

SUPPORTING INFORMATION

Title: Nucleosides with 5'-Fixed Lipid Groups – Synthesis and Anchoring in Lipid Membranes

Author(s): Nicolai Brodersen, Jun Li, Oliver Kaczmarek, Andreas Bunge, Ludwig Löser, Daniel Huster, Andreas Herrmann, Jürgen Liebscher*

Ref. No.: O200700521

General Procedure for the Synthesis of *O, O*-Dialkyl-*N,N*-diisopropylphosphoramidite **3b-d,h:**

A solution of the corresponding alcohol (10 mmol) and DIPEA (3.88 g, 30.0 mmol) in cyclohexane (10 ml) was added slowly (2 h) to a stirred solution of *N,N*-diisopropylphosphoramidite dichloride (1.01 g, 5.00 mmol) in hexane (10 ml) at 60 °C. The resulting mixture was stirred for further 2 h and the resulting precipitate was filtered off. The filtrate was concentrated and dried in vacuo, leaving the crude material **3b-d, h** as a colourless oil.

***O, O*-Di-(*n*-hexyl)-*N, N*-diisopropylphosphoramidite **3b**:** Yield: 1.17g (70%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.9 Hz, 6H, CH₃), 1.09, 1.11 (d, *J* = 6.0, 12H, CH₃), 1.23 (m, 12H, CH₂), 1.54 (m, 4H, CH₂), 3.52 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.0 (CH₃), 22.6 (CH₂), 24.5 (CH₃), 24.6 (CH₃), 25.6 (CH₂), 31.1 (CH₂), 31.2 (CH₂), 31.6 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.54, 139.79 ppm

***O, O*-Di-(*n*-octyl)-*N, N*-diisopropylphosphoramidite **3c**:** Yield: 1.46g (75%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.6 Hz, 6H, CH₃), 1.09, 1.11 (d, *J* = 6.0, 12H, CH₃), 1.20 (m, 20H, CH₂), 1.54 (m, 4H, CH₂), 3.52 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 22.6 (CH₂), 24.5 (CH₃), 24.6 (CH₃), 26.0 (CH₂), 29.3 (CH₂), 31.3 (CH₂), 31.4 (CH₂), 31.8 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.53, 139.79 ppm

***O, O*-Di-(*n*-dodecyl)-*N, N*-diisopropylphosphoramidite **3d**:** Yield: 1.83g (73%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.6 Hz, 6H, CH₃), 1.09, 1.11 (d, *J* = 6.0, 12H, CH₃), 1.19 (m, 36H, CH₂), 1.53 (m, 4H, CH₂), 3.51 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 22.7 (CH₂), 24.5 (CH₃), 24.6 (CH₃), 26.0 (CH₂), 29.4 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 31.3 (CH₂), 31.4 (CH₂), 31.9 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.54, 139.79 ppm

***O, O*-Di-(3,7-dimethyl-oct-6-enyl)-*N, N*-diisopropylphosphoramidite **3h**:** Yield: 1.61g (73%). ¹H-NMR (300 MHz, CDCl₃): δ = 0.97, 0.99 (d, *J* = 6.0 Hz, 6H, CH₃), 1.25, 1.27 (d, *J* = 6.0, 12H, CH₃), 1.47 (m, 6H, CH₂ + CH), 1.68-1.76 (m, 16H, CH₃ + CH₂), 2.06 (m, 4H, CH₂), 3.68 (m, 6H, CH₂O + NCH), 5.18 (t, *J* = 7.0 Hz, 2H, 2×CH=) ppm. ¹³C-NMR

(75.5 MHz, CDCl₃): δ = 17.6 (CH₃), 19.4 (CH₃), 19.5 (CH₃), 24.5 (CH₃), 24.6 (CH₃), 25.7 (CH₃), 25.7 (CH₂), 29.2 (CH), 29.3 (CH), 37.1 (CH₂), 37.2 (CH₂), 38.2 (CH₂), 38.4 (CH₂), 42.6 (NCH), 42.8 (NCH), 61.5 (CH₂O), 61.9 (CH₂O), 124.9 (CH=), 131.0 (=C(CH₃)) ppm. ³¹P-NMR (CDCl₃): δ = 145.53, 139.77 ppm

General Procedure for the Synthesis of *O, O*-Dialkyl-*N, N*-diisopropylphosphoramidite **3e-g:**

A solution of the corresponding alcohol (10mmol), Et₃N (3.03 g, 30.0 mmol), *N,N*-diisopropylphosphoramidite dichloride (1.01 g, 5.00 mmol) in hexane (50 ml) was refluxed under argon at 85°C for 3 h. The resulting precipitate was filtered off and the filtrate was concentrated and dried in vacuo, leaving the crude material **3e-g** as a colourless solid.

***O, O*-Di-(*n*-hexadecyl)-*N, N*-diisopropylphosphoramidite **3e**:** Yield: 2.29g (75%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.96 (t, J = 6.6 Hz, 6H, CH₃), 1.24, 1.26 (d, J = 6.0, 12H, CH₃), 1.33 (m, 52H, CH₂), 1.68 (m, 4H, CH₂), 3.60 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 22.7 (CH₂), 24.5 (CH₂O), 24.6 (CH₃), 26.0 (CH₂), 29.4 (CH₂), 29.7 (CH₂), 31.3 (CH₂), 31.4 (CH₂), 31.9 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.54, 139.79 ppm

***O, O*-Di-(*n*-octadecyl)-*N, N*-diisopropylphosphoramidite **3f**:** Yield: 2.93g (87%).

¹H-NMR (300 MHz, CDCl₃): δ = 1.07 (t, J = 6.6 Hz, 6H, CH₃), 1.36, 1.38 (d, J = 6.0, 12H, CH₃), 1.45 (m, 60H, CH₂), 1.80 (m, 4H, CH₂), 3.78 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 22.7 (CH₂), 24.6 (CH₃), 24.7 (CH₃), 26.0 (CH₂), 29.4 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 31.3 (CH₂), 31.4 (CH₂), 31.9 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.53, 139.79 ppm

***O, O*-Di-(*n*-docosyl)-*N, N*-diisopropylphosphoramidite **3g**:** Yield: 2.86g (68%).

¹H-NMR (300 MHz, CDCl₃): δ = 1.08 (t, J = 6.6 Hz, 6H, CH₃), 1.36, 1.38 (d, J = 6.0, 12H, CH₃), 1.45 (m, 76H, CH₂), 1.80 (m, 4H, CH₂), 3.78 (m, 6H, CH₂O + CH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 22.7 (CH₂), 24.6 (CH₃), 24.7 (CH₃), 26.0 (CH₂), 29.4 (CH₂), 29.7 (CH₂), 31.3 (CH₂), 31.4 (CH₂), 31.9 (CH₂), 42.6 (CH), 42.7 (CH), 63.3 (CH₂O), 63.6 (CH₂O) ppm. ³¹P-NMR (CDCl₃): δ = 145.51, 139.79 ppm

***O*-(3'-*O*-acetyl-2'-deoxyuridine-5'-yl)-*O*, *O*-Di-(n-hexyl)phosphate **5b**:** Yield: 80mg (77%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.3Hz, 6H, CH₃), 1.23 (m, 12H, CH₂), 1.61 (m, 4H, CH₂), 2.05 (s, 3H, CH₃O), 2.07-2.43 (m, 2H, CH₂''), 3.99 (q, *J* = 6.8Hz, 4H, CH₂O), 4.12 (m, 1H, CH₄'), 4.23 (m, 2H, CH₂5'), 5.22, 5.24 (d, *J* = 6.0Hz, 1H, CH₃'), 5.71, 5.73 (d, *J* = 6.0Hz, 1H, CH₅), 6.31 (q, *J* = 4.8Hz, 1H, CH₁'), 7.64, 7.67 (d, *J* = 9.0Hz, 1H, CH₆), 9.41 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.0 (CH₃), 20.9 (CH₃), 22.5 (CH₂), 25.0 (CH₂), 30.2 (CH₂), 30.2 (CH₂), 30.3 (CH₂), 30.3 (CH₂), 31.2 (CH₂), 37.6 (C₂'), 66.9 (C₅'), 68.4 (CH₂O), 68.5 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.8 (C₄'), 103.1 (C₅), 139.5 (C₆), 150.4 (C₂), 163.2 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.18 ppm. m/e, 518.00 (HPLC-MS).

***O*-(3'-*O*-Acetyl-2'-deoxyuridine-5'-yl)- *O*, *O*-di-(n-octyl)phosphate **5c**:** Yield: 96mg (83%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.3Hz, 6H, CH₃), 1.20 (m, 20H, CH₂), 1.62 (m, 4H, CH₂), 2.05 (s, 3H, CH₃O), 2.08-2.44 (m, 2H, CH₂''), 4.01 (q, *J* = 6.7Hz, 4H, CH₂O), 4.13 (m, 1H, CH₄'), 4.24 (m, 2H, CH₂5'), 5.22, 5.24 (d, *J* = 6.0Hz, 1H, CH₃'), 5.71, 5.74 (d, *J* = 9.0Hz, 1H, CH₅), 6.30 (q, *J* = 4.8Hz, 1H, CH₁'), 7.64, 7.67 (d, *J* = 9.0Hz, 1H, CH₆), 9.35 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 20.9 (CH₃), 22.6 (CH₂), 25.4 (CH₂), 29.0 (CH₂), 29.1 (CH₂), 30.2 (CH₂), 30.3 (CH₂), 31.7 (CH₂), 37.6 (C₂'), 66.9, 67.0 (C₅'), 68.5 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.9 (C₄'), 103.0 (C₅), 139.5 (C₆), 150.4 (C₂), 163.1 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.28 ppm. m/e, 574.48 (HPLC-MS).

***O*-(3'-*O*-Acetyl-2'-deoxyuridine-5'-yl)- *O*, *O*-di-(n-dodecyl)phosphate **5d**:** Yield: 90mg (66%).

¹H-NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.8Hz, 6H, CH₃), 1.18 (m, 18H, CH₂), 1.62 (m, 4H, CH₂), 2.05 (s, 3H, CH₃O), 2.08-2.44 (m, 2H, CH₂''), 4.01 (q, *J* = 6.8Hz, 4H, CH₂O), 4.12 (m, 1H, CH₄'), 4.24 (m, 2H, CH₂5'), 5.22, 5.24 (d, *J* = 6.0Hz, 1H, CH₃'), 5.71, 5.74 (d, *J* = 9.0Hz, 1H, CH₅), 6.31 (q, *J* = 4.9Hz, 1H, CH₁'), 7.64, 7.67 (d, *J* = 9.0Hz, 1H, CH₆), 9.38 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 20.9 (CH₃), 22.7 (CH₂), 25.4 (CH₂), 29.1 (CH₂), 29.5 (CH₂), 29.6 (CH₂), 30.2 (CH₂), 30.3 (CH₂), 31.9 (CH₂), 37.6 (C₂'), 66.9, 67.0 (C₅'), 68.5 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.9 (C₄'), 103.0 (C₅), 139.6 (C₆), 150.4 (C₂), 163.3 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.30 ppm.

***O*-(3'-*O*-Acetyl-2'-deoxyuridine-5'-yl)- *O,O*-di-(*n*-hexadecyl)phosphate 5e:** Yield: 120mg (75%). ¹H-NMR (300 MHz, CDCl₃): δ = 0.76 (t, *J* = 6.8Hz, 6H, CH₃), 1.13 (m, 52H, CH₂), 1.56 (m, 4H, CH₂), 1.99 (s, 3H, CH₃O), 2.01-2.37 (m, 2H, CH₂'), 3.94 (q, *J* = 6.9Hz, 4H, CH₂O), 4.06 (m, 1H, CH₄'), 4.17 (m, 2H, CH₂5'), 5.16, 5.18 (d, *J* = 6.0Hz, 1H, CH₃'), 5.66 (dd, *J*₁ = 9.0Hz, *J*₂ = 3.0Hz, 1H, CH₅), 6.26 (q, *J* = 4.9Hz, 1H, CH₁'), 7.58, 7.60 (d, *J* = 6.0Hz, 1H, CH₆), 9.24 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 20.9 (CH₃), 22.7 (CH₂), 25.4 (CH₂), 29.1 (CH₂), 29.4 (CH₂), 29.5 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 30.3 (CH₂), 30.3 (CH₂), 31.9 (CH₂), 37.6 (C₂'), 66.8, 66.9 (C₅'), 68.3 (CH₂O), 68.4 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.8 (C₄'), 103.1 (C₅), 139.4 (C₆), 150.4 (C₂), 163.0 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.15 ppm. HRMS, *m/z*: 799.55 [M+H]⁺, *m/e*, 799.67 (HPLC-MS)

***O*-(3'-*O*-Acetyl-2'-deoxyuridine-5'-yl)- *O, O*-di-(*n*-octadecyl)phosphate 5f:** Yield: 149mg (87%). ¹H-NMR (300 MHz, CDCl₃): δ = 1.14 (t, *J* = 6.9Hz, 6H, CH₃), 1.51 (m, 60H, CH₂), 1.94 (m, 4H, CH₂), 2.38 (s, 3H, CH₃O), 2.40-2.74 (m, 2H, CH₂'), 4.33 (q, *J* = 6.9Hz, 4H, CH₂O), 4.45 (m, 1H, CH₄'), 4.55 (m, 2H, CH₂5'), 5.55, 5.57 (d, *J* = 6.0Hz, 1H, CH₃'), 6.02, 6.05 (d, *J* = 9.0Hz, 1H, CH₅), 6.63 (q, *J* = 4.9Hz, 1H, CH₁'), 7.95, 7.98 (d, *J* = 9.0Hz, 1H, CH₆), 9.15 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 20.9 (CH₃), 22.7 (CH₂), 25.4 (CH₂), 29.1 (CH₂), 29.4 (CH₂), 29.5 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 30.3 (CH₂), 31.9 (CH₂), 37.6 (C₂'), 66.9 (C₅'), 68.4 (CH₂O), 68.5 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.8 (C₄'), 103.1 (C₅), 139.4 (C₆), 150.3 (C₂), 162.8 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.24 ppm.

***O*-(3'-*O*-Acetyl-2'-deoxyuridine-5'-yl)- *O, O*-di-(*n*-docosyl)phosphate 5g:** Yield: 172mg (89%). ¹H-NMR (300 MHz, CDCl₃): δ = 0.96 (t, *J* = 6.8Hz, 6H, CH₃), 1.33 (m, 76H, CH₂), 1.76 (m, 4H, CH₂), 2.20 (s, 3H, CH₃O), 2.22-2.56 (m, 2H, CH₂'), 4.15 (q, *J* = 6.9Hz, 4H, CH₂O), 4.27 (m, 1H, CH₄'), 4.38 (m, 2H, CH₂5'), 5.37, 5.39 (d, *J* = 6.0Hz, 1H, CH₃'), 5.85, 5.87 (d, *J* = 6.0Hz, 1H, CH₅), 6.45 (q, *J* = 4.8Hz, 1H, CH₁'), 7.78, 7.80 (d, *J* = 6.0Hz, 1H, CH₆), 9.05 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.1 (CH₃), 20.9 (CH₃), 22.7 (CH₂), 25.4 (CH₂), 29.1 (CH₂), 29.4 (CH₂), 29.5 (CH₂), 29.6 (CH₂), 29.7 (CH₂), 30.3 (CH₂), 31.9 (CH₂), 37.6 (C₂'), 66.9, 67.0 (C₅'), 68.4 (CH₂O), 68.5 (CH₂O), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.8 (C₄'), 103.1 (C₅), 139.4 (C₆), 150.3 (C₂), 162.9 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.24 ppm.

***O*-(3'-*O*-acetyl-2'-deoxyuridine-5'-yl)- *O*, *O*-di-(3,7-dimethyl-oct-6-enyl)phosphate **5h**:**

Yield: 95mg (76%). ¹H-NMR (300 MHz, CDCl₃): δ = 1.19 (dd, *J*₁ = 6.0Hz, *J*₂ = 3.0Hz, 6H, CH₃), 1.40-1.68 (m, 6H, CH₂ + CH), 18.78 (s, 6H, CH₃), 1.96 (s, 6H, CH₃), 1.99-2.07 (m, 4H, CH₂), 2.20-2.30 (m, 4H, CH₂), 2.40 (s, 3H, CH₃O), 2.41-2.78 (m, 2H, CH₂'), 4.35-4.38 (m, 4H, CH₂O), 4.47 (m, 1H, CH₄'), 4.57 (m, 2H, CH₂5'), 5.33-5.38 (m, 2H, CH=), 5.56, 5.58 (d, *J* = 6.0Hz, 1H, CH₃'), 6.05, 6.07 (d, *J* = 6.0Hz, 1H, CH₅), 6.65 (q, *J* = 4.9Hz, 1H, CH₁'), 7.98, 8.00 (d, *J* = 6.0Hz, 1H, CH₆), 9.42 (s, 1H, NH) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 17.6 (CH₃), 19.2 (CH₃), 20.9 (OCH₃), 25.7 (CH₃), 29.0 (CH), 36.9 (CH₃), 37.2 (CH₃), 37.5 (C₂'), 66.7 (CH₂O), 66.8 (CH₂O), 66.9 (C₅'), 74.5 (C₃'), 83.1, 83.2 (C₁'), 84.9 (C₄'), 103.1 (C₅), 124.3 (CH=), 131.5 (Me₂C=), 139.4 (C₆), 150.3 (C₂), 162.9 (C₄), 170.5 (O=CCH₃) ppm. ³¹P-NMR (CDCl₃): δ = -0.13 ppm.

2-Nitro-9,9-di-(n-octadecyl)-9H-fluorene:

2-Nitrofluorene (2.0g, 9.5mmol) was dissolved in DMF (120ml) and KOH-powder (1.6 g, 28.5 mmol) was added under vigorous stirring. After 30 minutes 1-octadecyl bromide (7.6 g, 22.7 mmol) was added to the dark-green coloured solution. Within 1 hour stirring at r.t. the reaction mixture became highly viscous and therefore further DMF (60ml) was added. The suspension was stirred at r.t. for 48 h and at 50°C for 24 h.

The solvent was evaporated and the residue was poured into ice-cold water (150ml).

The aqueous phase was extracted with DCM (50ml) four times and the combined organic phases were dried over MgSO₄. The filtrate was concentrated in vacuo. The product was obtained as brown oil. TLC EtOAc/Cyclohexane 1:2, R_f 0.8, Yield: 6.8g (99%). ¹H-NMR (300 MHz, CDCl₃): δ = 0.56 (s, 4H, -CH₂-), 0.87 (t, *J* = 6.8 Hz, 6H, -CH₃), 1.25 (s, 60H, -CH₂-), 2.01 (m, 4H, -CH₂-), 7.40 (m, 3H, C_{ar}-H), 7.77 (d, *J* = 7.5 Hz, 1H, C_{ar}-H), 7.79 (d, *J* = 8.3 Hz, 1H, C_{ar}-H), 8.19 (d, *J* = 1.9 Hz, 1H, C_{ar}-H), 8.25 (dd, *J* = 2.3 Hz, 1H, C_{ar}-H) ppm. ¹³C-NMR (75.5 MHz, CDCl₃): δ = 14.25 (CH₃), 22.82 (CH₂), 23.85 (CH₂), 29.22 (CH₂), 29.35 (CH₂), 29.49 (CH₂), 29.62 (CH₂), 29.65 (CH₂), 29.70 (CH₂), 29.82 (CH₂), 29.98 (CH₂), 32.05 (CH₂), 40.17 (CH₂), 55.79 (C_{ar}), 118.34 (C_{ar}), 119.88 (C_{ar}), 121.30 (C_{ar}), 123.32 (C_{ar}), 123.37 (C_{ar}), 127.49 (C_{ar}), 129.36 (C_{ar}), 138.83 (C_{ar}), 147.22 (C_{ar}), 147.76 (C_{ar}), 152.08 (C_{ar}), 152.43 (C_{ar}) ppm. C₄₉H₈₁NO₂ (716.17) calc. C 82.18, H 11.40, N 1.96, O 4.47; found C 78.70, H 11.96, N 2.08;

2-Amino-9,9-di-(n-octadecyl)-9H-fluorene:

2-Nitro-9,9-dioctadecyl-9H-fluorene (5.2g, 7.2mmol), zinc powder (3.8 g, 56.9mmol) and CaCl_2 (830mg) were suspended in iPrOH (100ml). Water (14ml) and glacial acetic acid (1.7ml) were added under vigorous stirring. The suspension was refluxed at 84 °C for 4 h and filtered at 60 °C. The precipitate was washed with CHCl_3 and the combined filtrates were concentrated in vacuo in combination with toluene. The resulting yellow residue was submitted to silica gel chromatography (EtOAc/Cyclohexane 1:9, R_f 0.4). The product was obtained as a yellow solid. M.p. 72-73°C. Yield: 2.4g (48%). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 0.62 (s, 4H, $-\text{CH}_2-$), 0.86 (t, J = 6.8 Hz, 6H, $-\text{CH}_3$), 1.32-0.98 (m, 60H, $-\text{CH}_2-$), 1.87 (m, 4H, $-\text{CH}_2-$), 3.82 (s, 2H, $-\text{NH}_2$), 6.64 (m, 2H, $\text{C}_{\text{ar}}-\text{H}$), 7.28-7.12 (m, 3H, $\text{C}_{\text{ar}}-\text{H}$), 7.46 (d, J = 8.5 Hz, 1H, $\text{C}_{\text{ar}}-\text{H}$), 7.53 (d, J = 8.0 Hz, 1H, $\text{C}_{\text{ar}}-\text{H}$) ppm. $^{13}\text{C-NMR}$ (75.5 MHz, CDCl_3): δ = 14.29 (CH_3), 22.85 (CH_2), 23.89 (CH_2), 29.48 (CH_2), 29.52 (CH_2), 29.74 (CH_2), 29.77 (CH_2), 29.79 (CH_2), 29.82 (CH_2), 29.85 (CH_2), 30.29 (CH_2), 32.08 (CH_2), 40.79 (CH_2), 54.91 (C_{ar}), 110.02 (C_{ar}), 114.12 (C_{ar}), 118.46 (C_{ar}), 120.56 (C_{ar}), 122.69 (C_{ar}), 125.48 (C_{ar}), 126.69 (C_{ar}), 132.73 (C_{ar}), 141.65 (C_{ar}), 145.79 (C_{ar}), 149.91 (C_{ar}), 152.76 (C_{ar}) ppm. $\text{C}_{49}\text{H}_{83}\text{N}$ (686.19) calc. C 85.77, H 12.19, N 2.04; found C 85.39, H 12.14, N 2.08; UV λ_{max} 293nm[0.13mmol/l]; ϵ_{max} 22465 l/mol·cm

5'-Di-(n-octylamino)-5'-deoxyuridine 10d:

Starting material **7** (250 mg, 0.4 mmol), dioctylamine **6** (1.4ml, 4.4mmol, 11 equiv.), 80°C, 10 h, THF 1 ml, TBAF(1 M in THF) (2 ml, 2 mmol), SC MeOH/ CHCl_3 1:30, R_f 0.1, Yield: 58 mg (31%). Colourless oil. $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 0.86 (t, J = 6.8 Hz, 6H, $-\text{CH}_2-\text{CH}_3$); 1.25 (s, 20H, $-\text{CH}_2-$); 1.53 (s, 4H, $-\text{NH}-\text{CH}_2-\text{CH}_2-$); 2.72 (m, 4H, $-\text{NH}-\text{CH}_2-\text{CH}_2-$); 3.08 (m, 2H, $-\text{CH}_25'$); 4.10 (m, 1H, $-\text{CH}-\text{OH}$, 4'); 4.20 (m, 1H, $-\text{CH}-\text{OH}$, 2'); 4.28 (m, 1H, $-\text{CH}-\text{OH}$, 3'); 5.72 (d, J = 8.3 Hz, 1H, $\text{CH}5$); 5.74 (d, J = 3.0 Hz, 1H, $-\text{CH}-$, 1'); 7.67 (d, J = 8.3 Hz, 1H, $\text{CH}6$) ppm. $^{13}\text{C-NMR}$ (75.5 MHz, CDCl_3): δ = 13.82 ($-\text{CH}_2-\text{CH}_3$); 19.87 ($-\text{CH}_2-$); 22.74 ($-\text{CH}_2-$); 24.28 ($-\text{CH}_2-$); 25.56 ($-\text{CH}_2-$); 27.36 ($-\text{CH}_2-$); 29.36 ($-\text{CH}_2-$); 29.51 ($-\text{CH}_2-$); 29.80 ($-\text{CH}_2-$); 31.89 ($-\text{CH}_2-$); 32.03 ($-\text{CH}_2-$); 54.37 ($-\text{CH}_2-$); 55.11(CH_25'); 59.21 ($-\text{CH}_2-$); 72.01 ($\text{CH}3'$); 74.12 ($\text{CH}2'$); 80.76 ($\text{CH}4'$); 92.24 ($\text{CH}1'$); 102.47 ($\text{CH}5$); 141.53 ($\text{CH}6$); 150.99 ($\text{C}2$); 164.09 ($\text{C}4$) ppm.

HRMS: calc. $\text{C}_{25}\text{H}_{46}\text{N}_3\text{O}_5^+$ 468.3432; found 468.3427