Supporting Information

Blue fluorescent deoxycytidine analogues: convergent synthesis, solid-state and electronic structure, and solvatochromism†

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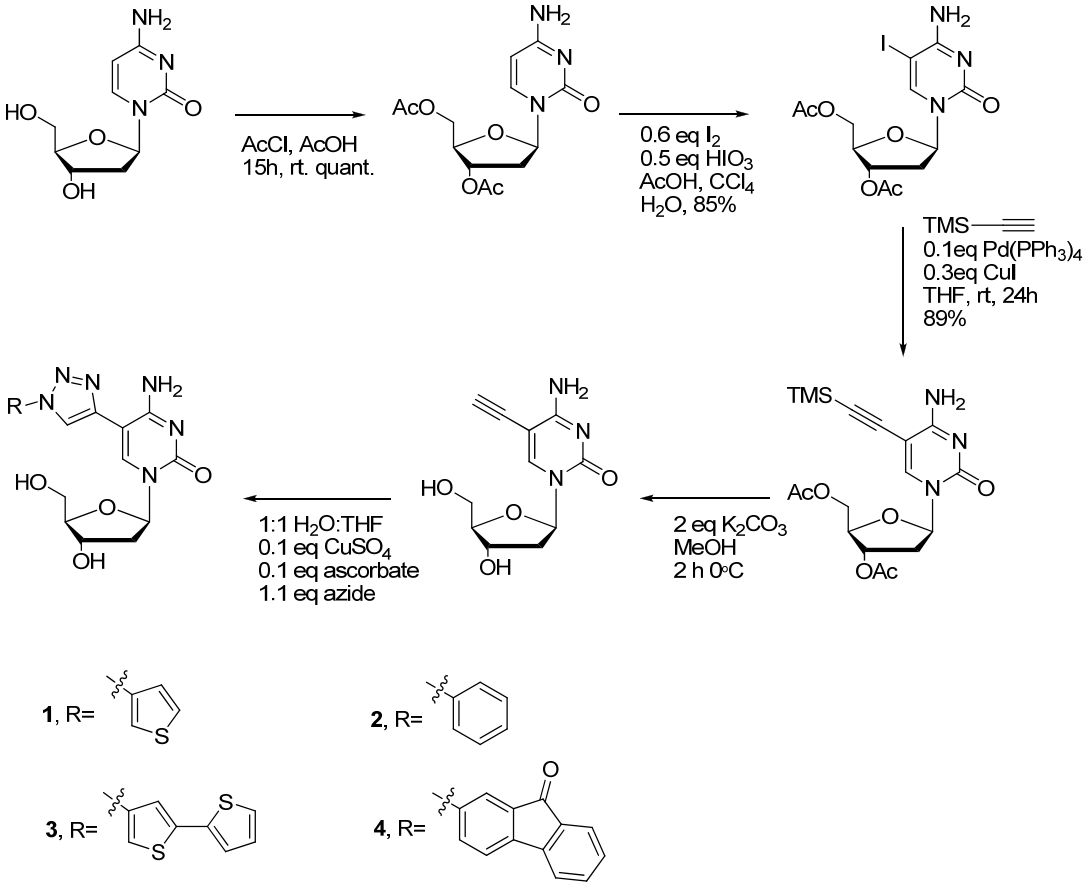
General Considerations:

All chemicals were obtained from commercial sources and were used without further purification. Solvents were dried by passing through columns of activated alumina. Flash column chromatography (FCC) was performed on Merck Kieselgel 60, 230-400 mesh and thin layer chromatography (TLC) was performed on Merck Kieselgel F-60 plates. Chemical shifts are reported in parts per million (δ), were measured from tetramethylsilane (0 ppm) and are referenced to the residual proton in the deuterated solvent: $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.48 ppm), D_2O (4.75 ppm) for ^1H NMR and $CDCl_3$ (77.0 ppm), DMSO-d_6 (39.5 ppm) for ^{13}C NMR. Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br s (broad singlet). Coupling constants (*J*) are reported in Hertz (Hz). Exchangeable protons were identified by their disappearance when the sample was shaken against D_2O. High resolution mass spectra (HRMS) were obtained using electrospray ionization time of flight methods (ESI-TOF). Solution ^1H NMR spectra were collected using a Varian 400 spectrometer (400.09 MHz for ^1H and 100.61 MHz for ^{13}C) at r.t. unless otherwise noted.



Scheme S1 Synthesis of 1-substituted 5-(1*H*-1,2,3-triazol-4-yl)-2'-deoxycytidines.

Synthesis of 3', 5'-diacetyl-2'-deoxycytidine

The following synthesis was based on a literature procedure.[1] 2'-Deoxycytidine HCl salt (0.95 g, 3.6 mmol) was dissolved in AcOH (10 mL) and stirred at 35°C until dissolution at which time the reaction was allowed to come to rt. A mixture of $CHCl_3$ (8 mL) and AcCl (3 mL) was added and the reaction continued to be stirred overnight after which time the colourless solution was concentrated to *ca.* 4.0 mL and placed under high vacuum. Subsequently, the residue was dissolved in MeOH (50 mL) and evaporated to yield a white foam which was left under high vacuum overnight and was of sufficient purity to be carried forward to the next step. Crude yield: 1.22 g (quant.). Spectroscopic data matched that of the literature compound.[1] ^{1}H NMR (DMSO-d_6) δ: 2.03 (s, 3H), 2.06 (s, 3H), 2.42 (dd, 2H, ^2J = 2.4, ^3J = 6.4), 4.22 (m, 1H), 5.18 (m, 1H), 6.08 (t, 1H, ^3J = 6.8), 6.13 (d, 2H, ^3J = 8.0), 7.95 (d, 2H, ^3J = 7.6), 8.51 (s, 1H, N*H*), 9.56 (s, 1H, N*H*).

Synthesis of 5-iodo-3', 5'-diacetyl-2'-deoxycytidine

This synthesis was based on a published report.[2] To a stirred solution of 3',5'-diacetyl-2'-deoxycytidine (3.42 g, 11.0 mmol) in H_2O (17.0 mL) was added I_2 (1.65 g, 6.50 mmol), HIO_3 (0.48 g, 2.73 mmol), CCl_4 (17 mL) and AcOH (25 mL). The resultant mixture was heated to 40°C and stirred vigourously for 24 h. Solvent was removed *in vacuo* to yield an orange solid. Crude product was purified by FCC (EtOAc:Acetone 1:1 – 1:2) to yield 4.14 g (86%) of an off-white foam. Spectral data conformed to literature precedent.[2] ^{1}H NMR (DMSO-d_6) δ: 2.06 (s, 3H), 2.09 (s, 3H), 3.65 (m, 1H), 4.20 (m, 2H), 4.25 (m, 2H), 5.17 (m, 1H), 6.10 (t, 1H, ^3J = 4.0), 7.24 (br s, 1H,), 8.01 (s, 1H), 8.16 (br s, 1H,).

Synthesis of 5-trimethylsilylethynyl-3',5'-diacetyl-2'-deoxycytidine

This synthesis was based on published reports.[3] Solid 5-iodo-3',5'-diacetyl-2'-deoxycytidine (1.20 g, 2.75 mmol), and $Pd(Ph_3)_4$ were dissolved in dry deoxygenated THF (8mL) under N_2 to which were added solid CuI (0.23 g, 1.21 mmol), trimethylsilylethyne (1.07 mL, 8.25 mmol) and Et_3N (1.15 mL, 8.25mmol). The solution was stirred in the dark for 24 h at rt. After removal of solvent *in vacuo* the product was purified by FCC (EtOAc:Acetone 2:1 – 1:1) to yield 997 mg (89%) of an off-white solid. ^{1}H NMR ($CDCl_3$) δ: 0.15 (s, 9H), 2.00 (s, 3H), 2.04 (s, 3H), 2.32 (m, 2H), 4.22 (overlapping, m, 3H), 5.13 (m, 1H), 6.31 (t, 1H, ^3J = 7.0), 6.75 (br s, 1H), 7.86 (br s, 1H), 7.91 (s, 1H). ^{13}C NMR (DMSO-d_6) δ: -0.5, 8.4, 20.3, 45.6, 63.2, 73.6, 81.3, 85.3, 90.0, 96.1, 99.6, 144.6, 152.9, 163.5, 169.6, 169.7. HRMS (ESI): Calcd. for $C_{18}H_{25}N_3O_6Si$ 407.1513 Found 407.1520.

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[1] Piton, N.; Mu, Y.; Stock, G.; Prisner, T. F.; Schiemann, O.; Engels, J. W. *Nucleic Acids Res.* **2007**, *35*, 3128-3143

[2] Chang, P.; Welch, A. D. *J. Med. Chem.* **1963**, *4*, 428-430.

[3] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313.

Synthesis of 5-ethynyl-2'-deoxycytidine

To a stirred mixture of K_2CO_3 (0.65 g, 4.72 mmol) and MeOH (15 mL)[4] was added 5-trimethylethynyl-3',5'-diacetyl-2'-deoxycytidine (0.55 g, 1.34 mmol). The mixture was stirred at 0°C for 2 h then filtered through Celite. The Celite plug was washed with MeOH (3 × 3 mL) and the filtrate was concentrated and purified by flash column chromatography (MeOH:EtOAc 20:80 Rf=0.2) to yield 306 mg (91%) of an off-white foam. ^{1}H NMR (D_2O) δ: 2.21 (m, 1H), 2.38 (m, 1H), 3.46 (s, 1H), 3.69 (dd, 1H, ^2J = 3.6, ^3J = 12.4), 3.78 (dd, 1H, ^2J = 5.2, ^3J = 12.4), 3.97 (m, 1H), 4.33 (m, 1H), 6.13 (t, 1H, ^3J = 4.0), 8.14 (s, 1H). ^{13}C NMR (DMSO-d_6) δ: 40.4, 61.3, 70.5, 81.3, 82.9, 89.1, 94.7, 110.3, 142.4, 155.1, 158.9. HRMS (ESI): Calcd. for $C_{11}H_{13}N_3O_4$ 251.0906 Found 251.0911.

General Procedure for the Huisgen cycloaddition

To a 1:1 THF/H_2O stirred solution of $CuSO_4$ (0.1 eq) and sodium ascorbate (0.2 eq) was added 5-ethynyl 2'-deoxycytidine (1 eq) and an organic azide (1.1 eq) at 0 °C. After these additions the solution was brought to rt and stirred until total consumption of 5-ethynyldeoxycytine as determined by TLC analysis. After evaporation of solvent, the residue was dissolved in THF, adsorbed onto silica gel, and purified by FCC.

Synthesis of 2'-deoxy-5-(1-(phenyl)-1*H*-1,2,3-triazol-4-yl)cytidine

The title compound was synthesised by following the general procedure. Thus, to a stirred 1:1 THF/H_2O solution (5 mL) was added 5-ethynyl 2'-deoxycytidine (250 mg, 0.99 mmol), azidobenzene (129 mg, 1.09 mmol), $CuSO_4 \cdot 5\ H_2O$ (22.4 mg, 0.09 mmol) and sodium ascorbate (39 mg, 0.18 mmol) yielding 335 mg (74%) of a light yellow powder after FCC. This material was recrystallized from 1:1 MeOH/H_2O to yield tan coloured needles suitable for X-ray diffraction studies. ^{1}HNMR (DMSO-d_6) δ: 2.10 (m, 1H), 2.22 (m, 1H), 3.60 (m, 1H), 3.67 (m, 1H), 3.81 (m, 1H), 4.25 (m, 1H), 5.18 (dd, 1H, J = 4.78, 4.96), 5.24 (d, 1H, ^3J = 4.27), 6.18 (t, 1H, ^3J = 6.32), 7.52 (t, 1H, ^3J = 7.35), 7.63 (overlapping, dd, ^3J = 8.03, 7.35), 7.67 (overlapping, br s, 1H), 7.83 (br s, 1H,), 7.91(d, 2H, J = 8.03), 8.48 (s, 1H), 8.85 (s, 1H). ^{13}C NMR (DMSO-d_6) δ: 40.8, 48.7, 60.8, 69.7, 85.5, 87.4, 119.4, 120.5, 129.1, 129.9, 136.4, 140.4, 153.8, 162.6. HRMS (ESI): Calcd. for $C_{17}H_{18}N_6O_4$ [+Na^+] 393.1277 Found 393.1287.

Synthesis of 2'-deoxy-5-(1-(thiophen-3-yl)-1*H*-1,2,3-triazol-4-yl)cytidine

Solid $CuSO_4 \cdot 5\ H_2O$ (35 mg, 0.14 mmol) and sodium ascorbate (84 mg, 0.43 mmol) was added to 5-ethynyl-2'-deoxycytidine (214 mg, 0.85 mmol) dissolved in THF:H_2O (1:1, 5 mL). Liquid 3-

[4] Bobek, M.; Kavai, I.; Sharma, R. A.; Grill, S.; Dutschman, G.; Cheng, Y.-C. *J. Med. Chem.* **1987**, *30*, 2154-2157.

azidothiophene (165 mg, 1.70 mmol) was added to the mixture which was stirred for 24 h at 35°C after which time the solvent was removed. Purification by flash column chromatography (TLC MeOH:DCM 1:1 Rf=0.8) gave the product as an off-white solid. Yield: 140 mg (43%). ^{1}H NMR (DMSO-d_6) δ: 2.11 (m, 1H), 2.20 (m, 1H), 3.64 (d, 2H, ^{3}J = 16.0), 3.82 (m, 1H), 4.26 (m, 1H), 5.19 (m, 1H), 5.25 (m, 1H), 6.18 (s, 1H), 7.59 (br s, 1H), 7.64 (s, 1H), 7.81 (br s, 1H), 7.84 (s, 1H), 8.06 (s, 1H), 8.46 (s, 1H), 8.77 (s, 1H). ^{13}C NMR (DMSO-d_6) δ: 48.6, 60.8, 69.7, 85.4, 87.3, 96.2, 115.5, 119.8, 120.8, 119.8, 120.8, 128.6, 135.1, 140.3, 142.1, 153.8, 162.5. HRMS (ESI): Calcd. for $C_{17}H_{16}N_6O_4$ [+H^+] 377.1041 Found 377.1032.

2'-Deoxy-5-(1-(2,2'-bithiophen-3-yl)-1*H*-1,2,3-triazol-4-yl)cytidine

Solid $CuSO_4 \cdot 5\ H_2O$ (58.2 mg, 0.23 mmol), sodium ascorbate (142 mg, 0.72 mmol), 5-ethynyl-2'-deoxycytidine (360 mg, 1.43 mmol), and 4-azido-2,2'-bithiophene (594 mg, 2.87 mmol) were combined and stirred at r.t. for 48 h in a solution of THF:H_2O (1:1, 10 mL). The solvent was removed and the crude product was purified by flash column chromatography (TLC MeOH:DCM 1:1 R_f=0.8) to give the title compound as a light brown solid. Yield: 100 mg (15%). ^{1}H NMR (DMSO-d_6) δ: 2.09 (m, 1H), 2.22 (m, 1H), 3.60 (d, 1H, ^{3}J = 12.5), 3.68 (d, 1H, ^{3}J = 11.8), 3.83 (dt, 1H, ^{3}J = 3.6, 7.0), 4.26 (m, 1H), 5.18 (s, 1H), 5.26 (s, 1H), 6.18 (t, 1H, ^{3}J = 6.3), 7.15 (dd, 1H, ^{3}J = 3.4, 5.1), 7.47 (dd, 1H, ^{3}J = 3.6, ^{4}J = 1.0), 7.63 (dd, 1H, ^{3}J = 5.1, ^{4}J = 1.0), 7.84 (d, 1H, ^{4}J = 1.5), 8.00 (d, 1H, ^{4}J = 1.4), 8.45 (s, 1H), 8.83 (s, 1H). ^{13}C NMR (DMSO-d_6) δ: 40.8, 60.8, 69.7, 85.4, 87.4, 96.2, 114.0, 116.9, 119.8, 125.2, 126.7, 128.6, 135.0, 135.2, 138.2, 140.4, 142.1, 153.9, 162.4. HRMS (ESI): Calcd. for $C_{19}H_{18}N_6O_4S_2$ [+Na^+] 481.0732 Found 481.0729.

Synthesis of 2'-deoxy-5-(1-(9*H*-fluoren-9-on-2-yl)-1*H*-1,2,3-triazol-4-yl)cytidine

Solid $CuSO_4 \cdot 5H_2O$ (39.6 mg, 0.16 mmol), sodium ascorbate (63.4 mg, 0.32 mmol), 5-ethynyl-2'-deoxycytidine (400 mg, 1.59 mmol), and 2-azido-9H-fluorenone (387 mg, 1.75 mmol) (prepared from 2-aminofluorenone *via* a literature procedure[5]) were combined and stirred at r.t. for 48 h in a solution of THF:H_2O (1:1, 10 mL). ^{1}H NMR (600MHz, DMSO-d_6) δ: 2.11 (m, 1 H), 2.23 (m, 1 H), 3.63 (m, 1 H), 3.67 (m, 1 H), 3.84 (m, 1 H), 4.27 (m, 1 H), 5.14 (t, 1 H, ^{3}J = 5.0), 5.26 (d, 1 H, ^{3}J = 4.1), 6.21 (t, 1 H, ^{3}J = 6.4), 7.46 (t, 1 H, ^{3}J = 7.6), 7.54 (br s, 1 H), 7.70 (m, 2 H), 7.77 (br s, 1 H), 7.93 (d, , 1 H, ^{3}J = 7.0), 8.09 (d, 1 H, ^{3}J = 8.2), 8.13 (s, 1 H), 8.21 (d, 1 H, ^{3}J = 8.2), 8.45 (s, 1 H), 9.04 (s, 1 H). ^{13}C NMR (DMSO-d_6) δ: 41.1, 61.4, 70.4, 85.8, 87.8, 116.2, 117.7, 120.2, 122.2, 124.8, 125.7, 127.0, 130.4, 134.0, 135.2, 136.3, 137.5, 140.9, 144.2, 145.1, 162.9, 192.3. HRMS (ESI): Calcd. for $C_{24}H_{22}N_6O_4$ [+Na^+] 495.1393 Found 495.1392.

[5] Nimura, S.; Kikuchi, O.; Ohana, T.; Yabe, A.; Kondo, S.; Kaise, M. *J. Phys. Chem. A* **1997**, *101*, 2083-2088.

Synthesis of 3-azidothiophene

This synthesis was based on a published report[6] and was conducted under Ar atmosphere using dry solvents and flame-dried glassware. A solution of *n*-BuLi (1.60 M, 32.9 mL, 52.7 mmol) in Et_2O and hexanes (1:1, 60 mL) was added dropwise to a solution of 3-bromothiophene (5.00 mL, 52.7 mmol) in Et_2O and hexanes (1:1, 120 mL). The mixture was cooled to -78°C and stirred for 30 min. The mixture was allowed to warm to r.t. and a solution of tosylazide (10.4 g, 52.7 mmol) in Et_2O and hexanes (1:1, 50 mL) was added dropwise. The mixture was again cooled to -78°C and stirred for 5 h during which time a pink precipitate formed. The pink solid, which turned green when dried, was collected by filtration and added to a cooled (0°C) solution of $Na_4P_2O_7$ (23.5 g, 52.7 mmol) in H_2O (50 mL). Hexanes (10 mL) was added and the mixture was stirred for 18 h at 0°C during which it became dark brown and a black precipitate formed; this was removed by filtration. The filtrate was diluted with hexanes (30 mL) then washed with deionized H_2O (3 × 30 mL) and brine (3 × 30 mL). The organic layer was dried over $MgSO_4$, filtered, and then concentrated *in vacuo* to a dark brown liquid which was purified by flash column chromatography (hexanes R_f=0.6). Yield: 2.35 g (36%). ^{1}H NMR ($CDCl_3$) δ: 6.80 (dd, 1H, ^4J = 1.2, 2.8), 6.83 (dd, 1H, ^3J = 4.8, ^4J = 1.2), 7.31 (dd, 1H, ^3J = 4.8, ^4J = 2.8). IR ν: 2115 (m, N_3). HRMS (ESI): Calcd. for $C_4H_3N_3S$ 125.0048 Found 125.0041.

Synthesis of 4-azido-2,2'-bithiophene

This synthesis was based on published reports[6] and was conducted under an Ar atmosphere using dry solvents and flame-dried glassware. A solution of *n*-BuLi (1.60 M, 11.9 mL, 19.1 mmol) in Et_2O (20 mL) was added dropwise to a solution of 4-bromo-2,2'-bithiophene (4.61 g, 19.1 mmol) in Et_2O (80 mL). The mixture was cooled to -78°C and stirred for 30 min. The yellow mixture was allowed to warm to r.t. and a solution of tosylazide (3.76 g, 19.1 mmol) in Et_2O (20 mL) was added dropwise. The mixture was again cooled to -78°C and stirred for 5 h during which time a yellow precipitate formed. The yellow solid was collected by filtration and added to a cooled (0°C) solution of $Na_4P_2O_7$ (8.52 g, 19.1 mmol) in H_2O (30 mL) and stirred for 24 h while being allowed to warm to r.t. The mixture became dark brown and a black precipitate formed; this was removed by filtration. The filtrate was diluted with hexanes (30 mL) then washed with deionized H_2O (3 × 30 mL) and brine (3 × 30 mL). The organic layer was dried over $MgSO_4$, filtered, and then concentrated to a dark brown liquid which was purified by flash column chromatography (hexanes R_f=0.3). Yield: 1.36 g (34%). ^{1}H NMR ($CDCl_3$) δ: 6.67 (d, 1H, ^4J = 1.2), 6.89 (d, 1H, ^4J = 2.0), 7.03 (dd, 1H, ^3J = 3.6, ^3J = 5.2), 7.18 (dd, 1H, ^3J = 3.6, ^4J = 1.2), 7.26 (dd, 1H, ^3J = 5.2, ^4J = 1.2). IR ν: 2109 (s, N_3). HRMS (ESI): Calcd. for $C_8H_5N_3S_2$ [+Na^+] 206.9925 Found 206.9929.

[6] (a) Spinelli, D.; Zanirato, P. *J. Chem. Soc. Perkin Trans 2* **1993**, 1129-1133. (b) Spagnolo, P.; Zanirato, P. *J. Org. Chem.* **1978**, *43*, 3539-3541.

Photophysical Data, Quantum Yields

Compound	Quantum Yield (solvent)		
	Φ (H_2O)	Φ (EtOH)	Φ (DMF)
1	0.0019	0.011	0.005
2	0.0025	0.013	0.004
3	0.0062	0.066	0.047
4	0.0055	0.089	0.060

Method

Photoluminescence quantum yields (Φ) were found by the relative method[7] using anthracene (Φf=0.32) and quinine sulphate in 0.1M H_2SO_4 (Φ=0.55) as a reference standard. The quantum yield of the unknown Φ(x) can be calculated by the following equation:

$$\Phi(x)= \Phi(ST)\ (A_{ST}/A_X)\ (F_X/F_{ST})\ (\eta^2_X/\eta^2_{ST})$$

Where Φ(ST) is the quantum yield of the standard, A is the absorbance at the excitation wavelength, F is the integrated area in the emission curve, the subscripts X and ST refer to unknown and standard and η is the refractive index of the solvent. When measuring a series of diluted solutions with various absorbance readings the following equation may be used:

$$\Phi(x)= \Phi(ST)\ (GradX/GradST)\ (\eta 2X/\eta 2ST)$$

Where Grad is the gradient from the plot of integrated area in the emission curve versus absorbance at the excitation wavelength. Prior to measuring the quantum yield of the unknown samples, the validity of the methodology was confirmed by measuring these characterized compounds: anthracene (Φf=0.29, in ethanol),[8] dichloroanthracene (Φf=0.58, in ethanol)[8] and deuterated anthracene (Φf=0.32, in cyclohexane),[9] and gave the following values 0.27, 0.58, 0.34 that are in very good agreement with the literature values.

[7] (a) Williams A. T. R.; Winfield S. A. *Analyst*, **1983**, 108, 1067-1071. (b) Lavabre, D.; Fery-Forgues, S. *J. Chem.Educ.*, **1999**, 76, 1260-1264. (c) Morris, J. V.; Mahaney, M. A.; Huber, J. R. *J. Phys. Chem.* **1976**, 80, 969-974.

[8] Guilbault, G. G. Practical Fluorescence, Second Edition, Marcel Dekker, Inc., New York, **1990**. p. 14-16.

[9] Berlman, I. B. Handbook of Fluorescence Spectra of Aromatic Molecules, Second Edition, Academic Press Inc., New York, **1971**, p. 357.

Selected data illustrating the dependence of fluorescence emission intensity on the nature of the medium.

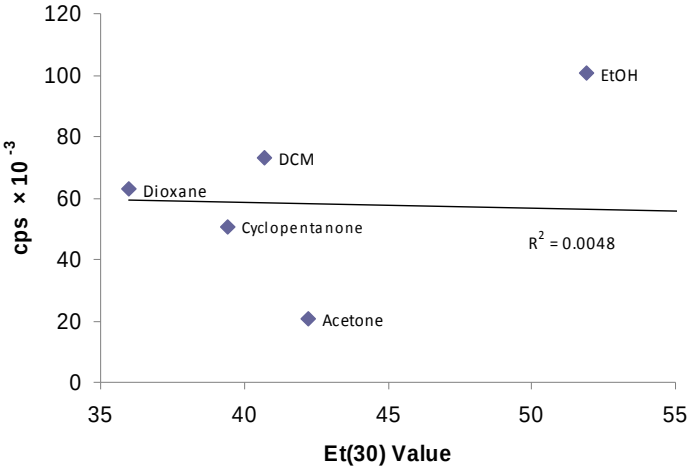


Figure S1. Representative data for compound **3**. The variation of fluorescence emission intensity versus Et(30) values for a variety of solvents. No correlation observed ($R^2 = 0.0048$)

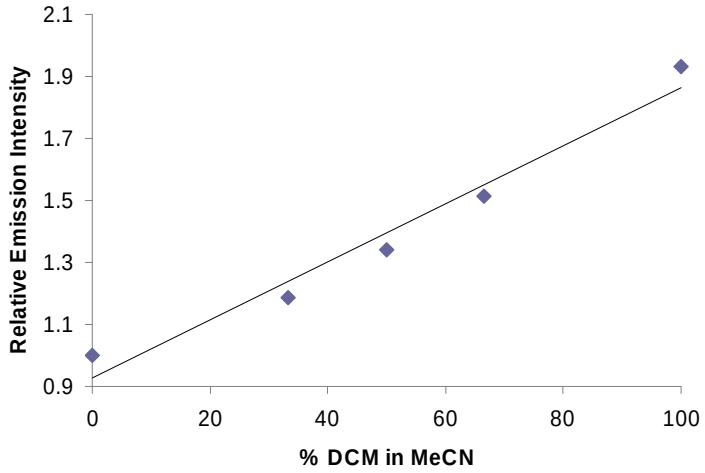


Figure S2. Representative data for compound **3**. The variation of fluorescence emission intensity upon changing percentage (v/v) of dichloromethane in acetonitrile.

Crystallographic Data for 2

Crystals of (5-(1-phenyl-1H-1,2,3-triazol-4-yl)-2'-deoxycytidine)•0.5MeOH•0.5H_2O were grown from a concentrated aqueous-methanol solution. A colourless needle was mounted on a glass fibre. Data were collected at low temperature (-80 °C)

A. Crystal Data

formula	$C_{17.50}H_{21}N_6O_5$
formula weight	395.40
crystal dimensions (mm)	0.48 × 0.09 × 0.06
crystal system	monoclinic
space group	$P2_1$ (No. 4)
unit cell parameters[a]	
α (Å)	11.3994 (14)
β (Å)	7.5273 (9)
χ (Å)	21.096 (3)
β (deg)	97.767 (2)
ς (Å^3)	1793.6 (4)
Z	4
ρcalcd (g cm^{-3})	1.464
μ (mm^{-1})	0.110

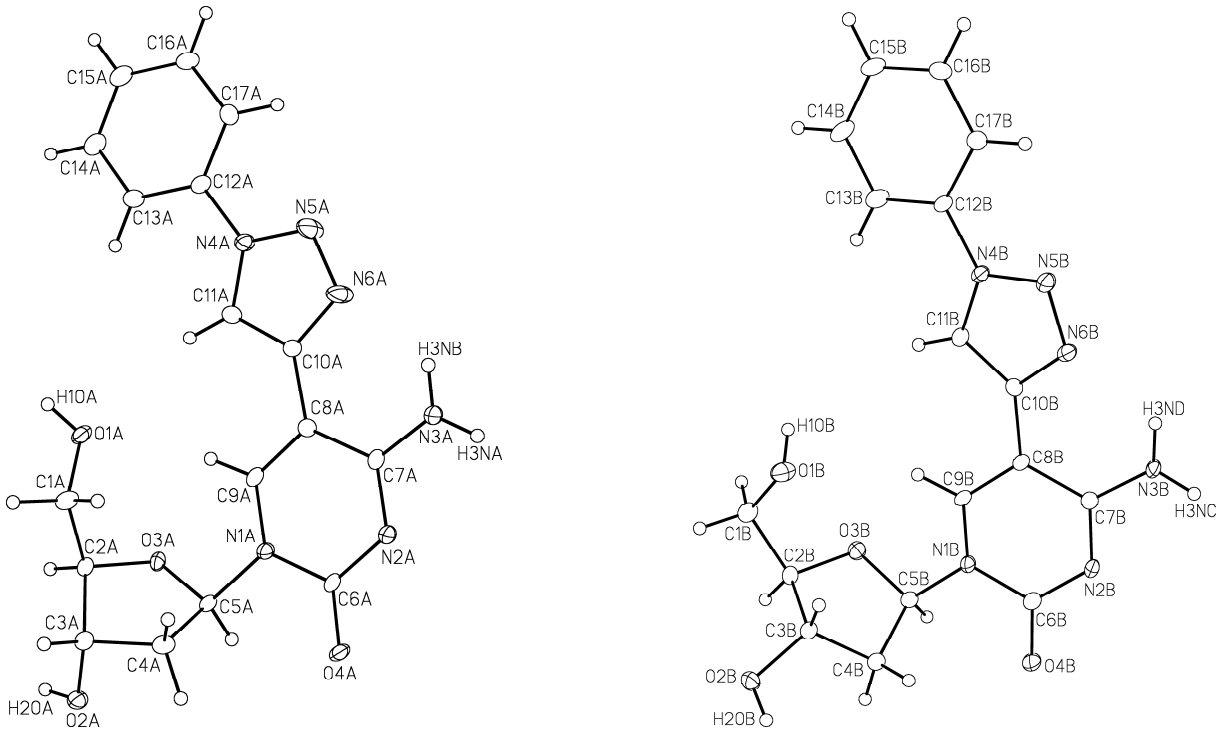


Figure S1. Perspective view of the two crystallographically independent 5-(1-phenyl-1*H*-1,2,3-triazol-4-yl)-2'-deoxycytidine molecules showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters. Right: *molecule A, molecule B* (only the major orientation of the disordered hydroxyl group (O1B) is shown).

B. Data Collection and Refinement Conditions

diffractometer	Bruker PLATFORM/SMART 1000 CCD[b]
radiation (λ [Å])	graphite-monochromated Mo Kα (0.71073)
temperature (°C)	–80
scan type	ω scans (0.3°) (20 s exposures)
data collection 2θ limit (deg)	54.30
total data collected	15357 ($-14 \le h \le 14$, $-9 \le k \le 9$, $-26 \le l \le 27$)
independent reflections	4291 (R_{int} = 0.0841)
number of observed reflections (*NO*)	2873 [$F_o^2 \ge 2\sigma(F_o^2)$]
structure solution method	direct methods (*SHELXS–97*[c])
refinement method	full-matrix least-squares on F^2 (*SHELXL–97*[c])
absorption correction method	multi-scan (*SADABS*)
range of transmission factors	0.9934–0.9490
data/restraints/parameters	4291 [$F_o^2 \ge -3\sigma(F_o^2)$] / 3[d] / 531
Flack absolute structure parameter[e]	0.2(15)
goodness-of-fit (*S*)[f]	1.034 [$F_o^2 \ge -3\sigma(F_o^2)$]
final *R* indices[g]	
R_1 [$F_o^2 \ge 2\sigma(F_o^2)$]	0.0521
wR_2 [$F_o^2 \ge -3\sigma(F_o^2)$]	0.1169
largest difference peak and hole	0.263 and –0.335 e Å^{-3}

a Obtained from least-squares refinement of 2380 reflections with $4.94° < 2\theta < 42.18°$.

b Programs for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

c Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.

d The O–H and H···H distances within the solvent water molecule were restrained to be 0.85(1) and 1.39(1) Å, respectively.

e Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881; Flack, H. D.; Bernardinelli, G. *Acta Crystallogr.* **1999**, *A55*, 908–915; Flack, H. D.; Bernardinelli, G. *J. Appl. Cryst.* **2000**, *33*, 1143–1148. The Flack parameter will refine to a value near zero if the structure is in the correct configuration and will refine to a value near one for the inverted configuration. The low anomalous scattering power of the atoms in this structure (none heavier than oxygen) implies that the data cannot be used for absolute structure assignment, thus the Flack parameter is provided for informational purposes only. Friedel pairs were merged prior to final refinement.

f $S = [\Sigma w(F_o^2 - F_c^2)^2/(n-p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.0506P)^2 + 0.2804P]^{-1}$ where $P = [\mathrm{Max}(F_o^2, 0) + 2F_c^2]/3$).

g $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^4)]^{1/2}$.

Computational Methods

Geometry optimizations on compounds **1**-**4** were performed with the B3LYP[10] 6-31+G* method and basis set using the Gaussian-03 program suite.[11] Frequency calculations were also executed at the same level of theory as the optimizations and the vibrational data confirmed that the structures were indeed minima on the potential energy surface.

Single point energy calculations were completed on the calculated structure of **1** and at un-optimized 10° increments about the dihedral angle involving nucleobase C4, C5 – triazole C4, N3.

[10] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, *GAUSSIAN 03 (Revision C.02)*, Gaussian, Inc., Wallingford CT, 2004.

[11] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.

Representations of calculated HOMOs and LUMOs of compounds 1, 3 and 4.

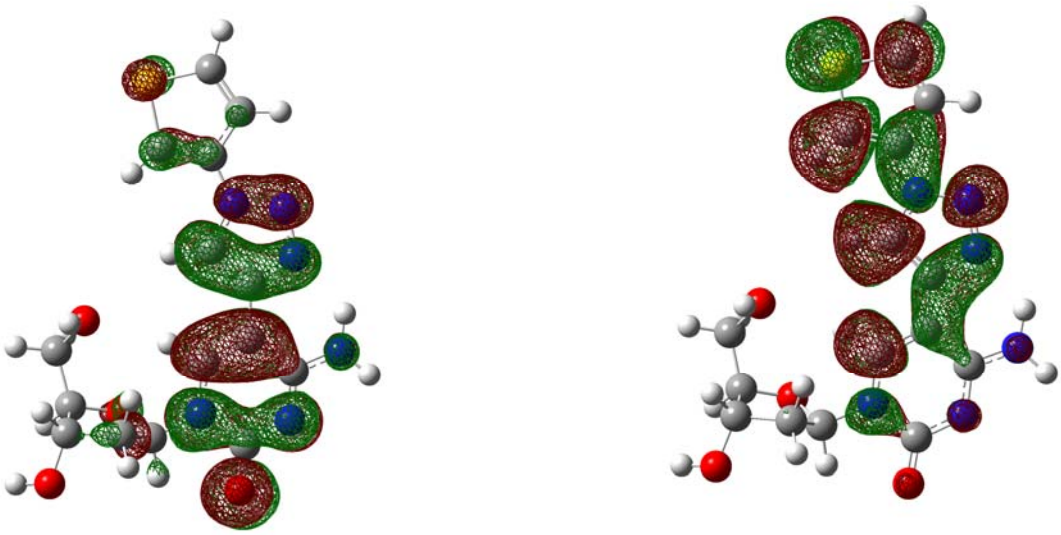


Figure S2. Representations of the calculated HOMO (left) and LUMO (right) of **1**.

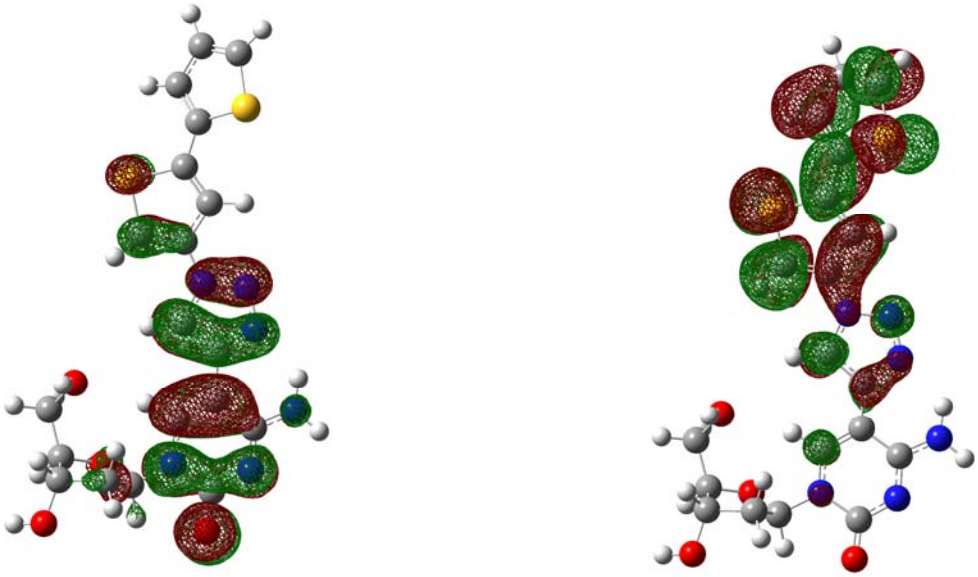


Figure S3. Representations of the calculated HOMO (left) and LUMO (right) of **3**.

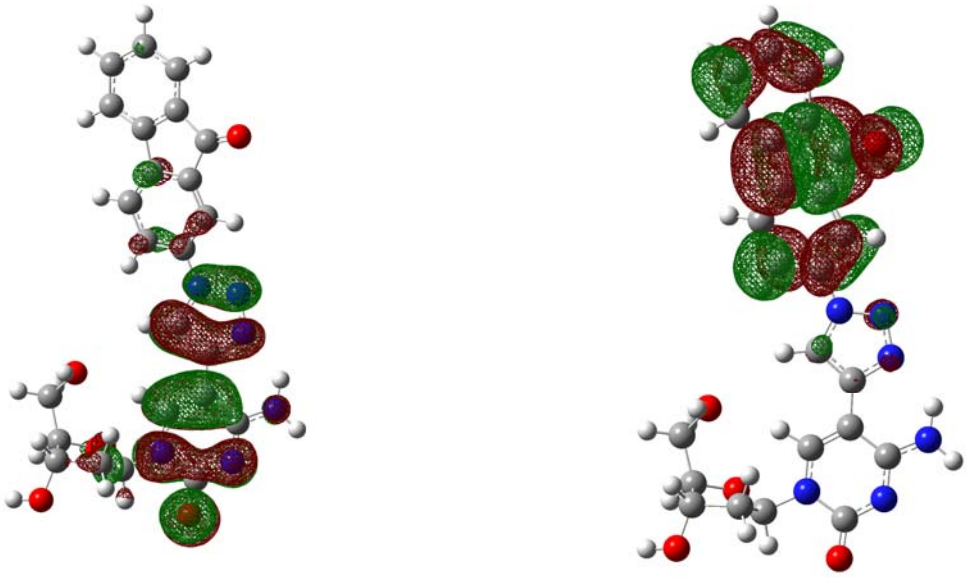
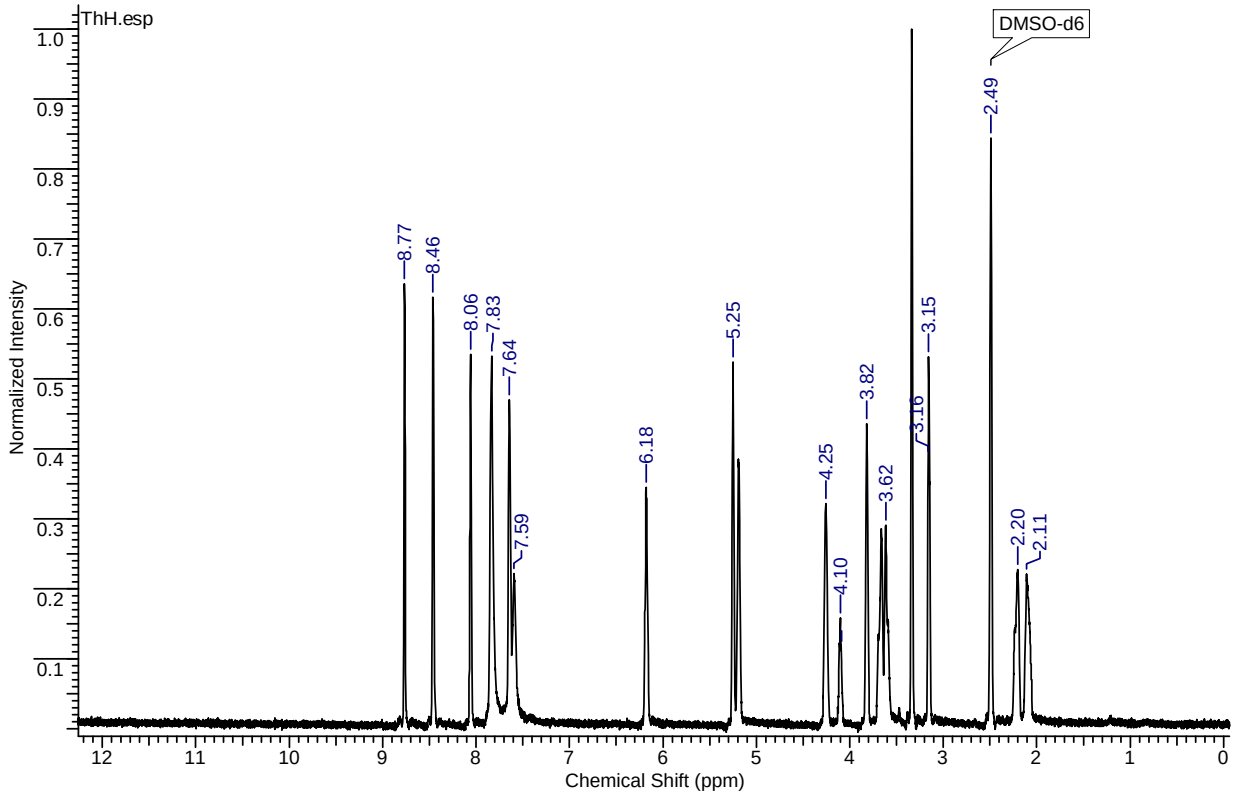


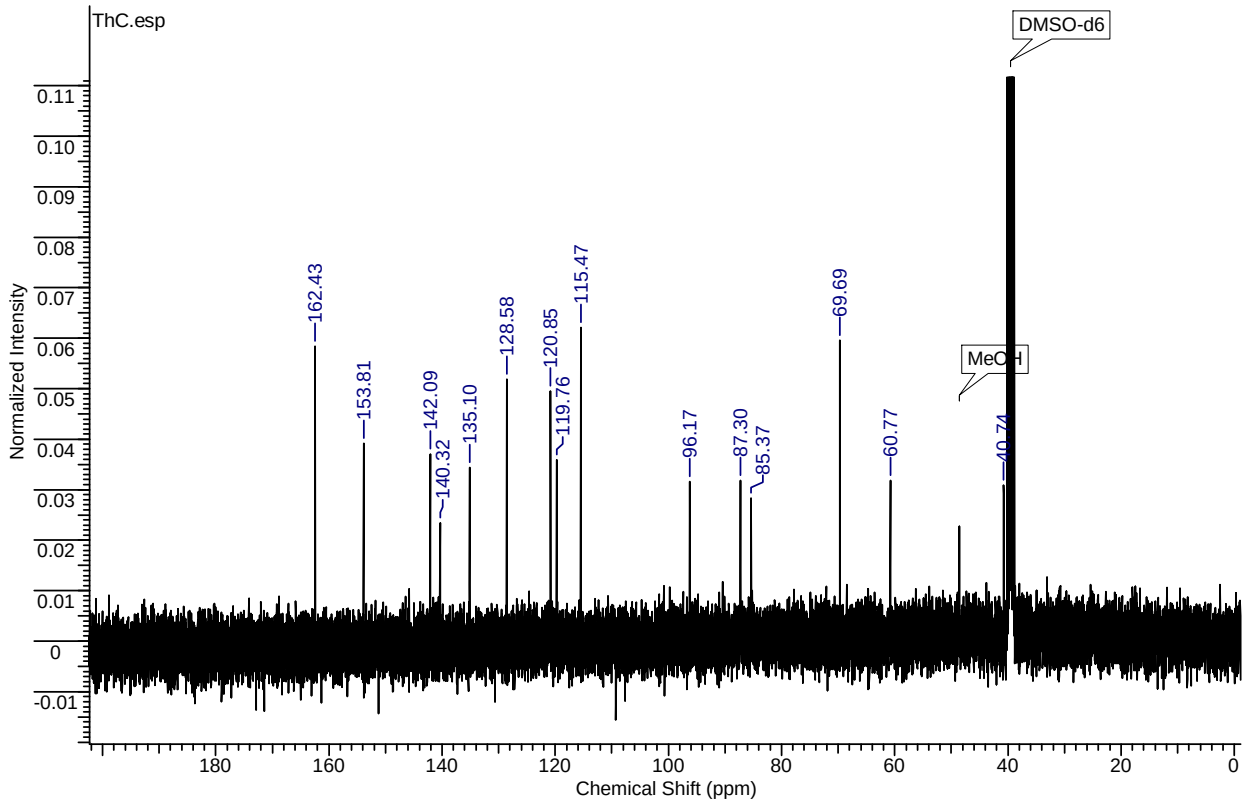
Figure S4. Representations of the calculated HOMO (left) and LUMO (right) of **4**.

2'-deoxy-5-(1-(thiophen-3-yl)-1*H*-1,2,3-triazol-4-yl)cytidine (1)

^{1}H

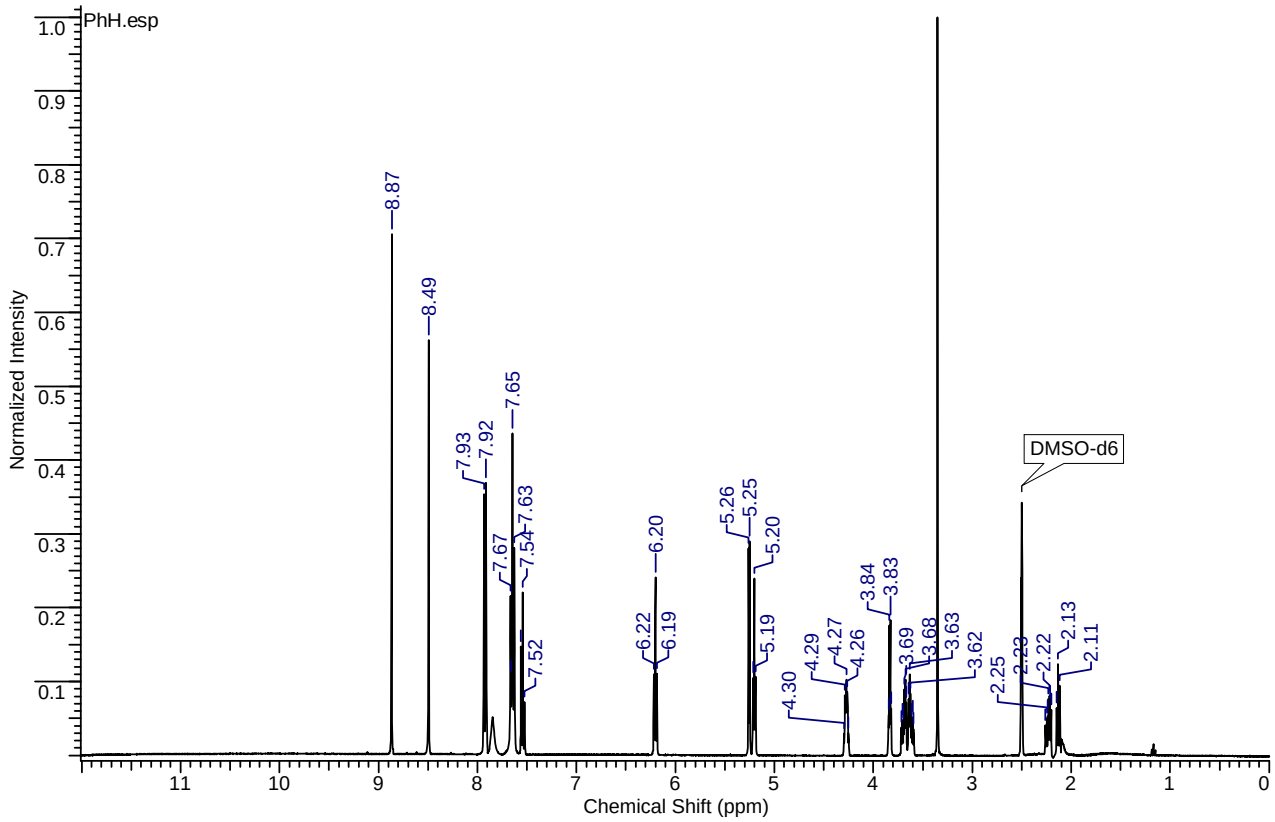


^{13}C

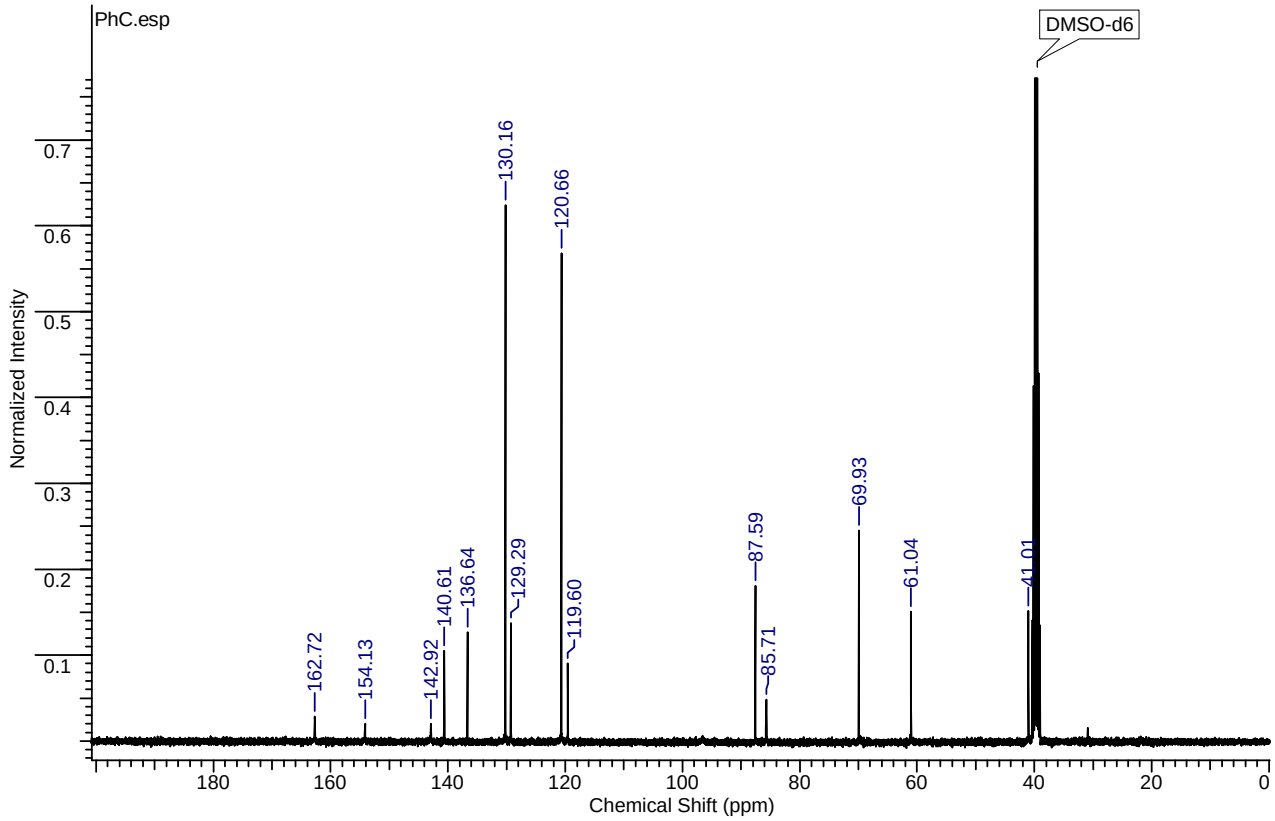


2'-deoxy-5-(1-(phenyl)-1*H*-1,2,3-triazol-4-yl)cytidine (2)

^{1}H

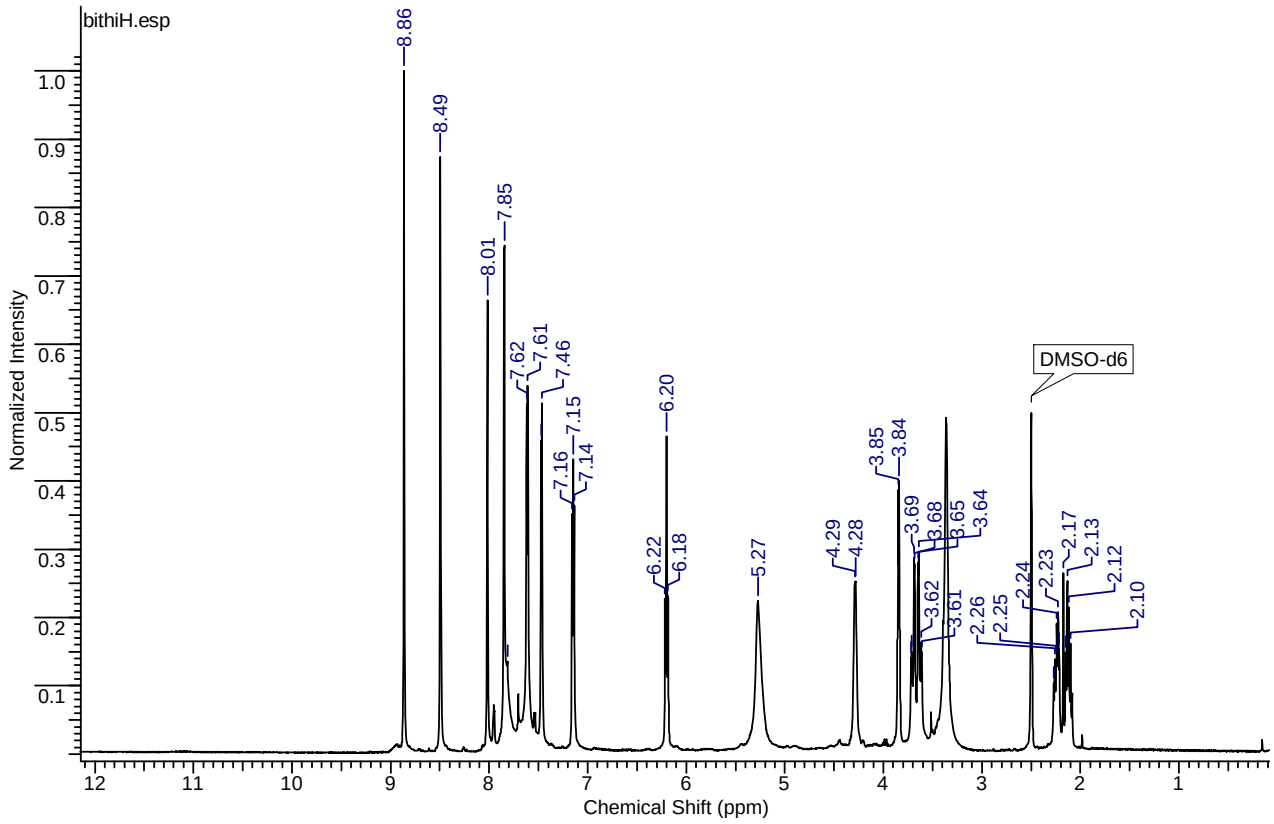


^{13}C

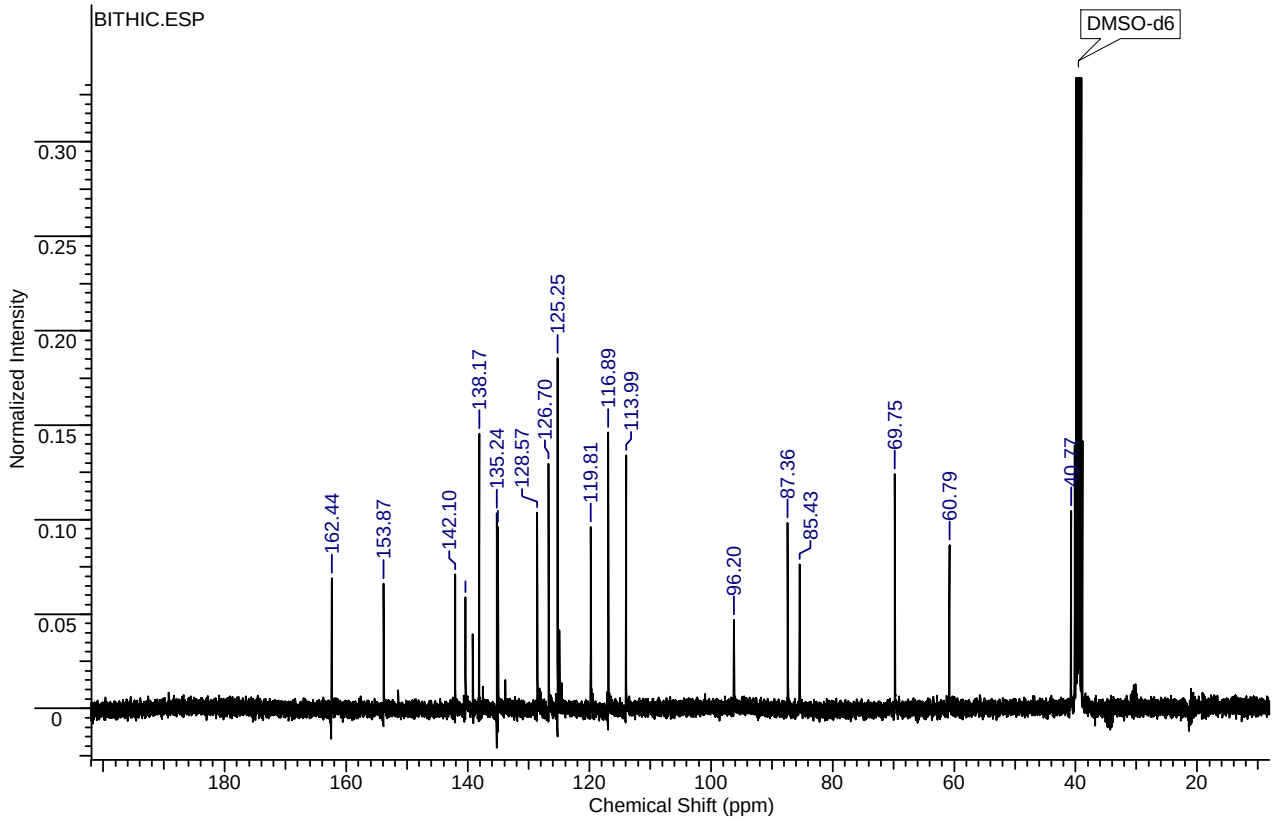


2'-Deoxy-5-(1-(2,2'-bithiophen-3-yl)-1*H*-1,2,3-triazol-4-yl)cytidine (3)

^{1}H

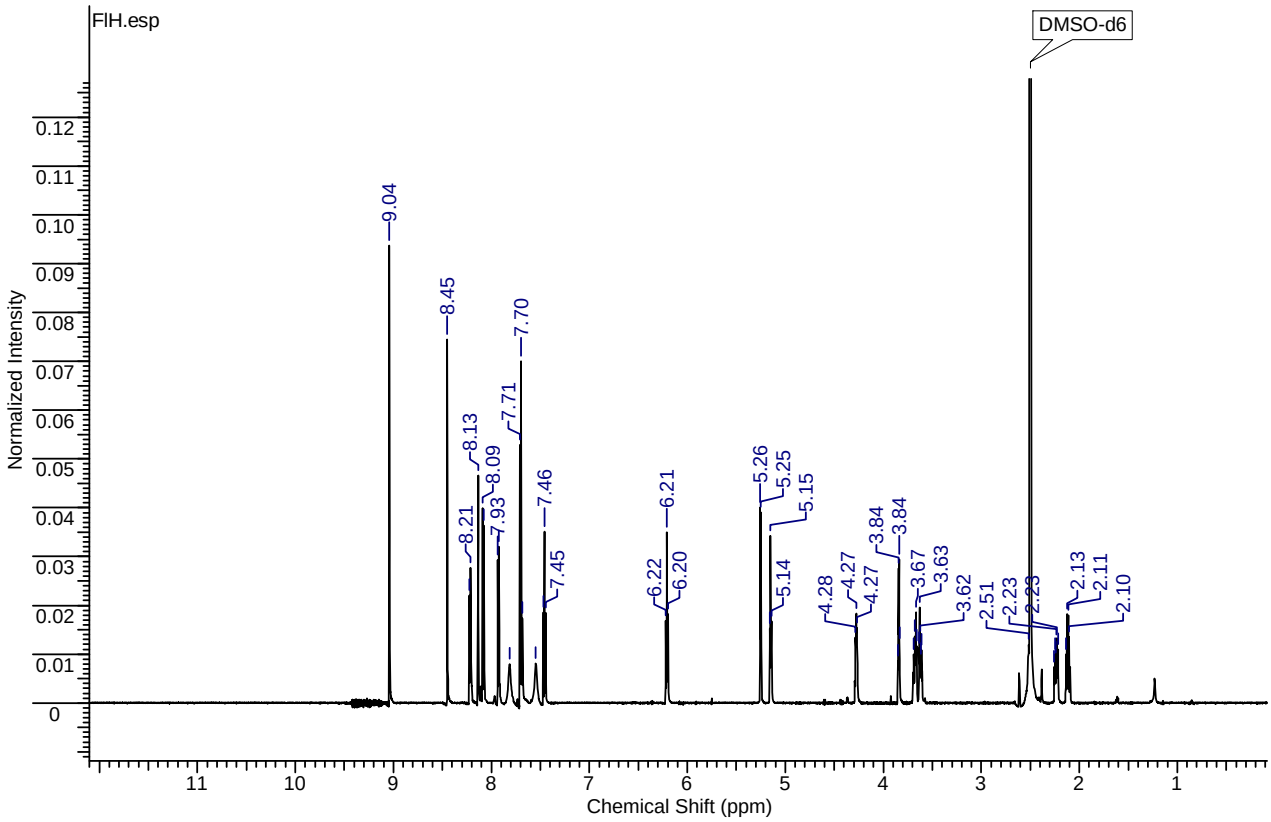


^{13}C



Synthesis of 2'-deoxy-5-(1-(9*H*-fluoren-9-on-2-yl)-1*H*-1,2,3-triazol-4-yl)cytidine (4)

^{1}H



^{13}C