SYNTHESIS OF 5-SUBSTITUTED PYRIMIDINE NUCLEOSIDES THROUGH A PALLADIUM-CATALYZED CROSS-COUPLING OF ALKENYLHALOSILANES

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Dedicated to the memory of late professor Yoshio Ban.

Abstract- Palladium-catalyzed cross-coupling of alkenylhalosilanes with 5-iodouracil and 5-iodouridine derivatives was described. 5-Iodo-1,3-dimethyluracil coupled with alkenylfluorodimethylsilanes to give the corresponding cross-coupled products in good yield. Fully protected 5-iodo-2'-deoxyuridine derivative also underwent the cross-coupling reaction. Noteworthy is that unprotected 5-iodo-2'-deoxyuridine could be converted into the corresponding cross-coupled products in good yields using alkenyl(difluoro)methylsilanes.

INTRODUCTION

Derivation of purine and pyrimidine nucleosides has attracted much attention because of potent antitumor or antiviral activity.[1] Modification of the nucleosides is well studied regarding to sugar and pyrimidine moiety. In particular, introduction of organic functional group to C5 and/or C6 position has been shown to be fruitful. Straightforward method for the synthesis of such derivatives is transition metal catalyzed cross-coupling reaction[2] by means of an organometallic reagent of mercury,[3] stannane,[4] boron,[4b] or aluminum.[5]

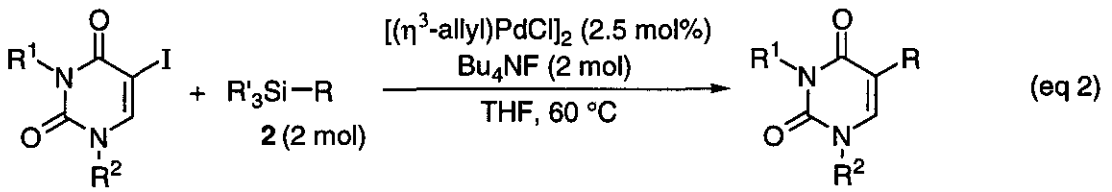
Palladium-catalyzed coupling of C5-mercuriouracil or -uridine with an organic halide or an alkene is well investigated by Bergstrom.[3] More recently, organostannanes are reported to undergo palladium-catalyzed cross-coupling with 5-iodouracil or -uridine derivatives.[4] However, these organometals are toxic to be used in large scale synthesis.

$$R\text{-}X + R'\text{-}SiR''_3 \xrightarrow[F^-]{\text{Pd cat.}} R\text{-}R' \qquad \text{(eq 1)}$$

We have studied the palladium-catalyzed cross-coupling of organofluorosilanes with organic electrophiles mediated by fluoride ion (eq 1).[6] Organosilicon compounds have some advantages over other metal reagents: Low toxicity, thermal and moisture stability, readily availability, and inexpensiveness. Thus we have applied this reaction to the synthesis of HMG-CoA reductase inhibitor.[7] In this article, we describe a convenient synthesis of 5-substituted uracil derivatives and 5-substituted 2'-deoxyuridines through a palladium-catalyzed cross-coupling of organofluorosilanes with 5-iodouracil and uridine derivatives.

RESULTS and DISCUSSION

At first, we studied the reaction with 5-iodo-1,3-dimethyluracil (**1a**) to optimize the structure of organofluorosilanes and a catalyst, and found that the reaction successfully proceeded in tetrahydrofuran (THF) at 60 °C with $[(\eta^3\text{-allyl})PdCl]_2$ catalyst and tetrabutylammonium fluoride (TBAF) (eq 2). Another Pd catalyst like $Pd(PPh_3)_4$ or $Pd(OAc)_2$ was less effective.



1a: $R^1 = R^2 = Me$
1b: $R^1 = Bn$, $R^2 = H$
1c: $R^1 = H$, $R^2 = H$

3a-3g (eq 2)

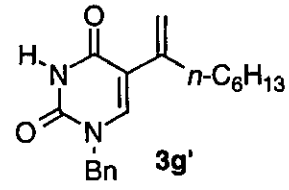
The results are summarized in Table 1. Alkenylfluorodimethylsilanes (**2a-2c**) smoothly reacted with **1a** to provide the cross-coupled products in moderate to good yields with retention of olefin geometry (runs 1, 2, and 3). It is worth to note that sterically congested alkenylsilane (**2c**) was reactive enough (run 3). We

found that alkenylchlorodimethylsilane (**2d**) and (**2e**) also exhibited enough reactivity in the presence of an excess amount of TBAF.[7] Mono protected substrate (**1b**) successfully coupled with alkenyl-(difluoro)methylsilane (**2f**) and (**2g**) to give the expected products. The reaction of **1b** and **2g** gave the desired cross-coupled product (**3g**) with considerable amount of regioisomer (**3g'**) (run 7). The isomerization process is not clear at this stage. Unfortunately, non-protected 5-iodouracil (**1c**) did not react under these reaction conditions.

Table 1. Cross-coupling of organosilanes with uracil derivatives

run	substrate	R'_3Si-R	time(h)	yield(%)
1	**1a**	Me_2FSi–(Ph) (**2a**)	16	**3a**(69)
2		Me_2FSi–(n-C_6H_{13}) (**2b**)	14	**3b**(70)
3		Me_2FSi–(Pr, Pr) (**2c**)	11	**3c**(63)
4[a)]		Me_2ClSi– (**2d**)	14	**3d**(82)
5[a)]		Me_2ClSi–(Ph) (**2e**)	14	**3a**(70)
6	**1b**	MeF_2Si–(Ph) (**2f**)	48	**3f**(58)
7		MeF_2Si–(n-C_6H_{13}) (**2g**)	44	**3g**(53)[b)]
8	**1c**	**2a**	72	no reaction

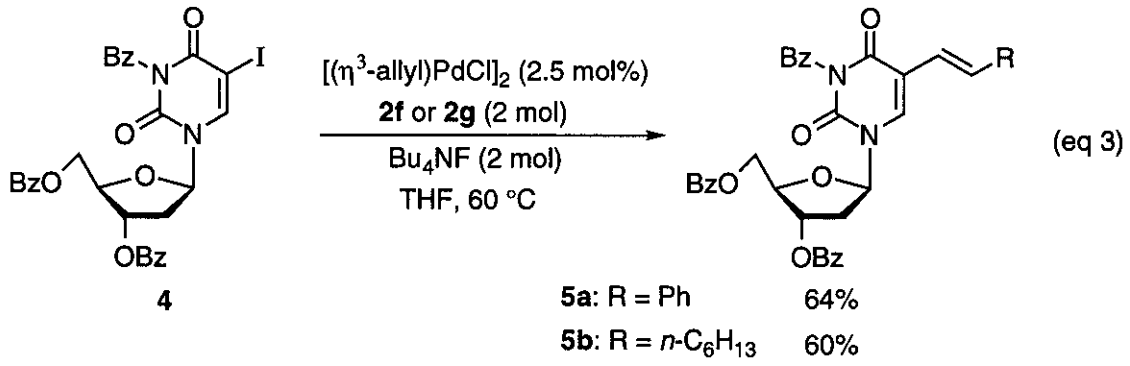
a) TBAF (4 eq.) was used. b) Regio isomer (**3g'**) was also obtained in 2 : 1 ratio of **3g** : **3g'**.

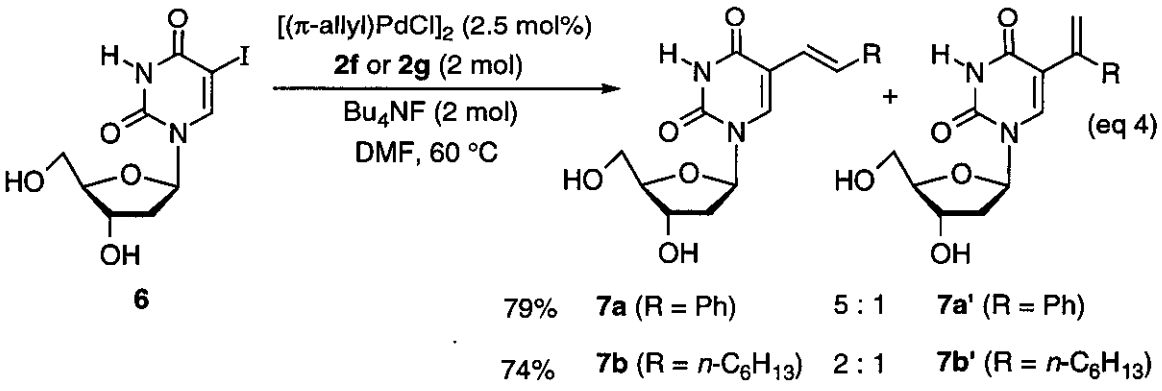


3g'

We next studied the reaction of 3,3',5'-tribenzoyl-5-iodo-2'-deoxyuridine (**4**) with alkenylfluoro-dimethylsilanes (**2a** or **2b**), but all attempts failed. However, alkenyl(difluoro)methylsilanes (**2f** or **2g**) was found to couple with **4** to give **5a** or **5b** (eq 3). Worthy to note is that non-protected 5-iodo-2'-deoxyuridine (**6**) also reacted with **2f** or **2g** in *N, N*-dimethylformamide (DMF) (eq 4). The reaction in

THF was very slow due to low solubility of the substrate. Both **2f** and **2g** reacted with **6**, giving undesirable regioisomers (**7a'**) and (**7b'**) in fair amounts.





CONCLUSION

We found that 5-iodouracil derivatives reacted with alkenylfluorosilanes and alkenylchlorosilanes in the presence of a Pd catalyst and TBAF. It should be noted that the cross-coupling reaction of non-protected 5-iodo-2'-deoxyuridine was achieved for the first time with alkenyl(difluoro)methylsilanes. The substituent at Si atom was found to be extremely important for the success of the cross-coupling: Alkenyl(difluoro)-methylsilanes are potent agent for the cross-coupling of 5-iodouracil derivatives.

EXPERIMENTAL SECTION

THF and ether were distilled from benzophenone/Na prior to use. Dichloromethane, DMF, DMSO, and hexane were distilled from CaH_2 and stored over Molecular Sieves 4A. All the reactions were carried out under an Ar atmosphere in a flame dried glass ware unless otherwise noted. Flash column chromatography

was performed using Merck Kieselgel (230-400 mesh). All the temperatures were uncorrected. Melting points were measured with a Yanagimoto Micro Melting Point apparatus. Ir spectra were recorded on a Hitachi Ir 260-10 or JASCO FT-IR 3A spectrometers. ^{1}H Nmr spectra were measured with a Bruker AC-200 (200.1 MHz) or JEOL EX-400 (400.1 MHz) spectrometers; ^{13}C nmr spectra with a Bruker AC-200 (50.3 MHz) or JEOL EX-400 (100.4 MHz). Mass spectra were measured by electron ionization method with a Hitachi M-80 spectrometer. Substrates 1-benzyl-5-iodouracil (**1b**)[9] and 3,3',5'-tribenzoyl-5-iodo-2'-deoxyuridine (**4**)[4c] were prepared according to the literature.

*5-Iodo-1,3-dimethyluracil (**1a**)*

Sodium hydride (60% oil dispersion, 0.24 g, 6.0 mmol) was washed with dry hexane for 3 times and suspended in DMF (7 ml). A solution of 5-iodouracil (0.48 g, 2.0 mmol) in DMF (5 ml) was added dropwise to NaH suspension, and the resultant mixture was stirred for 1 h at room temperature. Methyl iodide (0.37 ml, 6.0 mmol) was added dropwise to the mixture and stirring was continued for additional 30 min. The reaction was quenched with H_2O (20 ml) and extracted with dichloromethane for 2 times. Combined organic layer was washed with H_2O and dried over Na_2SO_4. After filtration, the filtrate was concentrated to give **1a** (0.47 g) as pale yellow powder. Pure **1a** (0.40 g) was obtained in 76% yield by recrystallization from ethyl acetate.

*Cross-coupling reaction of **1a-c** and **4**: A General Procedure.*

To a solution of a substrate (0.20 mmol) and $[(\eta^3\text{-allyl})PdCl]_2$ (1.8 mg, 5.0 μmol) in THF (1 ml) were added an alkenylsilane (0.40 mmol) and TBAF (1 M THF sol., 0.40 ml, 0.40 mmol) at room temperature in a glass tube. The reaction tube was sealed and heated at 60 °C until the substrate was consumed. THF was removed in vacuo, and the residue was purified by a short column chromatography on a silica gel (Wakogel C-200) to give a crude coupled product. Further purification was performed by flash column chromatography.

*1,3-Dimethyl-5-[(E)-2-phenylethenyl]uracil (**3a**)*

Purification by short column (hexane-ethyl acetate 1 : 1) followed by flash chromatography (hexane-ethyl acetate 2 : 1) provided **3a** as a colorless crystals. mp 149-152 °C. ^{1}H Nmr ($CDCl_3$) δ 3.42 (s, 3 H), 3.47 (s, 3 H), 6.84 (dd, J = 1.0, 16.0 Hz, 1 H), 7.20-7.49 (m, 7 H). ^{13}C Nmr ($CDCl_3$) δ 28.12, 37.19, 111.47, 119.92, 126.36, 127.64, 127.80, 128.63, 129.32, 137.31, 139.20, 151.03, 162.24. Ir (KBr) 3058, 1694, 1657, 1643, 1622, 1597, 1574, 1484, 1454, 1089, 973, 962, 792, 745, 687 cm^{-1}. Ms (70

eV, rel intensity) *m/z* 242 (M^+, 19), 157 (23), 115 (34), 108 (53), 77 (6.8), 42 (100). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.39; H, 5.78; N, 11.54.

1,3-Dimethyl-5-[(E)-1-octenyl]uracil (3b)

Purification by short column (hexane-ethyl acetate 1 : 1) followed by flash chromatography (hexane-ethyl acetate 2 : 1) provided **3b** as a colorless viscous oil. R_f 0.29 (hexane-ethyl acetate 2 : 1) ^1H Nmr ($CDCl_3$) δ 0.88 (m, 3 H), 1.26 (m, 6 H), 1.38 (m, 2 H), 2.13 (dt, *J* = 7.0, 7.0 Hz, 2 H), 3.35 (s, 3 H), 3.40 (s, 3 H), 6.10 (d, *J* = 16.0 Hz, 1 H), 6.33 (dt, *J* = 16.0, 7.0 Hz, 1 H), 7.12 (s, 1 H). ^{13}C Nmr ($CDCl_3$) δ 14.03, 22.54, 27.95, 28.83, 29.19, 31.66, 33.37, 111.82, 120.64, 132.43, 137.92, 151.19, 162.42. Ir (neat) 2920, 2850, 1705, 1655, 1460, 1350, 1090, 970, 915, 755, 730 cm^{-1}. Ms (70 eV, rel intensity) *m/z* 251 (M^+ + 1, 14), 222 (3.0), 180 (28), 166 (4.2), 154 (37), 123 (12), 81 (14), 42 (32), 32 (100).

1,3-Dimethyl-5-(1-propyl-1-pentenyl)uracil (3c)

Purification by short column (hexane-ethyl acetate 1 : 1) followed by flash chromatography (hexane-ethyl acetate 3 : 1) provided **3c** as a colorless viscous oil. R_f 0.30 (hexane-ethyl acetate 3 : 1) ^1H Nmr ($CDCl_3$) δ 0.87 (t, *J* = 7.5 Hz, 3 H), 0.94 (t, *J* = 7.0 Hz, 3 H), 1.22-1.52 (m, 4 H), 2.11 (q, *J* = 7.0 Hz, 2 H), 2.41 (br t, *J* = 7.5 Hz, 2 H), 3.35 (s, 3 H), 3.40 (s, 3 H), 5.46 (t, *J* = 7.0 Hz, 1 H), 6.98 (s, 1 H). ^{13}C Nmr ($CDCl_3$) δ 30.04, 30.86, 36.79, 117.42, 131.59, 134.68, 139.14, 151.73, 162.64. Ir (neat) 3005, 2940, 2850, 1680, 1630, 1440, 1320, 1250, 1215, 1180, 1065, 765, 715, 680 cm^{-1}. Ms (70 eV, rel intensity) *m/z* 250 (M^+, 47), 221 (54), 207 (95), 193 (45), 153 (56), 96 (22), 42 (100). Anal. Calcd for $C_{14}H_{22}N_2O_2$: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.05; H, 9.01; N, 11.28.

1-Benzyl-5-[(E)-2-phenylethenyl]uracil (3f)

Purification by short column (CH_2Cl_2-ethyl acetate 5 : 1) followed by flash chromatography (CH_2Cl_2-ethyl acetate 8 : 1) provided **3f** as a colorless crystals. mp 189-192 °C. ^1H Nmr ($CDCl_3$) δ 4.97 (s, 2 H), 6.72 (d, *J* = 16.5 Hz, 1 H), 7.25-7.44 (m, 12 H), 8.85 (br s, 1 H). ^{13}C Nmr ($CDCl_3$) δ 51.40, 112.97, 119.21, 126.41, 127.77, 128.01, 128.61, 129.19, 130.31, 135.06, 137.13, 140.02, 150.08, 162.06. Ms (10 eV, rel intensity) *m/z* 304 (M^+, 27), 213 (2.5), 128 (2.3), 115 (7.9), 91 (100), 65 (10). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30. Found: C, 74.91; H 5.20.

1-Benzyl-5-[(E)-1-octenyl]uracil (3g)

Chromatography through a short column (CH_2Cl_2-ethyl acetate 5 : 1) followed by flash column chromatography (CH_2Cl_2-ethyl acetate 10 : 1) provided an inseparable mixture of **3g** and **3g'** as a pale yellow viscous oil. R_f 0.26 (CH_2Cl_2-ethyl acetate 10 : 1) ^1H Nmr ($CDCl_3$) δ 0.87 (m, 3 H), 1.27 (m, 6

H), 1.40 (m, 2 H), 2.11 (dt, *J* = 6.5, 6.5 Hz, 2 H), 4.93 (s, 2 H), 6.02 (dd, *J* = 0.5, 16.0 Hz, 1 H), 6.39 (td, *J* = 6.5, 16.0 Hz, 1 H), 7.10 (s, 1 H), 7.26-7.43 (m, 5 H), 8.73 (br s, 1 H). Ms (70 eV, rel intensity) *m/z* 312 (M^+, 20), 255 (9.3), 243 (7.5), 229 (17), 221 (12), 151 (22), 91 (100), 65 (8.3).

*3,3',5'-Tribenzoyl-5-[(E)-2-phenylethenyl]-2'-deoxyuridine (**5a**)*

Purification by short column chromatography (hexane-ethyl acetate 1 : 1) followed by flash column chromatography (hexane-ethyl acetate 2 : 1) provided **5a** as a colorless amorphous solid. R_f 0.30 (hexane-ethyl acetate 3 : 1) ^{1}H Nmr ($CDCl_3$) δ 2.44 (ddd, *J* = 6.5, 9.0, 14.0 Hz, 1 H), 2.85 (ddd, *J* = 1.5, 5.5, 14.0 Hz, 1 H), 4.62 (m, 1 H), 4.77 (dd, *J* = 4.0, 12.5 Hz, 1 H), 4.87 (dd, *J* = 3.0, 12.5 Hz, 1 H), 5.69 (brd, *J* = 6.5 Hz, 1 H), 6.48 (d, *J* = 16.5 Hz, 1 H), 6.49 (dd, *J* = 5.5, 9.0 Hz, 1 H), 7.14-7.71 (m, 15 H), 7.78 (s, 1 H), 7.92-8.12 (m, 6 H). ^{13}C Nmr ($CDCl_3$) δ 38.83, 64.69, 75.24, 83.51, 86.03, 113.40, 119.23, 126.76, 128.08, 128.61, 128.76, 128.90, 129.14, 129.34, 129.52, 129.78, 130.05, 130.75, 131.50, 131.66, 134.08, 134.17, 135.10, 135.49, 137.24, 148.58, 161.24, 166.26, 166.34, 168.77. Ir (neat) 3060, 1745, 1710, 1660, 1600, 1450, 1375, 1315, 1270, 1175, 1110, 1100, 1075, 1025, 735, 710, 690 cm^{-1}. Ms (10 eV, rel intensity) *m/z* 642 (M^+, 0.9), 422 (1.0), 318 (18), 214 (17), 105 (90), 81 (100). Anal. Calcd for $C_{38}H_{30}N_2O_8$: C, 71.02; H, 4.71; N, 4.36. Found: C, 70.72; H, 4.61; N, 4.33.

*3,3',5'-Tribenzoyl-5-[(E)-1-octenyl]-2'-deoxyuridine (**5b**)*

Purification by short column chromatography (hexane-ethyl acetate 1 : 1) followed by flash column chromatography (hexane-ethyl acetate 3 : 1) provided **5b** as a pale yellow amorphous solid. R_f 0.30 (hexane-ethyl acetate 3 : 1) ^{1}H Nmr ($CDCl_3$) δ 0.88 (m, 3 H), 1.25 (m, 8 H), 1.92 (m, 2 H), 2.41 (ddd, *J* = 6.5, 9.0, 14.0 Hz, 1 H), 2.79 (ddd, *J* = 1.5, 5.5, 14.0 Hz, 1 H), 4.58 (m, 1 H), 4.72 (dd, *J* = 3.5, 12.5 Hz, 1 H), 4.83 (dd, *J* = 3.0, 12.5 Hz, 1 H), 5.68 (br d, *J* = 6.0 Hz, 1 H), 5.74 (d, *J* = 15.5 Hz, 1 H), 6.35 (dt, *J* = 15.5, 6.5 Hz, 1 H), 6.47 (dd, *J* = 5.5, 8.5 Hz, 1 H), 7.41-7.69 (m, 10 H), 7.90-8.10 (m, 6 H). ^{13}C Nmr ($CDCl_3$) δ 14.05, 22.52, 28.87, 28.94, 31.63, 33.48, 38.25, 64.33, 74.90, 82.93, 85.39, 113.49, 119.67, 128.54, 128.66, 128.79, 128.87, 129.12, 129.18, 129.49, 129.71, 130.36, 131.44, 133.29, 133.69, 134.46, 135.03, 148.45, 161.03, 165.90, 165.94, 168.61. Ir (neat) 2930, 1750, 1720, 1665, 1600, 1450, 1315, 1270, 1105, 735, 710, 685 cm^{-1}. Ms (10 eV, rel intensity) *m/z* 326 (M^+ - 324, 12), 222 (1.5), 122 (2.3), 105 (50), 81 (100). Anal. Calcd for $C_{38}H_{38}N_2O_8$: C, 70.14; H, 5.89; N, 4.30. Found: C, 70.04; H, 6.01; N, 4.29.

*Cross-coupling of **1a** with alkenylchlorodimethylsilanes (**2d**) and (**2e**).*

To a solution of **1a** (53.2 mg, 0.20 mmol) and $[(\eta^3\text{-allyl})PdCl]_2$ (1.8 mg, 5.0 μmol) in THF (1 ml) was added TBAF (1 M THF sol., 0.80 ml, 0.80 mmol) at room temperature in a glass tube. Then **2d** or **2e** (0.40 mmol) was added dropwise to this solution, the tube was sealed, and the reaction mixture was heated at 60 °C for 14 h. Workup and a short chromatography on a silica gel (Wakogel C-200, hexane-ethyl acetate 1:1) gave a pale yellow solid, which was further purified by flash column chromatography (hexane-ethyl acetate 1 : 1) to provide **3a** (33.9 mg, 70% yield) or **3d** (27.1 mg, 82% yield) respectively.

*5-Ethenyl-1,3-dimethyluracil (**3d**)*

Colorless crystal. mp 72-75 °C. ^{1}H Nmr ($CDCl_3$) δ 3.38 (s, 1 H), 3.44 (s, 3 H), 5.22 (dd, *J* = 1.5, 11.5 Hz, 1 H), 5.90 (dd, *J* = 1.5, 17.5 Hz, 1 H), 6.46 (ddd, *J* = 0.5, 11.5, 17.5 Hz, 1 H), 7.22 (s, 1 H). ^{13}C Nmr ($CDCl_3$) δ 27.96, 37.05, 111.53, 115.00, 128.12, 139.39, 151.17, 162.18. Ir (KBr) 1709, 1697, 1662, 1630, 1509, 1485, 1454, 1364, 1344, 902, 785, 756 cm^{-1}. Ms (70 eV, rel intensity) *m/z* 166 (M^+, 100), 135 (42), 93 (7.1), 81 (64), 57 (22). Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.71; H, 6.18; N, 16.86.

*Cross-coupling reaction of **6** with **2f** or **2g**.*

2f or **2g** (0.40 mmol) and TBAF (1 M THF sol., 0.40 ml, 0.40 mmol) were added to a solution of **6** (70 mg, 0.20 mmol) and $[(\eta^3\text{-allyl})PdCl]_2$ (1.8 mg, 5.0 μmol) in DMF (1 ml) and the reaction mixture was heated at 60 °C until all of **6** was consumed. Removing all solvents in vacuo followed by a short column chromatography (Wakogel C-200, CH_2Cl_2-MeOH 5 : 1) gave a crude brown oil, which was further purified by flash column chromatography (CH_2Cl_2-MeOH 9 : 1) to give a desired and undesired isomer as inseparable mixture.

*5-[(E)-2-Phenylethenyl]-2'-deoxyuridine (**7a**)*

Pale yellow amorphous solid. R_f 0.16 (CH_2Cl_2-MeOH 10 : 1). Following spectrum was assigned to **7a** and **7a'** respectively: **7a** ^{1}H Nmr (acetone-d_6) δ 2.35 (m, 2 H), 3.86 (dd, *J* = 3.0, 3.0 Hz, 2 H), 3.99 (dt, *J* = 3.0, 3.0 Hz, 1 H), 4.56 (m, 1 H), 6.34 (t, *J* = 6.5 Hz, 1 H), 6.89 (dd, *J* = 0.5, 16.5 Hz, 1 H), 7.15-7.48 (m, 5 H), 7.50 (d, *J* = 16.5 Hz, 1 H), 8.35 (s, 1 H). Protons of NH and OH could not be detected. **7a'** ^{1}H Nmr (acetone-d_6) δ 2.37 (m, 2 H), 3.62 (d, *J* = 3.0 Hz, 2 H), 3.93 (m, 1 H), 4.53 (m, 1 H), 5.45 (d, *J* = 1.5 Hz, 1 H), 5.66 (d, *J* = 1.5 Hz, 1 H), 6.32 (t, *J* = 6.0 Hz, 1 H), 7.15-7.48 (m, 5 H), 7.93 (s, 1 H). The ratio was determined by vinyl proton integration: **7a** (δ 6.89) : **7a'** (δ 5.45) = 5 : 1. Ms (10 eV, rel intensity) *m/z* 330 (M^+, 1.2), 215 (14), 214 (100), 143 (65), 116 (10), 73 (12).

5-[(E)-1-Octenyl]-2'-deoxyuridine (7b)

Pale yellow viscous oil. R_f 0.33 (CH_2Cl_2-MeOH 9 : 1). Following spectrum was assigned to **7b** and **7b'** respectively: **7b** ^{1}H Nmr (acetone-d_6) δ 0.88 (m, 3 H), 1.22-1.50 (m, 8 H), 2.11 (m, 2 H), 2.29 (m, 2 H), 2.81 (br s, 1 H), 3.31 (br s, 1 H), 3.82 (br d, *J* = 3.0 Hz, 2 H), 3.95 (dd, *J* = 3.0, 6.0 Hz, 1 H), 4.53 (m, 1 H), 6.09 (br d, *J* = 16.0 Hz, 1 H), 6.32 (dd, *J* = 7.0, 7.0 Hz, 1 H), 6.51 (dt, *J* = 6.5, 16.0 Hz, 1 H), 8.09 (s, 1 H), 9.94 (br s, 1 H). **7b'** ^{1}H Nmr (acetone-d_6) δ 0.88 (m, 3 H), 1.22-1.50 (m, 8 H), 2.29 (m, 2 H), 2.42 (t, *J* = 7.0 Hz, 2 H), 2.81 (br s, 1 H), 3.31 (br s, 1 H), 3.82 (m, 2 H), 3.97 (m, 1 H), 4.53 (m, 1 H), 5.01 (m, 1 H), 5.53 (d, *J* = 2.0 Hz, 1 H), 8.05 (s, 1 H), 9.94 (br s, 1 H). The ratio was determined by vinyl proton integration: **7b** (δ 6.51) : **7b'** (δ 5.53) = 2 : 1. Ms (10 eV, rel intensity) *m/z* 338 (M^+, 1.4), 223 (13), 222 (67), 179 (6.2), 152 (51), 138 (42), 117 (100), 99 (41), 73 (29).

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