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Uracil and Adenine Nucleosides Having a 2',3'-Bromovinyl Structure: Highly Versatile Synthons for the Synthesis of 2'-*C*- and 3'-*C*-Branched 2',3'-Unsaturated Derivatives

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Key Words β-hydroxyselenide, bromovinyl structure, branched-sugar nucleoside, anti-HIV agent, 2',3'-unsaturated nucleoside

Abstract *Preparation of 2'- and 3'-bromo derivatives of 2',3'-unsaturated uracil and adenine nucleosides has been carried out starting from the corresponding β-hydroxyselenides by way of bromination and successive selenoxide elimination These compounds have been shown to serve as versatile synthons for the preparation of anti-HIV candidates, 2'-C- and 3'-C-branched 2',3'-unsaturated nucleosides, through palladium-catalyzed cross-coupling and halogen-lithium exchange reactions*

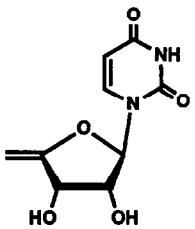
INTRODUCTION

Recent studies in our laboratory showed that a highly nucleophilic phenylselenide ion, generated by reducing $(PhSe)_2$ with $LiAlH_4$, enables to cleave various types of anhydro structures in uracil nucleosides and, thus, can be used as a suitable reagent for introducing a phenylseleno group to the furanosyl moiety [1,2] Since the resulting selenium-containing products are susceptible to selenoxide elimination under mild conditions, the whole sequence constitutes an efficient route for the preparation of various types of unsaturated-sugar uracil nucleosides that include rather unstable 1',2'-unsaturated derivative [3]

Although unsaturated-sugar nucleosides are expected to be versatile starting materials for C-C bond formation, majority of reactions regarding this class of compounds had been simple electrophilic additions with which only non-carbon substituents can be introduced [4] We have already shown through several publications that C-C bond formation in the furanosyl moiety of nucleosides can be accomplished by using certain unsaturated-sugar derivatives These are 1) a stereoselective addition of carbon radicals to the 5'-position of 1,[5]

2) an aldol reaction at the 3'-position of **2**,[6] and 3) reaction of carbon nucleophiles at the 4'-position of **3** *via* an allylic rearrangement.[7]

Promising anti-HIV (Human Immunodeficiency Virus) activity of 2',3'-didehydro-2',3'-dideoxynucleosides,[8] such as 3'-deoxy-2',3'-didehydrothymidine (D4T: **4**),[9] as well as the lack of a general method for the synthesis of their 2'-*C*- or 3'-*C*-branched analogues[10] prompted us to carry out the present investigation.[11] Since alkenyl halides are considered to serve both as vinyl cation- and as vinyl anion-equivalents through palladium-catalyzed cross-coupling[12] and halogen-lithium exchange reactions,[13] respectively, we anticipated that nucleosides having a bromovinyl structure in the sugar portion, such as **5** and **6**,[14] would work in both types of reactions and, therefore, permit a general entry to 2'-*C*- or 3'-*C*-branched 2',3'-unsaturated derivatives that could be active against HIV. In this paper, preparation of such synthons (**5** and **6**), starting from nucleoside derivatives having a phenylseleno group in the furanosyl moiety, and C-C bond forming reactions at their 2'- and 3'-positions are described.



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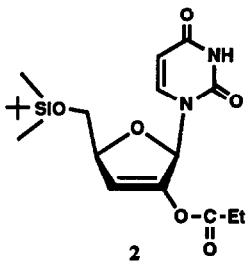

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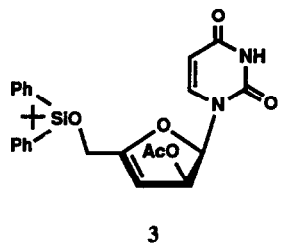

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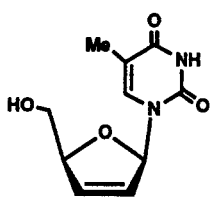

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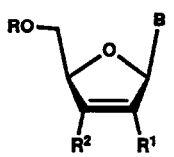


B= uracil-1-yl or adenin-9-yl

R= a protecting group

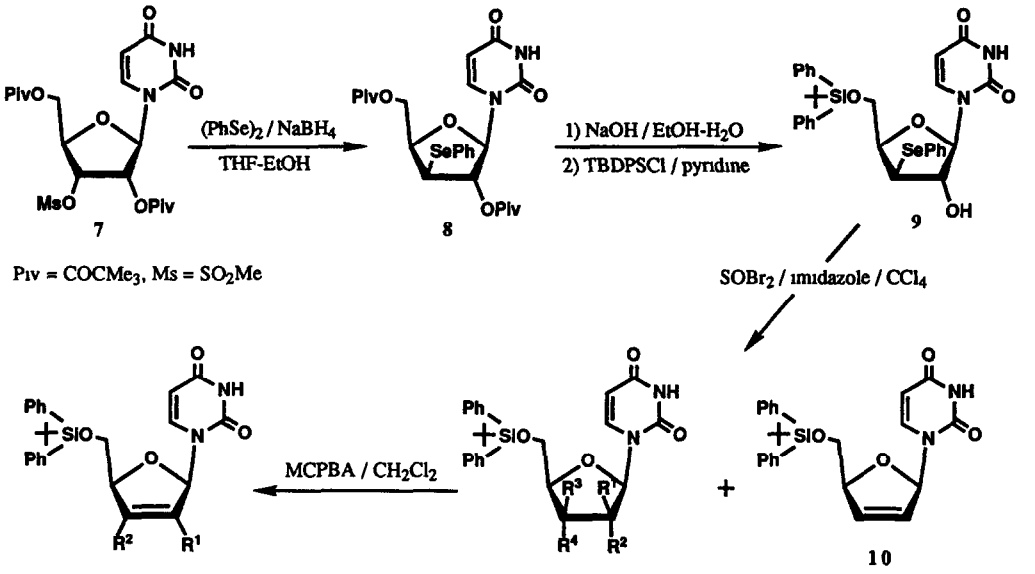
5 R^1= H, R^2= Br

6 R^1= Br, R^2= H

PREPARATION OF URACIL AND ADENINE NUCLEOSIDES HAVING A BROMOVINYL STRUCTURE

We reasoned that bromination and successive selenoxide elimination of nucleosidic β-hydroxyselenides would lead to the formation of the desired nucleosides having a bromovinyl structure As shown in Scheme 1, 3'-*O*-mesyl-2',5'-di-*O*-pivaloyluridine (**7**) was selected as a substrate for introduction of a phenylseleno group to the 3'-position, because this compound can be readily prepared in a fairly large scale according to the procedure reported by Ishido and his co-workers [15]

In our recent paper, it has been shown that, despite the successful reaction between 3'-*O*-mesyl-2',5'-di-*O*-trityluridine and $(PhSe)_2/LiAlH_4$, the reaction of **7** gave only a trace amount of the corresponding selenide (**8**).[3] In contrast to this, when **7** was reacted with $(PhSe)_2$ (0.8 mol equiv)/$NaBH_4$ (1.6 mol equiv)[16] in refluxing THF-EtOH, **8** was obtained in 81% yield.[17] Stereochemistry regarding the introduced phenylseleno group in **8** was confirmed based on its X-ray crystallographic analysis,[18] the result of which indicates that no participation of the base moiety had been involved during its formation. Quite unexpectedly, use of larger amounts of the reagents in this reaction resulted in a decreased yield of **8**. 49% by the use of $(PhSe)_2$ (1.6 mol equiv)/$NaBH_4$ (3.2 mol equiv); trace amount by the use of $(PhSe)_2$ (2.4 mol equiv.)/$NaBH_4$ (4.8 mol equiv). Compound **8** was converted to the β-hydroxyselenide **9** in almost quantitative yield by deacylation followed by 5'-*O*-silylation with *tert*-butyldiphenylsilyl chloride (TBDPSCl)



Scheme 1

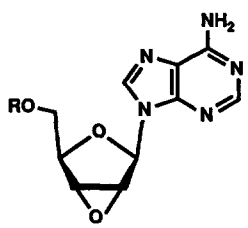
Although β-hydroxyselenides undergo, in general, elimination reaction to give olefins upon treatment with $SOCl_2$ in the presence of Et_3N,[19,20] it has been briefly mentioned in a review[21] that chlorination of the hydroxyl group can be accomplished by omitting the base from the reaction medium. When **9** was brominated in CCl_4 with $SOBr_2$ (5 equiv.) (0 °C, for 5 h), TLC analysis (hexane–EtOAc = 2:1) of the reaction mixture showed the formation of a highly nonpolar product (Rf 0.56) in addition to the starting material (**9**, Rf 0.17) and a trace amount of an elimination product, 5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyuridine (**10**, Rf 0.27).[22] The ^1H NMR spectrum of this nonpolar product, isolated by silica gel column chromatography, revealed that it consists of two isomeric products with a ratio of *ca.* 2:1 (H-1' of the major product δ 6.44 ppm, $J_{1',2'}$ = 6.6 Hz *vs* H-1' of the minor product δ 6.19 ppm, $J_{1',2'}$ = 4.4 Hz). Together with its characteristic MS spectrum due to the presence of Br and Se [*m/z* 629, 627, and 625 (M^+–Bu-*t*)], structures

of these isomeric products were tentatively assigned to be the β-bromoselenides **11a** and **11b** The yield of **11** was 38% (recovery of **9**, 29%) Attempts to improve the yield of **11** by employing prolonged reaction time (overnight) or a large excess of $SOBr_2$ (10 equiv.) uniformly gave a complex mixture of products On the other hand, when the bromination was conducted in the presence of Et_3N (1 2 equiv), the reaction appeared not to follow the reported trend of elimination pathway dominating, but produced **11** in 56% yield along with **10** (10%). To optimize the reaction conditions, we examined the use of various types of bases and found that the presence of imidazole (3.0 equiv) gave **11** in a higher yield of 72%.

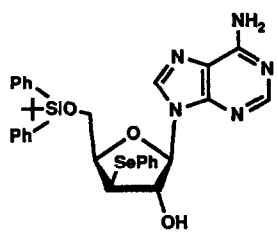
The mixture of β-bromoselenides (**11a** and **11b**) thus obtained was subjected to selenoxide elimination in CH_2Cl_2 by treatment with MCPBA (1 3 equiv , at room temperature for 3 h) The resulting bromovinyl uracil nucleosides **12** and **13** were separated by column chromatography and fully characterized by ^1H NMR and MS spectroscopies.[23] Since selenoxide elimination is known to proceed in syn stereochemistry,[24] the formation of **12** clearly indicates that its precursor should be **11a** and that the aforementioned bromination took place through a "2',3'-up" seleniranium intermediate which then underwent ring-opening by bromide ion [25]

During repeated preparation of **12** and **13**, we noticed that isolated yield and ratio of the two β-bromoselenides (**11a** and **11b**) varied considerably, presumably due to their decomposition upon evaporation and subsequent purification by column chromatography This led us to carry out the preparation of **12** and **13** without isolating **11** After quenching the bromination mixture with cold aqueous $NaHCO_3$, **11** was extracted with cold CH_2Cl_2 and then reacted with MCPBA By following this procedure, the overall yield of **12** plus **13** from **9** attained to 80% (**12**, 42% *vs* **13**, 38%) A 9% yield of **10** was also isolated

For the preparation of adenine counterparts, 2',3'-anhydroadenosine (**14**)[26] was used as the starting material The 5'-hydroxyl group of **14** was protected with a *tert*-butyldiphenylsilyl (TBDPS) group to give **15** in 76% yield. Cleavage of the 2',3'-oxirane ring of **15** with phenylselenide ion was performed in dioxane at 60-70 °C for 3 5 h by using $(PhSe)_2$ (2 4 mol equiv)/$LiAlH_4$ (1 8 mol equiv) [27] This gave **16** as the sole product in 86% yield When **16** was treated with $SOBr_2$/imidazole followed by MCPBA in a similar manner to the case of **9**, the desired **17** and **18** were isolated in 41 and 33% yields, respectively, by column chromatography The two dimensional nuclear Overhauser enhancement spectra (NOESY-spectra) of **17** and **18** provided confirmation for their structures That is, the enhancement correlation was observed between H-8 and H-2' in the former, while between H-3' and H-5' in the latter



14 R= H
15 R= TBDPS



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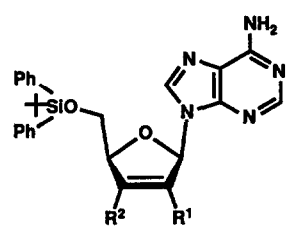
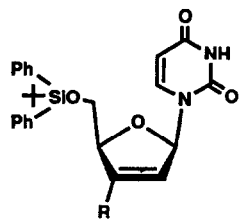


17 R^1= H, R^2= Br
18 R^1= Br, R^2= H

PALLADIUM-CATALYZED CROSS-COUPLING OF THE BROMOVINYL NUCLEOSIDES

Although palladium-catalyzed cross-coupling reaction is a frequently employed synthetic operation for C-C bond formation, its application in nucleoside field had been limited to the reaction at the base moiety.[28] To the best of our knowledge, the reactions described herein constitute the first example of its application to the sugar portion of nucleosides

The results obtained by the use of bromovinyl uracil nucleosides (**12** and **13**) are summarized in Table 1 together with detailed reaction conditions Either $(Ph_3P)_2PdCl_2$ or $(Ph_3P)_4Pd$ was used as a palladium catalyst throughout these reactions, except entry 3 Treatment of the 3'-bromo derivative (**12**) with terminal alkynes, under the conditions reported by Sonogashira and his co-workers,[12b] effected smooth coupling to give **19** and **20** (entries 1 and 2) On the other hand, despite ample precedents of the reaction between vinylic halides and electron-deficient alkenes,[12a] no reaction took place upon treatment with ethyl acrylate in DMF at 100 °C for 2 h



19 R= C≡CPh
20 R= C≡CSiMe$_3$
21 R= CH=CH$_2$
22 R= Ph
23 R= Me

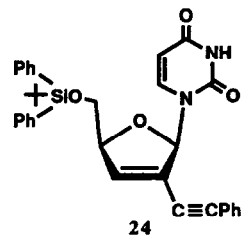


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Table 1. Palladium-catalyzed cross-coupling reactions of **12** and **13**

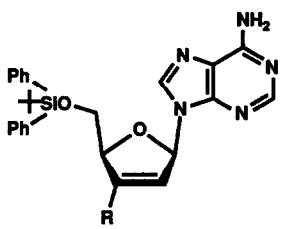
Entry	Compd	Catalyst[a)]	Reagent (equiv)	Conditions	Product	Isolated yield (%)
1	**12**	A/CuI	PhC≡CH (4)	DMF/Et_3N 80 °C, 5 h	**19**	68
2	**12**	A/CuI	Me_3SiC≡CH (10)	DMF/Et_3N 80 °C, 1 h	**20**	62
3	**12**	$Pd(OAc)_2$ PPh_3	CH_2=$CHCO_2Et$ (2)	DMF/Et_3N 100 °C, 2 h	no reaction	
4	**12**	A	Bu_3SnCH=CH_2(5)	DMF, 60 °C, 1 h	**21**	37
5	**12**	A	Ph_4Sn (5)	dioxane 100 °C, 24 h	**22**	39
6	**12**	B	Me_4Sn (5)	dioxane 100 °C, 48 h	**23**	14
7	**13**	A/CuI	PhC≡CH (4)	DMF/Et_3N 80 °C, 1 h	**24**	72

[a)] Catalysts A and B refer to $(Ph_3P)_2PdCl_2$ and $(Ph_3P)_4Pd$, respectively
All experiments were carried out by the use of 10 mol% of the catalyst.

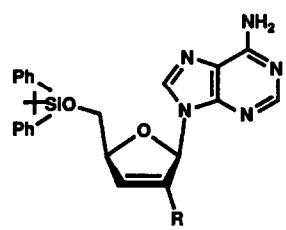
(entry 3). When this reaction was carried out in MeCN at refluxing temperature for 12 h, again **12** remained unchanged, but at a higher temperature of 120 °C (in a sealed tube, for 20 h), a product was formed besides a large amount of uracil. From its ^{1}H NMR spectrum, it appeared that the product had no sugar moiety and instead had one $CH_2CH_2CO_2Et$ structure as well as one D_2O exchangeable proton In corroboration with the MS spectrum, we assume the likely structure of this product to be 1-[2-(ethoxycarbonyl)ethyl]uracil (17% yield), which had apparently resulted from a Michael addition of uracil to ethyl acrylate.[29]

As an alternative method, organotin reagents were used as coupling partners. In accord with the reported reactivity order of tin ligands,[30] introduction of a vinyl group to the 3'-position of **12** was achieved under relatively mild conditions to give **21** (entry 4). Such transfer of a phenyl or methyl ligand required heating in dioxane at 100 °C for 1-2 days (entries 5 and 6), giving the corresponding 3'-*C*-substituted products (**22** and **23**). Although the use of dipolar aprotic solvents can be expected to increase the nucleophilicity of the tin reagent, when the reaction of Ph_4Sn was carried out at 100 °C in either DMF or MeCN, the starting material (**12**) was recovered. As shown in entry 7, the 2'-bromo derivative **13** can also be used as a substrate

In a similar manner, bromovinyl adenine nucleosides (**17** and **18**) were subjected to the cross-coupling reaction to afford **25-32** The results are summarized in Table 2 The reactions with terminal alkynes (entries 1, 2, 7, and 8) gave the respective products in good yields It should be mentioned that, when these reactions were conducted for a longer reaction time, formation of adenine was observed Although readily transferable tin ligands such as vinyl and allyl (entries 3, 4, 9, and 10) can be introduced to the 3'- or 2'-position, none of 3'-*C*-substituted product was obtained when **17** was reacted with Ph_4Sn or Me_4Sn (entries 5 and 6)



25 R= C≡CPh
26 R= C≡CSiMe$_3$
27 R= CH=CH$_2$
28 R= CH$_2$CH=CH$_2$



29 R= C≡CPh
30 R= C≡CSiMe$_3$
31 R= CH=CH$_2$
32 R= CH$_2$CH=CH$_2$

Table 2. Palladium-catalyzed cross-coupling reactions of **17** and **18**.

Entry	Compd	Catalyst[a)]	Reagent (equiv)	Conditions	Product	Isolated yield (%)
1	**17**	A/CuI	PhC≡CH (15)	DMF/Et_3N 70 °C, 20 min	**25**	70
2	**17**	A/CuI	Me_3SiC≡CH (15)	DMF/Et_3N 50 °C, 20 min	**26**	42
3	**17**	A	$Bu_3SnCH=CH_2$(15)	DMF, 70 °C, 2 h	**27**	41
4	**17**	B	$Bu_3SnCH_2CH=CH_2$ (10)	benzene 100 °C, 24 h	**28**	21
5	**17**	A	Ph_4Sn (15)	dioxane 100 °C, 24 h	no reaction	
6	**17**	B[b)]	Me_4Sn (5)	dioxane reflux, 48 h	an intractable mixture	
7	**18**	A/CuI	PhC≡CH (15)	DMF/Et_3N 70 °C, 20 min	**29**	64
8	**18**	A/CuI	Me_3SiC≡CH (15)	DMF/Et_3N 70 °C, 40 min	**30**	92
9	**18**	A	$Bu_3SnCH=CH_2$(15)	DMF, 70 °C, 2 h	**31**	72
10	**18**	B	$Bu_3SnCH_2CH=CH_2$ (10)	benzene 100 °C, 18 h	**32**	97

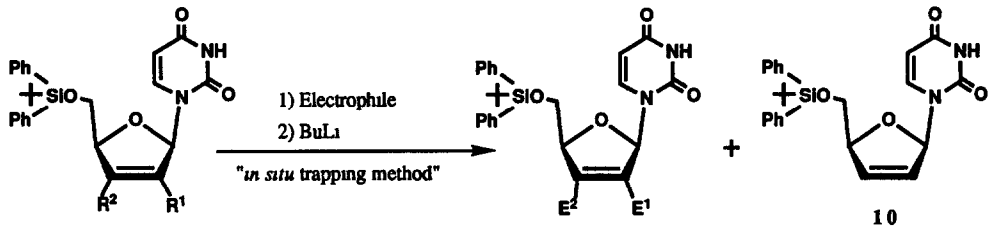
[a)] Catalysts A and B refer to $(Ph_3P)_2PdCl_2$ and $(Ph_3P)_4Pd$, respectively
All experiments were carried out by using 10 mol% of the catalyst
[b)] This particular reaction was carried out in the presence of 30 mol% of B

HALOGEN-LITHIUM EXCHANGE OF THE BROMOVINYL NUCLEOSIDES

Halogen-lithium exchange reaction was investigated in detail by using 3'-bromo-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyuridine (**12**) as a substrate When **12** was treated with 2 equiv of BuLi in THF below –70 °C for 10 min and quenched with AcOH, the 2',3'-didehydro-2',3'-dideoxy derivative **10** was formed (31%) along with uracil (52%) Similar treatment of **12** with 1 equiv of BuLi gave again both **10** and uracil in much the same yields (**10**, 27% and uracil, 49%) as those in the first experiment. The latter experiment suggests that the halogen-lithium exchange reaction is an earlier event than the anticipated deprotonation from N^3H [31,32] Since the most likely pathway of the observed formation of uracil can be δ-elimination (between 1'- and 4'-positions) and since uracil was formed even by the use of 1 equiv of BuLi , we assume that a considerable amount of the vinyllithium intermediate would be protonated, not only with N^3H but also with H-4', before quenching with AcOH

When **12** was lithiated under the above conditions (2 equiv. of BuLi for 10 min) and then allowed to react with benzaldehyde (5 equiv), the desired 3'-*C*-substituted product (**33**) was not formed even in a trace amount, but instead, a 55% yield of **10** was isolated together with uracil In contrast to this, addition of

benzaldehyde immediately after the lithiation did produce **33**, albeit in low yield (8%). Based on these observations, we reasoned that the vinyllithium intermediate generated from **12** is highly basic and thus would be protonated before reacting with the added electrophile. It should be mentioned that, under these conditions, neither C-5 nor C-6 position of the base moiety had been lithiated as evidenced by ^{1}H NMR spectrum of **10** obtained upon quenching of the lithiated reaction mixture with MeOD



12 R^1= H, R^2= Br
13 R^1= Br, R^2= H

33 E^1= H, E^2= CH(OH)Ph
23 E^1= H, E^2= Me
34 E^1= H, E^2= CH(OH)CHMe$_2$
35 E^1= CH(OH)Ph, E^2= H
36 E^1= Me, E^2= H

10

Scheme 2

We finally found that an "*in situ* trapping method" gave a synthetically valuable yield of **33** That is, when a hexane solution of BuLi was added dropwise to a mixture of **12** and benzaldehyde (10 equiv) in THF below –70 °C, **33** was isolated in 84% yield. It was neccessaryt to use 8 equiv of BuLi to assure complete disappearence of the starting materail Diastereomeric ratio of **33** was determined to be *ca* 1 1 by inspecting the integrated ^{1}H NMR spectrum Although formation of uracil was completely suppressed by using this method, an 8% yield of **10** was inevitably formed as shown in Table 3 (entry 1) As an electrophilic trap, MeI (entry 2) and Me_2CHCHO (entry 3) can also be used to give satisfactory yields of products (**23** and **34**, respectively) In a similar manner, 2'-*C*-branched products **35** and **36** were synthesized from **13** through the reaction with PhCHO (entry 4) and MeI (entry 5) When the two vinyllithium intermediates, generated from

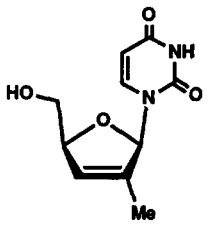
Table 3. Halogen-lithium exchange reactions of **12** and **13** by *in situ* trapping method [a)]

Entry	Compd	Electrophile[b)]	BuLi (equiv)	Isolated yield (%)	Value of Product / **10**
1	**12**	PhCHO	8	**33** (84), **10** (8)	10 5
2	**12**	MeI	3 5	**23** (53), **10** (19)	2 8
3	**12**	Me_2CHCHO	8	**34** (75), **10** (4)	18 8
4	**13**	PhCHO	8	**35** (54), **10** (23)	2 3
5	**13**	MeI	3 5	**36** (38), **10** (38)	1 0

[a)] All reactions were carried out below -70 °C in THF
[b)] Amount of electrophile 10 equiv

12 and 13, are compared within the same electrophile, there can be seen a trend that the latter produces a lower yield of *C*-substituted product with an increased yield of **10** As a result, ratios of the product and **10** listed in Table 3 are significantly smaller in the cases of the latter.

Desilylation of **36** was carried out in a conventional way (TBAF in THF, at room temperature) to give **37** in high yield. The ^{1}H NMR data of **37** in $CDCl_3$ were fully in accord with those previously reported by Wu and Chattopadhyaya,[10c] which gave confirmation regarding the regiochemistry of the bromovinyl derivatives **12** and **13**



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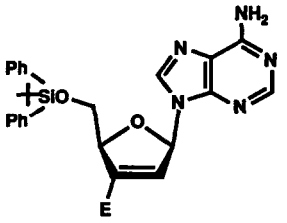

38 E= CH(OH)Ph
39 E= H
40 E= CH(OAc)Ph

We next examined synthesizing adenine counterparts by applying the above mentioned *in situ* trapping method When a THF solution of the 3'-bromovinyl derivative **17** and PhCHO (10 equiv.) was treated with portionwise addition of BuLi (total 10 equiv), TLC analysis ($CHCl_3$ EtOH = 15 1) of the reaction mixture indicated that neither the expected 3'-*C*-substituted product (**38**) nor the 2',3'-didehydro-2',3'-dideoxy derivative (**39**) was formed Quite different from the case of the uracil nucleoside, the greater part of **17** remained intact. We also found that the use of more than 10 equiv of BuLi in this reaction gave a complex mixture of products. Although no clear explanation is available at present, this fact may suggest that **17** would be less reactive than PhCHO toward BuLi When **17** was first treated with BuLi (2 equiv.) and then with PhCHO (5 equiv), **38** was obtained in 27% yield along with unreacted **17** (19%), **39** (34%), and a small amount of adenine The structure of **38** was fully characterized by converting to the two diastereomeric acetates (**40**) Use of 3 equiv of BuLi in the above halogen-lithium exchange reaction led to complete consumption of **17** but the yield of **38** remained much the same (28%) [33]

CONCLUSION

The palladium-catalyzed cross coupling and halogen-lithium exchange reactions investigated in the present study have provided a highly general synthetic approach to 2'-*C*- and 3'-*C*-branched 2',3'-unsaturated nucleosides, utilizing the bromovinyl derivatives as common starting materials Removal of the 5'-*O*-*tert*-butyldiphenylsilyl group of the compounds synthesized in this study can be carried out by the procedure used for the preparation of **37**. Since these nucleoside derivatives are expected to serve as promising anti-HIV candidates, the present methods will find growing application in this field.[34] Biological results of the free nucleosides will be reported elsewhere in due course.

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EXPERIMENTAL SECTION

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H-NMR spectra were measured at 23 °C (internal standard, Me_4Si) either with a JEOL JNM-FX 100 or with a JEOL JNM-GX 400 spectrometer Mass spectra were taken either on a JEOL JMS-D 300 in electron impact mode or on a JEOL SX-102A spectrometer in fast-atom-bombardment (FAB) mode (*m*-nitrobenzyl alcohol as a matrix). Ultraviolet spectra (UV) were recorded on a JASCO Ubest-55 spectrophotometer. Commercially available hexane solution of BuLi was titrated before use with diphenylacetic acid in THF THF was distilled from benzophenone ketyl Column chromatography was carried out on silica gel (Wakogel® C-200) Thin layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck)

1-(3-Deoxy-3-phenylseleno-2,5-di-*O*-pivaloyl-β-D-xylofuranosyl)uracil (8) To a solution of $(PhSe)_2$ (2 50 g, 8 0 mmol) in EtOH (20 mL), $NaBH_4$ (606 mg, 16 0 mmol) was added portionwise under atmosphere of dry Ar To the resulting colorless solution, a THF (20 mL) solution of **7** (4 90 g, 10 0 mmol) was added and the mixture was refluxed for 48 h. After being neutralized with 10% AcOH in MeOH, the reaction mixture was evaporated to dryness and the whole residue was chromatographed on a silica gel column (1% EtOH in $CHCl_3$) This gave **8** (2 05 g, 81%), which was crystallized from EtOAc-hexane (mp 158-160 °C) UV (MeOH) λ_{max} 264 nm (ε 13100), ^{1}H NMR ($CDCl_3$) δ 1 16 and 1 27 (18H, each as s, $COCMe_3$), 3 90 (1H, t, $J_{2',3'} = J_{3',4'} = 6$ 4 Hz, H-3'), 4 52 (2H, m, H-5'), 4 65 (1H, m, H-4'), 5 38 (1H, dd, $J_{1',2'} = 4$ 9 Hz, H-2'), 5 78 (1H, dd, $J_{5,6} = 8$ 1, $J_{5,NH} = 2$ 2 Hz, H-5), 5 93 (1H, d, H-1'), 7 31-7 34 (3H, m, SePh), 7 51-7 68 (3H, m, H-6 and SePh), 8 46 (1H, br, NH), MS *m/z* 552 and 550 (M^+) *Anal* Calcd for $C_{25}H_{32}N_2O_7Se$ C, 54 45, H, 5 85, N, 5 08 Found C, 54 55, H, 5 86, N, 4 99

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-3-phenylseleno-β-D-xylofuranosyl]uracil (9) A mixture of **8** (536 mg, 0.97 mmol) and aqueous N NaOH (4 mL) in EtOH (4 mL) was stirred for 24 h. After being neutralized with aqueous N HCl, the reaction mixture was evaporated to dryness and the whole residue was chromatographed on a silica gel column (5% EtOH in $CHCl_3$) The eluate was evaporated to dryness and the residue was treated with TBDPSCl (0 63 mL, 2 42 mmol) in pyridine (3 mL) for 24 h. The reaction mixture was evaporated and chromatographed on a silica gel column (2.5% EtOH in $CHCl_3$). This gave **9** (576 mg, 96%) as a foam which was analytically pure UV (MeOH) λ_{max} 265 nm (ε 11700), ^{1}H NMR ($CDCl_3$, after addition of D_2O) δ 1 11 (9H, s, Bu-*t*), 3 80 (1H, t, $J_{2',3'}$= $J_{3',4'}$= 6.4 Hz, H-3'), 4 04 (2H, m, H-5'), 4 43 (1H, dd, $J_{1',2'}$= 3 8 Hz, H-2'), 4 62 (1H, m, H-4'), 5 40 (1H, d, $J_{5,6}$= 8.4 Hz, H-5), 5 69 (1H, d, H-1'), 7 21-7 25 (2H, m, SePh), 7 38-7 51 (9H, SiPh and SePh), 7 65-7 74 (5H, m, SiPh and H-6), MS *m/z* 622 (M^+), 565 (M^+–Bu-*t*) *Anal* Calcd for $C_{31}H_{34}N_2O_5SeSi$ C, 59 89, H, 5 51, N, 4 51 Found C, 59 67; H, 5 54, N, 4 36

3'-Bromo-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyuridine (12), 2'-Bromo-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyuridine (13), and 5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyuridine (10) To a suspension of imidazole (102 mg, 1 50 mmol) in CCl_4 (3 mL), distilled $SOBr_2$ (194 μL, 2 50 mmol) was added dropwise with stirring at 0 °C under positive pressure of dry Ar After 30 min, a solution of **9** (311 mg, 0 5 mmol) in CCl_4 (3 mL) was added and the mixture was gradually allowed to warm to room temperature over 6 h After being quenched with cold aqueous saturated $NaHCO_3$, the reaction mixture was extracted with cold CH_2Cl_2 (70 mLx3) The resulting CH_2Cl_2 solution containing **11** was dried (Na_2SO_4) and filtered The filtrate was treated with MCPBA (173 mg, 1 0 mmol) at room temperature overnight and partitioned between $CHCl_3$ and aqueous 0 1 N $Na_2S_2O_3$ The organic layer was further washed with aqueous saturated $NaHCO_3$ and chromatographed on a silica gel column (hexane EtOAc = 3 1) This gave **13** (101 mg, 38%), **12** (111 mg, 42%), and **10** (20 mg, 9%) Compound **12** was crystallized from hexane-EtOAc (mp 175-178 °C) UV (MeOH) λ_{max} 259 nm (ε 8900), ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s, SiBu-*t*), 3 87 and 3 98 (2H, each as dd, J_{gem}= 11.7, $J_{4',5'}$= 2 9 Hz, H-5'), 4 85 (1H, m, H-4'), 5 24 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 1 8 Hz, H-5), 6 36 (1H, m, H-3'), 6.96 (1H, m, H-1'), 7 37-7 47 (6H, m, SiPh), 7 57-7 67 (5H, m, SiPh and H-6), 9.36 (1H, br, NH), MS *m/z* 471 and 469 (M^+–Bu-*t*), 359 and 357 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{25}H_{27}BrN_2O_4Si$ C, 56 93, H, 5 16, N, 5 31 Found C, 56 97, H, 5 29, N, 5 04 Compound **13** was obtained as an analytically pure foam UV (MeOH) λ_{max} 260 nm (ε 9200), ^{1}H NMR ($CDCl_3$) δ 1 10 (9H, s, SiBu-*t*), 4 07 (2H, m, H-5'), 4 78 (1H, m, H-4'), 4 87 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 1 8 Hz, H-5), 6 06 (1H, m, H-2'), 7 00 (1H, m, H-1'), 7 35-7 46 (6H, m, SiPh), 7 55-7 68 (4H, m, SiPh), 7 80 (1H, d, H-6), 9 53 (1H, br, NH), MS *m/z* 471 and 469 (M^+–Bu-*t*), 359 and 357 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{25}H_{27}BrN_2O_4Si$ C, 56 93, H, 5 16, N, 5 31 Found· C, 56 98, H, 5 32, N, 5 21 Compound **10** was obtained as an analytically pure solid UV (MeOH) λ_{max} 260 nm (ε 10200), ^{1}H NMR ($CDCl_3$) δ 1 07 (9H, s, SiBu-*t*), 3 87 and 3 98 (2H, each as dd, J_{gem}= 11 7, $J_{4',5'}$= 3 3, 2 9 Hz, H-5'), 4 90 (1H, m, H-4'), 5 21 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 1 8 Hz, H-5), 5 86 (1H, m, H-2'), 6 30 (1H, m, H-3'), 7 03 (1H, m, H-1'), 7 36-7 47 (6H, m, SiPh), 7 59-7 68 (5H, m, H-6 and SiPh), 9 22 (1H, br, NH), MS *m/z* 391 (M^+–Bu-*t*) *Anal* Calcd for $C_{25}H_{28}N_2O_4Si\,H_2O$ C, 64 35, H, 6 48, N, 6 00 Found C, 64 11, H, 6 19, N, 5 95

2',3'-Anhydro-5'-*O*-(*tert*-butyldiphenylsilyl)adenosine (15) To a solution of **14** (8 0 g, 32 1 mmol) in pyridine (120 mL), TBDPSCl (21 mL, 80.0 mmol) was added and the mixture was stirred at room temperature overnight After being quenched with aqueous saturated $NaHCO_3$, the reaction mixture was extracted with $CHCl_3$ The extract was evaporated to dryness and the residue was chromatographed on a silica gel column (6% EtOH in $CHCl_3$). This gave **15** (11 9 g, 76%) as an analytically pure foam. UV (MeOH) λ_{max} 260 nm (ε 12300), $\lambda_{shoulder}$ 296 nm (ε 2600); ^{1}H NMR ($CDCl_3$) δ 1 03 (9H, s, SiBu-*t*), 3 73 and 3 85 (2H, each as dd, J_{gem}= 10 8, $J_{4',5'}$= 5 5, 7.0 Hz, H-5'), 4.12 (1H, m, H-4'), 4.39-4 42 (2H, m, H-2' and H-3'), 5 65 (2H, br, NH_2), 6 15 (1H, s, H-1'), 7 30-7 46 (3H, m, SiPh), 7.54-7.62 (2H, m, SiPh), 7.90 and 8.24 (2H, each as s, H-8 and H-2) , MS *m/z* 430 (M^+–Bu-*t*) *Anal* Calcd for $C_{26}H_{29}N_5O_3Si$ 1/4H_2O: C, 63 45, H, 6 04, N, 14 23 Found· C, 63.59, H, 6.07; N, 14 37.

9-[5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-3-phenylseleno-β-D-xylofuranosyl]adenine (16) To a solution of $(PhSe)_2$ (4 61 g, 14 8 mmol) in dioxane (20 mL), $LiAlH_4$ (426 mg, 11 2 mmol) was added portionwise under atmosphere of dry Ar and the mixture was stirred until a colorless suspension resulted A dioxane (45 mL) solution of **15** (3 0 g, 6.2 mmol) was added to the above mixture and the reaction was conducted first at room temperature for 1 h and then at 60-70 °C for 3.5 h After neutralization with 10% AcOH in MeOH, the reaction mixture was evaporated and the residue was chromatographed on a silica gel column (4% EtOH in $CHCl_3$) This gave **16** (3.4 g, 86%) as a pale yellow foam. UV (MeOH) λ_{max} 262 nm (ε 17200), ^{1}H NMR ($CDCl_3$) δ 0 92 (9H, s, SiBu-*t*), 3 97-4.00 (2H, m, H-3' and H-5'a), 4.08 (1H, dd, J_{gem}= 11 7, $J_{4',5'}$= 2 9 Hz, H-5'b), 4 68 (1H, m, H-4'), 4 98 (1H, dd, $J_{1',2'}$= 5.5 , $J_{2',3'}$= 9 2 Hz, H-2'), 5 78 (1H, d, H-1'), 6 63 (2H, br, NH_2), 7 27-7 71 (15H, m, SePh and SiPh), 8 03 and 8.26 (2H, each as s, H-8 and H-2), MS *m/z* 588 (M^+–Bu-*t*) *Anal.* Calcd for $C_{32}H_{35}N_5O_3SeSi$· C, 59 62, H, 5.47, N, 10 86. Found C, 59 52; H, 5 50; N, 10 87

3'-Bromo-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyadenosine (17) and 2'-Bromo-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyadenosine (18) These compounds were prepared from **16** by the procedure described for the preparation of **12** and **13** from **9** The following amounts of reagents and **16** (519 mg, 0 80 mmol) in CCl_4 (13 mL) were used: imidazole (57 mg, 0 83 mmol) in CCl_4 (5 mL), $SOBr_2$ (180 μL, 2 32 mmol), and MCPBA (214 mg, 1.24 mmol) The bromination and selenoxide elimination were conducted at 0 °C for 2 h and at room temperature overnight, respectively Silica gel column chromatography (hexane·EtOAc = 1 1~1 4) gave **18** (145 mg, 33%) and then **17** (180 mg, 41%) Compoun **17** was obtained as an analytically pure foam UV (MeOH) λ_{max} 261 nm (ε 12100), ^{1}H NMR ($CDCl_3$) δ 1 08 (9H, s, SiBu-*t*), 3 98 (2H, d, H-5'), 4 90 (1H, m, H-4'), 6.09 (2H, br, NH_2), 6 28 (1H, m, H-2'), 7 05 (1H, dd, *J*= 1 5, 3 4 Hz, H-1'), 7 26-7.40 (6H, m, SiPh), 7 54-7 62 (4H, m, SiPh), 8 08 and 8 37 (2H, each as s, H-8 and H-2), MS *m/z* 494 and 492 (M^+–Bu-*t*) *Anal.* Calcd for $C_{26}H_{28}BrN_5O_2Si$ C, 56 72, H, 5 13, N, 12 72 Found C, 56 68, H, 5 13, N, 12 43 Compound **18** was obtained as an analytically pure foam UV (MeOH) λ_{max} 261 nm (ε 14700), ^{1}H NMR ($CDCl_3$) δ 1.08 (9H, s, SiBu-*t*), 3 86 (2H, d, H-5'), 4 97 (1H, m, H-4'), 5 78 (2H, br, NH_2), 6.50 (1H, m, H-3'), 6 91 (1H, dd, *J*= 1 8, 3 3 Hz, H-1'), 7 31-7 46 (6H, m, SiPh), 7 59-7 63 (4H, m, SiPh), 7 88 and 8 34 (2H, each as s, H-8 and H-2), MS *m/z* 494 and 492 (M^+–Bu-*t*) *Anal* Calcd for $C_{26}H_{28}BrN_5O_2Si$ C, 56 72, H, 5 13, N, 12 72 Found C, 56 45, H, 5 20, N, 12 33

Preparation of 5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(phenylethynyl)uridine (19) by palladium-catalyzed cross-coupling (a typical procedure) To a mixture of **12** (27.5 mg, 0 05 mmol), $(Ph_3P)_2PdCl_2$ (3.5 mg, 10 mol%), and CuI (1.0 mg, 10 mol%) in DMF (1 5 mL), phenylacetylene (22 9 μL, 0.20 mmol) and Et_3N (0.1 mL) were added and the mixture was stirred at 80 °C for 5 h under positive pressure of dry Ar. After evaporation of the solvent, the residue was chromatographed on a silica gel column (10% EtOH in $CHCl_3$). The resulting crude product was further purified by preparative TLC (benzene EtOAc = 5 1) This gave **19** (19.4 mg, 68%) as a syrup. UV (MeOH) λ_{max} 261 (ε 25200), 273 (ε 32600), and 290 nm (ε 24300), ^{1}H NMR ($CDCl_3$) δ 1 08 (9H, s, SiBu-*t*), 4 10 and 4 15 (2H, each as dd, J_{gem}= 12.1, $J_{4',5'}$= 1 5, 2 2 Hz, H-5'), 4 91 (1H, m, H-4'), 4.98 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2 2 Hz, H-5), 6 11 (1H, m, H-2'), 7 14 (1H, m, H-1'), 7 25-7 46 (11H, m, Ph and SiPh), 7 57-7 67 (4H, m, SiPh), 7 87 (1H, d, H-6), 8 31 (1H, br, NH), MS *m/z* 491 (M^+–Bu-*t*). *Anal.* Calcd for $C_{33}H_{32}N_2O_4Si$ 1/4H_2O C, 71 64, H, 5 92, N, 5 06 Found· C, 71.56, H, 6 19, N, 4 73.

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(trimethylsilylethynyl)uridine (20) This compound was obtained as a syrup (191 4 mg) from **12** (300 mg). UV (MeOH) λ_{max} 236 (ε 18300) and 248 nm (ε 18700), $\lambda_{shoulder}$ 258 nm (ε 12900), ^{1}H NMR ($CDCl_3$) δ 0 24 (9H, s, $SiMe_3$), 1 10 (9H, s, SiBu-*t*), 4 05 and 4 13 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 1 5, 2 2 Hz, H-5'), 4.78 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2 2 Hz, H-5), 4 82 (1H, m, H-4'), 6 05 (1H, m, H-2'), 7 09 (1H, m, H-1'), 7 34-7 44 (6H, m, SiPh), 7 56-7 73 (4H, m, SiPh), 7 72 (1H, d, H-6), 8.56 (1H, br, NH), MS *m/z* 487 (M^+–Bu-*t*), 375 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{30}H_{36}N_2O_4Si_2$ 1/2H_2O C, 65 06; H, 6.74, N, 5 06 Found C, 65 30; H, 6 69, N, 4 91

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-vinyluridine (21) This compound was obtained as a syrup (14 4 mg) from **12** (43 4 mg) UV (MeOH) λ_{max} 260 nm (ε 9900), ^{1}H NMR ($CDCl_3$) δ 1 05 (9H, s, SiBu-*t*), 4 04 and 4 09 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2.8, 1 8 Hz, H-5'), 5 00-5 03 (2H, m, H-4' and H-5), 5 31 and 5 34 (2H, each as d, *J*= 11 4, 17 6 Hz, CH=C$\underline{H}_2$), 5 79 (1H, s, H-2'), 6 50 (1H, dd, C$\underline{H}$=CH_2), 6 99 (1H, m, H-1'), 7.35-7 48 (6H, m, SiPh), 7 51-7 77 (4H, m, SiPh), 7 82 (1H, d, $J_{5,6}$= 8 1 Hz, H-6), 8 74 (1H, br, NH), MS *m/z* 417 (M^+–Bu-*t*). *Anal* Calcd for $C_{27}H_{30}N_2O_4Si$ 1/2H_2O· C, 67 05, H, 6 46, N, 5 79 Found C, 67 20, H, 6 58, N, 5 48

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-phenyluridine (22) This compound was obtained as a syrup (11 6 mg) from **12** (30 0 mg) UV (MeOH) λ_{max} 257 nm (ε 21800), ^{1}H NMR ($CDCl_3$) δ 0 86 (9H, s, SiBu-*t*), 4 00 and 4 08 (2H, each as dd, J_{gem}= 12.1, $J_{4',5'}$= 2 6, 1 1 Hz, H-5'), 5 10 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2 2 Hz, H-5), 5.36 (1H, m, H-4'), 6 04 (1H, m, H-2'), 7 14 (1H, m, H-1'), 7 23-7 47 (15H, m, SiPh and Ph), 8 01 (1H, d, H-6), 8 20 (1H, br, NH), FAB-MS *m/z* 467 (M^+–Bu-*t*) *Anal* Calcd for $C_{31}H_{32}N_2O_4Si$ 1/4H_2O C, 70 36, H, 6 19, N, 5 29 Found C, 70 23, H, 6 45, N, 4 97

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-methyluridine (23) This compound was obtained as a syrup (6.7 mg) from **12** (54 3 mg). UV (MeOH) λ_{max} 261 nm (ε 8300); ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s, SiBu-*t*), 1.91 (3H, d, *J*= 1 1 Hz, 3'-Me), 3.88 and 4 05 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2.2, 1 8 Hz, H-5'), 4 65 (1H, m, H-4'), 4 94 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2 2 Hz, H-5), 5 50 (1H, m, H-2'), 6.95 (1H, m, H-1'), 7.35-7.47 (6H, m, SiPh), 7 54-7 66 (4H, m, SiPh), 7 76 (1H, d, H-6), 8 66 (1H, br, NH), FAB-MS *m/z* 405 (M^+–Bu-*t*). *Anal.* Cacld for $C_{26}H_{30}N_2O_4Si$ 1/4H_2O: C, 66.85; H, 6.58, N, 6 00 Found: C, 66 95; H, 6.86, N, 5.78.

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-(phenylethynyl)-uridine (24) This compound was obtained as a syrup (38.0 mg) from **13** (50 7 mg). UV (MeOH) λ_{max} 259 (ε 23400), 272 (ε 26000), and 289 nm (ε 18800); ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s, SiBu-*t*), 3.90 and 3.97 (2H, each as dd, J_{gem}= 11.7, $J_{4',5'}$= 3 3 Hz, H-5'), 5.01 (1H, m, H-4'), 5.24 (1H, dd, $J_{5,6}$= 8.1, $J_{5,NH}$= 2 2 Hz, H-5), 6.49 (1H, m, H-3'), 7 04 (1H, m, H-1'), 7 29-7 48 (11H, m, Ph and SiPh), 7 59-7 67 (5H, m, SiPh and H-6), 8 66 (1H, br, NH), MS *m/z* 491 (M^+–Bu-*t*) *Anal* Calcd for $C_{33}H_{32}N_2O_4Si$ 1/2H_2O C, 71 07; H, 5 96; N, 5.02 Found C, 70 71; H, 6.05, N, 4 84

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(phenylethynyl)-adenosine (25) This compound was obtained as a foam (76 mg) from **17** (108.5 mg) UV (MeOH) λ_{max} 261 (ε 31000), 273 (ε 37800), and 289 nm (ε 25200), ^{1}H NMR ($CDCl_3$) δ 1 06 (9H, s, SiBu-*t*), 4.03 (2H, m, H-5'), 5 03 (1H, m, H-4'), 5 94 (2H, br, NH_2), 6 32 (1H, m, H-2'), 7.15-7 44 (7H, m, H-1' and SiPh), 7 58-7 63 (4H, m, SiPh), 8 14 and 8 39 (2H, each as s, H-8 and H-2), MS *m/z* 380 (M^+–B–Bu-*t*) *Anal.* Calcd for $C_{34}H_{33}N_5O_2Si$ C, 71 42, H, 5 82, N, 12 25 Found C, 71 11, H, 5 99, N, 12 06

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(trimethylsilylethynyl)adenosine (26) This compound was obtained as a syrup (35 mg) from **17** (81 mg) UV (MeOH) λ_{max} 235 (ε 20500), 247 (ε 22100), and 259 nm (ε 18400), ^{1}H NMR ($CDCl_3$) δ 0.23 (9H, s, $SiMe_3$), 1 07 (9H, s, SiBu-*t*), 3 97-3 98 (2H, m, H-5'), 4.95 (1H, m, H-4'), 6 00 (2H, br, NH_2), 6.26 (1H, m, H-3'), 7 16 (1H, m, H-1'), 7 24-7.61 (10H, m, SiPh), 7 98 and 8 37 (2H, each as s, H-8 and H-2); MS *m/z* 376 (M^+–B–Bu-*t*) *Anal* Calcd for $C_{31}H_{37}N_5O_2Si_2$ C, 65 57, H, 6 57, N, 12 34 Found C, 65 51, H, 6 85, N, 12 10

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-vinyladenosine (27) This compound was obtained as a syrup (62 mg) from **17** (166 mg) UV (MeOH) λ_{max} 260 nm (ε 15200), ^{1}H NMR ($CDCl_3$) δ 1 03 (9H, s, SiBu-*t*), 3 90 and 4 01 (2H, each as dd, J_{gem}= 11 7, $J_{4',5'}$= 4 0, 2 6 Hz, H-5'), 5 14 (1H, m, H-4'), 5 29 and 5 33 (2H, each as d, *J*= 17 2, 10 3 Hz, CH=CH_2), 5 97 (2H, br, NH_2), 6.01 (1H, m, H-2'), 6 52 (1H, dd, CH=CH_2), 7 07 (1H, m, H-1'), 7 24-7 56 (10H, m, SiPh), 8 05 and 8 37 (2H, each as s, H-8 and H-2), MS *m/z* 306 (M^+–B–Bu-*t*) *Anal* Calcd for $C_{28}H_{31}N_5O_2Si$ C, 67 58, H, 6 28, N, 14 07 Found C, 67 36, H, 6 58, N, 13 72

3'-Allyl-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyadenosine (28) This compound was obtained as a syrup (21.8 mg) from **17** (150.7 mg). UV (MeOH) λ_{max} 260 nm; ^{1}H NMR ($CDCl_3$) δ 1.07 (9H, s, SiBu-*t*), 2.89-3.07 (2H, m, $C\underline{H}_2CH=CH_2$), 3.79 and 3.93 (2H, each as dd, J_{gem}= 11 7, $J_{4',5'}$= 2 9, 3 3 Hz, H-5'), 4.82 (1H, m, H-4'), 5.09-5.18 (2H, m, $CH_2CH=C\underline{H}_2$), 5 69 (2H, br, NH_2), 5 75 (1H, m, H-2'), 5 86-5.90 (1H, m, $CH_2C\underline{H}=CH_2$), 7 03 (1H, m, H-1'), 7.27-7.83 (10H, m, SiPh), 8 03 and 8 38 (2H, each as s, H-8 and H-2); MS *m/z* 454 (M^+–Bu-*t*) HRMS (FAB), Calcd for $C_{29}H_{34}N_5O_2Si$ [MH^+]. *m/z* 512 2481 Found *m/z* 512.2458

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-(phenylethynyl)-adenosine (29) This compound was obtained as a foam (100 mg) from **18** (150.7 mg) UV (MeOH) λ_{max} 259, 265, 272, and 289 nm, ^{1}H NMR ($CDCl_3$) δ 1 08 (9H, s, SiBu-*t*), 3.80 and 3 87 (2H, each as dd, J_{gem}= 11 0, $J_{4',5'}$= 4.4, 5 1 Hz, H-5'), 5 12 (1H, m, H-4'), 6 03 (2H, br, NH_2), 6.64 (1H, m, H-3'), 7 06 (1H, m, H-1'), 7 23-7 68 (15H, m, SiPh and Ph), 7.93 and 8 38 (2H, each as s, H-8 and H-2), MS *m/z* 514 (M^+–Bu-*t*) HRMS (FAB), Calcd for $C_{34}H_{34}N_5O_2Si$ [MH^+]· *m/z* 572.2482 Found. *m/z* 572 2497

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-(trimethylsilyl-ethynyl)adenosine (30) This compound was obtained as a powder (142 mg) from **18** (149 8 mg) UV (MeOH) λ_{max} 237 (ε 20300) and 247 nm (ε 22300), $\lambda_{shoulder}$ 255 nm (ε 17000), ^{1}H NMR ($CDCl_3$) δ 0 08 (9H, s, $SiMe_3$), 1 06 (9H, s, SiBu-*t*), 3 74 and 3 83 (2H, each as dd, J_{gem}= 11 0, $J_{4',5'}$= 5 5, 4.8 Hz, H-5'), 5 05 (1H, m, H-4'), 5 97 (2H, br, NH_2), 6 60 (1H, m, H-3'), 6 96 (1H, m, H-1'), 7 29-7 70 (10H, m, SiPh), 7 85 and 8 36 (2H, each as s, H-8 and H-2), MS *m/z* 510 (M^+–Bu-*t*) *Anal* Calcd for $C_{31}H_{37}N_5O_2Si_2$ C, 65 57, H, 6 57, N, 12 33 Found C, 65 84, H, 6 80, N, 12 21

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-vinyladenosine (31) This compound was obtained as a foam (99 mg) from **18** (151.5 mg) UV (MeOH) λ_{max} 260 nm (ε 14600), ^{1}H NMR ($CDCl_3$) δ 1 07 (9H, s, SiBu-*t*), 3 76 and 3 84 (2H, each as dd, J_{gem}= 10 8, $J_{4',5'}$= 4 8, 5 1 Hz, H-5'), 4 88 and 5 11 (2H, each as d, *J*= 11 0, 18 0 Hz, $CH=C\underline{H}_2$), 5 01 (1H, m, H-4'), 5 76 (2H, br, NH_2), 6 30 (1H, m, H-3'), 6 44 (1H, dd, $C\underline{H}=CH_2$), 7 19 (1H, m, H-1'), 7 29-7 62 (10H, m, SiPh), 7 75 and 8 37 (2H, each as s, H-8 and H-2), MS *m/z* 440 (M^+–Bu-*t*) *Anal* Calcd for $C_{28}H_{31}N_5O_2Si$ C, 67.58, H, 6 28, N, 14 07 Found C, 67 69, H, 6 43, N, 13 80

2'-Allyl-5'-*O*-(*tert*-butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyadenosine (32) This compound was obtained as a foam (94 2 mg) from **18** (104 1 mg) UV (MeOH) λ_{max} 260 nm (ε 14700), ^{1}H NMR ($CDCl_3$) δ 1 08 (9H, s, SiBu-*t*), 2 71 (2H, m, $C\underline{H}_2CH=CH_2$), 3 84-3 85 (2H, m, H-5'), 4 96-5.06 (3H, m, H-4' and $CH_2CH=C\underline{H}_2$), 5 73 (1H, m, $CH_2C\underline{H}=CH_2$), 5 99 (1H, m, H-3'), 6.38 (2H, br, NH_2), 6 95 (1H, m, H-1'), 7 27-7 70 (10H, m, SiPh), 7 92 and 8 33 (2H, each as s, H-8 and H-2), MS *m/z* 454 (M^+–Bu-*t*) *Anal* Calcd for $C_{29}H_{33}N_5O_2Si$ C, 68 07, H, 6 50, N, 13 69. Found C, 68 16, H, 6.58, N, 13 34

General procedure for the halogen-lithium exchange reaction of 12 and 13. To a mixture of **12** or **13** (300 mg, 0.57 mmol) and an appropriate electrophile (5.7 mmol) in THF (10 mL), a hexane solution of BuLi was added dropwise (*ca* 2.5 mL/hr) under atmosphere of dry Ar, while maintaining the temperature below –70 °C. The reaction mixture was quenched with AcOH. The whole mixture was evaporated and chromatographed on a silica gel column (hexane-EtOAc) When neccessary, further purification of the product(s) was carried out by preparative TLC

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(phenyl)hydroxymethyluridine (33) This compound composed of two diastereomers (*ca* 1:1), each of which was isolated by preparative TLC (benzene·EtOAc = 3 1). Physical data of less polar isomer obtained as a syrup are given below UV (MeOH) λ_{max} 261 nm (ε 9100), ^{1}H NMR ($CDCl_3$) δ 1 14 (9H, s, SiBu-*t*), 2.89 (1H, br, OH), 4 08 and 4.14 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2 2 Hz, H-5'), 4 94-4 97 (2H, m, H-5 and H-4'), 5 36 (1H, s, C<u>H</u>(OH)Ph), 5 55 (1H, s, H-2'), 6 92 (1H, m, H-1'), 7 32-7 46 (11H, m, Ph), 7.57-7 59 (2H, m, Ph), 7 67-7 69 (3H, m, Ph and H-6), 8 80 (1H, br, NH), FAB-MS *m/z* 425 (M^+–B–H_2O), 385 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{32}H_{34}N_2O_5Si$ 1/3H_2O C, 68 54, H, 6 23, N, 5.00 Found C, 68 62, H, 6 39, N, 4 90 Physical data of more polar isomer obtained as a syrup are given below UV (MeOH) λ_{max} 260 nm (ε 10600), ^{1}H NMR ($CDCl_3$) δ 1 13 (9H, s, SiBu-*t*), 2 77 (1H, br, OH), 3 74 and 3 98 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2 2 Hz, H-5'), 4 37 (1H, m, H-4'), 5 16 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 1.8 Hz, H-5), 5.24 (1H, s, C<u>H</u>(OH)Ph), 5 94 (1H, d, $J_{1',2'}$= 1 1 Hz, H-2'), 7 01 (1H, m, H-1'), 7 07-7 10, 7 28-7 31, 7 38-7 51, 7 57-7 59, 7.68-7 72 (15H, each as m, Ph), 7 84 (1H, d, H-6), 8 97 (1H, br, NH), FAB-MS *m/z* 425 (M^+–B–H_2O), 385 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{32}H_{34}N_2O_5Si$· C, 69 29, H, 6 18, N, 5 05 Found C, 69 08, H, 6 28, N, 4 82

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-[(1-hydroxy-2-methyl)propyl]uridine (34) This compound composed of two diastereomers (*ca* 1 1), each of which was isolated by preparative TLC (1% EtOH in $CHCl_3$). Physical data of less polar isomer obtained as a syrup are given below. UV (MeOH) λ_{max} 261 nm (ε 8800), ^{1}H NMR ($CDCl_3$) δ 0 90 (3H d, *J*= 6 6 Hz, CH<u>Me</u>$_2$), 1 07-1 09 (12H, m, CH<u>Me</u>$_2$ and SiBu-*t*), 1 88 (1H, m, C<u>H</u>Me$_2$), 2 88 (1H, d, *J*= 5 9 Hz, OH), 4.00 and 4 07 (2H, each as dd, J_{gem}= 11 4, $J_{4',5'}$= 3 7, 2 4 Hz, H-5'), 4 13 (1H, t, *J*= 6.8 Hz, C<u>H</u>OH), 4 86 (1H, m, H-4'), 5 03 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 1 8 Hz, H-5), 5 67 (1H, s, H-2'), 6 93 (1H, m, H-1'), 7 36-7 46 (6H, m, SiPh), 7 55-7 66 (5H, m, H-6 and SiPh), 8 39 (1H, br, NH), FAB-MS *m/z* 521 (M^++1), 463 (M^+–Bu-*t*), 351 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{29}H_{36}N_2O_5Si$ 3/4H_2O. C, 65 20; H, 7 08, N, 5.24 Found C, 65 08, H, 6 94, N, 5.03 Physical data of more polar isomer obtained as a syrup are given below. UV (MeOH) λ_{max} 261 nm (ε 9400), ^{1}H NMR ($CDCl_3$) δ 0 84 and 0 97 (6H, each as d, *J*= 6 6 Hz, CH<u>Me</u>$_2$), 1 08 (9H, s, SiBu-*t*), 1 72 (1H, m, C<u>H</u>Me$_2$), 2 36 (1H, s, OH), 3 83 and 4 20 (2H, each as dd, J_{gem}= 11 7, $J_{4',5'}$= 2 6 Hz, H-5'), 4.20 (1H, m, C<u>H</u>(OH)CHMe$_2$), 4 70 (1H, m, H-4'), 5 12 (1H, d, $J_{5,6}$= 8 1 Hz, H-5), 5.78 (1H, d, $J_{1',2'}$= 1 5 Hz, H-2'), 7.00 (1H, m, H-1'), 7 35-7 46 (6H, m, SiPh), 7 55-7 66 (4H, m, H-6 and SiPh), 7 74 (1H, d, H-6), 9 48 (1H, br, NH), FAB-MS *m/z* 463 (M^+–Bu-*t*), 351 (M^+–B–Bu-*t*–1) *Anal.* Calcd for $C_{29}H_{36}N_2O_5Si$ 1/2H_2O C, 65 76, H, 7 04, N, 5 29 Found C, 65 70, H, 7 27, N, 4 99

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-(phenyl)hydroxymethyluridine (35) This compound was obtained as a foam, which composed of two inseparable diastereomers (*ca* 1:1) UV (MeOH) λ_{max} 261 nm (ε 9900), ^{1}H NMR ($CDCl_3$) δ 1 07 and 1 10 (9H, each as s, SiBu-*t*), 3 80 and 3 85 (1H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2 6 Hz, H-5'a), 4.00-4 03 (1H, m, H-5'b), 4 87 and 4 89 (1H, each as m, H-4'), 5 01 and 5 09 (1H, each as dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2.2 Hz, H-5), 5 21 and 5 44 (1H, each as s, CHOH), 6 00 and 6 13 (1H, each as d, *J*= 1 5 Hz, H-3'), 6 89 and 7 05 (1H, each as m, H-1'), 7 29-7 46 and 7 57-7.74 (16H, m, H-6, Ph, and SiPh), 7.85 and 7 91 (1H, each as br, NH); MS *m/z* 425 (M^+–B–H_2O), 385 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{32}H_{34}N_2O_5Si$ 5/4H_2O C, 66.58; H, 6 37, N, 4 85. Found C, 66 59, H, 6.03, N, 4 65

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-2'-methyluridine (36) This compound was obtained as a solid UV (MeOH) λ_{max} 260 nm (ε 9700), ^{1}H NMR ($CDCl_3$) δ 1 07 (9H, s, SiBu-*t*), 1 71 (3H, s, 2'-Me), 3 82 and 3 95 (2H, each as dd, J_{gem}= 11.7, $J_{4',5'}$= 3 3, 2 9 Hz, H-5'), 4.83 (1H, m, H-4'), 5 20 (1H, dd, $J_{5,6}$= 8.1, $J_{5,NH}$= 2 2 Hz, H-5), 5 86 (1H, dd, *J*= 1 5, 3.3 Hz, H-3'), 6 84 (1H, m, H-1'), 7 36-7 47 (6H, m, SiPh), 7 59-7 65 (5H, m, SiPh and H-6), 8 56 (1H, br, NH), MS *m/z* 405 (M^+–Bu-*t*), 293 (M^+–B–Bu-*t*–1) *Anal* Calcd for $C_{26}H_{30}N_2O_4Si$ 1/4H_2O C, 66 85, H, 6 58, N, 6 00 Found C, 67 09, H, 6 48, N, 5 77

2',3'-Didehydro-2',3'-dideoxy-2'-methyluridine (37) A THF (2 mL) solution of **36** (94 mg, 0 20 mmol) was treated with TBAF $3H_2O$ (83 4 mg, 0 26 mmol) at room temperature for 40 min. After evaporation of the solvent, the whole residue was chromatographed on a silica gel column (10% EtOH in $CHCl_3$) This gave **37** (41 9 mg, 92%) as an analytically pure solid. UV (MeOH) λ_{max} 260 nm (ε 9200), ^{1}H NMR ($CDCl_3$) δ 1 72 (3H, s, 2'-Me), 3 75 and 3.91 (2H, each as dd, J_{gem}= 12 1, $J_{4',5'}$= 2 9 Hz, H-5'), 4 88 (1H, m, H-4'), 5 70 (1H, dd, $J_{5,6}$= 8 1, $J_{5,NH}$= 2 2 Hz, H-5), 5 92 (1H, d, $J_{3',4'}$= 1 8 Hz, H-3'), 6 84 (1H, m, H-1'), 7 63 (1H, d, H-6), 8 34 (1H, br, NH); MS *m/z* 113 (M^+–B) *Anal* Calcd for $C_{10}H_{12}N_2O_4$ C, 53 57, H, 5 40, N, 12.49 Found C, 53 27, H, 5 34, N, 12.43

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxy-3'-(phenyl)hydroxymethyladenosine (38) and its two diastereomeric acetates (40) To a THF (2 mL) solution of **17** (54 1 mg, 0 098 mmol), under atmosphere of dry Ar, a hexane solution of BuLi (0 196 mmol) and PhCHO (60 μL, 0 588 mmol) were added successively while maintaining the temperature below –70 °C After 10 min, the reaction mixture was quenched by adding AcOH (12 μL) and the whole mixture was chromatographed on a silica gel column (8% EtOH in $CHCl_3$) This gave **38** (15 5 mg, 27%), **39** (15 1 mg, 34%), and **17** (10 1 mg, 19%) Compound **38** obtained as a syrup was characterized by ^{1}H NMR and MS spectroscopies ^{1}H NMR ($CDCl_3$) δ 1 09 (9H, s, SiBu-*t*), 3 73, 3 90, and 3 95 (2H, each as m, H-5'), 4.58 and 5 03 (1H, each as m, H-4'), 5 36, 5 62, 5 66, and 6 04 (2H, each as s, H-2' and CH(OH)Ph), 5 72 and 5 79 (2H, each as br, NH_2), 6 98 and 7 03 (1H, each as s, H-1'), 7 19-7 66 (15H, m, Ph), 7 95, 8 08, 8 31, and 8 33 (2H, each as s, H-8 and H-2), MS *m/z* 521 (M^+–Bu-*t*+1), 386 (M^+–B–Bu-*t*) Acetylation of **38** (Ac_2O in pyridine, room temperature, overnight) gave **40** as two diastereomers, each of which was isolated by preparative TLC ($CHCl_3$ EtOH = 15 1). Physical data of less polar isomer obtained in 33% yield as a syrup are given below UV (MeOH) λ_{max} 260 nm, ^{1}H NMR ($CDCl_3$) δ 1 09 (9H, s, SiBu-*t*), 2 03 (3H, s, OAc), 3 83 and 3 93 (2H,

each as dd, J_{gem}= 11.9, $J_{4',5'}$= 3.7, 2 2 Hz, H-5'), 5 11 (1H, m, H-4'), 5 58 (2H, br, NH_2), 5.60 (1H, m, H-2'), 6.56 (1H, s, CH(OAc)Ph), 7.04 (1H, m, H-1'), 7.22-7.57 (15H, m, Ph), 7.93 and 8.35 (2H, each as s, H-2 and H-8) HRMS (FAB), Calcd. for $C_{35}H_{38}N_5O_4Si$ [MH^+] *m/z* 620.2693 Found: *m/z* 620.2684. Physical data of more polar isomer obtained in 35% yield as a syrup are given below. UV (MeOH) λ_{max} 260 nm, ^1H NMR ($CDCl_3$) δ 1 11 (9H, s, SiBu-*t*), 2.10 (3H, s, OAc), 3.64 and 3 91 (2H, each as dd, J_{gem}= 11 7, $J_{4',5'}$= 2 9, 3 3 Hz, H-5'), 4.48 (1H, m, H-4'), 5.72 (2H, br, NH_2), 6.16 (1H, m, H-2'), 6.46 (1H, s, CH(OAc)Ph), 7.12 (1H, m, H-1'), 7.26-7 70 (15H, m, Ph), 8.20 and 8 39 (2H, each as s, H-2 and H-8) HRMS (FAB), Calcd. for $C_{35}H_{38}N_5O_4Si$ [MH^+]. *m/z* 620 2693. Found· *m/z* 620 2662

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-2',3'-dideoxyadenosine (39) This compound was obtained as an analytically pure powder UV (MeOH) λ_{max} 260 nm (ε 14700); ^1H NMR ($CDCl_3$) δ 1.06 (9H, s, SiBu-*t*), 3.84 (2H, m, H-5'), 5.04 (1H, m, H-4'), 6 08 and 6 45 (2H, each as m, H-2' and H-3'), 6.64 (2H, br, NH_2), 7 08 (1H, m, H-1'), 7.30-7 70 (10H, m, SiPh), 8.00 and 8 34 (2H, each as s, H-2 and H-8); MS *m/z* 414 (M^+–Bu-*t*) *Anal* Calcd for $C_{26}H_{29}N_5O_2Si$ C, 66 21, H, 6 20; N, 14 85 Found: C, 66.26, H, 6 40; N, 15 01

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26 For the preparation of **14**· (a) Robins, M J , Fouron, Y., Mengel, R *J Org Chem* **1974**, *39*, 1564-1570 (b) Robins, M J , Mengel, R , Jones, R A , Fouron, Y *J Am Chem Soc* **1976**, *98*, 8204-8213

27 When the 5'-hydroxyl group of **14** was protected with an acetyl group, reaction with $(PhSe)_2/LiAlH_4$ can be conducted at room temperature to give the corresponding 3'-selenide in 65% yield after 18 h

28 (a) Bergstrom, D E , Ogawa, M K *J Am Chem Soc* **1978**, *100*, 8106-8112 (b) Robins, M J , Barr, P J *J Org Chem* **1983**, *48*, 1854-1862 (c) Goodchild, J , Porter, R A , Raper, R H , Sim, I S , Upton, R M , Viney, J , Wadsworth, H J. *J Med Chem* **1983**, *26*, 1252-1257 (d) Tanaka, H , Haraguchi, K , Koizumi, Y , Fukui, M , Miyasaka, T *Can J Chem* **1986**, *64*, 1560-1563 (e) Nair, V , Turner, G A , Buenger, G S , Chamberlain, S D *J Org Chem* **1988**, *53*, 3051-3057 (f) Crisp, G T *Synth Commun* **1989**, *19*, 2117-2123

29 The ^{1}H NMR and MS data of this product are as follows. ^{1}H NMR ($CDCl_3$) δ 1 26 (3H, t, J= 7 0 Hz, $CO_2CH_2C\underline{H}_3$), 2 77 (2H, t, $NCH_2C\underline{H}_2CO_2Et$), 3 99 (2H, t, J= 5.9 Hz, $NC\underline{H}_2CH_2CO_2Et$), 4 16 (2H, q, $CO_2C\underline{H}_2CH_3$), 5 66 (1H, dd, $J_{5,6}$= 8.1, $J_{5,NH}$= 2 2 Hz, H-5), 7 39 (1H, d, H-6), 8 38 (1H, br, NH), MS *m/z* 212 (M^+), 167 (M^+–OEt), 138 (M^+–CO_2Et–1)

30 For a review. Stille, J K *Angew Chem Int Ed Engl* **1986**, *25*, 508-524

31 It has been reported that halogen-lithium exchange reaction takes place even in the presence of ^3H_2O or an intramolecular carboxylic group (a) Taylor, R *Tetrahedron Lett* **1975**, 435-436 (b) Sydnes, L K , Skare, S. *Can J Chem* **1984**, *62*, 2073-2078.

32 There have been arguments concerning whether halogen-lithium exchange is faster than loss of an acidic proton (a) Narasimhan, N S , Ammanamanchi, R *J Chem Soc Chem Commun* **1985**, 1368-1369 (b) Beak, P , Musick, T. J , Chen, C *J Am Chem Soc* **1988**, *110*, 3538-3542. (c) Narasimhan, N S , Sunder, N M ; Ammanamanchi, R , Bonde, B D *ibid* **1990**, *112*, 4431-4435 (d) Beak, P ; Allen, D J *ibid* **1992**, *114*, 3420-3425

33 Compound **39** was also isolated in a significantly decreased yield of 3% in this reaction. TLC analysis of the reaction mixture showed that formation of adenine became a dominant reaction pathway

34 Very recently, formation of 2',3'-unsaturated adenine and uracil nucleosides having a 2'-*C*-ethyl group has been reported through a radical-induced ring-opening of their 2'-spirocyclopropane derivatives Samano, V , Robins, M J *J Am Chem Soc* **1992**, *114*, 4007-4008