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SYNTHESIS OF VARIOUS 5-(3-SUBSTITUTED PHENYL)-2'-DEOXYURIDINES*

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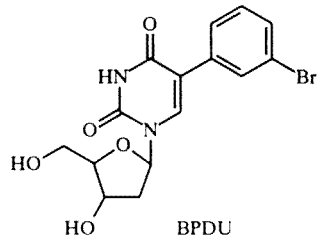
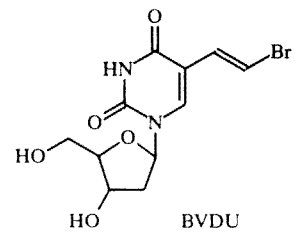
A series of 5-aryl-2'-deoxyuridines has been prepared and evaluated as antiviral agents. The following substituents have been used in position 3 of the phenyl ring: chloro, iodo, amino, azido, methylthio, and vinyl. None of the new compounds showed any significant activity when tested against human immunodeficiency virus 1 (HI V-1), herpes simplex virus 1 (HSV-1), or human cytomegalovirus (HCMV).

5-(3-Bromophenyl)-2'-deoxyuridine (BPDU) is structurally reminiscent of (*E*)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU). BVDU has potent activity against herpes simplex virus type 1 (HSV-1), for a review see [1]. We have previously reported that BPDU has some activity against HSV-1, and in contrast to BVDU also a weak activity against human cytomegalovirus (HCMV) [2].

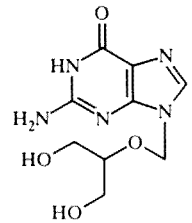


BPDU

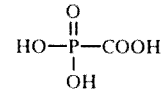


BVDU

5-(Heteroaryl)-substituted 2'-deoxyuridines have earlier been reported to possess potent anti-HSV-1 activities [3-6]. However, we have found that in contrast to BVDU, the anti-HSV-1 activity of this class of compounds is highly dependent on the cells and virus strains used in the assay and differ by a factor 500 or more [2]. HCMV infections often lead to severe diseases in immunocompromised individuals, such as acquired immunodeficiency syndrome (AIDS) patients and transplant recipients [7-11].



DHPG, GCV ganciclovir



PFA, foscarnet

*Dedicated to Professor Édmund Lukevits on the occasion of his 60th birthday.

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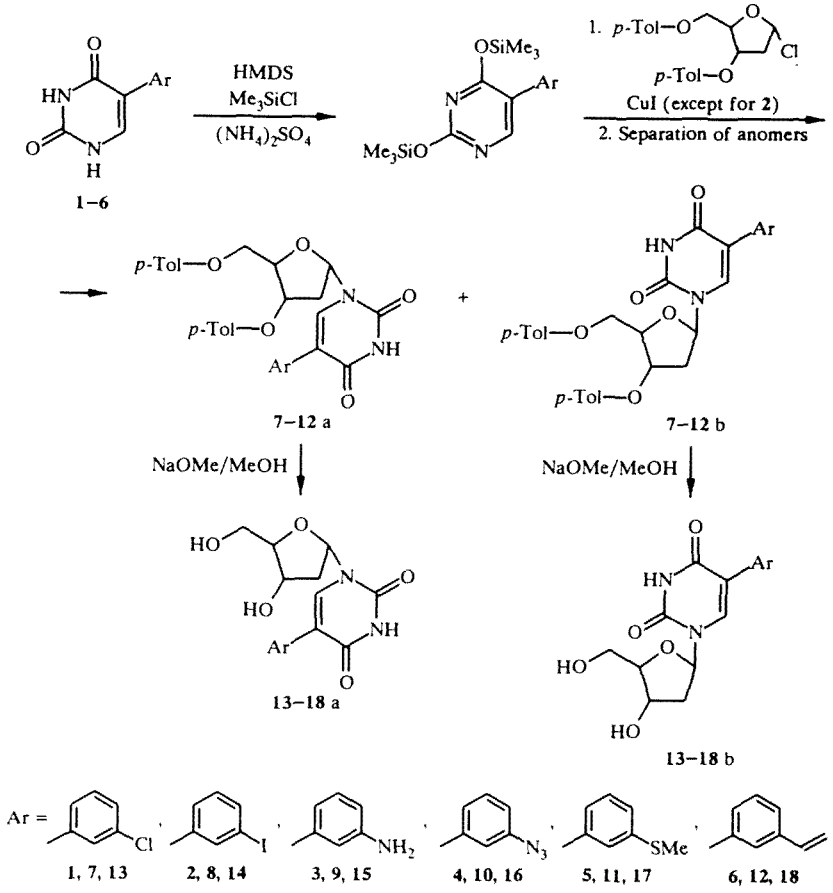
The two drugs currently of choice for the treatment of HCMV, 9-(1,3-dihydroxy-2-propoxymethyl)guanine (DHPG, GCV ganciclovir) and phosphonoformic acid (PFA, foscarnet) [12-15], both result in serious side effects as well as the emergence of drug-resistant virus [15, 16].

In view of this we have studied, and earlier reported, antiviral activities of structural variations on the lead compound BPDU. A second *meta*-substituent on the 5-phenyl function does not alter the activity against HSV-1 and HCMV [17]. Bromo substituted 5-furyl- and 5-thienyl-2′-deoxyuridines also have about the same anti-HCMV activities and slightly differing anti-HSV-1 activities [2]. The ribofuranosyl, arabinofuranosyl, and 2′-deoxy-2′-fluoroarabinofuranosyl analogues of BPDU were slightly more active against HCMV but inactive against HSV-1 [18]. In continuing this structure-activity investigation we decided to prepare some 5-(3-substituted phenyl)-2′-deoxyuridines with 3-substituents that would be able to closely mimic the bromo group. The considerations in choosing the appropriate 3-substituents as well as the preparation of the corresponding uracils has been reported elsewhere [19]. In the present work these uracils have been coupled with 2-deoxy-3,5-di-O-*p*-toluoyiribofuranosyl chloride. The α- and β-anomers were separated and the sugar moiety deprotected, giving the desired 5-(3-substituted phenyl)-2′-deoxyuridines.

5-(3-Chlorophenyl)-, 5-(3-iodophenyl)-, 5-(3-aminophenyl)-, 5-(3-azidophenyl)-, 5-(3-methylthiophenyl)-, and 5-(3-styryl)uracils **1-6** (Scheme 1) were prepared as previously described [18]. The coupling between 2,4-di-(trimethylsiloxy)pyrimidines and 2-deoxy-3,5-di-O-*p*-toluoyl-*D*-erythropentosyl chloride [20] usually results in a mixture of α- and β-anomers. By performing the reaction in anhydrous chloroform [21] with copper(I) iodide catalysis [22], the α/β-ratio can be lowered due to less anomerization of the chloro sugar and faster coupling. Since it has been shown that the unnatural α-anomers of certain nucleosides show biological activity [23-25], we were also interested in obtaining the α-anomers of the 5-(3-substituted phenyl)-2′-deoxyuridines presented in this paper.



Scheme 1. Preparation of 5-(3-substituted phenyl)-2′-deoxyuridines.

The β-optimized conditions gave satisfactory yields (55-92%) except for the coupling with 2,4-di-(trimethylsiloxy)-5-(3-iodophenyl)pyrimidine. This could be due to Ullmann homo-coupling, and when performing the reaction without copper (I) iodide catalysis, 90% of the desired product (**8**) was isolated. For the coupling with 2,4-di-(trimethylsiloxy)-5-(3′-aminophenyl)-

TABLE 1. Antiviral Activity

Compound	HCMV (μg/ml)		HSV-1 (μg/ml)
	ED_{50}[a]	CD_{50}	ED_{50}[b]
13a	120	*	†
13b	120	*	†
14a	75	200	†
14b	85	200	†
15b	*	*	†
16a	140	*	†
16b	160	*	†
17a	*	*	†
17b	*	*	†
18a	*	*	†
18b	*	*	†
BPDU	60(10[c])	150	50(7[d])

*> 200 μg/ml.

†0-5% inhibition at 100 μg/ml.

[a]ELISA assay; HEL cells.

[b]XTT assay; vero cells; C42 strain.

[c]CMV cytopathic assay (see text).

[d]HSV-1 plaque assay (see text).

pyrimidine no α-anomer could be detected, while for the other five products the α/β-ratio varied from 0.21 to 1.17. This allowed the isolation of sufficient amounts of both the α- and the β-anomers.

The anomers of compounds **7**, **8**, and **10-12** could easily be separated by column chromatography using dichloromethane/ethyl acetate as eluent. Compound **9** was purified using dichloromethane/ethyl acetate/triethylamine as eluent.

The protecting *p*-toluoyl groups on the sugar unit were easily removed with a dilute solution of sodium methoxide in methanol. After being washed through a short column of silica gel 60 with methanol in order to remove the excess of sodium methoxide, the 5-(3-substituted phenyl)-2′-deoxyuridines **13-18** (Scheme 1) were obtained pure after column chromatography using dichloromethane/methanol as eluent.

ANTIVIRAL ACTIVITY

Results and Discussion

The anomers of compounds **13-18** were tested for inhibition of HCMV and HSV-1 multiplication in cell culture using ELISA and XTT assay conditions, respectively. The results are listed in Table 1. As can be seen, both α- and β-anomers of the *meta*-iodo analogue (**14**) of BPDU were about equally active to BPDU in inhibition of HCMV, and both anomers of the *meta*-chloro (**13**) and *meta*-azido (**16**) analogues had diminished activities. All other analogues were inactive against HCMV, and compounds **13-18** did not inhibit HSV-1 under the assay conditions used.

Compounds **13-18** were also tested for inhibition of HIV-1 in an XTT assay and all were inactive at 100 μg/ml. The mode of action for some of the weak anti-HCMV compounds is not known. Usually nucleoside analogues are active as triphosphates. However, HCMV does not encode a virus-specific nucleoside kinase enzyme capable of monophosphorylation, in contrast to HSV and varicella zoster virus [26, 27]. A protein kinase encoded by the HCMV UL97 gene is, however, capable of phosphorylating the acyclic nucleoside analogue ganciclovir [28, 29]. If this is the case also for the weakly active anti-HCMV compounds discussed here or if some other mechanism at hand is not known.

Results on anti-HSV-1 activities for this class of compounds obtained by using different cell lines and virus strains, and referred to in the introduction above, will be reported [30].

EXPERIMENTAL

Melting points were recorded on a Lietz Wetzlar Microscope Heating Stage 350 Melting Point Apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a Varian XL-300 spectrometer. The mass spectra were recorded on a JEOL-SX 102 spectrometer. The ^{1}H NMR data for the four groups of compounds presented in this paper (α- and β-anomers of protected and unprotected 2′-deoxyuridines) are very similar within the groups. Complete ^{1}H NMR data are therefore only presented for one representative compound out of each class (**7a**, **7b**, **13a**, and **13b**). For compounds **14-18**, only data for the 5-substituent are presented. Elemental analyses were only performed on the β-anomers.

General Procedure for the Coupling Between 5-(3-Substituted Phenyl)-2,4-di-(trimethylsiloxy)pyrimidines and 2-Deoxy-3,5-di-O-*p*-toluoyl-*D*-erythropentosyl Chloride. A 250 ml flask equipped with a magnetic stirrer, a condenser and a nitrogen inlet was charged with 13.48 mmol of the 5-aryluracil (**1-6**), 70 ml of 1,1,1,3,3,3-hexamethyldisilazane, 1 ml of trimethylchlorosilane, and 0.5 g of ammonium sulfate. The reaction mixture was refluxed with stirring for 12 h. After cooling to room temperature, the excess of 1,1,1,3,3,3-hexamethyldisilazane was evaporated *in vacuo*. The residue was dissolved in 120 ml of anhydrous chloroform and added at 0°C to a solution of 4.76 g (12.26 mmol) of 2-deoxy-3,5-di-O-*p*-toluoyl-*D*-erythropentosyl chloride dissolved in 180 ml of anhydrous chloroform in a 500 ml flask equipped with a magnetic stirrer and a drying tube. Then 2.34 g (12.26 mmol) of copper (I) iodide was added, the ice bath was removed and the reaction mixture was allowed to stand with stirring at room temperature for 2 h. The chloroform was evaporated *in vacuo* and the residue was dissolved in 10 ml of chloroform. This solution was applied onto a column of silica gel 60 and the anomers were eluted with dichloromethane/ethyl acetate (**7**, **8**, **10-12**) or dichloromethane/ethyl acetate/triethyl amine (**9**).

5-(3-Iodophenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyluridine (8) was obtained as described above but without adding copper (I) iodide.

5-(3-Chlorophenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyluridine (7a and 7b). Column chromatography using dichloromethane/ethyl acetate 9:1 as eluent gave 1.27 g (18%) of 7a as a syrup and 4.72 g (67%) of 7b as a white solid.

7a: ^{1}H NMR (deuteriochloroform): δ 2.33 (3H, s, Ph—CH_3), 2.41 (3H, s, Ph—CH_3), 2.56 (1H, d, J = 15.5 Hz, H2′b), 2.99 (1H, dt, J = 6.6, 15.6 Hz, H2′a), 4.49 (1H, dd, J = 4.3, 11.9 Hz, H5′b), 4.56 (1H, dd, J = 4.2, 12.0 Hz, H5′a), 4.93 (1H, t, J = 4.0 Hz, H4′), 5.60 (1H, d, J = 5.9 Hz, H3′), 6.39 (1H, d, T = 5.8 Hz, H 1′), 6.98-7.95 (17H, m, aromatic), 9.36 (1H, s, N—H_3). HRMS: Found: 575.1577 (MH^+). Calculated for $C_{31}H_{28}ClN_2O_7$: 575.1585.

7b: mp 186-188°C; ^{1}H NMR (deuteriochloroform) : δ 2.26-2.43 (1H, m, H2′a), 2.34 (3H, s, Ph—CH_3), 2.43 (3H, s, Ph—CH_3), 2.81 (1H, ddd, J = 1.3, 5.4, 14.2 Hz, H2′b), 4.58 (1H, q, J = 2.7 Hz, H4′), 4.68 (1H, dd, J = 3.3, 12.3 Hz, H5′b), 4.77 (1H, dd, J = 2.8, 12.3 Hz, H5′a), 5.62 (1H, dt, J = 1.4, 6.5 Hz, H3′), 6.47 (1H, dd, J = 5.3, 8.8 Hz, H1′), 7.02-7.97 (17H, m, aromatic), 8.75 (1H, s, 3-NH). HRMS: Found: 575.1584 (MH^+). Calculated for $C_{31}H_{28}ClN_2O_7$: 575.1585. Found, %: C 64.66; H 4.73; N 4.93. $C_{31}H_{28}ClN_2O_7$. Calculated, %: C 64.76; H 4.73; N 4.8.

5-(3-Iodophenyl)-2′-deoxy-3′,5′-di-O-p-toluoyluridine (8a and 8b). Column chromatography using dichloromethane/ethyl acetate 9:1 as eluent gave 0.93 g (12%, with copper(I) iodide) or 2.21 g (27%, without copper(I) iodide) of **8a** and 1.19 g (14%, with copper (I) iodide) or 5.14 g (63%, without copper(I) iodide) of **8b**, both as white solids.

8a: mp 65-69°C. HRMS: Found: 667.0925 (MH^+). Calculated for $C_{31}H_{28}IN_2O_7$: 667.0941.

8b: mp 190-193°C. HRMS: Found: 667.0926 (MH^+). Calculated for $C_{31}H_{28}IN_2O_7$: 667.0941.

Found, %: C 55.66; H 4.09; N 4.24. $C_{31}H_{27}IN_2O_7$. Calculated, %: C 55.87; H 4.08; N 4.20.

5-(3-Aminophenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyluridine (9b). Column chromatography using dichloromethane/ethyl acetate/triethylamine 23:1:1 as eluent gave 3.75 g (55%) of **9b** as a white solid. Mp 81-86°C. HRMS: Found: 556.2078 (MH^+). Calculated for $C_{31}H_{30}N_3O_7$: 556.2084.

Found, %: C 65.69; H 6.13; N 7.97. $C_{31}H_{29}N_3O_7$. Calculated, %: C 67.02; H 5.26; N 7.56 (better EA could not be obtained).

5-(3-Azidophenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyluridine (10a and 10b). Column chromatography using dichloromethane/ethyl acetate 9:1 as eluent gave 2.14 g (30%) of **10a** as a syrup and 3.56 g (50%) of **10b** as a white solid.

10a: HRMS: Found: 582.1987 (MH^+). Calculated for $C_{31}H_{28}N_5O_7$: 582.1989.

10b: mp 162-164°C. HRMS: Found: 582.1987 (MH^+). Calculated for $C_{31}H_{28}N_5O_7$: 582.1989.

Found, %: C 63.85; H 4.75; N 12.10. $C_{31}H_{27}N_5O_7$. Calculated, %: C 64.02; H 4.68; N 12.04.

5-(3-Methylthiophenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyluridine (11a and 11b). Column chromatography using dichloromethane/ethyl acetate 9:1 as eluent gave 1.15 g (16%) of **11a** as a syrup and 5.47 g (76%) of **11b** as a white solid.

11a: HRMS: Found: 587.1851 (MH^+). Calculated for $C_{32}H_{31}N_5O_7S$: 587.1852.

11b: mp 89-94°C. HRMS: Found: 587.1860 (MH^+). Calculated for $C_{32}H_{31}N_5O_7S$: 587.1852.

Found, %: C 65.44; H 5.22; N 4.82. $C_{32}H_{30}N_5O_7S$. Calculated, %: C 65.52; H 5.15; N 4.78.

5-(3-Styryl)-2″-deoxy-3′,5′-di-0-*p*-toluoyluridine (12a and 12b). Column chromatography using dichloromethane/ethyl acetate 9:1 as eluent gave 2.36 g (34%) of **12a** as a syrup and 2.09 g (30%) of **12b** as a white solid.

12a: HRMS: Found: 567.2128 (MH^+). Calculated for $C_{33}H_{31}N_2O_7$: 567.2131.

12b: mp 163-165°C. HRMS: Found: 567.2131 (MH^+). Calculated for $C_{33}H_{31}N_2O_7$: 567.2131.

Found, %: C 69.99; H 5.44; N 4.92. $C_{33}H_{30}N_2O_7$. Calculated, %: C 69.96; H 5.34; N 4.94.

General Procedure for the Deprotection of 5-(3-Substituted Phenyl)-2′-deoxy-3,5-di-O-*p*-toluoyl Uridines. A 250 ml flask equipped with a magnetic stirrer and a drying tube was charged with 1.74 mmol of the 5-(3-substituted phenyl)-2′-deoxy-3′,5′-di-O-*p*-toluoyl uridines and 165 ml of methanol. Then 26 ml (5.20 mmol) of 0.20 M sodium methoxide in methanol was added dropwise. The reaction mixture was allowed to stand at room temperature for 24 h and was then poured onto a short column of silica gel 60. The silica was washed with methanol and after the addition of 2.5 g of coarse silica gel, the methanol was evaporated *in vacuo*. The coarse silica gel was applied onto a column of silica gel 60 and the product was eluted with dichloromethane/methanol.

5-(3-Chlorophenyl)-α-2′-deoxyuridine (13a).

Yield: 481 mg (63%); mp 203-207°C; ^{1}H NMR (deuteriomethanol): δ 2.14 (1H, d, J = 14.8 Hz, H2′b), 2.72 (1H, ddd, J = 5.9, 7.7, 14.8 Hz, H2′a), 3.56 (1H, dd, J = 4.6, 12.0 Hz, H5′b), 3.61 (1H, dd, J = 4.5, 12.0 Hz, H5′a), 4.34-4.41 (2H, m, H3′ and H4″), 6.31 (1H, dd, J = 2.1, 7.7 Hz, H1″), 7.31 (1H, dt, J = 1.8, 8.2 Hz, H6″), 7.36 (1H, t, J = 7.4 Hz, H5″), 7.47 (1H, dt, J = 1.6, 7.3 Hz, H4″), 7.63 (1H, t, J = 1.4 Hz, H2″), 8.20 (1H, s, H6). HRMS: Found: 339.0747 (MH^+). Calculated for $C_{15}H_{16}ClN_2O_5$: 339.0748.

5-(3-Chlorophenyl)-β-2′-deoxyuridine (13b).

Yield: 578 mg (98%); mp 67-72°C; ^{1}H NMR (deuteriomethanol): δ 2.32-2.36 (2H, m, H2′a and H2′b), 3.75 (1H, dd, J = 3.1, 12.0 Hz, H5′b), 3.83 (1H, dd, J = 2.9, 12.0 Hz, H5′a), 3.96 (1H, q, J = 3.2 Hz, H4′), 4.45 (1H, q, J = 4.6 Hz, H3′), 6.34 (1H, t, J = 6.4 Hz, H1′), 7.30 (1H, dt, J = 1.8, 8.2 Hz, H6″), 7.35 (1H, t, J = 7.9 Hz, H5″), 7.48 (1H, dt, J = 1.6, 7.3 Hz, H4″), 7.66 (1H, t, J = 1.9 Hz, H2″), 8.37 (1H, s, H6). HRMS: Found: 339.0756 (MH^+). Calculated for $C_{15}H_{16}ClN_2O_5$: 339.748.

Found, %: C 52.89; H 4.54; N 8.23. $C_{15}H_{15}ClN_2O_5$. Calculated, %: C 53.19; H 4.46; N 8.27.

5-(3-Iodophenyl)-α-2′-deoxyuridine (14a).

Yield: 576 mg (77%); mp 322-325°C (starts to decompose at ~230°C) ; ^{1}H NMR (deuteriomethanol): δ 7.14 (1H, t, J = 7.8 Hz, H5″), 7.54 (1H, dt, J = 1.6, 7.8 Hz, H6″), 7.66 (1H, dt, J = 1.6, 7.9 Hz, H4″), 7.96 (1H, t, J = 1.6 Hz, H2″). HRMS: Found: 431.0107 (MH^+). Calculated for $C_{15}H_{16}IN_2O_5$: 431.0104.

5-(3-Iodophenyl)-β-2′-deoxyuridine (14b).

Yield: 524 mg (70%) as a syrup; ^{1}H NMR (deuteriomethanol): δ 7.14 (1H, t, J = 7.8 Hz, H5″), 7.53 (1H, ddd, J = 1.0, 1.6, 7.9 Hz, H6″), 7.65 (1H, ddd, J = 1.0, 1.7, 7.9 Hz, H4″), 8.00 (1H, t, J = 1.7 Hz, H2″). HRMS: Found: 431.0096 (MH^+). Calculated for $C_{15}H_{16}IN_2O_5$: 431.0104.

Found, %: C 41.65; H 3.82; N 6.21. $C_{15}H_{15}IN_2O_5$. Calculated, %: C 41.88; H 3.51; N 6.51.

5-(3-Aminophenyl)-β-2′-deoxyuridine (15b).

Yield: 539 mg (97%); mp 93-98°C; ^{1}H NMR (deuteriomethanol): δ 6.69 (1H, ddd, J = 1.0, 2.3, 8.0 Hz, H6″), 6.87 (1H, ddd, J = 1.0, 1.6, 7.7 Hz, H4″), 7.91 (1H, t, J = 1.8 Hz, H2″), 7.10 (1H, t, J = 7.7 Hz, H5″); HRMS: Found: 320.1249 (MH^+). Calculated for $C_{15}H_{17}N_3O_5$: 320.1246.

Found, %: C 55.84; H 5.85; N 12.15. $C_{15}H_{16}N_3O_5$. Calculated, %: C 56.42; H 5.37; N 13.16 (better EA could not be obtained).

5-(3-Azidophenyl)-α-2′-deoxyuridine (16a).

Yield: 547 mg (91%); mp 97-102°C; ^{1}H NMR (deuteriomethanol): δ 7.01 (1H, ddd, J = 1.4, 2.3, 7.6 Hz, H6″), 7.31 (1H, m, H4″), 7.34 (1H, t, J = 1.5 Hz, H2″), 7.39 (1H, dt, J = 0.8, 7.5 Hz, H5″). HRMS: Found: 346.1157 (MH^+). Calculated for $C_{15}H_{16}N_5O_5$: 346.1151.

5-(3-Azidophenyl)-β-2′-deoxyuridine (16b).

Yield: 589 mg (98%); mp 160-163°C; ^{1}H NMR (deuteriomethanol): δ 7.01 (1H, dt, J = 2.2, 6.9 Hz, H6″), 7.02-7.38 (2H, m, H2″ and H4″), 7.39 (1H, t, J = 8.1 Hz, H6″). HRMS: Found: 368.0957 (MNa^+). Calculated for $C_{15}H_{15}N_5NaO_5$: 368.0971.

Found, %: C 51.94; H 4.39; N 20.33. $C_{15}H_{15}N_5O_5$. Calculated: C 52.17%, H 4.38%, N 20.28%.

5-(3-Methylthiophenyl)-α-2′-deoxyuridine (17a).

Yield: 597 mg (98%); mp 156-160°C; ^{1}H NMR (deuteriomethanol): δ 2.48 (1H, s, SCH_3), 7.18-7.33 (3H, m, H4″, H5″ and H6″), 7.46 (1H, m, H2″). HRMS: Found: 351.1007 (MH^+). Calculated for $C_{16}H_{19}N_2O_5S$: 351.1015.

5-(3-Methylthiophenyl)-β-2′-deoxyuridine (17b).

Yield: 597 mg (98%); mp 157-160°C; ^{1}H NMR (deuteriomethanol): δ 2.49 (1H, s, SCH_3), 7.18-7.34 (3H, m, H4″, H5″ and H6″), 7.48 (1H, m, H2″). HRMS: Found: 351.1025 (MH^+). Calculated for $C_{16}H_{19}N_2O_5S$: 351.1015.

Found, %: C 54.79; H 5.24; N 8.23. $C_{16}H_{18}N_2O_5S$. Calculated, %: C 54.85; H 5.18; N 8.00.

5-(3-Styryl)-α-2′-deoxyuridine (18a).

Yield: 546 mg (95%) as a syrup; ^{1}H NMR (deuteriomethanol): δ 5.25 (1H, dd, J = 1.0, 11.0 Hz, $CH=CH_2$ (*cis*)), 5.81 (1H, dd, J = 1.0, 17.6 Hz, $CH=CH_2$ (*trans*)), 6.75 (1H, dd, J = 10.8, 17.7 Hz, $CH=CH_2$), 7.33 (1H, t, J = 7.8 Hz, H5″), 7.39 (1H, dt, J = 1.6, 7.8 Hz, H6″), 7.44 (1H, dt, J = 1.6, 7.3 Hz, H4″), 7.62 (1H, t, J = 1.8 Hz, H2″). HRMS: Found: 331.1287 (MH^+). Calculated for $C_{17}H_{19}N_2O_5$: 331.1294.

5-(3-Styryl)-β-2′-deoxyuridine (18b).

Yield: 552 mg (96%); mp 104-107°C; ^{1}H NMR (deuteriomethanol): δ 5.24 (1H, dd, J = 1.0, 10.9 Hz, $CH=CH_2$ (*cis*)), 5.81 (1H, dd, J = 1.0, 17.6 Hz, $CH=CH_2$ (*trans*)), 6.75 (1H, dd, J = 10.9, 17.7 Hz, $CH=CH_2$), 7.33 (1H, t, J = 7.6 Hz, H5″), 7.39 (1H, dt, J = 1.5, 7.6 Hz, H6″), 7.44 (1H, dt, J = 1.7, 7.4 Hz, H4″), 7.63 (1H, t, J = 1.7 Hz, H2″). HRMS: Found: 331.1292 (MH^+). Calculated for $C_{17}H_{19}N_2O_5$: 331.1294.

Found, %: C 61.47; H 5.54; N 8.28. $C_{17}H_{18}N_2O_5$. Calculated, %: C 61.81; H 5.49; N 8.48.

Materials and Experimental Procedures: Virology

Inhibition of HIV-1 and HSV-1 (C42 strain) were performed as XTT assays in MT4 cells (human T cell line) and Vero cells, respectively. Effect on cell growth was determined as an XTT assay on non-confluent HEL cells without presence of any virus. In the CMV assay, reduction in cytopathic effect caused by the virus was determined in MRC-5 cells (human embryonic lung cells). These assays were performed as previously described [31]. The CMV ELISA was an *in situ* determination of viral antigens in HEL cells and performed essentially as described [32].

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