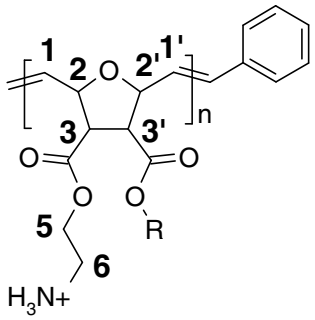
**4d**: R = Butyl: $^1$H-NMR (300 MHz, $CDCl_3$): 0.87 (m, 3H, $CH_2$-C*H*$_3$), 1.29 (m, 2H, γ-$CH_2$), 1.43 (s, 9H, H9), 1.59 (m, 2H, β-$CH_2$), 3.11 (br m, 2H, H3 & H3'), 3.37 (br m, 2H, H6), 4.10 (m, 4H, α-$CH_2$ and H5), 4.73 (br m, 1H, H2 & H2' trans), 5.11 (br m, 1H, H2 & H2' cis), 5.35 (br s, 1H, NH), 5.59 (br m, 1H, H1 & H1' cis), 5.88 (br m, 1H, H1 & H1' trans).

**4e**: R= iso-Pentyl: $^1$H-NMR (300 MHz, $CDCl_3$): 0.91 (m, 6H, CH-C*H*$_3$), 1.43 (s, 9H, H9), 1.52 (m, 1H, C*H*-$CH_3$), 1.62 (m, 2H, β-$CH_2$), 3.10 (br m, 2H, H3 & H3'), 3.35 (br m, 2H, H6), 4.15 (m, 4H, α-$CH_2$ and H5), 4.69 (br m, 1H, H2 & H2' trans), 5.11 (br m, 1H, H2 & H2' cis), 5.34 (br s, 1H, NH), 5.59 (br m, 1H, H1 & H1' cis), 5.88 (br m, 1H, H1 trans).

**4f**: R = Hexyl: $^1$H-NMR (300 MHz, $CDCl_3$): 0.88 (m, 3H, $CH_2$-C*H*$_3$), 1.29 (m, 2H, γ-ε-$CH_2$), 1.43 (s, 9H, H9), 1.56 (m, 2H, β-$CH_2$), 3.10 (br m, 2H, H3 & H3'), 3.36 (br m, 2H, H6), 4.10 (m, 4H, α-$CH_2$ and H5), 4.70 (br m, 1H, H2 & H2' trans), 5.12 (br m, 1H, H2 & H2' cis), 5.38 (br s, 1H, NH), 5.58 (br m, 1H, H1 & H1' cis), 5.89 (br m, 1H, H1 & H1' trans).

**(ii)** The crude polymers were dissolved in 2 mL dichloromethane. An excess of TFA (2 mL, 2.97 g, 26.0 mmol) was added and the solution was stirred at room temperature over night. The excess acid was removed by azeotropic distillation with dichloromethane (2x 15 mL) and methanol (1x 15 mL) at the rotary evaporator. The samples were dried in vacuum over night and dissoved in 30 mL Milli-Q water or DMSO depending on solubility. They were dialyzed against

Milli-Q water until the conductivity of the water was 0.1 µS after 12 h of dialysis (total dialysis time 4-7 days). The hydrolyzed polymers were then freeze dried.




**5a**: R = Methyl: $^1$H-NMR (300 MHz, DMSO): 3.04 (br m, 2H, H3 & H3'), 3.30 (br m, 2H, H6), 3.59 (s, 3H, $CH_3$), 4.16 (br m, 2H, H5), 4.57 (m, 1H, H2 & H2' trans), 4.91 (br m, 1H, H2 & H2' cis), 5.61 (br m, 1H, H1 & H1' cis), 5.82 (br m, 1H, H1 & H1' trans).

**5b**: R = Ethyl: $^1$H-NMR (300 MHz, $D_2O$): 1.28 (br s, 3H, $CH_2$-C*H*$_3$), 3.12 (br m, 2H, H3 & H3'), 3.32 (br m, 2H, H6), 3.49-3.81 (br m, 4H, C*H*$_2$-$CH_3$ and H5), 5.10-5.40 (br m, 2H, H2 & H2'), 5.30-5.90 (br m, 2H, H1 & H1').

**5c**: R = Propyl: $^1$H-NMR (300 MHz, $D_2O$): 0.94 (br m, 3H, $CH_2$-C*H*$_3$), 1.67 (br m, 2H, β-$CH_2$), 3.31 (br m, 2H, H3 & H3'), 3.50 (br m, 2H, H6), 4.12 (m, 4H, α-$CH_2$ and H5), 4.39 (br m, 1H, H2 & H2' trans), 5.12 (br m, 1H, H2 & H2' cis), 5.31 (br m, 1H, H1 & H1' cis), 5.88 (br m, 1H, H1 & H1' trans).

**5d**: R = Butyl: $^1$H-NMR (300 MHz, $D_2O$): 0.93 (m, 3H, $CH_2$-C*H*$_3$), 1.36 (m, 2H, γ-$CH_2$), 1.61 (m, 2H, β-$CH_2$), 3.10 (br m, 2H, H3 & H3'), 3.48 (br m, 2H, H6), 4.14 (m, 4H, α-$CH_2$ and H5), 4.38 (br m, 1H, H2 & H2' trans), 5.11 (br m, 1H, H2 & H2' cis), 5.35-6.20 (br m, 2H, H1 & H1').

**5e**: R= iso-Pentyl: $^1$H-NMR (300 MHz, DMSO): 0.91 (m, 6H, CH-C*H*$_3$), 1.55 (m, 1H, C*H*-$CH_3$), 1.69 (m, 2H, β-$CH_2$), 3.31 (br m, 2H, H3 & H3'), 3.48 (br m, 2H, H6), 4.15 and 4.40 (m, 4H, α-$CH_2$ and H5), 4.69 (br m, 1H, H2 & H2' trans), 5.11 (br m, 1H, H2 & H2' cis), 5.34 (br m, 1H, H1 & H1' cis), 5.88 (br m, 1H, H1 & H1' trans).

**5f**: R = Hexyl: $^1$H-NMR (300 MHz, $D_2O$): 0.90 (m, 3H, $CH_2$-C*H*$_3$), 1.31 (m, 2H, γ-ε-$CH_2$), 1.62 (m, 2H, β-$CH_2$), 3.30 (br m, 2H, H3 & H3'), 3.47 (br m, 2H, H6), 4.13 and 4.40 (m, 4H, α-$CH_2$ and H5), 4.70-5.12 (br m, 2H, H2 & H2'), 5.50-6.20 (br m, 2H, H1 & H1').

**Copolymer Synthesis, Deprotection and Characterization:** Copolymers were synthesized and hydrolyzed using the same methods as for the homopolymers. Each comonomer was dissolved in 0.7 mL dichloromethane separately under argon. The monomer solutions were mixed, and the respective amount of G3 catalyst in 1 mL dichloromethane was added in one shot. Details are given in Table S2. The NMR spectroscopic data for each repeat unit proton matched the assignment of the analogous protons in the homopolymers. Where possible (no peak overlap), integration revealed that the copolymer composition matched the monomer feed ratio. Deprotection was performed as described for the homopolymers.

Table S2: Experimental parameters for copolymer synthesis: a) ethyl-propyl copolymers, b) methyl-ethyl copolymers, c) methyl-propyl copolymers.

a)

| Sample | Monomers | $N_{repeat\ units}$ | $M_{n\ Target}$ g mol$^{-1}$ | $n_{Ethyl}$ mmol | $m_{Ethyl}$ mg | $n_{Propyl}$ mmol | $m_{Propyl}$ mg | $n_{Catalyst}$ mmol | $m_{Catalyst}$ mg |
|---|---|---|---|---|---|---|---|---|---|
| E1:P9 | Ethyl:Propyl | 10 | 3500 | 0.06 | 20.2 | 0.54 | 192 | 0.060 | 53.1 |
| E1:P2 | Ethyl:Propyl | 10 | 3400 | 0.20 | 68.3 | 0.40 | 137 | 0.060 | 53.1 |
| E1:P1 | Ethyl:Propyl | 9 | 3000 | 0.14 | 48.0 | 0.14 | 51.4 | 0.037 | 32.2 |
| E2:P1 | Ethyl:Propyl | 10 | 3500 | 0.40 | 130 | 0.20 | 70.0 | 0.060 | 53.1 |
| E9:P1 | Ethyl:Propyl | 10 | 3400 | 0.54 | 183 | 0.06 | 20.1 | 0.060 | 53.1 |

b)

| Sample | Monomers | $N_{repeat\ units}$ | $M_{n\ Target}$ g mol$^{-1}$ | $n_{Methyl}$ mmol | $m_{Methyl}$ mg | $n_{Ethyl}$ mmol | $m_{Ethyl}$ mg | $n_{Catalyst}$ mmol | $m_{Catalyst}$ mg |
|---|---|---|---|---|---|---|---|---|---|
| M1:E9 | Methyl-Ethyl | 10 | 3400 | 0.81 | 276.5 | 0.09 | 32.0 | 0.09 | 79.7 |
| M1:E1 | Methyl-Ethyl | 10 | 3500 | 0.45 | 153.6 | 0.45 | 159.9 | 0.09 | 79.7 |
| M9:E1 | Methyl-Ethyl | 10 | 3550 | 0.09 | 30.7 | 0.81 | 287.9 | 0.09 | 79.7 |

c)

| Sample | Monomers | $N_{repeat\ units}$ | $M_{n\ Target}$ g mol$^{-1}$ | $n_{Methyl}$ mmol | $m_{Methyl}$ mg | $n_{Ethyl}$ mmol | $m_{Ethyl}$ mg | $n_{Catalyst}$ mmol | $m_{Catalyst}$ mg |
|---|---|---|---|---|---|---|---|---|---|
| M1:P9 | Methyl-Propyl | 10 | 3400 | 0.81 | 276.5 | 0.09 | 33.2 | 0.09 | 79.7 |
| M1:P1 | Methyl- Propyl | 10 | 3600 | 0.45 | 153.6 | 0.45 | 166.2 | 0.09 | 79.7 |
| M9:P1 | Methyl- Propyl | 10 | 3700 | 0.09 | 30.7 | 0.81 | 299.2 | 0.09 | 79.7 |

**Propyl Oligomer Synthesis**

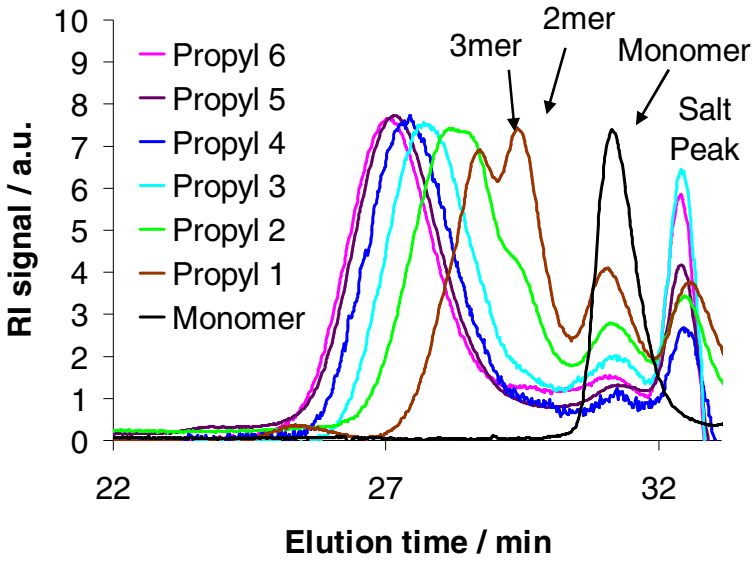
Propyl Oligomers were synthesized and hydrolyzed using the same methods as for the homopolymers. Experimental data are included in Table S3. GPC traces and distribution functions obtained from the MALDI-TOF MS spectra of all oligomers are included in Fig. S1.

Table S3: Experimental parameters for oligomer synthesis

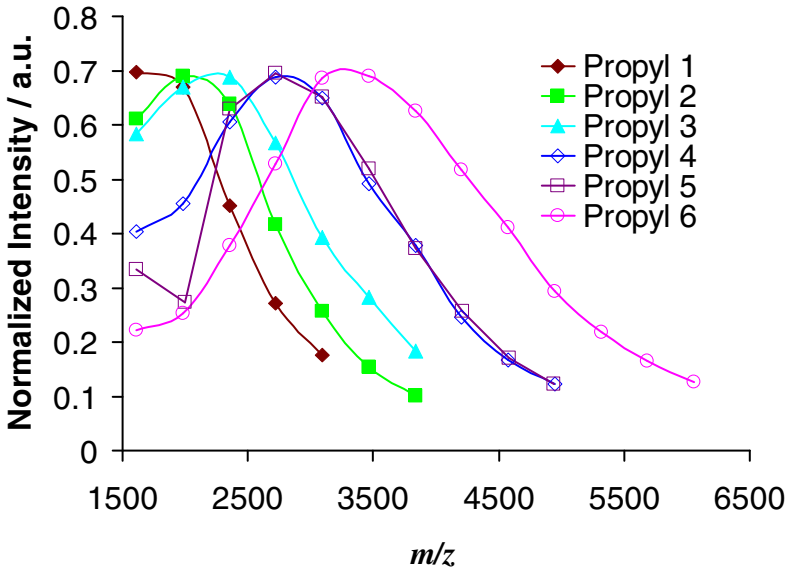
| Sample | Monomers | $N_{repeat\ units}$ | $M_{n\ Target}$ g mol$^{-1}$ | $n_{Propyl}$ mmol | $m_{Propyl}$ mg | $n_{Catalyst}$ mmol | $m_{Catalyst}$ mg |
|---|---|---|---|---|---|---|---|
| **Oligo 1** | Propyl | 2 | 740 | 0.18 | 66.5 | 0.09 | 79.7 |
| **Oligo 2** | Propyl | 3 | 1100 | 0.27 | 99.7 | 0.09 | 79.7 |
| **Oligo 3** | Propyl | 4 | 1480 | 0.36 | 133.0 | 0.09 | 79.7 |
| **Oligo 4** | Propyl | 5 | 1850 | 0.45 | 166.2 | 0.09 | 79.7 |
| **Oligo 5** | Propyl | 6 | 2220 | 0.54 | 199.5 | 0.09 | 79.7 |
| **Oligo 6** | Propyl | 7 | 2600 | 0.18 | 66.5 | 0.09 | 79.7 |

Fig S1: Characterization of ALL propyl oligomers. a) GPC traces, b) MALDI-TOF MS peaks and distributions

a)



b)




**Biological Data**

Representative curves for the determination of the $MIC_{90}$ as well as the $HC_{50}$ values are given in the following section. The experiments were performed as described previously:[2] The $MIC_{90}$ data was obtained from the plot of % growth vs. concentration. The concentration value below 10% growth was taken as the $MIC_{90}$. Controls with inactive polymers and polymers with known activity were included on each plate to ensure data reproducibility. Additionally, the data was collected in quadruplicate. Representative examples are given below (Fig. S2-S3). An example of the dose-response behavior for the different bacteria is shown in Fig. S2 c) and d). The shape of the dose-response curve is largely the same for both bacteria. What is sometimes seen for hydrophobic polymers such as **Propyl_3k** is that they appear to become less toxic at higher concentrations. This is an artifact that comes from decreased solubility or aggregation at these concentrations. When the bacterial count is determined in these wells, there are zero remaining

viable bacteria, or CFUs. Examples of typical $HC_{50}$ curves are shown in Fig S4. The $HC_{50}$ value was taken as the average value of the data at 50 % lysis.

Fig. S2: Examples of a highly active polymer: a) **E1:M1** copolymer, MIC testing against *S. aureus*, $MIC_{90}$ = 12.5 µg/mL, Trial 1 and 2, b) same system, Trial 3 and 4, c) **Proyl_3k**, MIC testing against *E. coli*, d) Proyl_3k, MIC testing against *S. aureus.*

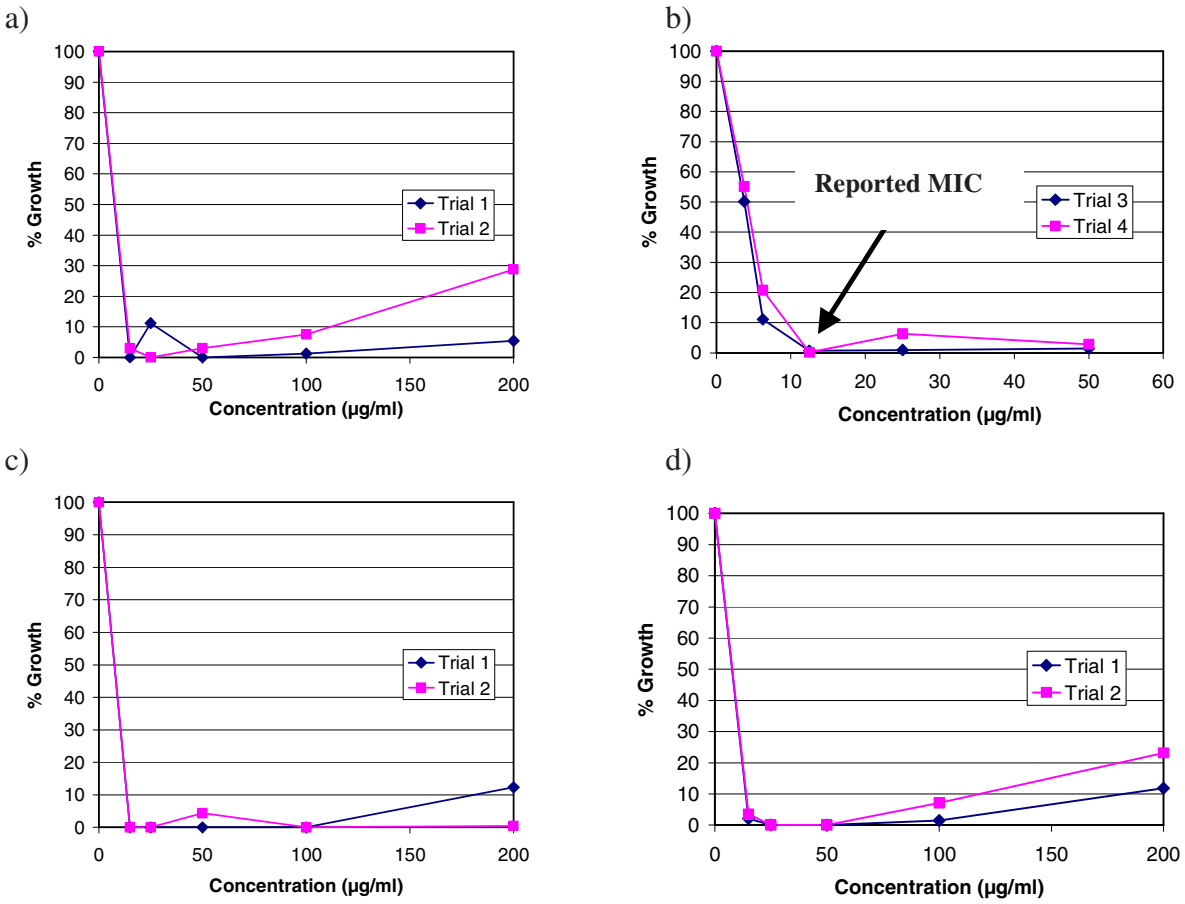
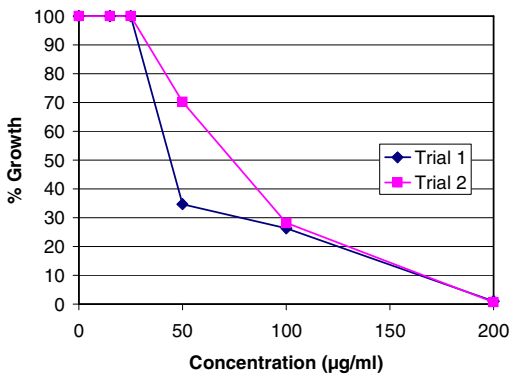


Fig. S3: Example of a) a moderately active polymer: **Propyl_10k**, MIC testing against *S. aureus,*, $MIC_{90}$ = 200 µg/mL, and b) an inactive polymer: **Propyl_10k**, MIC testing against *E. coli,*, $MIC_{90}$ >200 µg/mL

a)




b)

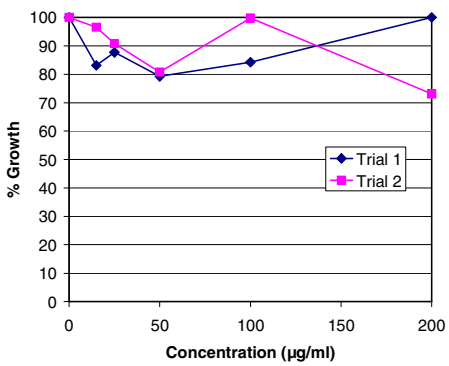
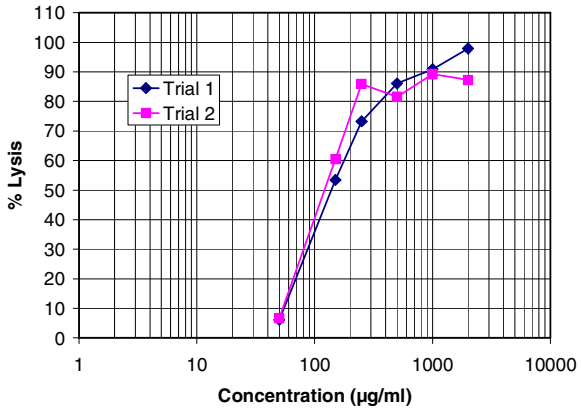
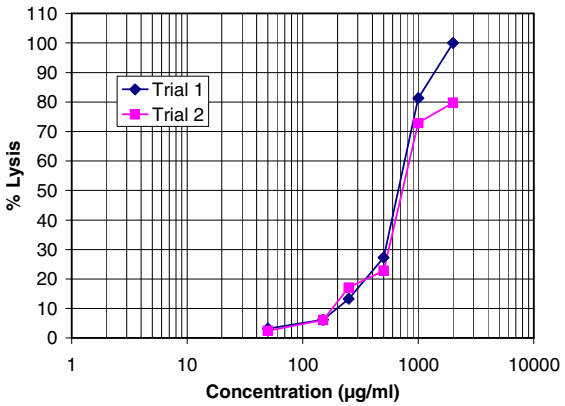


Fig. S4: $HC_{50}$ curve of a) a very hemolytic polymer: Oligo 6, $HC_{50}$ = 150 µg/mL; b) a moderately hemolytic polymer: E1:M9, $HC_{50}$ = 700 µg/mL; and c) a non-hemolytic polymer: M9:P1, $HC_{50}$ > 2000 µg/mL

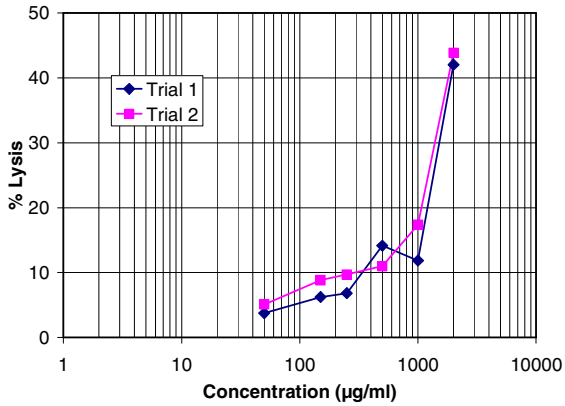
a)




b)




c)




**To compare the differences between our reported $MIC_{90}$** (Tables 1b, 2b and 3b), **and the value of $MIC_{100}$ which is sometime reported, Table S4 reports these $MIC_{100}$ values. When they differ from the $MIC_{90}$ values in the main text, they are highlighted in blue.**

As can be seen when comparing the tables, the difference is usually a factor of two and for the very high selectivities polymers the difference is less since we obtained a clean 100% kill.

Table S4: Characterization of the antimicrobial homopolymers by biological assays: Inhibitory activity towards bacterial growth of *E. coli* and *S. aureus* bacteria. ($MIC_{100}$ = minimal inhibitory concentration preventing 100% bacterial growth) and hemolytic activity towards red blood cells ($HC_{50}$ = concentration lysing 50% of blood cells). a) Homopolymers, b) oligomers, and c) copolymers.

a)

| Sample | $MIC_{100}$ µg mL$^{-1}$ | | $HC_{50}$ µg mL$^{-1}$ | Selectivty | |
|---|---|---|---|---|---|
| | *E. coli* | *S. aureus* | | *E. coli* | *S. aureus* |
| **Methyl_3k** | >200 | >200 | 2000 | <10 | 10 |
| **Ethyl_3k** | 50 | 200 | 1400 | 28 | 7 |
| **Propyl_3k** | 6.25 | 25 | 50 | 8.0 | 2.0 |
| **Butyl_3k** | 15 | 25 | <50 | <3.3 | <2.0 |
| **Isopentyl_3k** | 12.5 | 50 | <50 | <4.0 | <1.0 |
| **Hexyl_3k** | >200 | >200 | <50 | <0.3 | <0.3 |
| **Methyl_10k** | >200 | >200 | 50 | <10 | <10 |
| **Ethyl_10k** | >200 | >200 | 1250 | <6.3 | <6.3 |
| **Propyl_10k** | 6.25 | >200 | <50 | <8.0 | <0.25 |
| **Butyl_10k** | 20 | >200 | <50 | <2.5 | <0.3 |
| **Isopentyl_8k** | 50 | >200 | <50 | <0.3 | <0.3 |
| **Isopentyl_10k** | 50 | 200 | <50 | <0.3 | <0.3 |
| **Hexyl_10k** | 100 | >200 | n.d. | n.d. | n.d. |

b)

| Sample | $MIC_{100}$ µg mL$^{-1}$ | | $HC_{50}$ µg mL$^{-1}$ | Selectivty | |
|---|---|---|---|---|---|
| | *E. coli* | *S. aureus* | | *E. coli* | *S. aureus* |
| Monomer (**3c,** hydrolyzed) | >200 | >200 | n.d. | n.d. | n.d. |
| **Oligo 1** | >200 | 6.25 | 1050 | 5.25 | 168 |
| **Oligo 2** | 200 | 12.5 | 800 | 4.0 | 64 |
| **Oligo 3** | 200 | 25 | 1250 | 6.3 | 50 |
| **Oligo 4** | >200 | 50 | >2000 | >10 | 40 |
| **Oligo 5** | 100 | >200 | 1000 | 10 | 5.0 |
| **Oligo 6** | 50 | 50 | 150 | 3.0 | 3.0 |
| **Propyl_3k** | 6.25 | 25 | 50 | 8.3 | 2.0 |
| **Propyl_10k** | 6.25 | >200 | <50 | <8.0 | <0.25 |

c)

| Sample | Monomer | $MIC_{90}$ μg mL$^{-1}$ | | $HC_{50}$ μg mL$^{-1}$ | Selectivty | |
|---|---|---|---|---|---|---|
| | | *E. coli* | *S. aureus* | | *E. coli* | *S. aureus* |
| Propyl_3k | Propyl | 6.25 | 25 | 50 | 8.0 | 2.0 |
| E1:P9 | Ethyl:Propyl | 50 | 15 | <50 | <1.0 | <3.3 |
| E1:P2 | Ethyl:Propyl | 15 | 15 | <50 | <3.3 | <3.3 |
| E1:P1 | Ethyl:Propyl | 100 | 200 | 1000 | 10 | 5.0 |
| E2:P1 | Ethyl:Propyl | >200 | 200 | >2000 | 10 | >10 |
| E9:P1 | Ethyl:Propyl | >200 | 50 | 500 | <2.5 | 10 |
| Ethyl_3k | Ethyl | 50 | 200 | 1400 | 28 | 7 |
| Methyl_3k | Methyl | >200 | >200 | 2000 | <10 | <10 |
| M9:E1 | Methyl-Ethyl | >200 | 12.5 | 700 | <3.5 | 56 |
| M1:E1 | Methyl-Ethyl | >200 | 25 | 1200 | <6.0 | 48 |
| M1:E9 | Methyl-Ethyl | >200 | 12.5 | 1500 | <7 | 120 |
| Ethyl_3k | Ethyl | 50 | 200 | 1400 | 28 | 7 |
| Methyl_3k | Methyl | >200 | >200 | 2000 | 10 | <10 |
| M9:P1 | Methyl-Propyl | >200 | 3.75 | > 2000 | 10 | 533 |
| M1:P1 | Methyl-Propyl | >200 | 3.75 | > 2000 | 10 | 533 |
| M1:P9 | Methyl-Propyl | >200 | 3.75 | > 2000 | 10 | 533 |
| Propyl_3k | Propyl | 6.25 | 25 | 50 | 8.3 | 2.0 |

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3. Mantovani, G.; Lecolley, F.; Tao, L.; Haddleton, D. M.; Clerx, J.; Cornelissen, J. J. L. M.; Velonia, K., *J. Am. Chem. Soc.* **2005,** *127*, 2966