Published in final edited form as:

Chemistry. 2009 August 3; 15(31): 7569–7577. doi:10.1002/chem.200900481.

Synthesis and ESR studies of 2'-deoxyuridines tethered with alkynyl, rod-like linkages[#]

Dr. Adam Sniady^[a], Prof. Michael D. Sevilla^[a], Dr. Srinivasarao Meneni^[a], Prof. Tadeusz Lis^[b], Assoc. Prof. Slawomir Szafert^[b], Ms. Deepthi Khanduri^[a], Assist. Prof. John M. Finke^[a], and Assoc. Prof. Roman Dembinski^{[a],*}

^[a]Department of Chemistry and Center for Biomedical Research, Oakland University, 2200 N. Squirrel Rd., Rochester, Michigan 48309-4477, USA ^[b]Department of Chemistry, University of Wroclaw, F. Joliot-Curie 14, 50-383 Wroclaw, Poland

Abstract

Sonogashira coupling of diacetyl 5-ethynyl-2'-deoxyuridine with diacetyl 5-iodo-2'-deoxyuridine gave the acylated ethynediyl-linked 2'-deoxyuridine dimer (**3b**) (63%) that was deprotected with ammonia/methanol to ethynediyl-linked 2'-deoxyuridines (**3a**) (79%). Reaction of 5-ethynyl-2'-deoxyuridine (**1a**) with 5-iodo-2'-deoxyuridine gave the furopyrimidine linked to 2'-deoxyuridine (78%). Catalytic oxidative coupling of **1a** (O₂, CuI, Pd/C, DMF) gave the butadiynediyl-linked 2'-deoxyuridines (**4**) (84%). Double Sonogashira coupling of 5-iodo-2'-deoxyuridine with 1,4-bis(ethynyl)benzene gave 1,4-phenylenediethyne-bridged 5-ethynyl-2'-deoxyuridines (**5**, 83%). Cu-catalyzed cycloisomerization of dimers **4** and **5** gave their furopyrimidine derivatives. One electron addition to **1a**, **3a** and **4** gave the anion radical whose ESR spectra showed the unpaired electron largely localized at C6 of one uracil ring (17 G doublet) at 77 K. For the ethynediyl- and butadiynyl-linked uridines **3a** and **4** the ESR spectra of their one electron oxidized species at 77 K showed that the unpaired electron is delocalized over both rings. Thus structures **3a** and **4** provide an efficient electronic link for hole conduction between the uracil rings. However, for the excess electron, an activation barrier prevents coupling to both rings. These dimeric structures could provide a gate that could separate hole transfer from electron transport between strands in DNA systems. In the crystal structure of acylated dimer **3b** the bases were found in the *anti* position to each other across the ethynyl link. Similar *anti* conformation was preserved in the derived furopyrimidine–deoxyuridine dinucleoside.

Keywords

Alkynes; Electron delocalization; ESR; Deoxyuridine; Furopyrimidine; Nucleosides; Synthesis

[#]Presented in part: R. Dembinski, M. S. Rao, 225th National Meeting of the American Chemical Society, New Orleans, LA, Mar 23–27, 2003; *Abstract of Papers*, Vol. 225, American Chemical Society: Washington, DC, 2003; 54-CARB (p U260).

*dembsinsk@oakland.edu.

Supporting Information. NMR spectra for compounds **3-8**; X-ray tables for compounds **1b**, **3b**, and **6b**, ORTEPs for **1b** and **3b**; fluorescence figures; computational figure for anion of analogue of **3** and Figure 6 in color. This material is available free of charge via the Internet at <http://onlinelibrary.wiley.com/doi/10.1002/chem.200900481/abstract>.

Introduction

Covalently linked nucleosides have been synthesized for a variety of applications. For example, DNA duplexes with interstrand cross-linkers,^{[i],[ii],[iii],[iv],[v],[vi]} hydrogen (Watson-Crick) base pair bonding models (Figure 1),^{[vii],[viii]} inhibitors of ribonucleotide reductase^[ix] or HIV reverse transcriptase,^[x] a model of the mechanism for the repair of DNA photolysis,^[xi] supramolecular self-assembly,^[xii] as well as protein binding^[8] have all been studied with their aid. Some of the interstrand cross-linked oligonucleotides exhibit interesting biological properties such as thrombin inhibition.^{[5],[xiii]}

Acetylenes and their higher conjugated homologues have been found to promote strong electronic communication between terminal subunits and to favor rigid, rod-like structures, which have found application in the design of molecular wires.^[xiv] The linear, *sp* carbon chain facilitates exact positioning of the alkynyl substituents for oligonucleotides arrays, and provides an opportunity for substituent-nucleobase communication. Interest in the utilization of the ethynyl (acetylenic) fragment for modification of nucleoside bases, in particular uridines, has resulted in a great number of contributions in recent years.^{[xv],[xvi]} By comparison, butadiynyl or 1,4-phenylenediethynediyl fragments have been used for nucleoside modifications to a much lesser extent.^{[xvii],[xviii]}

Internucleoside alkynyl modifications involving sugar groups are also known. For example, for backbone modification purposes, the phosphodiester bridge has been replaced by acetylenic links.^{[xix],[xx]} Homo- and heterodimers of uridine and adenosine linked at C-3' by a butadiynyl group have also been reported.^[xxi]

Purine-purine,^[xxii] purine-pyrimidine,^[xxiii] and pyrimidine-pyrimidine^[xxiv] base conjugates linked with ethynyl or butadiynyl fragments have also been synthesized.^[xxv] Initial screening has shown cytostatic activity of bis(purin-6-yl)ethyne and –butadiyne.^[22]

We have approached alkynyl-nucleoside chemistry of the μ -ethynediyl,^[xxvi] μ -butadiynediyl,^[xxvii] and μ -1,4-phenylenediethynediyl^[xxviii] linked uridines to study electronic communication or electron delocalization between the linked pyrimidines for hole and excess electron states that are of interest to DNA electronic chips.^{[xxix],[xxx]} Since the alkynyl conformationally well-defined rigid linker may also serve as an interstrand linkage,^[6] detailed investigation of dimers' properties has been warranted. In addition, the tethered nucleosides offer a starting point for further synthetic transformations, such as cyclization to furopyrimidine nucleosides. Such structures, containing a bicyclic base, are known for their highly potent and selective antiviral properties.^[xxxi] Furthermore, synthesis of halofuopyrimidines^[xxxii] or metallation to dicobalt hexacarbonyl complexes,^[xxxiii] with a resulting potential for biological activity, can be envisioned.

Results and Discussion

Synthesis

Preparation of the 2'-deoxyuridine dinucleosides, which contain rod-like tethers of different lengths anchored to position C5 of their pyrimidine base, have been approached in a systematic way. A series of compounds with conformationally well-defined units, namely

ethynediyl, butadiyndiyl, and 1,4-phenylenediethynediyl (lengths^[xxxiv] ca. 4.0,^[xxxv] 6.5, and 10.8 Å respectively), were synthesized. Two key substrates, 5-ethynyl-2'-deoxyuridine (**1a**), and 5-iodo-2'-deoxyuridine (**2a**), were used (Scheme 1). Both unprotected nucleosides **1a** and **2a** are commercially available, although it has been more economically feasible to synthesize **1a** from **2a**.^{[16],[xxxvi]}

The ethynediyl-linked 2'-deoxyuridines (**3a**) were prepared first by Sonogashira coupling at 37 °C,^[xxxvii] as we also observed that elevated temperature leads to a cyclization product.^{[36],[xxxviii]} Although the ethynediyl-linked dimer **3a** was obtained in 64% yield, due to its poor solubility synthesis of ribose-acetylated derivative **3b** was explored. A DMF solution of diacetyl 5-ethynyl-2'-deoxyuridine (**1b**, 2.5 equiv) was used in an excess when reacted with diacetyl 5-iodo-2'-deoxyuridine (**2b**, 1 equiv) in the presence of Pd(PPh₃)₄ (0.1 equiv), CuI (0.1 equiv), and Et₃N (37 °C). After workup tetraacetyl ethynyl-bridged dimer of 2'-deoxyuridine **3b** was isolated in 63% yield (Scheme 1). Deprotection with NH₃/MeOH gave **3a** in 79% yield.

A homocoupling reaction was subsequently investigated. The dimer of 5-ethynyl-2'-deoxyuridine was obtained by Eglinton-Glaser oxidative coupling.^[xxxix] The unprotected ethynyl deoxyuridine **1a** (1.0 equiv) and Cu(OAc)₂ (1.5 equiv) were combined in pyridine below 55°C, to avoid formation of the cyclized product(s). Column chromatography gave the μ -butadiynediyl 2'-deoxyuridine (**4**).^[27] However, the leaching of Cu^{II} salts during column chromatography was occasionally observed. Thus, an alternative catalytic procedure, utilizing less copper, was sought. Oxidative coupling of ethynyl nucleoside **1a** (1.0 equiv) in the presence of oxygen and catalytic amounts of Pd/C (0.01 equiv) and CuI (0.03 equiv, DMF, rt)^[x] gave, after workup, an identical dimer **4** in 84% yield, as shown in Scheme 1. In this case ribose acylation was not applied since purification was accomplished effectively.

Subsequently, the internucleoside linkage was elongated by a phenylene group. Unprotected iododeoxyuridine **2a** (2 equiv) was combined with 1,4-bis(ethynyl)benzene (1 equiv) under Sonogashira conditions at 40°C to yield dimer **5** in 83% yield.

The temperature of the reactions needs to be precisely controlled to find an optimum balance between the rate of coupling and of cyclization to furopyrimidines. Since furopyrimidines, as mentioned earlier, constitute an antiviral-active class of structures, we were stimulated to investigate the cyclization process of dimers that will lead to novel furopyrimidine-pyrimidine or furopyrimidine-furopyrimidine dinucleosides. When the above-mentioned reaction of **1a** and **2a** was carried out in a higher temperature (45 °C), dinucleoside **6a** with a bicyclic base component were isolated and characterized. To increase the potential crystallinity, dimer **6a** was acylated to yield **6b**. When dimers **4** and **5** were treated with CuI in the presence of Et₃N in DMF at an elevated temperature, furopyrimidine dimers **7** and **8** were obtained with 46% and 60% yields, respectively.

The ¹H and ¹³C NMR spectra confirmed the structural integrity of compounds **3–8**. The ¹H NMR spectra for **3–5** exhibited resonances at 11.68–11.76 and 8.01–8.48 ppm corresponding to the NH and H6 protons, respectively ([D₆]DMSO). The characteristic signals were

observed for fuoropyrimidines. In the spectrum of **6-8** peaks at 8.58–8.91 and 7.13–7.41 ppm, consistent with a H4 and H5 resonances, respectively, were present.^[xli] The isomer **6a** exhibited both NH, H6 (11.81, 8.41 ppm) and H4, H5 proton signals, as expected for pyrimidine and fuoropyrimidine rings, respectively. Monitoring of these ¹H NMR signals is convenient for observation of reaction progress. The C≡C ¹³C signals for **3-5** showed chemical shifts characteristic for alkynyl uridines.^[xlii] Assignment of carbons, where possible, was established for **4** by a gated decoupling experiment based upon C-H coupling constants *J*(C,H). Strong parent ions and adequate fragmentation were commonly observed in the MS spectra. Elemental analyses usually indicated hydrates that were also observed by X-ray crystallography for **3b**.

Fluorescence of fuoropyrimidines has been noted in previous studies.^{[32a],[xliii],[xliv]} The properties of **3a** and **6a** were investigated as fluorescent nucleosides may find practical applications as nucleic acids probes.^{[44],[xlv],[xlv]} Due to the limited solubility of **3a/6a** in water, fluorescence measurements were carried out in water/DMSO 1:1. The excitation maxima were found at $\lambda_{\text{ex}} = 344/356$ nm and the emissions maxima were found at $\lambda_{\text{em}} = 425/441$ nm for **3a/6a** (Figure 2). Both fluorescence emission spectra were slightly red-shifted relative to the alkynyl mononucleosides.^[xlvii] Measurements of the fluorescence lifetime of **3a** indicated a very fast (<0.1 ns) decay, which could not be accurately determined with the available instrumentation. However, the fluorescence decay of **6a** (for $\lambda_{\text{ex}} = 295$ nm) produced experimentally accessible lifetime(s) in the ns regime. Based on the χ_r^2 parameters and inspection of the fit residuals, a two-exponential model gave the optimal fit with a 0.8 ns component (41% amplitude) and a 3.7 ns component.^[xlviii]

Crystallography

Molecular structures of **3b**, **6b** (and **1b**) were confirmed by X-ray analysis. Crystallization of acylated dinucleoside from dichloromethane/hexanes gave single crystals of a hydrate **3b•(H₂O)_{1.25}** suitable for X-ray analysis. Figure 3 illustrates the selected molecular structure of the expected ethynediyl dimer. Views of all ORTEPS for **3b** as well as an X-ray structure data for **1b** are available in the Supporting Information. Compound **3b** crystallized in space group *P1* with both uracil rings positioned almost in the same plane similarly for crystallographically independent molecules (*Z* = 4). The dihedral angle between the two calculated planes of six atoms of pyrimidine rings ranges from 1.8(5) to 15.2(5)°, with all conformations being *anti*. However, molecules of **3b** differ more significantly in ribose configuration. Similar *anti* conformation of heterocyclic bases was also observed for **6b** (*P2₁*; Figure 3). The angles/distances for **1b**, **6b**, and all four crystallographically independent molecules of **3b** were provided in the Supporting Information.

ESR Experiments

Electronic coupling between DNA components is becoming of increasing interest for DNA electronic technologies such as DNA chips,^[xlix] and electronic DNA sequence recognition.^[i] In this work we have produced one electron reduced radical species of **1a**, **3a**, and **4** and one electron oxidized radical species of **3a** and **4**.^[ii] The radicals were produced in aqueous glassy solutions at low temperature after gamma irradiation. A critical measure of the electronic coupling between the two uracil rings in the anion radicals of **3a**, and **4** is

the ESR hyperfine structure. The ESR spectrum of the anion radical of **1a** at 77 K in 7 M LiBr (D₂O) is shown in Figure 4, where we find a 17 G doublet. This results from a single proton hyperfine coupling from the hydrogen at C6 of the uracil ring. This spectrum shows identical coupling to that found for the uridine anion radical and other substituted uracil anion radicals (such as thymidine anion radical).^{[lii],[liii],[liv]} Thus in structure **1a** at 77 K no significant delocalization into the side chain at C5 occurs. The 17 G hyperfine coupling clearly indicates the spin density distribution is largely localized to the C6 position (ca. 70%).^[lv] The ESR spectra of the anion radical for both of the dimeric structures **3a** and **4** are nearly identical to that of mononucleoside **1a** (Figure 4). No significant delocalization to the second ring on an ESR time scale is found for **3a** or **4**. The electron transfer rate between rings is therefore slow at 77 K as compared to the ESR time scale.^[lvi] However, at elevated temperature the small activation barrier to exchange in the anion radicals of **3a** and **4** would be overcome and these dimers would also be expected to show fast electron exchange between rings.^[56]

The spectra of one electron oxidized dimeric structures **3a** and **4** are shown in Figure 5.^[lvii] Both show unresolved singlets spectra, which are consistent with delocalization over both rings of the structures at 77 K. If the radical were localized to one of the structures, a resolved nitrogen hyperfine coupling from N1 and a proton hyperfine coupling from the beta proton at C1' would be observed.^[lviii] Thus the sharp singlets are strong evidence for delocalization between rings. A second ESR signal seen at low intensity in the spectrum is observed for **4** that can be attributed to a side reaction during the production of oxidized form.

The exchange between the two rings in these dimeric structures is influenced by several factors. First, in the anion radical of uracil and its analogues its major spin distribution occurs at C6 with little at C5, thus the coupling between the rings is weak (Figure 6).^[55] This is not so for the cation radical, which has a maximum in its spin density at the C5 position (Figure 6)^[58] and thus p-type conduction is expected to be favored over n-type conduction through this coupling site. Other factors that influence the transfer between rings is nuclear reorganization,^[lix] counter ion placement, and possible reversible protonation of the anion radical at a carbonyl group.^{[lx],[lxi]} These events create an activation energy toward electron exchange between the rings.

These results were in line with the theoretical calculations. Using density functional theory (DFT) the structure of an analogue of **3a** (ribose moieties were replaced by methyl groups), in its anionic, cationic, and O4-protonated (anion protonated at O4) radical states, was fully optimized in *anti* conformation as observed in an X-ray structure of **3b**. Figure 6 illustrates the B3LYP/6-31G* calculated spin densities for an analogue of **3a**. In cationic state (top/left) the spin densities are delocalized on both of the uracil ring. The calculated spin density is spread over both rings in the anion radical as well. However, the corresponding anion protonated at O4 (bottom/right), that corresponds to experimentally investigated anion (*pK_a* ca. 7),^[60] shows localization of the spin densities within a single uracil ring (for color figures see Supporting Information; nodal negative spin densities are visualized in green).

In conclusion, the synthesis and characterization of alkynyl modified nucleoside dimers with conformationally rigid linkages that may serve as interstrand cross-linkers, as well as their furopyrimidine derivatives, have been presented. In the crystal structure of acylated ethynediyl-linked 2'-deoxyuridine dimer and its furopyrimidine analogue the bases have been found in the *anti* position to each other across the link. It was experimentally established by ESR spectroscopy that the unpaired electron was mainly localized at C6 of the one uracil ring in one electron reduced **3a** and **4**, but for the one electron oxidized species delocalization to both rings has been found. These results show that these dimeric structures may provide a gate that could separate hole transfer from electron transport in DNA electronic systems.

Experimental

General

Commercial chemicals were treated as follows: DMF, distilled from CaH₂ and degassed (freeze and thaw) three times prior to use; Et₃N and pyridine distilled from P₂O₅. 5-Iodo-2'-deoxyuridine (Yamasa Corporation), *p*-diethynylbenzene (GFS Chemicals), Pd(PPh₃)₄ (Pressure Chemicals), copper(I) iodide 99.999%, and copper(II) acetate (Aldrich) were used as received. Chromatography media: silica gel 40-63 μm and TLC plates (Dynamic Adsorbents). Other materials not listed were used as received. Sonogashira coupling reactions were carried out under an N₂ atmosphere. IR and UV-visible spectra were recorded on a Varian 3100 Excalibur or Bio Rad FTS-175C and Cary 50 or 100 spectrometers. NMR spectra were obtained on a Bruker Avance III 400 and Avance 200 spectrometers. Mass spectra were recorded on a Bruker MicrOTOF-Q (ESI) instrument. Microanalyses were conducted by Atlantic Microlab. Fluorescence including time-resolved was observed on a Photon Technologies Quantum Master/Easy Life instrument.

5,5'-ethyne-1,2-diylbis(3',5'-di-*O*-acetyl-2'-deoxyuridine) (**3b**)

A Schlenk flask was charged with 3',5'-di-*O*-acetyl-5-iodo-2'-deoxyuridine **2b**^[38] (0.280 g, 0.639 mmol), Pd(PPh₃)₄ (0.074 g, 0.064 mmol), CuI (0.012 g, 0.064 mmol), DMF (6 mL), Et₃N (0.18 mL, 1.3 mmol), and 3',5'-di-*O*-acetyl-5-ethynyl-2'-deoxyuridine **1b**^[16] (0.537 g, 1.60 mmol). The yellow mixture was stirred at 37°C for 20 h (¹H NMR showed complete conversion of the substrate). The solvent was removed by oil pump vacuum. Silica gel column chromatography (25 × 2.5 cm; hexanes/EtOAc 100:0 → 0:100) gave a pale-yellow fraction. Solvent was removed by rotary evaporation and the residue was dried by oil pump vacuum. MeOH (ca. 10 mL) was added and the solid residue after column chromatography was extracted/sonicated (ultrasonic bath) for 0.5 h. The precipitate was filtered off and the product was dried by oil pump vacuum for 3 h to give **3b** as a white powder (0.260 g, 0.402 mmol, 63%).

¹H NMR (200 MHz, CDCl₃, 22°C, TMS): δ = 11.76 (s, 2 H; N3), 8.01 (s, 2 H; H6), 6.15 (t, ³J(H,H) = 6.5 Hz, 2 H; H1'), 5.26-5.11 (m, 2 H; H3'), 4.39-4.09 (m, 6 H; H4', H5'), 2.63-2.21 (m, 4 H; H2'), 2.07 (s, 6 H; 2COCH₃), 2.06 ppm (s, 6 H; 2COCH₃); ¹³C NMR (50 MHz, CDCl₃, 22°C, TMS): δ = 170.1 (s; COCH₃), 170.0 (s; COCH₃), 161.2 (d, ²J(C,H) = 9.2 Hz; C4), 149.3 (d, ²J(C,H) = 7.5 Hz; C2), 143.5 (d, ¹J(C,H) = 184.5 Hz; C6), 98.7

(d, $^2J(\text{C},\text{H}) = 4.2$ Hz; C5), 84.9 (d, $^1J(\text{C},\text{H}) = 178.4$ Hz; C1'),^[lxiii] 84.5 (d, $^3J(\text{C},\text{H}) = 5.1$ Hz; C≡C), 81.5 (d, $^1J(\text{C},\text{H}) = 153.2$ Hz; C4'),^[62] 73.7 (d, $^1J(\text{C},\text{H}) = 158.5$ Hz; C3'), 63.5 (t, $^1J(\text{C},\text{H}) = 148.9$ Hz; C5'), 36.3 (d, $^1J(\text{C},\text{H}) = 135.4$ Hz; C2'), 20.8 (q, $^1J(\text{C},\text{H}) = 129.7$ Hz; COCH₃), 20.6 ppm (q, $^1J(\text{C},\text{H}) = 129.7$ Hz; COCH₃); IR (KBr): ν bar = 3194 br, 3076 br, 1701 vs, 1459 s, 1367 m, 1297 s, 1236 vs, 1105 m, 1063 m cm⁻¹; UV/Vis (CH₃OH, 2.0×10^{-5} M): λ_{max} (ϵ) = 321 (19000), 252 sh (11000), 238 nm ($13000 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$); MS (ESI): m/z (%): 669 ((M + Na)⁺, 100%), 469 ((M – ribose + Na)⁺, 23%); elemental analysis calcd (%) for C₂₈H₃₀N₄O₁₄•0.5H₂O: C 51.30, H 4.77; found: C 51.17, H, 4.66.

5,5'-ethyne-1,2-diylbis(2'-deoxyuridine) (3a)

A round bottom flask was charged with **3b** (0.111 g, 0.170 mmol), MeOH (5 mL), and ammonia (7.0 M in MeOH; 0.80 mL, 5.6 mmol). The solution was stirred at rt for 20 h. ¹H NMR showed complete conversion of the substrate. Solvent was removed by oil pump vacuum and the residue was extracted (sonicated) with CHCl₃/MeOH (80:20, 15 mL) for 1 h. The precipitate was filtered off and washed with CHCl₃/MeOH (80:20, 3 × 5 mL). The solid was dried by oil pump vacuum for 3 h to give **3a** (0.054 g, 0.11 mmol, 66%). The solvent was removed from the filtrate by rotary evaporation and the residue was suspended extracted (sonicated) with CHCl₃/MeOH (80:20, 5 mL) for 0.5 h. Filtration and drying by oil pump vacuum gave an additional amount of **3a** as a white solid (0.010 g, 0.021 mmol, 12%; total 0.064 g, 1.3 mmol, 79%).

¹H NMR (200 MHz, [D₆]DMSO, 22°C, TMS): δ = 11.68 (s, 2 H; N3), 8.24 (s, 2 H; H6), 6.12 (t, $^3J(\text{H},\text{H}) = 6.5$ Hz, 2 H; H1'), 5.25 (d, $^3J(\text{H},\text{H}) = 4.2$ Hz, 2 H; OH3'), 5.11 (t, $^3J(\text{H},\text{H}) = 4.8$ Hz, 2 H; OH5'), 4.23 (p, $^3J(\text{H},\text{H}) = 3.5$ Hz, 2 H; H3'), 3.89-3.72 (m, 2 H; H4'), 3.71-3.47 (m, 4 H; H5'), 2.13 ppm (t, $^3J(\text{H},\text{H}) = 6.0$ Hz, 4 H; H2'); ¹³C NMR (50 MHz, [D₆]DMSO, 22°C, TMS): δ = 161.5 (d, $^2J(\text{C},\text{H}) = 9.2$ Hz; C4), 149.4 (d, $^2J(\text{C},\text{H}) = 8.5$ Hz; C2), 144.0 (d, $^1J(\text{C},\text{H}) = 183.5$ Hz; C6), 98.3 (s; C5), 87.6 (d, $^1J(\text{C},\text{H}) = 146.3$ Hz; C4'),^[61] 84.8 (d, $^1J(\text{C},\text{H}) = 168.1$ Hz; C1'),^[61] 84.5 (d, $^3J(\text{C},\text{H}) = 5.4$ Hz; C≡C), 70.2 (d, $^1J(\text{C},\text{H}) = 150.6$ Hz; C3'), 61.0 (t, $^1J(\text{C},\text{H}) = 140.3$ Hz; C5'), 40.3 ppm (d, $^1J(\text{C},\text{H}) = 133.0$ Hz; C2'); IR (KBr): ν bar = 3404 br, 3066 br, 1701 vs, 1466 m, 1297 s, 1293 m, 1101 m cm⁻¹; UV/Vis (H₂O/DMSO 1:1, 1.0×10^{-5} M): λ_{max} (ϵ) = 238 nm ($13000 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$); MS (ESI): m/z (%): ((2M + Na)⁺, 55%), 737 (unassigned, 38%), 501 ((M + H + Na)⁺, 100%), 479 ((M + H)⁺, 48%), 385 ((M – ribose + Na)⁺, 33%); elemental analysis calcd (%) for C₂₀H₂₂N₄O₁₀•H₂O: C 48.39, H, 4.87; found: C 48.01, H, 4.58.

5,5'-buta-1,3-diyne-1,4-diylbis(2'-deoxyuridine) (4)^[6b]

A Schlenk flask was charged with **1a** (0.253 g, 1.00 mmol), Pd/C (10%; 0.011 g, 0.01 mmol), CuI (0.0057 g, 0.03 mmol), and DMF (1 mL). The flask was sealed with septum, the air inside the flask was replaced with oxygen by five vacuum-oxygen (balloon) cycles. The mixture was stirred for 12 h at rt. ¹H NMR showed complete conversion of the substrate. The reaction mixture was passed through a 1 cm silica gel pad, followed by an additional amount of DMF (10 mL). Solvent was removed by oil pump vacuum and the residue was extracted (sonicated) with CHCl₃/MeOH (60:40, 25 mL) for 2 h. The precipitate was filtered off, washed with CHCl₃/MeOH (60:40, 3 × 10 mL), and dried by oil pump vacuum for 3 h to give **4** as a white solid (0.210 g, 0.418 mmol, 84%).

¹H NMR and MS spectra matched those reported earlier;^[6b] ¹³C NMR (50 MHz, [D₆]DMSO, 22°C, TMS): δ = 161.6 (d, ²J(C,H) = 9.0 Hz; C4), 149.2 (d, ²J(C,H) = 8.1 Hz; C2), 146.1 (d, ¹J(C,H) = 184.3 Hz; C6), 96.7 (s; C5), 87.7 (d, ¹J(C,H) = 147.8 Hz; C4'),^[61] 85.2 (d, ¹J(C,H) = 170.2 Hz; C1'),^[61] 76.5 (s; C≡CC≡C), 75.4 (d, ³J(C,H) = 5.6 Hz; C≡CC≡C), 69.7 (d, ¹J(C,H) = 149.2 Hz; C3'), 60.7 (t, ¹J(C,H) = 141.2 Hz; C5'), 40.9 ppm (d, ¹J(C,H) = 134.8 Hz; C2'); IR (KBr): ν̄ = 3426 br, 3181 br, 3061 br, 1702 vs, 1459 m, 1281 m, 1087 m cm⁻¹; UV/Vis (CH₃OH, 2.6 × 10⁻⁵ M): λ_{max} (ε) = 359 (19000), 336 (28000), 316 (25000), 295 sh (20000), 274 (16000), 255 sh (23000), 240 nm (26000 mol⁻¹ dm³ cm⁻¹); elemental analysis calcd (%) for C₂₂H₂₂N₄O₁₀•H₂O: C 50.77, H, 4.65; found: C 50.98, H 4.34.

5,5'-(1,4-phenylenediethyne-2,1-diyl)bis(2'-deoxyuridine) (5)

A Schlenk flask was charged with 5-iodo-2'-deoxyuridine **2a** (1.70 g, 4.80 mmol), Pd(PPh₃)₄ (0.555 g, 0.480 mmol), CuI (0.092 g, 0.48 mmol), DMF (5 mL), Et₃N (1.4 mL, 9.6 mmol), and 1,4-bis(ethynyl)benzene (0.303 g, 2.40 mmol). The yellow mixture was stirred at 40°C for 18 h (¹H NMR showed complete conversion of the substrate). Solvent was removed by oil pump vacuum and the residue was extracted (sonicated) with CHCl₃/MeOH (50:50, 25 mL) for 20 h. The precipitate was filtered off and extracted in a Soxhlet apparatus (CHCl₃/MeOH (50:50, 150 mL) for 20 h. The solid was dried by oil pump vacuum for 3 h to give **5** as a pale-yellow solid (1.15 g, 1.99 mmol, 83%).

¹H NMR (200 MHz, [D₆]DMSO, 22°C, TMS): δ = 11.72 (br s, 2 H; NH), 8.43 (s, 2 H; H6), 7.48 (s, 4 H; C₆H₄), 6.13 (t, ³J(H,H) = 6.3 Hz, 2 H; H1'), 5.27 (d, ³J(H,H) = 4.3 Hz, 2 H; OH3'), 5.19 (t, ³J(H,H) = 4.7 Hz, 2 H; OH5'), 4.26 (p, ³J(H,H) = 3.9 Hz, 2 H; H3'), 3.88-3.77 (m, 2 H; H4'), 3.75-3.52 (m, 4 H; H5'), 2.17 ppm (t, ³J(H,H) = 5.3 Hz, 4 H; H2'); ¹³C{¹H} NMR (50 MHz, [D₆]DMSO, 22°C, TMS): δ = 161.4 (C4), 149.4 (C2), 144.3 (C6), 131.4 (*m,o*-C₆H₄), 122.4 (*i,p*-C₆H₄), 97.9 (C5), 91.4 (C≡CC₆H₄), 87.6 and 84.9 (C4' and C1'), 84.7 (C≡CC₆H₄), 69.9 (C3'), 60.8 ppm (C5');^[lxiii] IR (KBr): ν̄ = 3413 br, 3055 br, 2690 vs, 1461 s, 1301 s, 1274 s, 1091 s cm⁻¹; UV/Vis (DMSO, 1.9 × 10⁻⁵ M): λ_{max} (ε) = 343 (38000), 365 sh nm (28000 mol⁻¹ dm³ cm⁻¹); MS (ESI): m/z (%): 1179 ((2M + Na)⁺, 9%), 601 ((M + Na)⁺, 44%), 413 (unassigned, 100%); elemental analysis calcd (%) for C₂₈H₂₆N₄O₁₀•H₂O: C 56.37, H 4.73; found: C 56.63, H 4.73.

1-(2-deoxy-β-D-erythro-pentofuranosyl)-5-[3-(2-deoxy-β-D-erythro-pentofuranosyl)-2-oxo-2,3-dihydrofuro[2,3-*d*]pyrimidin-6-yl]uracil (6a)

A Schlenk flask was charged with 5-iodo-2'-deoxyuridine **2a** (1.00 g, 2.90 mmol), Pd(PPh₃)₄ (0.335 g, 0.290 mmol), CuI (0.055 g, 0.29 mmol), DMF (8 mL), Et₃N (0.84 mL, 5.8 mmol), and 5-ethynyl-2'-deoxyuridine (1.10 g, 4.35 mmol). The yellow mixture was stirred at 45°C for 55 h (¹H NMR showed complete conversion of the substrate). Solvent was removed by oil pump vacuum and the residue was extracted (sonicated) with MeOH (30 mL). The precipitate was filtered off, washed with MeOH (3 × 5 mL), and extracted (sonicated) in CHCl₃/MeOH (95:5, 30 mL). The precipitate was filtered off and washed with cold CHCl₃ (3 × 5 mL). The solid was dried by oil pump vacuum for 3 h to give **6a** (0.760 g, 1.59 mmol, 55%). The solvent was removed from filtrate by rotary evaporation and remaining product was suspended in CHCl₃/MeOH (95:5, 5 mL) and sonicated. Filtration

and drying by oil pump vacuum gave an additional amount of **6a** as a white solid (0.320 g, 0.670 mmol, 23%; total 1.08 g, 2.26 mmol, 78%).

^1H NMR (200 MHz, $[\text{D}_6]\text{DMSO}$, 22°C, TMS):^[lxiv] δ = 11.82 (s, 1 H; NH), 8.77 (s, 1 H), 8.41 (s, 1 H), 7.13 (s, 1 H; H5), 6.18 (q, $^3J(\text{H,H})$ = 6.3 Hz, 2 H; 2H1'), 5.30 (d, $^3J(\text{H,H})$ = 4.2 Hz, 2 H; 2OH3'), 5.12 (q, $^3J(\text{H,H})$ = 4.6 Hz, 2 H; 2OH5'), 4.35–4.18 (m, 2 H; 2H3'), 3.98–3.82 (m, 2 H; 2H4'), 3.76–3.58 (m, 4 H; 2H5'), 2.54–2.32 (m, 1 H), 2.22 (t, $^3J(\text{H,H})$ = 5.4 Hz, 2 H), 2.16–1.98 ppm (m, 1 H); ^{13}C NMR (50 MHz, $[\text{D}_6]\text{DMSO}$, 22°C, TMS): δ = 170.3 (t, $^2J(\text{C,H})$ = 9.2 Hz; C7A), 160.1 (d, $^2J(\text{C,H})$ = 9.2 Hz), 153.9 (d, $^2J(\text{C,H})$ = 5.6 Hz), 149.2 (d, $^2J(\text{C,H})$ = 8.1 Hz), 147.8 (m; C6), 137.6 (d, $^1J(\text{C,H})$ = 187.6) Hz, 137.2 (d, $^1J(\text{C,H})$ = 182.9 Hz), 106.8 (s; C4A), 103.5 (s; C5), 101.2 (d, $^1J(\text{C,H})$ = 187.2 Hz; C5A), 88.3/87.9 (d, $^1J(\text{C,H})$ = 148.6 Hz/d, $^1J(\text{C,H})$ = 147.3 Hz; C4' and C4'A),^[62] 87.7/85.3 (d, $^1J(\text{C,H})$ = 174.5 Hz/d, $^1J(\text{C,H})$ = 172.0 Hz; C1' and C1'A),^[62] 70.4/69.8 (d, $^1J(\text{C,H})$ = 148.6 Hz/d, $^1J(\text{C,H})$ = 148.5; C3' and C3'A), 61.1/60.9 ppm (t, $^2J(\text{C,H})$ = 140.2 Hz/t, $^2J(\text{C,H})$ = 141.6 Hz; C5' and C5'A);^[63] IR (KBr): ν bar = 3415 br, 1697 vs, 1093 m, 1057 m cm^{-1} ; UV/Vis (CH_3OH , 2.5×10^{-5} M): λ_{max} (ϵ) = 355 (22000), 316 sh (13000), 274 sh (13000), 260 (18000), 243 sh nm ($14000 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$); MS (ESI): m/z (%): 1457 ((3M + Na)⁺, 10%), 979 ((2M + Na)⁺, 48%), 479 ((M + H)⁺, 100%), 363 ((M – ribose + H)⁺, 32%); elemental analysis calcd (%) for $\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_{10} \cdot 0.5\text{H}_2\text{O}$: C 49.28, H 4.76; found: C 49.30, H 4.54.

1-(3,5-di-O-acetyl-2-deoxy- β -D-erythro-pentofuranosyl)-5-[3-(3,5-di-O-acetyl-2-deoxy- β -D-erythro-pentofuranosyl)-2-oxo-2,3-dihydrofuro[2,3-d]pyrimidin-6-yl]uracil (6b**)**

A flask was charged with **6a** (0.205 g, 0.429 mmol), pyridine (2 mL), and acetic anhydride (1.0 mL, 1.1 mmol). The mixture was stirred at rt for 16 h (time not optimized), then poured into HCl (1 N; ca. 20 mL) and extracted with chloroform (3×15 mL). The organic layer was washed with water (2×100 mL), brine (100 mL), and dried over anhydrous MgSO_4 . The solvent was removed by rotary evaporation. Ethyl acetate (10 mL) was added to the oily residue, and the solid was collected on a fritted funnel. The solid was dried by oil pump vacuum for 2 h to give **6b** (0.194 g, 0.300 mmol, 70%) as a white powder.

^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$, 22°C, TMS):^[64] δ = 11.96 (s, 1 H; NH), 8.58 (s, 1 H; H4), 8.11 (s, 1 H; H6A), 7.24 (s, 1 H; H5), 6.37–6.23 (m, 2 H; 2H1'), 5.33–5.12 (m, 2 H; 2H3'), 4.49–4.10 (m, 6 H; 2H4' and 2H5'), 2.73–2.25 (m, 4 H; 2H2'), 2.20 (s, 3 H; CH_3), 2.09 (s, 6 H; 2 CH_3), 2.01 ppm (s, 3 H; CH_3); ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$, 22°C, TMS): δ = 170.5, 170.3, 170.1, 170.02, 170.00, 159.9 (d, $^2J(\text{C,H})$ = 9.3 Hz; C4), 153.7 (d, $^2J(\text{C,H})$ = 6.1), 149.0 (dd, $^2J(\text{C,H})$ = 8.1, 2.0 Hz), 147.5 (dd, $^2J(\text{C,H})$ = 8.6, 4.9 Hz), 137.6 (dd, $^1J(\text{C,H})$ = 189.0 Hz, $^2J(\text{C,H})$ = 2.8 Hz), 136.2 (dd, $^1J(\text{C,H})$ = 182.3 Hz, $^2J(\text{C,H})$ = 3.0 Hz), 107.0 (dd, $^2J(\text{C,H})$ = 4.5, 2.9 Hz; C4A), 103.8 (s; C5), 101.6 (d, $^1J(\text{C,H})$ = 188.9 Hz; C5A), 88.1/85.6 (dm, $^1J(\text{C,H})$ = 173.1 Hz/dm, $^1J(\text{C,H})$ = 169.8 Hz; C1' and C1'A),^[62] 82.5/82.0 (d, $^1J(\text{C,H})$ = 152.4 Hz/d, $^1J(\text{C,H})$ = 152.9 Hz; C4' and C4'A),^[62] 74.2/74.1 (br d, $^1J(\text{C,H})$ = 158.6 Hz/br d, $^1J(\text{C,H})$ = 157.7 Hz; C3' and C3'A), 63.6 (t, $^1J(\text{C,H})$ = 149.2 Hz, C5' and C5'A), 37.9/37.0 (dd, $^1J(\text{C,H})$ = 137.7, 134.6 Hz/dd, $^1J(\text{C,H})$ = 137.1, 134.4 Hz; C2' and C2'A), 20.73 (q, $^1J(\text{C,H})$ = 129.7 Hz; 2 CH_3), 20.71 (q, $^1J(\text{C,H})$ = 129.8 Hz; CH_3), 20.5 ppm (q, $^1J(\text{C,H})$ = 129.6 Hz; CH_3); IR (KBr): ν bar = 3075 br, 1747 vs, 1716 vs, 1671 vs,

1233 vs cm^{-1} ; UV/Vis (CH_3OH , 1.9×10^{-5} M): λ_{max} (ϵ) = 355 (24000), 260 nm (18000 $\text{mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$); MS (ESI): m/z (%): 1315 ($(2\text{M} + \text{Na})^+$, 15%), 669 ($(\text{M} + \text{Na})^+$, 100%), 447 ($(\text{M} - \text{ribose} + \text{H})^+$, 54%); elemental analysis calcd (%) for $\text{C}_{28}\text{H}_{30}\text{N}_4\text{O}_{14}$: C 52.01, H 4.68; found: C 51.72, H 4.61.

3,3'-bis(2-deoxy- β -D-erythro-pentofuranosyl)-6,6'-bifuro[2,3-*d*]pyrimidine-2,2'(3*H*,3'*H*)-dione (7)

A flask was charged with **4** (0.196 g, 0.390 mmol), CuI (0.015 g, 0.075 mmol), DMF (7 mL), and Et_3N (3 mL). The brown mixture was stirred at 120°C for 60 h. ^1H NMR showed complete conversion of the substrate. The precipitate was filtered off and dried by oil pump vacuum for 3 h and extracted (sonicated) with $\text{CHCl}_3/\text{MeOH}$ (70:30, 20 mL) for 1 h. The solid was filtered off, washed with $\text{CHCl}_3/\text{MeOH}$ (70:30, 3×10 mL), and dried by oil pump vacuum for 3 h to give **7** as a grey-brown solid (0.090 g, 0.18 mmol, 46%).

^1H NMR (200 MHz, $[\text{D}_6]\text{DMSO}$, 22°C , TMS): δ = 8.91 (s, 2 H; H4), 7.20 (s, 2 H; H5), 6.16 (t, $^3J(\text{H,H})$ = 6.0 Hz, 2 H; C1'), 5.31 (d, $^3J(\text{H,H})$ = 4.3 Hz, 2 H; OH3'), 5.16 (t, $^3J(\text{H,H})$ = 5.1 Hz, 2 H; OH5'), 4.35-4.15 (m, 2 H; H3'), 4.03-3.87 (m, 2 H; H4'), 3.80-3.55 (m, 4 H; H5'), 2.55-2.35 (m, 2 H; H2'), 2.20-2.00 ppm (m, 2 H; H2'); ^{13}C NMR (50 MHz, $[\text{D}_6]\text{DMSO}$, 22°C , TMS): δ = 171.0 (apparent t, $^3J(\text{C,H})$ = 7.5 Hz; C7a), 153.6 (d, $^2J(\text{C,H})$ = 5.7 Hz; C2), 143.5 (d, $^2J(\text{C,H})$ = 9.6 Hz; C6), 139.6 (d, $^1J(\text{C,H})$ = 188.0 Hz; C4), 105.7 (s; C4a), 102.8 (d, $^1J(\text{C,H})$ = 186.5 Hz; C5), 88.4 (d, $^1J(\text{C,H})$ = 145.1 Hz; C4'),^[62] 88.0 (d, $^1J(\text{C,H})$ = 176.0 Hz; C1'),^[62] 69.6 (d, $^1J(\text{C,H})$ = 147.9 Hz; C3'), 60.7 ppm (t, $^1J(\text{C,H})$ = 139.2 Hz; C5');^[63] IR (KBr): ν bar = 3410 br, 1660 vs, 1572 m, 1175 w cm^{-1} ; UV/Vis (CH_3OH , 3.2×10^{-5} M): λ_{max} (ϵ) = 416 sh (18000), 387 sh (26000), 374 (27000), 291 nm (27000 $\text{mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$); MS (ESI): m/z (%): 503 ($(\text{M} + \text{H})^+$, 100%); HRMS ($\text{C}_{22}\text{H}_{22}\text{N}_4\text{O}_{10} + \text{Na}$ 525.1228) 525.1254.

6,6'-(1,4-phenylene)bis[3-(2-deoxy- β -D-erythro-pentofuranosyl)furo[2,3-*d*]pyrimidin-2(3*H*)-one] (8)

A flask was charged with **5** (0.500 g, 0.864 mmol), CuI (0.050 g, 0.255 mmol), DMF (10 mL), and Et_3N (3 mL). The brown mixture was stirred at 70°C for 15 h (^1H NMR showed complete conversion of the substrate). The precipitate during was filtered off and dried by oil pump vacuum for 3 h. The precipitate was extracted (sonicated) with $\text{CHCl}_3/\text{MeOH}$ (70:30, 20 mL) for 1 h. The solid was filtered off, washed with $\text{CHCl}_3/\text{MeOH}$ (70:30, 3×10 mL), and dried by oil pump vacuum for 3 h to give **8** as a dark yellow solid (0.300 g, 0.518 mmol, 60%). ^1H NMR (200 MHz, $[\text{D}_6]\text{DMSO}$, 22°C , TMS): δ = 8.91 (s, 2 H; H4), 7.95 (s, 4 H; C_6H_4), 7.41 (s, 2 H; H5), 6.18 (t, $^3J(\text{H,H})$ = 5.8 Hz, 2 H; H1'), 5.31 (d, $^3J(\text{H,H})$ = 4.1 Hz, 2 H; OH3'), 5.20 (t, $^3J(\text{H,H})$ = 5.0 Hz, 2 H; OH5'), 4.33-4.19 (m, 2 H; H3'), 4.00-3.88 (m, 2 H; H4'), 3.81-3.57 (m, 4 H; H5'), 2.50-2.35 (m, 2 H; H2'), 2.21-2.03 ppm (m, 2 H; H2'); $^{13}\text{C}\{^1\text{H}\}$ NMR (50 MHz, $[\text{D}_6]\text{DMSO}$, 22°C , TMS): δ = 170.8 (C7a), 153.3/152.6 (C6 and C2), 138.1 (*i*- C_6H_4), 128.6 (C4), 128.6 (4C, C_6H_4), 106.4 (C4a), 100.2 (C5), 88.0/87.4 (C4' and C1'), 69.5 (C3'), 60.6 ppm (C5');^[63] IR (KBr): ν bar = 3387 br, 1664 vs, 1571 vs, 1382 s, 1342 s, 1179 s, 1099 s, 1059 s, 1026 s, 1000 s, 832 m, 779 s, 695 w cm^{-1} ; UV/Vis (DMSO , 1.3×10^{-5} M): λ_{max} (ϵ) = 413 (52000), 390 (50000), 321 (13000), 258 nm (10000

mol⁻¹ dm³ cm⁻¹); MS (ESI): m/z (%): 601 ((M + Na)⁺, 100%); elemental analysis calcd (%) for C₂₈H₂₆N₄O₁₀•2H₂O: C 54.72, H 4.92; found: C 55.10, H 4.54.

Crystallography

X-ray quality crystals of **1b**, **3b**, and **6b** (all colorless plates) were grown by slow evaporation from the chloroform (**1b** and **6b**), and dichloromethane/hexanes (**3a**) solutions. Selected crystallographical tables are provided in Supporting Information. Crystallographic data for the structures of **1b**, **3b**, and **6b** were also deposited with Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-711025, CCDC-711026, and CCDC-715301, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

ESR

Samples for ESR investigation were prepared by dissolving approximately 1 mg of **1a**, **3a**, or **4** in 7 M LiBr (D₂O) or 7M LiCl (D₂O). These solutions were drawn into 4 mm suprasil quartz tubes and cooled to 77 K. On cooling these solutions form glasses and are essentially supercooled liquid states. These samples were γ -irradiated (500 Gy, ⁶⁰Co) at 77 K, which forms excess electrons and Br²⁻• (Cl²⁻•) from the irradiation of the 7 M LiBr (LiCl) solution. The solute which makes up only 0.1% of the sample mass is not directly irradiated to any observable extent. The electrons formed by the irradiation add to the solute and the Br²⁻• (Cl²⁻•) formed by the ionization of the matrix produces a very broad background ESR signal that does not interfere in the g = 2 region significantly.^[54]

The ESR spectra observed of the solute anions are a result of addition to the π electron system (LUMO) of the structures. One electron oxidation is performed by attack of Cl²⁻• on the solutes (**3a**, **4**) on annealing of the 7 M LiCl glasses to 155K where the glass softens and Cl²⁻• becomes mobile. For these oxidative studies 5mg/mL K₂S₂O₈ was added to scavenge the electrons. This results in the sulfate radical (SO⁴⁻•) which simply forms additional Cl²⁻•.^[xv] Thus the system has only one electron oxidative processes. All ESR spectra were recorded at 77 K after γ -irradiation and were taken with a Varian Century Series EPR spectrometer operating at X-band with a dual cavity and a 200-mW klystron, with Frémy's salt (g = 2.0056, A_N = 13.09 G) as a reference.

Computations

The geometries of dimer **3a** methyl analogue in their cationic, O4-protonated (and anionic, Supporting Information) radical states were fully optimized using DFT as implemented in Gaussian 03 suite of programs.^[lxvi] The B3LYP functional with 6-31G* basis set was used in the calculation. The B3LYP functional is a combination of Becke's three-parameter hybrid exchange functional^{[lxvii],[lxviii]} and the Lee-Yang-Parr correlation functional.^[lxix] The use of B3LYP functional, for the study of radicals, is well documented in the literature.^{[lxx],[lxxi]} GaussView molecular modeling software^[lxxii] was used to plot the spin density distributions in the molecules.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

We thank the National Institute of Health (NIH, CA111329, CA045424), Oakland University, and its Research Excellence Program in Biotechnology for support of this research. National Science Foundation instrumentation award (NSF, CHE-0821487) is also acknowledged. T.L. and S.S. thank the Polish State Committee for Scientific Research (Grant N204 140 31/3236) for support. A.S. is grateful for the Provost's Graduate Student Research Award. Dr. Agnieszka Mikus and Dr. Anil Kumar are acknowledged for assistance with fluorescence experiments and DFT calculations, respectively. We are also thankful to Dr. Hiroyuki Hayakawa (Yamasa Corporation, Biochemicals Division) for generous supply of idonucleosides.

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Figure 1.
An example of covalently linked uridines.^[7a]

Figure 2.

Comparison of excitation (---) and emission (—, λ_{ex} 320 nm) spectra for **3a** (top) and **6a** (bottom) ($\text{H}_2\text{O}/\text{DMSO}$ 1:1, 22°C).

Figure 3.

An ORTEP view of the representative molecule of **3b** (top), and **6b** (bottom) illustrating atom labeling scheme and thermal ellipsoids (50% probability level, asymmetric unit). Selected interatomic distances: **3b** C5–C7 1.411(12), C7–C7A 1.219(12), C5A–C7A 1.436(12), N1–C1' 1.472(10), N1A–C1'A 1.482(10); **6b** C4A–C5 1.447(2), C5–C6 1.363(2), C6–C5A 1.440(2), N3–C1' 1.497(2), N1A–C1'A 1.465(2). Key angles: **3b** C5–C7–C7A 177.1(11), C7–C7A–C5A 175.9(9); **6b** C4A–C5–C6 105.74(14), C5–C6–C5A 133.74(14).

Figure 4. First derivative X-band Electron Spin Resonance spectra of the one electron reduced radicals of **1a**, **3a**, and **4**, in a aqueous glassy matrix (7 M LiBr, D₂O) at 77 K. The three vertical dashed lines in the figure are field calibration (13.09 G separations) and g value (2.0056 central line) markers.

Figure 5. First derivative X-band Electron Spin Resonance spectra of the one electron oxidized radicals of **3a** and **4** (7 M LiCl, D₂O) at 77 K. The three vertical dashed lines in the figure are field calibration (13.09 G separations) and g value (2.0056 central line) markers.

Figure 6. Calculated spin densities for analogue of **3** (ribose rings replaced by methyl; B3LYP/6-31G*). Protonated anion at O4 (left) and cation radical (right).

Scheme 1.

Synthesis of ethynediyl-, butadiynediyl-, phenylenediethynediyl-bridged 2'-deoxyuridine dimers **3a**, **4**, **5**, and their furopyrimidine derivatives **6a**, **7**, and **8**.