

2'-O-{2-[N,N-(dialkyl)aminooxy] ethyl}

Modified Antisense Oligonucleotides

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5'-O-DMT-2'-O-[2-N,N-(dimethyl)aminooxyethyl]-5-methyluridine (11)

R_f 0.44 ((10% MeOH in CH_2Cl_2); ^1H NMR (200 MHz, CDCl_3) δ 1.35 (s, 3H), 2.60 (s, 6H), 3.43 (dd, $J = 2.721$, 8.2 Hz, 1H), 3.57 (dd, $J = 1.86$ Hz, 9.06 Hz, 1H), 3.7-3.89 (m, 3H), 3.80 (s, 6H), 4.03-4.19 (m, 4H), 4.45 (q, $J = 5.38$ Hz, 7.36 Hz, 1H), 5.99 (d, $J = 3.2$ Hz, 1H), 6.84 (d, $J = 8.84$ Hz, 4H), 7.2-7.44 (m, 9H), 7.68 (s, 1H), 8.22 (s, 1H); ^{13}C (50 MHz, CDCl_3) δ 11.75, 47.54, 55.23, 62.42, 69.23, 70.10, 70.76, 83.05, 83.67, 86.91, 87.87, 110.92, 113.34, 123.69, 127.10, 127.95, 128.28, 126.28, 130.17, 135.37, 135.50, 144.45, 149.76, 150.45, 156.81, 163.95; MS (FAB) m/z 648 (M+H) $^+$, MS (ES) m/z 646 [M-H] $^-$, HRMS (MALDI) Calcd for $\text{C}_{35}\text{H}_{41}\text{O}_9\text{N}_3\text{Na}^\oplus$ 670.2735, found 670.2731.

5'-O-DMT-2'-O-[2-N,N-(dimethyl)aminoxyethyl]-5-methyluridine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramidite] (13)

R_f 0.25 (ethyl acetate:hexane, 1:1). ^1H NMR (400 MHz, CDCl_3) δ 1.17 (d, $J = 8.8$ Hz, 2H), 1.25 (m, 10H), 1.34 (s, 3H), 2.37 (t, $J = 6$ Hz, 1H), 2.57, (s, 6H), 2.62 (m, 1H), 3.33 (m, 1H), 3.59 (m, 5H), 3.92 (m, 11 H), 4.11-4.3 (m, 2H), 4.51 (m, 1H), 6.09 (m, 2H), 6.84 (m, 4H), 7.21-7.44 (m, 9H), 7.7 (s, 1H), 7.74 (s, 1H), 8.31 (brs, 1H); ^{31}P NMR (50 MHz, CDCl_3) δ 150.73, HRMS (FAB) Calcd for $\text{C}_{44}\text{H}_{58}\text{O}_{10}\text{N}_5\text{PNa}^\oplus$ 870.3819, found 870.3796.

5'-O-DMT-2'-O-[2-N,N-(diethyl)aminoxyethyl]-5-methyluridine (12)

R_f = 0.47 (10% MeOH in CH_2Cl_2). ^1H NMR (200 MHz, $\text{DMSO}-d_6$) δ 0.98 (t, 6H, $J = 7.12$ Hz), 1.39 (s, 3H), 2.6 (q, 4H, $J = 7.22$ Hz), 3.22 (m, 2H), 3.73 (brs, 10H), 3.98 (brs, 1H), 4.07 (m, 1H), 4.23 (m, 1H), 5.18 (d, 1H, $J = 5.76$ Hz), 5.9 (d, 1H, $J = 5.38$ Hz), 6.9 (d, 4H, $J = 8.42$ Hz), 7.24-7.41 (m, 9H), 7.49 (s, 1H), 11.39 (s, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ 11.7, 11.87, 52.27, 55.11, 62.17, 69.03, 70.36, 72.24, 82.76, 83.47, 86.73, 87.52, 110.83, 113.16, 126.99, 127.88, 128.1, 130.03, 135.26, 144.27, 150.46, 158.59, 164.22; HRMS (FAB), Calcd for $\text{C}_{37}\text{H}_{46}\text{N}_3\text{O}_9^\oplus$ 676.3234, Found 676.3214.

5'-O-DMT-2'-O-[2-N,N-(diethyl)aminoxyethyl]-5-methyluridine-3'-O-[(2-cyanoethyl)N,N-diisopropyl]phosphoramidite (14)

R_f = 0.58 (CH_2Cl_2 : MeOH : Pyridine, 94 : 5 : 1), ^{31}P NMR (80 MHz, CDCl_3) 150.84, 150.54; HRMS (FAB), Calcd for $\text{C}_{46}\text{H}_{62}\text{N}_5\text{O}_{10}\text{PNa}^\oplus$ 898.4132 Found 898.4113.