Backbone conformation affects duplex initiation and duplex propagation in hybridisation of synthetic H-bonding oligomers

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Supporting information

Synthesis .......................................................................................................................... S2
Binding studies ................................................................................................................ S50
Molecular mechanic calculations ..................................................................................... S52
X-ray structure of the AA 2-mer of backbone N8 ............................................................ S53
References ...................................................................................................................... S54
Synthesis

Synthesis of 1a

![Chemical Structure](image)

A mixture of *para*-aminophenol (2.10 g, 19 mmol), 2-methoxybenzaldehyde (2.10 ml, 17 mmol) and NaBH(AcO)₃ (5.40 g, 25 mmol) in DCM (120 ml) was stirred under nitrogen at room temperature for 1 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 100 ml), water (1 x 100 ml) and brine (1 x 100 ml), dried with MgSO₄, and the solvent was removed under reduced pressure. The crude product was then purified by column chromatography on silica eluting with hexane/EtOAc (70:30). The product was isolated as a brown solid (2.25 g, 58%).

**¹H NMR (400 MHz, CD₃CN):** δ 7.30-7.23 (m, 2H), 6.99-6.88 (m, 2H), 6.63-6.51 (m, 4H), 6.30 (s, 1H), 4.43 (s, 1H), 4.23 (s, 2H), 3.87 (s, 3H);

**¹³C NMR (100.6 MHz, CDCl₃):** δ 157.5, 149.0, 141.4, 129.6, 128.6, 127.1, 120.6, 116.4, 116.1, 110.4, 55.4, 45.8;

**MS (ES+):** m/z (%) = 230.1184 (100) [M+H⁺];

**HRMS (ES+):** calcld for C₁₄H₁₆NO₂ 230.1181, found 230.1184;

**FT-IR (thin film):** νmax /cm⁻¹ 3328, 3028, 2938, 2836, 1588, 1601.

**m.p.:** 116-118 °C.
Synthesis of 1b

A mixture of di-tert-butyl((4-((2-methoxybenzyl)amino)phenoxy)methyl)phosphine oxide (0.17 g, 0.6 mmol), 2-methoxybenzaldehyde (0.06 ml, 0.5 mmol) and NaBH(AcO)₃ (0.16 g, 0.75 mmol) in DCE (10 ml) was stirred under nitrogen at room temperature for 1 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄, and the solvent was removed under reduced pressure. The crude product was then purified by column chromatography on silica eluting with DCM/EtOH (95:5). The product was isolated as a brown solid (0.105 g, 48%).

^1H NMR (400 MHz, CD₃CN): δ 7.27-7.20 (m, 2H), 6.96-6.85 (m, 2H), 6.81-6.79 (m, 2H), 6.61-6.58 (m, 2H), 4.27 (d, J = 6, 2H), 4.24 (s, 2H), 3.84 (s, 3H);

^31P NMR (162.0 MHz, CD₃CN): δ 55.6;

^13C NMR (100.6 MHz, CD₃CN): δ 157.6, 150.9, 150.9, 143.3, 128.6, 128.2, 127.5, 120.2, 115.3, 114.1, 110.5, 63.6, 62.9, 55.1, 43.1, 35.2, 34.6, 25.8;

MS (ES+): m/z (%) = 404.2 (100) [M+H⁺];

HRMS (ES+): calcd for C₂₃H₃₅NO₃P 404.2355, found 404.2339;

FT-IR (thin film): νmax/cm⁻¹ 3306, 2953, 1510.

m.p.: 129-130 °C.
Synthesis of 3

A mixture of 2 (3.0 g, 7.6 mmol), ethane-1,2-diol (0.4 ml, 7.6 mmol) and a catalytic amount of p-toluenesulfonic acid in toluene (50 ml) was refluxed for 12 h under nitrogen. After cooling to room temperature, the solution was washed with water (3 x 30 mL) and brine (1 x 30 ml), dried with MgSO₄, and the solvent was removed under reduced pressure. The crude product was then purified by column chromatography on silica eluting with hexane/DCM (90:10). The product was isolated as a yellow oil (1.3 g, 40%).

\(^1\)H NMR (250 MHz, CDCl₃):  δ 10.47 (s, 1H), 7.32 (s, 1H), 7.20 (s, 1H), 6.10 (s, 1H), 4.19-4.01 (m, 4H), 4.07-3.87 (m, 4H), 1.78-1.71 (m, 2H), 1.51-1.30 (m, 16H), 0.96-0.88 (m, 12H);

\(^13\)C NMR (62.9 MHz, CDCl₃):  δ 189.5, 156.3, 151.5, 134.0, 125.6, 111.7, 110.0, 98.7, 71.7, 71.5, 65.4, 39.6, 39.4, 30.7, 30.6, 29.2, 29.0, 24.1, 23.9, 23.1, 23.0, 14.1, 11.2, 11.1;

MS (ES+): m/z (%) = 435.3 (100) [M+H⁺];

HRMS (ES+): calcd for C₂₆H₄₃O₅ 435.3110, found 435.3115;

FT-IR (thin film): ν_max /cm⁻¹ 2956, 2927, 2873, 2859, 1682.
Synthesis of 4a

A mixture of 3 (0.66 g, 1.5 mmol), 1a (0.17 g, 0.74 mmol) and NaBH(AcO)$_3$ (0.45 g, 5.9 mmol) in DCE (2.5 ml) dried with molecular sieves, was stirred under nitrogen at room temperature for 4 h. The solution was then washed with saturated aqueous NaHCO$_3$ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml) and the solvent was removed under reduced pressure. The crude product was then diluted with DCM (10 ml) and left stirring with HCl 4M (10 ml) for 12 h at room temperature. The solution was then washed with saturated aqueous NaHCO$_3$ (1 x 20 ml), water (1 x 20 ml) and brine (1 x 20 ml), dried with MgSO$_4$, and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with CHCl$_3$/MeOH (99:1). The product was isolated as a yellow oil (0.42 g, 94%).

$^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 10.35 (s, 1H), 7.22-7.15 (m, 3H), 6.94-6.91 (m, 2H), 6.84 (td, $J = 7, J = 1$, 1H), 6.61-6.52 (m, 4H), 6.27 (bs, 1H), 4.55-4.54 (m, 4H), 3.88 (d, 2H), 3.77 (s, 3H), 3.74 (d, $J = 6$, 2H), 1.69-1.58 (m, 2H), 1.48-1.23 (m, 16H), 0.91-0.83 (m, 12H);
$^{13}$C NMR (125.7 MHz, CD$_3$CN): $\delta$ 189.5, 158.4, 157.3, 151.7, 149.5, 143.5, 138.4, 128.9, 128.8, 127.7, 124.6, 121.1, 116.7, 115.3, 114.3, 111.5, 109.2, 72.4, 71.6, 56.0, 52.0, 51.5, 40.3, 40.0, 31.5, 31.2, 29.8, 29.7, 24.8, 24.6, 23.7, 23.7, 14.4, 14.4, 11.6, 11.4;
MS (ES$^+$): m/z (%) = 604.4 (100) [M+H$^+$];
HRMS (ES$^+$): calcd for C$_{38}$H$_{54}$NO$_5$ 604.4002, found 604.4016;
FT-IR (thin film): $\nu_{\text{max}}$/cm$^{-1}$ 2961, 2928, 2864, 1661, 1492, 1489, 1515
Synthesis of 4b

A mixture of 3 (0.19 g, 0.45 mmol), 1b (0.09 g, 0.22 mmol) and NaBH(AcO)_3 (0.13 g, 0.60 mmol) in DCE (0.7 ml) dried with molecular sieves, was stirred under nitrogen at room temperature for 12 h. The solution was then washed with saturated aqueous NaHCO_3 (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO_4, and the solvent was removed under reduced pressure. The crude product was then diluted with DCM (10 ml) and left stirring with HCl 4M (10 ml) for 12 h at room temperature. The solution was then washed with saturated aqueous NaHCO_3 (1 x 20 ml), water (1 x 20 ml) and brine (1 x 20 ml) and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with CHCl_3/MeOH (99:1). The product was isolated as an orange oil (0.93 g, 60%).

\[^{1}\text{H} \text{NMR} (400 \text{ MHz, aceton-}d_6): \delta 10.42 (s, 1H), 7.28 (s, 1H), 7.24 (t, J = 8, 2H), 7.03\text{-}7.01 (m, 2H), 6.92\text{-}6.89 (m, 3H), 6.69 (d, J = 9, 2H), 4.7\text{-}4.3 (m, 4H), 4.30 (d, J = 7, 2H), 4.00 (d, J = 5, 2H), 3.87 (s, 3H), 3.84 (d, J = 6, 2H), 1.81\text{-}171 (m, 1H), 1.71\text{-}1.65 (m, 1H), 1.53\text{-}1.28 (m, 34H), 0.98\text{-}0.86 (m, 12H);

\[^{31}\text{P} \text{NMR} (162.0 \text{ MHz, aceton-}d_6): \delta 53.8;

\[^{13}\text{C} \text{NMR} (100.6 \text{ MHz, aceton-}d_6): \delta 187.8, 157.5, 156.3, 150.7, 150.7, 150.7, 143.9, 136.9, 128.0, 127.7, 126.3, 123.8, 120.2, 115.1, 113.7, 113.1, 110.4, 108.3, 71.3, 70.6, 63.7, 63.0, 54.8, 51.1, 50.5, 39.4, 39.1, 35.2, 34.7, 30.6, 30.3, 28.1, 25.9, 23.9, 23.7, 22.8, 22.7, 13.5, 13.4, 10.6, 10.5;

\text{MS (ES+): m/z (%) = 778.5 (100) [M+H]^+, 800.5 (10) [M+Na];

\text{HRMS (ES+): calcd for C}_{47}H_{73}NO_6P 778.5176, found 778.5142.}
A mixture of 4a (90 mg, 0.140 mmol), of para-aminophenol (4.0 g, 0.036 mmol) and NaBH(AcO)₃ (44 mg, 0.09 mmol), AcOH (4 eq) in DCE (100 µl) dried with molecular sieves, was stirred under nitrogen at room temperature for 24 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄, and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with hexane/Et₂O (60:40). The product was isolated as a brown oil (26 mg, 56%).

**1H NMR (500 MHz, CD₃CN):** δ 7.18 (td, J = 8, J = 1, 2H), 7.12 (d, J = 7, 2H), 6.92 (d, J = 8, 2H), 6.82 (td, J = 7, J = 1, 2H), 6.74 (s, 2H), 6.72 (s, 2H) 6.58-6.51 (m, 12H), 6.15 (bs, 3H), 4.48-4.46 (m, 12H), 3.77 (s, 6H), 3.63-3.60 (m, 8H), 1.57-1.53 (m, 4H), 1.38-1.20 (m, 32H), 0.83-0.78 (m, 24H);

**13C NMR (125.7 MHz, CD₃CN):** δ 158.4, 151.5, 151.4, 149.4, 149.2, 144.0, 143.9, 128.7, 128.6, 127.9, 127.4, 121.1, 116.6, 116.5, 115.5, 115.1, 113.1, 113.0, 111.4, 71.8, 56.0, 51.4, 51.2, 40.2, 31.4, 31.4, 29.8, 24.8, 24.7, 23.8, 23.7, 14.4, 14.4, 11.6, 11.5;

**MS (ES+):** m/z (%) = 1284.8 (100) [M+H⁺];

**HRMS (ES+):** calcd for C₈₂H₁₁₄N₃O₉ 1284.8555, found 1284.8569;

**FT-IR (thin film):** ν_max /cm⁻¹ 3368, 2927, 2871, 1602, 150.
**Synthesis of 5b**

A mixture of 4b (130 mg, 0.16 mmol), of di-tert-butyl((4-((2-methoxybenzyl)amino)phenoxy)methyl)phosphine oxide (12.0 mg, 0.04 mmol), NaBH(AcO)₃ (50.0 mg, 0.20 mmol) and AcOH (4 eq) in DCE (100 µl) dried with molecular sieves, was stirred under nitrogen at room temperature for 24 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄, and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with EtOAc/MeOH (90:10). The product was isolated as an orange oil (13.0 mg, 18%).

**¹H NMR (500 MHz, CD₂CN):** δ 7.21-7.17 (m, 2H), 7.10-7.08 (m, 2H), 6.94-6.92 (m, 2H), 6.83-6.76 (m, 8H), 6.70 (d, J = 8, 4H), 6.63 (d, J = 9, 2H), 6.57 (d, J = 9, 4H), 4.54 (s, 4H), 4.51 (s, 8H), 4.23 (d, J = 7, 6H), 3.78 (s, 6H), 3.62-3.60 (m, 8H), 1.54-1.50 (m, 4H), 1.33-1.17 (m, 86H), 0.81-0.76 (m, 24H);

**³¹P NMR (202.4 MHz, CD₂CN):** δ 55.3;

**¹³C NMR (125.7 MHz, CD₂CN):** δ 158.4, 151.4, 151.3, 151.3, 151.3, 151.2, 151.1, 145.1, 145.0, 128.9, 128.5, 127.6, 127.2, 121.1, 116.0, 116.0, 114.8, 114.5, 113.1, 112.9, 111.5, 71.8, 71.8, 64.4, 64.1, 63.8, 63.8, 56.0, 51.3, 51.2, 51.1, 40.1, 40.1, 36.1, 35.6, 31.3, 31.3, 29.8, 26.8, 24.8, 24.7, 23.8, 23.8, 14.5, 14.5, 11.6, 11.6;

**MS (ES+):** m/z (%) = 1807.2 (70) [M+H⁺], 1830.2 (100) [M+Na];

**HRMS (ES+):** calcd for C₁₀₉H₁₇₁N₃O₁₂P₃ 1807.2076, found 1807.2063;

**FT-IR (thin film):** ν_max /cm⁻¹ 2957, 2927, 2871, 1680, 1601, 1511,
Synthesis of 7a

A mixture of 4a (0.390 g, 0.64 mmol), of 6a (0.093 g, 0.16 mmol) and NaBH(AcO)₃ (0.190 g, 0.9 mmol), AcOH (4 eq) in DCE (1 ml) dried with molecular sieves, was stirred under nitrogen at room temperature for 6 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄, and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with hexane/Et₂O (60:40). The product was isolated as a brown oil (0.203 g, 72%).

¹H NMR (500 MHz, CD₃CN): δ 7.17 (td, J = 8, J = 1, 2H), 7.11 (dd, J = 7, J = 1, 2H), 6.91-6.89 (m, 2H), 6.81 (td, J = 7, J = 1, 2H), 6.74-6.72 (m, 6H), 6.59-6.50 (m, 16H), 6.20 (bs, 4H), 4.47-4.46 (m, 16H), 3.76 (s, 6H), 3.63-3.59 (m, 12H), 1.56-1.50 (m, 6H), 1.38-1.16 (m, 48H), 0.81-0.76 (m, 36H);

¹³C NMR (125.7 MHz, CD₃CN): δ 158.4, 151.5, 151.4, 151.3, 149.3, 149.1, 144.0, 143.9, 128.7, 128.5, 127.9, 127.3, 127.3, 121.1, 116.5, 116.5, 115.5, 115.0, 113.0, 113.0, 112.9, 111.3, 71.8, 55.9, 51.4, 51.2, 51.1, 51.1, 40.2, 40.1, 40.1, 31.4, 31.4, 31.3, 29.8, 24.7, 24.7, 23.7, 23.7, 14.4, 14.4, 11.5, 11.5;

MS (ES+): m/z (%) = 1753.2 (100) [M+H⁺];

HRMS (ES+): calcd for C₁₁₂H₁₅₉N₄O₁₂ 1752.1955, found 1752.1964;

FT-IR (thin film): ν max /cm⁻¹ 3625, 3541, 3441, 2964, 2929, 2867, 1500.
**Synthesis of 7b**

A mixture of 4b (60 mg, 0.07 mmol), of 6b (18 mg, 0.02 mmol) and NaBH(AcO)₃ (23 mg, 0.1 mmol), AcOH (4 eq) in DCE (100 µl) dried with molecular sieves, was stirred under nitrogen at room temperature for 24 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄, and the solvent was removed under reduced pressure then purified by column chromatography on silica eluting with EtOAc/MeOH (90:10). The product was isolated as an orange oil (10 mg, 20%).

**¹H NMR (500 MHz, CD₃CN):** δ 7.19 (td, J = 8, J = 1, 2H), 7.09 (dd, J = 7, J = 1, 2H), 6.93-6.92 (m, 2H), 6.83-6.76 (m, 10H), 6.71-6.69 (m, 6H), 6.64-6.57 (m, 8H), 4.53-4.51 (m, 16H), 4.23 (d, J = 7, 8H), 3.78 (s, 6H), 3.62-3.59 (m, 12H), 1.53-1.51 (m, 12H), 1.32-1.16 (m, 120H), 0.79-0.76 (m, 36H);

**³¹P NMR (202.4 MHz, CD₃CN):** δ 55.4;

**¹³C NMR (125.7 MHz, CD₃CN):** δ 157.3, 150.3, 150.3, 150.2, 150.2, 150.2, 150.1, 150.0, 144.1, 143.9, 127.7, 127.3, 126.4, 126.0, 125.9, 125.9, 120.0, 114.9, 114.8, 113.7, 113.7, 111.8, 111.7, 110.3, 70.7, 63.3, 63.2, 62.7, 62.7, 54.9, 50.2, 50.1, 50.0, 49.9, 39.0, 39.0, 38.9, 35.0, 34.5, 30.2, 30.2, 28.7, 25.7, 23.6, 23.6, 23.5, 22.6, 22.6, 13.3, 13.3, 10.5, 10.4;

**MALDI MS:** m/z (%) = 2448.9 (100) [M+H⁺], calcd for C₁₄₈H₂₃₄N₄O₁₆P₄ 2447.66;

**FT-IR (thin film):** ν max /cm⁻¹ 2960, 2920, 2873.
Synthesis of 9

A mixture of 8 (3.8 g, 14 mmol), ethane-1,2-diol (0.08 ml, 14 mmol) and a catalytic amount of p-toluenesulfonic acid in toluene (80 ml) was refluxed for 12 h under nitrogen. After cooling to room temperature, the solution was washed with water (3 x 100 mL) and brine (1 x 100 ml), dried with MgSO₄, and the solvent was removed under reduced pressure. The crude product was then purified by column chromatography on silica eluting with hexane / DCM from 0 to 20% DCM. The product was isolated as a yellow oil (1.87 g, 44%).

\[ ^1 \text{H NMR (400 MHz, CD}_3\text{CN):} \delta \ 9.95 \text{ (s, 1H), 7.54 (s, 1H), 7.39 (s, 1H), 7.28 (s, 1H), 5.78 (s, 1H), 4.10-3.94 (m, 6H), 1.75-1.69 (m, 1H), 1.51-1.29 (m, 8H), 0.94-0.86 (m, 6H);} \]
\[ ^13 \text{C NMR (100.6 MHz, CD}_3\text{CN):} \delta \ 192.1, 160.0, 141.4, 138.2, 120.3, 119.1, 114.2, 102.5, 70.9, 65.3, 39.2, 30.2, 28.8, 23.6, 22.8, 13.4, 10.4; \]
\[ \text{MS (ES+:} m/z (%) = 307.2 (30) [M+H\textsuperscript{+}], 348.2 (100) [M+H\textsuperscript{+} CH}_3\text{CN];} \]
\[ \text{HRMS (ES+):} \text{calcd for C}_{18}\text{H}_{27}\text{O}_4 307.1909 \text{ found 307.1906;} \]
\[ \text{FT-IR (thin film):} \nu_{\text{max}} / \text{cm}^{-1} 3054, 2962, 2931, 2875, 1699, 1597. \]
Synthesis of 10a

A mixture of 9 (1.0 g, 3.2 mmol), 1a (0.37 g, 1.6 mmol) and NaBH(AcO)₃ (0.95 g, 4.5 mmol) in DCE (6 ml) dried with molecular sieves, dried with molecular sieves, was stirred under nitrogen at room temperature for 2 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml) and the solvent was removed under reduced pressure. The crude product was then diluted with DCM (20ml) and left stirring with HCl 4M (20ml) for 12 h at room temperature. The solution was then washed with saturated aqueous NaHCO₃ (1 x 20 ml), water (1 x 20 ml) and brine (1 x 20 ml). The solution was dried with MgSO₄ and the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica eluting with hexane/EtOAc (85:15). The product was isolated as a yellow oil (0.50 g, 65%).

¹H NMR (400 MHz, CD₃CN): δ 9.84 (s, 1H), 7.33 (s, 1H), 7.23-7.08 (m, 4H), 6.93-6.91 (m, 1H), 6.84 (t, J = 7, 1H), 6.62-6.55 (m, 4H), 6.28 (s, 1H), 4.54 (s, 4H), 3.85 (d, J = 6, 2H), 3.78 (s, 3H), 1.70-1.64 (m, 1H), 1.48-1.27 (m, 8H), 0.91-0.87 (m, 6H).

¹³C NMR (100.6 MHz, CD₃CN): δ 192.4, 160.1, 157.5, 148.6, 143.0, 142.5, 138.2, 128.03, 127.9, 126.6, 120.8, 120.2, 119.8, 115.8, 114.6, 112.0, 110.5, 70.7, 55.0, 54.9, 50.5, 39.1, 30.3, 28.8, 23.6, 22.8, 13.5, 10.5;

MS (ES+): m/z (%) = 476.3 (100) [M+H⁺];

HRMS (ES+): calcld for C₃₀H₃₈NO₄ 476.2801 found 476.2786;

FT-IR (thin film): $v_{max} / \text{cm}^{-1}$ 3386, 2929, 2872, 2958, 1695, 1593, 1514.
Synthesis of 10b

A mixture of 9 (0.80 g, 2.6 mmol), 1b (0.45 g, 1.1 mmol) and NaBH(AcO)$_3$ (0.66 g, 3.1 mmol) in DCE (5 ml) dried with molecular sieves, was stirred under nitrogen at room temperature for 12 h. The solution was then washed with saturated aqueous NaHCO$_3$ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml) and the solvent was removed under reduced pressure. The crude product was then diluted with DCM (10ml) and left stirring with HCl 4M (10ml) for 12 h at room temperature. The solution was then washed with saturated aqueous NaHCO$_3$ (1 x 20 ml), water (1 x 20 ml) and brine (1 x 20 ml), dried with MgSO$_4$, and the solvent was removed under reduced pressure. The crude material was purified by column chromatograph on silica eluting with CHCl$_3$/MeOH (99:1). The product was isolated as a orange oil (0.51 g, 71%).

$^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 9.86 (s, 1H), 7.34 (s, 1H), 7.24-7.20 (m, 2H), 7.11 (d, J = 7, 1H), 7.06 (s, 1H), 6.95 (d, J = 8, 1H), 6.86-6.83 (m, 1H), 6.79 (d, J = 9, 2H), 6.61 (d, J = 9, 2H), 4.62 (s, 2H), 4.58 (s, 2H), 4.24 (d, J = 6, 2H), 3.87 (d, J = 6, 2H), 3.80 (s, 3H), 1.69-1.64 (m, 1H), 1.48-1.25 (m, 26 H), 0.90-0.86 (m, 6H);

$^{31}$P NMR (202.4 MHz, CD$_3$CN): $\delta$ 55.29;

$^{13}$C NMR (126 MHz, CD$_3$CN): $\delta$ 193.4, 161.1, 158.5, 151.5, 144.6, 143.8, 139.2, 129.1, 128.6, 127.3, 121.4, 121.2, 120.6, 116.1, 114.8, 113.2, 111.5, 71.7, 64.3, 63.8, 56.0, 55.6, 51.4, 40.1, 36.1, 35.6, 31.2, 29.7, 26.8, 24.6, 23.8, 14.4, 11.4;

MS (ES+): m/z (%) = 650.4 (100) [M+H$^+$];

HRMS (ES+): calcd for C$_{39}$H$_{57}$NO$_3$P 650.3974 found 650.3993.

FT-IR (thin film): $\nu_{max}$/cm$^{-1}$ 2958, 2929, 2871, 1698, 1593, 1512.
Synthesis of 11a

A mixture of 10a (0.17 g, 0.37 mmol), of para-aminophenol (0.01 g, 0.092 mmol) and NaBH(AcO)₃ (0.11 mg, 0.51 mmol), AcOH (4 eq) in DCE (300 μl) dried with molecular sieves, was stirred under nitrogen at room temperature for 12 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1x 10 ml) dried with MgSO₄ and the solvent was removed under reduced pressure. The crude product was then purified by column chromatograph on silica eluting with hexane/EtOAc (70:30). The product was isolated as a red oil (10 mg, 11%).

¹H NMR (500 MHz, CD₃CN): δ 7.19-7.16 (td, J = 8, J = 1, 2H), 7.10-7.09 (m, 2H), 6.91 (d, J = 8, 2H), 6.81 (td, J = 7, J = 1, 2H), 6.71 (s, 2H), 6.62 (s, 2H), 6.59 (s, 2H), 6.57-6.49 (m, 12H), 4.42 (s, 8H), 4.29 (s, 4H), 3.77 (s, 6H), 3.70 (d, J = 6, 4H), 1.60-1.56 (m, 2H), 1.42-1.22 (m, 16H), 0.87-0.83 (m, 12H);

¹³C NMR (126.7 MHz, CD₃CN): δ 160.8, 158.5, 149.9, 149.4, 143.8, 142.6, 142.4, 128.9, 128.9, 127.9, 121.2, 119.2, 117.1, 116.6, 116.5, 115.7, 112.7, 112.5, 111.5, 71.3, 56.7, 56.5, 56.0, 51.4, 40.2, 31.3, 29.8, 24.6, 23.8, 14.5, 11.5;

MS (ES⁺): m/z (%) = 1028.6 (100) [M+H⁺];

HRMS (ES⁺): calcd for C₆₆H₸₂N₃O₇ 1028.6153 found 1028.6177;

FT-IR (thin film): ν max/cm⁻¹ 3347, 2956, 2923, 2853, 1596, 1513.
Synthesis of 11b

A mixture of 10b (195 mg, 0.31 mmol), of di-tert-butyl((4-((2-methoxybenzyl)amino)phenoxy)methyl)phosphine oxide (21.0 mg, 0.07 mmol), NaBH(AcO)₃ (90.0 mg, 0.42 mmol) and AcOH (4 eq) in DCE (300 μl) dried with molecular sieves, was stirred under nitrogen at room temperature for 12 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄ and the solvent was removed under reduced pressure. The crude product was then purified by column chromatograph on silica eluting with EtOAc/MeOH (90:10). The product was isolated as an orange oil (91 mg, 83%).

¹H NMR (500 MHz, CD₃CN): δ 7.17-7.14 (m, 2H), 7.02 (d, J = 7, 2H), 6.89 (d, J = 8.0, 2H), 6.77 (t, J = 7, 2H), 6.73-6.70 (m, 6H), 6.64 (s, 2H), 6.60 (s, 2H), 6.56-6.50 (m, 18H), 4.43 (s, 4H), 4.41 (s, 4H), 4.29 (s, 4H), 4.22-4.19 (m, 6H), 3.73 (s, 6H), 3.67 (d, J = 6, 4H), 3.67 (d, J = 6, 4H), 1.57-1.52 (m, 2H), 1.35-1.19 (m, 70H), 0.84-0.78 (m, 12H);
³¹P NMR (202.4 MHz, CD₃CN): δ 55.43, 55.41;
¹³C NMR (125.7 MHz, CD₃CN): δ 160.8, 158.4, 151.68, 151.6, 151.3, 151.2, 145.0, 145.0, 142.3, 142.1, 128.9, 128.4, 127.3, 121.2, 118.6, 116.1, 116.0, 115.7, 114.7, 112.5, 112.2, 111.4, 71.2, 64.4, 63.8, 56.1, 56.1, 55.9, 51.2, 40.1, 36.1, 35.6, 31.2, 29.8, 26.8, 23.8, 14.5, 11.5;
MS (ES+): m/z (%) = 1550.9 (100) [M+H⁺];
HRMS (ES+): calcd for C₉₃H₁₃₉N₅O₁₀P₃ 1550.9673 found 1550.9702.
FT-IR (thin film): ν max /cm⁻¹ 2957, 2924, 2855, 1596.
Synthesis of 13a

A mixture of 10a (0.21 g, 0.44 mmol), of 12a (0.05 g, 0.11 mmol) and NaBH(AcO)₃ (0.13 g, 0.61 mmol), AcOH (4 eq) in DCE (500 μl) dried with molecular sieves, was stirred under nitrogen at room temperature for 6h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄ and the solvent was removed under reduced pressure. The crude product was then purified by column chromatograph on silica eluting with hexane /Et₂O (50:50). The product was isolated as a red oil (0.56 g, 37%).

¹H NMR (400 MHz, CD₃CN): δ 7.19-7.15 (m, 2H), 7.09-7.07 (m, 2H), 6.91-6.89 (m, 2H), 6.82-6.78 (m, 2H), 6.69 (s, 2H), 6.66 (s, 1H), 6.61-6.47 (m, 2H), 6.301 (s, 2H), 6.236 (s, 2H), 4.40 (s, 8H), 4.27 (s, 8H), 3.75 (s, 6H), 3.70-3.67 (m, 6H), 1.61-1.54 (m, 3H), 1.42-1.19 (m, 24H), 0.86-0.81 (m, 18H);

¹³C NMR (100.6 MHz, CD₃CN): δ 159.7, 157.4, 148.9, 148.3, 142.8, 142.7, 141.6, 141.3, 141.2, 127.8, 127.7, 126.8, 120.1, 118.6, 118.2, 116.0, 115.5, 115.4, 114.6, 111.7, 111.6, 111.4, 110.4, 70.2, 55.6, 55.5, 55.0, 50.3, 39.1, 30.2, 28.8, 23.6, 22.8, 13.4, 10.4;

MS (ES+): m/z (%) = 1367.8 (100) [M+H⁺];

HRMS (ES+): calcd for C₈₈H₁₁₁N₄O₉ 1367.8351 found 1367.8411;

FT-IR (thin film): ν max /cm⁻¹ 3342, 2962, 2923, 2854, 1595, 1513.
Synthesis of 13b

A mixture of 10b (85 mg, 0.1 mmol), of 12b (26 mg, 0.03 mmol) and NaBH(AcO)₃ (40 mg, 0.2 mmol), AcOH (4 eq) in DCE (100 μl) dried with molecular sieves, was stirred under nitrogen at room temperature for 24 h. The solution was then washed with saturated aqueous NaHCO₃ (1 x 10 ml), water (1 x 10 ml) and brine (1 x 10 ml), dried with MgSO₄ and the solvent was removed under reduced pressure. The crude product was then purified by column chromatograph on silica eluting with EtOAc/MeOH (90:10). The product was isolated as an orange oil (24 mg, 36%)

¹H NMR (400 MHz, CD₃CN): δ 7.18-7.14 (m, 2H), 7.02-7.00 (m, 2H), 6.90-6.88 (m, 2H), 6.79-6.69 (m, 10H), 6.63-6.49 (m, 17H), 4.42 (s, 4H), 4.41 (s, 4H), 4.28 (s, 8H), 4.21-4.18 (m, 8H), 3.73 (s, 6H), 3.65 (d, J = 6, 6H), 1.57-1.51 (m, 3H), 1.34-1.17 (m, 3H), 0.84-0.77 (m, 18H);

³¹P NMR (162.0 MHz, CD₃CN): δ 55.24, 55.22;

¹³C NMR (100.6 MHz, CD₃CN): δ 159.81, 159.76, 157.4, 150.74, 150.63, 150.36, 150.25, 144.08, 144.00, 141.4, 141.09, 141.01, 127.9, 127.4, 126.3, 120.2, 118.0, 117.6, 115.07, 115.03, 114.7, 113.7, 111.58, 111.52, 111.2, 110.4, 70.2, 63.5, 62.8, 55.14, 55.02, 50.2, 39.1, 35.2, 34.6, 30.2, 28.8, 25.9, 23.6, 22.8, 13.5, 10.5;

MS (ES+): m/z (%) = 2064.3 (100) [M+H⁺];

HRMS (ES+): calcd for C₁₂₄H₁₈₇N₄O₁₃P₄ 2064.3045 found 2064.3040;

FT-IR (thin film): ν max /cm⁻¹ 2957, 2925, 2871, 1595, 1512.
Binding studies

All binding constants were measured by means of NMR titrations. A known concentration of host solution (0.5-1 mM) in deuterated toluene or chloroform was prepared. A fraction of the host stock solution (0.45-0.6 ml) was transferred to a NMR tube. The guest solution (1-10 mM) was then prepared by dissolving it in the host stock solution. In this way the concentration of host is maintained constant throughout the titration. $^{31}$P NMR spectra were recorded after successive additions of aliquots of guest solution. The observed changes in chemical shift were analysed using a purpose-written fitting program in Microsoft Excel. Errors are quoted as two times the standard deviation.

Figure S1 a) $^{31}$P NMR chemical shift as a function of guest concentration for addition of 5a to 5b. The line represents the best fit to a 1:1 binding isotherm; b) 162 MHz $^{31}$P NMR titration data for addition of 5a to 5b in toluene-$d_8$ at 298 K; c) $^{31}$P NMR chemical shift as a function
of guest concentration for addition of 7a to 7b. The line represents the best fit to a 1:1 binding isotherm; d) 162 MHz $^{31}$P NMR titration data for addition of 7a to 7b in toluene-$d_8$ at 298 K.

Figure S2 a) $^{31}$P NMR chemical shift as a function of guest concentration for addition of 11a to 11b. The line represents the best fit to a 1:1 binding isotherm; b) 162 MHz $^{31}$P NMR titration data for addition of 11a to 11b in toluene-$d_8$ at 298 K; c) $^{31}$P NMR chemical shift as a function of guest concentration for addition of 13a to 13b. The line represents the best fit to a 1:1 binding isotherm; d) 162 MHz $^{31}$P NMR titration data for addition of 13a to 13b in toluene-$d_8$ at 298 K.
Molecular mechanic calculations

Molecular mechanic calculations were performed using MacroModel version 9.8 (Schrödinger Inc.). All structures were minimized first and the minimized structures were then used as the starting molecular structures for all MacroModel conformational searches. The force field used was MMFFs as implemented in this software. The charges were defined by the force field library and no cut off were used for non-covalent interaction. H-bonds were fixed by constraining the distance between the phenolic hydroxyl and phosphine oxide functionalities to 2 ± 1 Å. A Polak-Ribiere Conjugate Gradient (PRCG) was used and each structure was subjected to 10000 iterations. The minima converged on a gradient with a threshold of 0.01. Conformational search was performed from previously minimized structures using 10000 steps. Only the structures in a 5 kJ·mol⁻¹ windows from the global minimum were analysed.
**X-ray structure of the AA 2-mer of backbone N8**

Pure compound (3 mg) was dissolved in MeCN (1 mL) in an NMR tube, resulting in crystallization after 3 days at room temperature. Crystals suitable for X-ray crystallography were selected using an optical microscope and examined at 100 K on a Bruker SMART APEX-II CCD diffractometer operating with a Cu Kα sealed tube X-ray source. The structures were solved using SHELXL-97 and refined using WinGX V1.64.05.23.24. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in idealised position.

![Figure S3. X-ray structure of derivative AA 2-mer (backbone N8) in ORTEP view (ellipsoids are drawn at 50% probability level).](image)

| **Formula**     | C\textsubscript{70}H\textsubscript{107}N\textsubscript{2}O\textsubscript{8}P\textsubscript{2} |
|-----------------|--------------------------------------------------|
| **Temperature / K** | 100                                               |
| **Space Group**  | P2\textsubscript{1}/c                             |
| **Cell Lengths/ Å** | a 21.0973 (5) b 11.5790 (3) c 14.960 (4)         |
| **Cell Angles/ °** | α 90 β 109.03 (2) γ 90                           |
| **Cell Volume/ Å\textsuperscript{3}**     | 3454.81                                           |
| **Z**            | 2                                                 |
| **R factor**     | 15.4                                              |
References

1  C. Xue; F. T., J. Org. Chem., 2003, 68, 4417.

2  MacroModel, version 9.8, Schrödinger, LLC, New York, NY, 2014.