C-5-Substituted Pyrimidine Nucleosides. 3. Reaction of Allylic Chlorides, Alcohols, and Acetates with Pyrimidine Nucleoside Derived Organopalladium Intermediates

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The reaction of allylic chlorides with pyrimidine nucleoside derived organopalladium intermediates was investigated. The organopalladium intermediates were generated in situ by the reaction of 5-(chloromercuri)-2'-deoxyuridine (1), 5-(chloromercuri)cytidine, and 5-(chloromercuri)-2'-deoxycytidine with a catalytic amount of Li_2PdCl_4 in methanol. With allyl chloride, 1 gives principally 5-allyl-2'-deoxyuridine, some of which reacts further with 1 to give the cross-linked nucleosides (*E*)-5-[3-(2'-deoxyuridin-5-yl)-1-propen-1-yl]-2'-deoxyuridine (**5**) and 5-[3-(2'-deoxyuridin-5-yl)-1-methoxyprop-1-yl]-2'-deoxyuridine (**6**). 3-Chloro-1-butene couples with 1 to give mainly (*E*)-5-(2-buten-1-yl)-2'-deoxyuridine (**9**) and lesser amounts of the *Z* isomer **10** and 5-(1-methyl-2-propen-1-yl)-2'-deoxyuridine (**11**). Nucleoside **11** appears to be the product of a coupling reaction between 1-methoxy-2-butene and the organopalladium intermediate derived from 1. Allylic chlorides are transformed to allyl methyl ethers in 0.1 M Li_2PdCl_4 at a slightly slower rate than the coupling reaction. Higher allylic chloride homologues show greater regioselectivity and stereoselectivity. 3-Chloro-1-pentene leads to (*E*)-5-(2-penten-1-yl)-2'-deoxyuridine (**14**) as the sole major product in 50% yield. When a cyano group was attached to C-5 of 3-chloro-1-pentene, the resultant allylic chloride coupled regioselectivity but gave both cis and trans isomers. The mechanism of the coupling reaction is discussed and a basis for stereoselectivity proposed. Allylic alcohols and acetates couple more slowly and less cleanly, leading to lower yields of the same allylic-substituted pyrimidine nucleosides obtained with allylic chlorides. In some instances other products could be isolated. Nucleoside 1 and 3-hydroxy-4-methyl-1-pentene gave 5-(4-methyl-2-penten-1-yl)-2'-deoxyuridine (**16**) as well as 5-(4-methyl-3-oxopentyl)-2'-deoxyuridine (**20**). 3-Acetoxy-4-methyl-1-pentene led to (*E*)-5-(4-methyl-1,3-pentadien-1-yl)-2'-deoxyuridine (**23**). Mechanisms leading to these products are discussed.

The development of a route to C-5-substituted pyrimidine nucleosides based on the coupling of alkenes to nucleoside-derived organopalladium intermediates has been underway in our laboratory for a number of years. We recently described details for the synthesis of 5-allylcytosine and 5-allyluracil ribo- and deoxyribonucleosides from 5-mercuripyrimidine nucleosides, allyl chloride, and Li_2PdCl_4 in methanol.[1]

Two features of the allyl chloride coupling reaction, regioselectivity and the requirement for only catalytic amounts of palladium, led us to investigate further to determine the feasibility of utilizing allylic chlorides of the general structure CH_2=CHCHClR (R = alkyl or functionalized alkyl) in order to obtain nucleosides substituted at C-5 by CH_2CH=CHR. Simple alkenes of structures CH_2=$CHCH_2R$ (R = alkyl) generally led to complex mixtures of products and required a stoichiometric amount of Pd^{II}.[2]

Ideally, a coupling reaction was desired which would (1) be applicable to the synthesis of complex functionalized side chains, (2) be regiospecific, with addition occurring only at C-1 of terminal alkenes, (3) yield a single product (olefins such as 4-hydroxy-1-pentene add regioselectivity at C-1 but subsequently lead to both olefinic and α-methoxy-derived side chains[2]), and (4) be catalytic in palladium. In the present paper we describe not only developments in this direction (utilization of allylic chlorides) but also efforts to exploit the more readily available allylic alcohols and acetates. Specifically we wished to develop methodology which would allow synthesis of pyrimidine and pyrrolo[2,3-*d*]pyrimidine nucleosides and nucleotides substituted by variable-length alkyl chains linked to functional groups intended as reacting and/or reporting probes for biological macromolecules and allow directed regioselective substitution at the polynucleotide level. The palladium-catalyzed coupling of allylic chlorides has been studied by others but not extensively.

Heck[3] and Larock[4] investigated the coupling of arylmercurials and vinylmercurials, respectively, to allylic halides as catalyzed by LiCl and $PdCl_2$. The reactions were generally highly specific. For example, phenylmercuric chloride, 3-chloro-1-butene, and a catalytic amount of $LiPdCl_3$ in acetonitrile gave 1-phenyl-2-butene (eq 1). Allylic chlorides longer than four carbons were not included in these studies.

$$CH_2{=}CH{-}CHClCH_3 + PhHgCl \xrightarrow[CH_3CN]{LiPdCl_3} PhCH_2CH{=}CHCH_3 \quad (1)$$

Results and Discussion

Allylic Chloride Coupling. Preliminary to a full investigation of coupling reactions of higher allylic chlorides, the reaction of allyl chloride was examined in further detail. Previously we reported that allyl chloride and 5-(chloromercuri)-2'-deoxyuridine (1) with 20 mol % of Li_2PdCl_4 in methanol gave a single major product, 5-allyl-2'-deoxyuridine (**3**).[1] Further investigation of the reaction showed two additional products running at low R_f on silica gel thin-layer chromatography. One of these was established to be (*E*)-5-[3-(2'-deoxyuridin-5-yl)-1-propen-1-yl]-2'-deoxyuridine (**5**), and the other was tentatively identified as 5-[3-(2'-deoxyuridin-5-yl)-1-methoxyprop-1-yl]-2'-deoxyuridine (**6**, Scheme I). The combined yield was 12%. Both products are formed logically via coupling of 5-allyl-2'-deoxyuridine to the organopalladium species **2** to give intermediate **4** which can either eliminate HPdCl to give **5** or, following a pathway observed previously,[2] give **6**.

In an experiment to determine the possible intermediacy of a π-allyl complex, $[(\pi\text{-}C_3H_5)PdCl]_2$[5] was combined with

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(1) Ruth, J. L.; Bergstrom, D. E. *J. Org. Chem.* **1978**, *43*, 2870.
(2) Bergstrom, D. E.; Ogawa, M. K. *J. Am. Chem. Soc.* **1978**, *100*, 8106.
(3) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5531.
(4) Larock, R. C.; Bernhardt, J. C.; Driggs, R. J. *J. Organomet. Chem.* **1978**, *156*, 45-54.
(5) Hartley, F. R.; Jones, S. R. *J. Organomet. Chem.* **1974**, *66*, 465.

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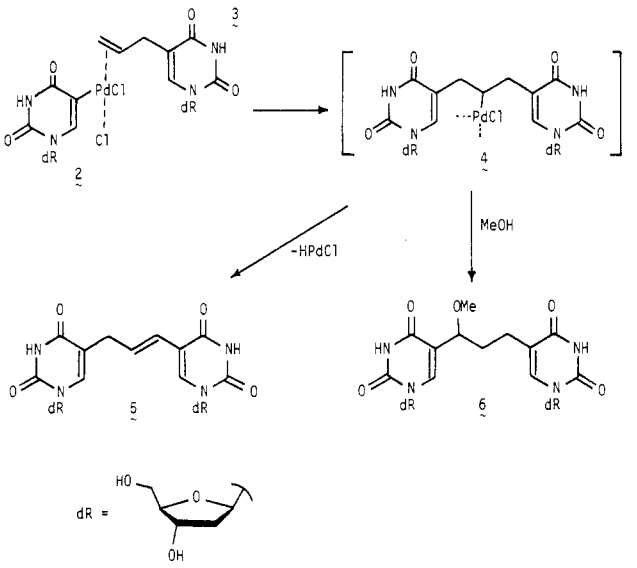
Scheme I



1 in methanol. Nucleosides **5** and **6** were obtained in a combined yield of 20%, but no 5-allyl-2′-deoxyuridine could be detected. Apparently $[(\pi\text{-}C_3H_5)PdCl]_2$ either couples at a significantly slower rate than allyl chloride or is slowly converted in situ to allyl chloride (or an equivalent species such as allyl methyl ether). The reaction of **2** with **3** would then predominate.

The next higher homologue, 3-chloro-1-butene, proved a useful model in a study of problems in regioselectivity. When pure 3-chloro-1-butene (97% by GLC) was allowed to react with 5-(chloromercuri)-2′-deoxyuridine (**1**) in 0.1 M Li_2PdCl_4 in methanol, three products, (*E*)- and (*Z*)-5-(2-buten-1-yl)-2′-deoxyuridines (**9** and **10**) and 5-(1-methyl-2-propen-1-yl)-2′-deoxyuridine (**11**), were formed in a ratio of 6:3:1 (Scheme II). Nucleoside **11** was not isolated but was considered the best fit on the basis of the doublet (J = 7 Hz) at 1.13 ppm in the combined spectrum of nucleosides **9**–**11**. The ratio of *E* to *Z* isomers could not be established by ^1H NMR at 100 NHz since the olefinic protons of both isomers fell at nearly identical chemical shifts. At 360 MHz the allylic methylene groups were distinguishable, but absolute assignment was not possible. The ^{13}C NMR offered the one unambiguous method for assigning stereochemistry. Reference to the literature[29] shows that C-4 of (*E*)-4-methyl-2-pentene absorbs at 31.4 ppm relative to Me_4Si while C-4 of (*Z*)-4-methyl-2-pentene falls at 26.4 ppm. The respective C-1's absorb at 17.8 and 12.7 ppm. In comparison, peaks in the ^{13}C NMR spectrum of the mixture of **9** and **10** were found at 35.10 and 24.21 ppm and are approximately 3 times the area of two peaks at 29.62 and 18.09 ppm. A more accurate value for the relative amounts of the two isomers was obtained by integrating the allylic methylene signals in the 360-MHz ^1H spectrum. The ratio of *E* to *Z* isomers here was 2.1:1. Initially we believed **11** to be the result of coupling between 1-chloro-2-butene and the organopalladium intermediate derived from **1**. There was no question about a possible source for 1-chloro-2-butene. Heck reported that palladium halides are catalysts for allylic rearrangement. In control experiments with 3-chloro-1-butene he found that in 0.1 M $LiPdCl_3$ in acetonitrile each was converted into the same equilibrium mixture of allylic chlorides at a rate comparable to the rate of the coupling reaction between *trans*-1-chloro-2-butene and the intermediate organopalladium species generated from phenylmercuric chloride.[3]

Following Heck's proposal for phenylmercuric chloride and allyl chloride, one sees that nucleosides **9**–**11** would be formed from **1** via the pathways outlined in Scheme II. Initially palladium exchanges for mercury to give the transient organopalladium intermediate **2** which may form π complexes with any available olefin. The π complex of **2** with 3-chloro-1-butene reacts with complete regioselectivity to yield an intermediate σ complex, **7**, in which the pyrimidine is bonded only to the terminal carbon of the olfein. Elimination of $PdCl_2$ then gives nucleosides **9** and **10**. The 1-methyl-2-propen-1-yl side chain of **11** is a result of coupling by the same mechanism but at C-3 of 1-chloro-2-butene. For the determination of the relative rates of reaction of the two isomeric chlorobutenes, a 1:1 mixture was allowed to react with **1** in 0.1 M Li_2PdCl_4. The ratio of the relative yields of nucleosides **9** and **10** to **11** was 2.2:1. Hence, as expected, the terminal alkene (3-chloro-1-butene) reacted at a faster rate than the disubstituted alkene (1-chloro-2-butene). In actuality the overall process is not this simple. Our results demonstrated that in 0.1 M Li_2PdCl_4 in *methanol* very little 3-chloro-1-butene isomerizes to 1-chloro-2-butene. By GLC 1-chloro-2-butene is seen as a transient species comprising at most 5% of the total olefinic material. The major products of 3-chloro-1-butene transformation are 1-methoxy-2-butene and 3-methoxy-1-butene formed in a ratio

Scheme II

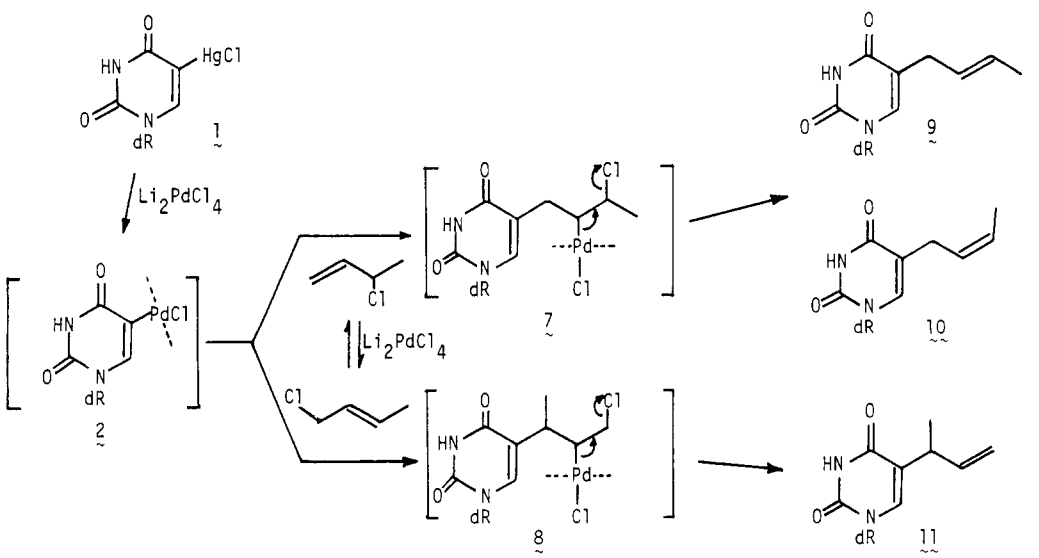
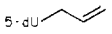
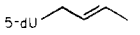
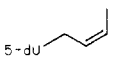
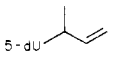
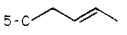
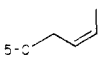
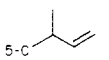
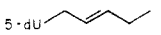
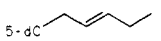
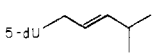
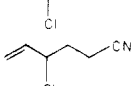
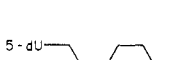
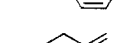


Table I. Reaction of 5-(HgCl)C, 5-(HgCl)dC, and 5-(HgCl)dU with Li_2PdCl_4 and H_2C=CHCHClR in MeOH

H_2C=CHC(Cl)HR	mercurinucleoside	product	no.	% yield[a]
	5-(HgCl)dU			64–84
	5-(HgCl)C			70
	5-(HgCl)dU		9	64
			10	
			11	7
	5-(HgCl)C		12a	72
			12b	
			13	<5
	5-(HgCl)dU		14	50
	5-(HgCl)dC		15	44
	5-(HgCl)dU		16	
	5-(HgCl)dU		17a	38[b]
			17b	
	5-(HgCl)dU		18	

[a] Yield of isolated product after column chromatography. [b] Yield for 17a plus 17b.

of 4:1. Under conditions identical with those used for the coupling reaction, $t_{1/2}$ for this reaction was 4 h. The presence of 5-(chloromercuri)-2′-deoxyuridine (1) had no detectable influence on the course or rate of the reaction.

The palladium-catalyzed transformation of allylic chlorides to allylic ethers has precedent in the $PdCl_2$-catalyzed conversion of allyl chloride to allyl acetate.[6] The π complex between Pd^{II} and 3-chloro-1-butene (Scheme III) could be attacked by the predominant nucleophile, methanol, at either C-1 or C-2 to give intermediate palladium σ complexes i and ii. Of these only ii could subsequently eliminate palladium chloride to give 1-methoxy-2-butene. 3-Methoxy-1-butene could be either formed by isomerization of 1-methoxy-2-butene via the intermediate σ complex iii as shown in Scheme III or by reaction of the π complex between Pd^{II} and 1-chloro-2-butene with methanol. If 11 is not formed via coupling to 1-chloro-2-butene (Scheme II), then is it reasonable to suppose that it results from coupling to C-3 of 1-methoxy-2-butene? The answer to that question is not entirely clear. The major products from a coupling reaction between 1, 0.1 M Li_2PdCl_4 in methanol, and a mixture of 1-methoxy-2-butene and 3-methoxy-1-butene prepared by methoxide treatment of 3-chloro-1-butene were nucleosides 9–11; however, the yields were low, and many other unidentified side products were observed. This and one other example[7] show that allylic ethers can give the same products as allylic chlorides in the organopalladium coupling reaction, but the reactions are slower, go in lower yield, produce more side products, and give Pd^0 in the process. The reaction between the methyl allylic ethers and 1 could conceivably proceed by a mechanism paralleling that accepted for coupling to allylic chloride as outlined in Scheme II, except the final step would require elimination of PdClOMe rather than $PdCl_2$.

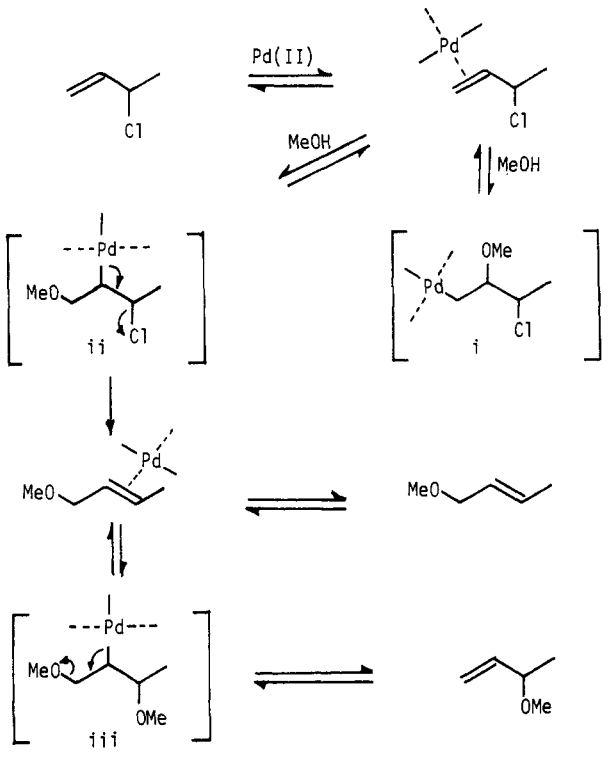
As outlined in Scheme I, an important side reaction in the preparation of 5-allyl-2′-deoxyuridine (3) was the coupling between 2 and 3 to give the C-5-bridged nucleosides 5 and 6. No evidence of a similar side reaction between (*E*)- and (*Z*)-5-(2-buten-1-yl)-2′-deoxyuridines (9 and 10) and the intermediate nucleoside-derived organopalladium intermediate 2 was observed. Since in the former reaction yields of 5 and 6 as low as 5% were easily detected, we can safely conclude that the C-5 butenyl nucleosides give far lower yields if any of C-5-bridged nucleosides.

In comparison to the reaction of 1 with 3-chloro-1-butene, 5-(chloromercuri)cytidine showed significantly greater selectivity. The ratio of straight-chain (12) to branched-chain (13) product was greater than 14:1 (Table I). A number of factors may be responsible. For one, the coupling reactions proceed slowly and in low yield unless cupric chloride is included. Presumably the complexation of palladium by N-4 of cytosine is responsible. The results of the coupling reaction between a series of allylic chlorides and the three mercurinucleosides 5-(chloromercuri)-2′-deoxyuridine (1), 5-(chloromercuri)-2′-deoxycytidine, and 5-(chloromercuri)cytidine are summarized in Table I. Minor structural variations in the allylic chlorides have a significant effect on the outcome of the coupling reaction. Addition of a single methylene unit increased selectivity beyond our limits of detection. Unlike 3-chloro-1-butene, 3-chloro-1-pentene gave only the straight-chain product (*E*)-5-(2-penten-1-yl)-2′-deoxyuridine (14). It is unlikely

(6) Brady, D. G. *Chem. Commun.* **1970**, 434–5.

(7) The reaction of ethyl allyl ether with 5-(chloromercuri)-2′-deoxyuridine and 0.1 M Li_2PdCl_4 in methanol gave 5-allyl-2′-deoxyuridine (3) in 32% yield and other minor products. One of these (15% yield) was tentatively identified as 5-(2,2-dimethoxy-1-methylethyl)-2′-deoxyuridine.

Scheme III



that the homologous allylic chlorides would undergo palladium-catalyzed exchange of methanol for chloride at significantly different rates since the structural modification is removed from the site of reactivity. However, in the resultant methoxy-substituted internal olefins, particularly when 1-methoxy-2-butene and 1-methoxy-2-pentene are compared, there would be a significant steric difference for addition of the pyrimidine to C-3.

The coupling reactions of 3-chloro-4-methyl-1-pentene and 4-chlorohex-5-enenitrile displayed equivalent selectivity for terminal additions. From a synthetic standpoint these results are significant, especially in light of the purity of the starting allylic chlorides. 3-Chloro-1-pentene, 3-chloro-4-methyl-1-pentene, and 4-chlorohex-5-enenitrile were prepared from the corresponding allylic alcohols by treatment with triphenylphosphine in hexachloroacetone.[8] The alternative reagent combination of carbon tetrachloride and triphenylphosphine[9,10] would probably have been suitable but was not investigated. The latter two allylic chlorides were not separated from their isomeric internal olefins prior to coupling to 5-(chloromercuri)-2′-deoxyuridine.

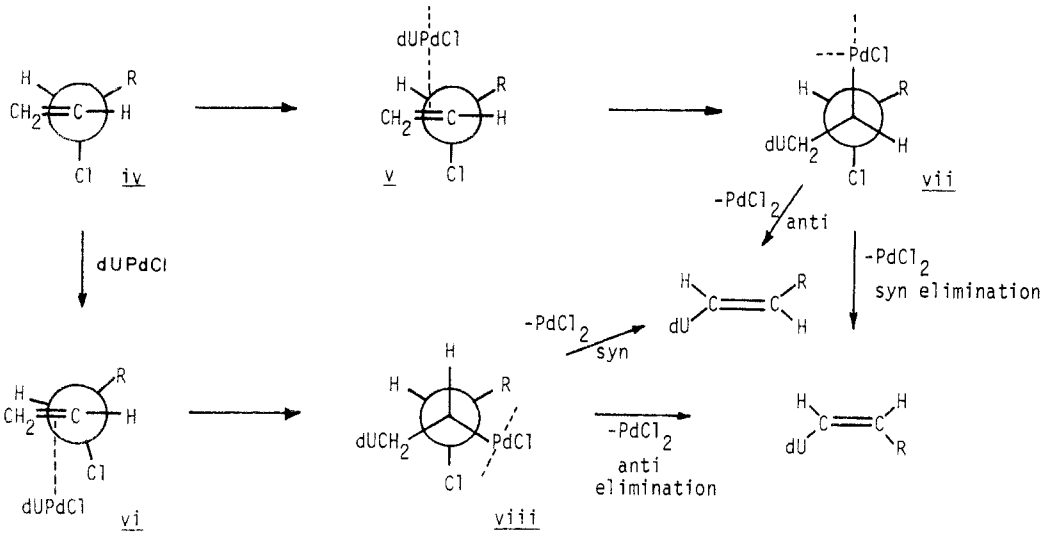
The reactions of 3-chloro-1-pentene and 3-chloro-4-methyl-1-pentene were highly stereoselective as well as regioselective. Within the limits of detection of ^1H and ^{13}C NMR spectroscopy, the sole products were the *E* isomers **14** and **16**. The stereochemical outcome could be established during any of a number of steps in the overall reaction. This is most conveniently depicted by the use of Newman projection (Scheme IV). An allylic chloride of structure CH_2=CHCHClR[11] in its most stable conformation (iv) can form a π complex with the palladium-derived nucleoside from either the top (v) or the bottom (vi). Because of potentially destabilizing steric interaction between the Cl of the allylic chloride and the nucleoside, the former would be more favorable. Olefin insertion from π complex v gives the σ palladium complex vii, which is sterically less crowded than the σ palladium complex viii, which results when the olefin inserts into π complex vi. Then, if $PdCl_2$ elimination was only anti, σ complex vii would give trans product and viii would give cis product. The stereochemistry would have been established during the π-complexation–insertion stage.

However, there is no firm evidence to suggest that elimination of $PdCl_2$ has to be anti. On the contrary, Henry[12] has shown that of all palladium-catalyzed exchange and isomerization reactions involving the reversible addition of PdX across a carbon–carbon double bond, only chloropalladation and dechloropalladation are nonstereospecific. This leads to a plausible explanation for the unusual result when the nucleoside palladium complex **2** was coupled with 4-chlorohex-5-enenitrile. Although only products of terminal addition were found, the cis isomer, **17b**, comprised a sizable portion of products. The ratio of cis to trans isomer was 1:3. Sterically the cyanoethyl group is at least as large as an ethyl group so that a priori one would predict that 4-chlorohex-5-enenitrile would couple at least as stereoselectively as 3-chloro-1-pentene. Since this is not the case, the cyano group must participate in the reaction. We have observed that 4-acetoxy-hex-5-enenitrile forms a red complex with Pd^{II} that is significantly less reactive than other allylic acetates. If 4-acetoxyhex-5-enenitrile can function as a bidentate ligand for Pd^{II}, then intermediates vii and viii may also exist with the cyano group complexed to palladium. Both intermediates could be formed via π complexes involving the bidentate interaction. However, elimination of $PdCl_2$ from either vii or viii would have to be antiperiplanar if the cyano group is to remain complexed to the palladium throughout the reaction. In this way complex viii leads solely to the cis isomer **17b**, and vii gives only the trans isomer. Syn elimination would require that the palladium and chloride be rotated into a synperiplanar conformation, thereby losing the complexation to the R group. When R is large and not a ligand for palladium, viii may normally eliminate by a syn mechanism to give the thermodynamically more stable trans alkene. By this argument both intermediates vii and viii are formed, and the relative proportion of stereoisomers is determined during the elimination step.

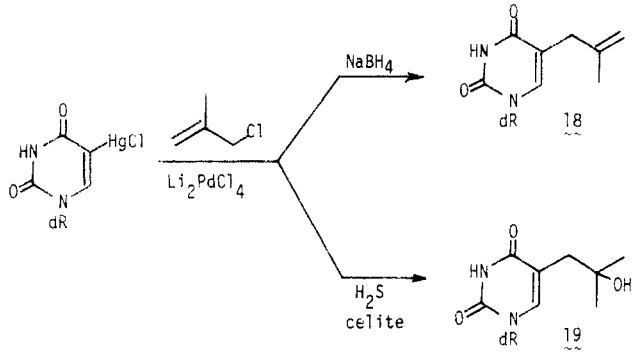
With one exception the allylic chlorides react rapidly and cleanly with 5-(chloromercuri)-2′-deoxyuridine and a catalytic amount (generally 20–25 mol %) of Li_2PdCl_4. 2-Methyl-3-chloropropene reacted significantly more slowly than the monosubstituted terminal olefins. Pd^0 was precipitated during the course of the reaction, this being evidence that other undetermined side reactions were occurring. To prevent Pd^0 precipitation, 1 equiv of $CuCl_2$ was added to the reaction mixture. When the mercuric and palladium ions were removed by sodium borohydride reduction to the insoluble metals, the major product isolated after silica gel chromatography was 5-(2-methyl-2-propenyl)-2′-deoxyuridine (**18**, Scheme V). A minor side product was not identified. Throughout most of this work metals were removed by precipitation with H_2S followed by filtration through Celite. The 2-methyl-3-chloropropene reaction was the first where working conditions were critical. When treated in the conventional way with H_2S and Celite, the major product (42% yield) was 5-(2-

(8) Magid, R. M.; Fruchey, O. S.; Johnson, W. L.; Allen, T. G. *J. Org. Chem.* **1979**, *44*, 359.
(9) Snyder, E. I. *J. Org. Chem.* **1972**, *37*, 1466.
(10) Collington, E. W.; Meyers, A. I. *J. Org. Chem.* **1971**, *36*, 3044.
(11) The allylic chlorides used in these studies were racemic. The mechanism shown in Scheme IV for the *R* configuration would apply to the *S* configuration as well.
(12) Henry, Patrick M. *Acc. Chem. Res.* **1973**, *6*, 16–24.

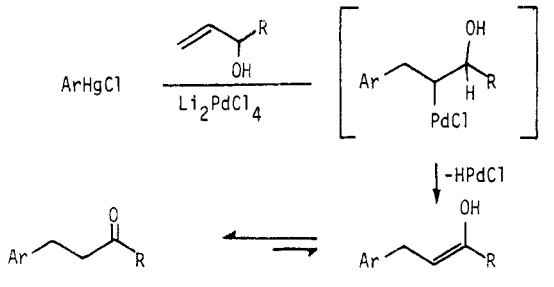
Scheme IV



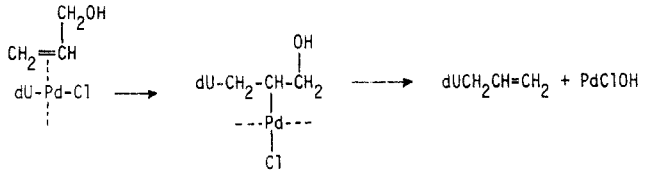
Scheme V



Scheme VI



Scheme VII



hydroxy-2-methylpropyl)-2′-deoxyuridine (**19**). The occurrence of a hydroxy-substituted side chain has been observed in other instances after H_2S–Celite workup. 5-(1-Hydroxy-3,3,3-trifluoropropyl)-2′-deoxyuridine was the predominant product from reaction of 3,3,3-trifluoropropene with **1** and Li_2PdCl_4 when the H_2S-treated reaction mixture was filtered hot through Celite.[13] The normal products of this reaction are 5-(1-methoxy-3,3,3-trifluoropropyl)-2′-deoxyuridine and 5-(3,3,3-trifluoro-1-propenyl)-2′-deoxyuridine.[14] 3,3,3-Trifluoropropene was one of two allylic fluorides whose reaction was investigated. The other, allyl fluoride, behaved just like allyl chloride, giving 5-allyl-2′-deoxyuridine as the major product.

Allylic Alcohol Coupling. Concomitant with investigation of the allylic chloride coupling, we studied the reaction of allylic alcohols with 5-(chloromercuri)-2′-deoxyuridine. Heck established that arylmercurials react regioselectively with allylic alcohols to give 3-aryl aldehydes and ketones.[15] Presumably a mechanism involving elimination of HPdCl to give an enol is responsible[15] (Scheme VI). With aryl halides the overall reaction (oxidative addition of Pd^0, organopalladium–olefin insertion, and elimination of Pd^0) is catalytic in palladium.[16–18] In most instances yields and regioselectivity have been good. Because of the availability of 5-mercuripyrimidine nucleosides, we focused on the noncatalytic pathway.

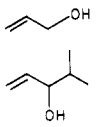
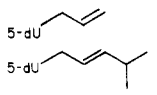
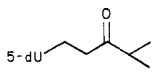
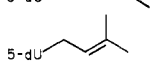
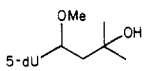
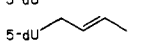
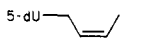
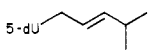
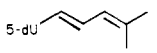
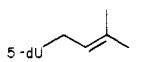
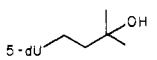
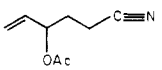
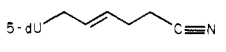
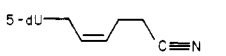
In an attempt to synthesize 3-(2′-deoxyuridin-5-yl)]-propionaldehyde, allyl alcohol and **1** were allowed to react with Li_2PdCl_4 in methanol. The only isolable monomeric product was 5-allyl-2′-deoxyuridine. In contrast, 5-allylbenzene has been observed as only a minor product in the coupling reaction of phenylmercuric chloride with allyl alcohol.[15] During the reaction of **1**, allyl alcohol was slowly converted to allyl methyl ether. Consequently the allyl side chain is most likely produced by elimination of PdClOH or PdClOMe following coupling to either allyl alcohol or allyl methyl ether (Scheme VII).

Why this elimination should be so much more favorable in methanol solution with pyrimidine nucleoside intermediates than under the conditions and with the substrates used by others is unknown. Two other allylic alcohols were examined. 4-Methyl-1-penten-3-ol gave both the allylic product, (*E*)-5-(4-methyl-2-penten-1-yl)-2′-deoxyuridine (**16**), and the expected ketone, 5-(4-methyl-3-oxopentyl)-2′-deoxyuridine (**20**, Table II).

3-Methyl-1-buten-3-ol with 1 equiv of Li_2PdCl_4 and 5-(chloromercuri)-2′-deoxyuridine in methanol gave low yields of 5-(3-methyl-2-buten-1-yl)-2′-deoxyuridine (**21**) and 5-(1-methoxy-3-hydroxy-3-methylbutyl)-2′-deoxyuridine (**22**). The latter compound, which predominated, is pre-

(13) Bergstrom, D. E.; Ruth, J. L., unpublished data.
(14) Wataya, Y.; Matsuda, A.; Santi, D. V.; Bergstrom, D. E.; Ruth, J. L. *J. Med. Chem.* **1979**, *22*, 339.
(15) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5526.
(16) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265.
(17) Tamaru, Y.; Yamada, Y.; Yoshida, Z.-I. *Tetrahedron* **1979**, *35*, 329–40.
(18) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273, 1206.

Table II. Reaction of dUHgCl with Li_2PdCl_4, Allylic Alcohols, and Acetates

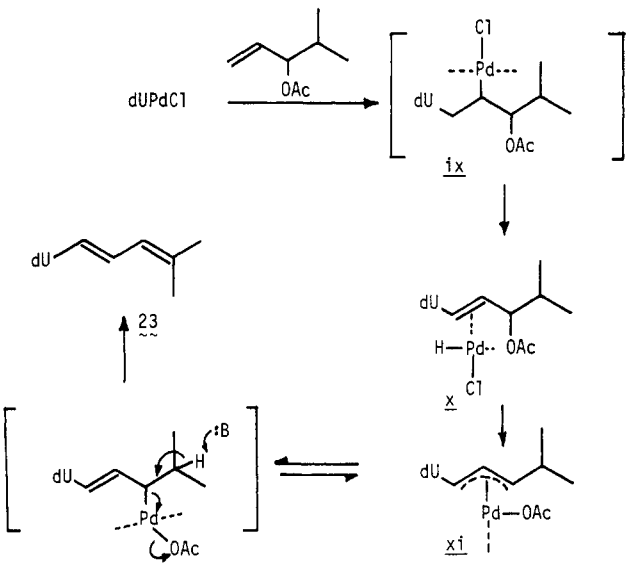
H_2C=CHCHXR	product	no.	% yield
		16	18
		20	24
		21	5
		22	16
		9	24[a]
		10	
		16	5
		23	13
		21	15
		24	10
		17a	16[b]
		17b	

[a] Yield for 9 plus 10. [b] Yield for 17a plus 17b.

sumably formed by a mechanism outlined previously for the addition of simple aliphatic olefins to 1.[2] Yields were low with both the five- and six-carbon-chain allylic alcohols.

Allylic Acetate Coupling. To avoid the problems of allylic chloride synthesis and purification, allylic acetates were examined as potential side-chain precursors. Allylic acetates are readily available by the reaction of allylic alcohols with acetic anhydride in pyridine.[19] The major products from the reaction of most allylic acetates with 5-(chloromercuri)-2′-deoxyuridine (1) were identical with those obtained from allylic chlorides. However, the yields were poor and many additional side products were detected by TLC. Allyl acetate is converted to allyl methyl ether in 0.1 M Li_2PdCl_4 in methanol with $t_{1/2}$ approximately 2 h. Since the rate of the coupling reaction is similar, the allylic products could result via coupling to either (or both) allylic acetates or allylic methyl ethers. The only unusual product was diene **23**, from 1, Li_2PdCl_4, and 3-acetoxy-4-methyl-1-pentene in methanol. The structure was established as (*E*)-5-(4-methyl-1,3-pentadien-1-yl)-2′-deoxyuridine on the basis of ^1H NMR and ^{13}C NMR spectroscopic data. The ^1H NMR spectrum of the side chain correspond to that for (*E*)-1-phenyl-4-methyl-1,3-pentadiene synthesized by Heck[20] from 1-bromo-2-methylpropene and styrene. The fluorescence and strong absorptions in the UV at 322 nm (ε 14000) and 309 (13700) confirm the presence of the extended chromophore. The reaction of 1 with 3-acetoxy-4-methyl-1-pentene typically gave the diene in yields up to 13% and the allylic product

Scheme VIII



16 in yields of 5%. In comparison, 3-hydroxy-4-methyl-1-pentene gave ketone **20** in 24% yield and nucleoside **16** in 18% yield. Finally, the reaction of 3-chloro-4-methyl-1-pentene with 1 gave only (*E*)-5-(4-methyl-2-penten-1-yl)-2′-deoxyuridine (**16**) in good yield. Thus even though the same mixture of methoxy ethers is produced from each of these alkenes in methanolic Li_2PdCl_4, the reactions with 1 are clearly different and thereby establish that the leaving group at the allylic position of the alkene is a critical factor in the outcome of the coupling reactions.

Since diene **23** was a product of only the allylic acetate and not the chloride or alcohol, we have sought a reasonable explanation for its formation. Two groups working independently discovered that allylic acetates are transformed to conjugated dienes by Pd^0.[21,22] We have concluded that diene **23** is not produced by coupling of 1 to 4-methyl-1,3-pentadiene from the reaction of 3-acetoxy-4-methyl-1-pentene with Pd^0. First of all, Heck has demonstrated that when dienes couple with organopalladium intermediates derived from arylmercurials, the products are aryl-coupled π-allyl complexes and not dienes.[23] Second, we synthesized 4-methyl-1,3-pentadiene and found that it does not react with 1 under the usual reaction conditions. Consequently the diene must be formed by elimination of acetate after coupling occurs. A mechanism similar to that proposed by Tsuji[22] is possible if, as shown in Scheme VIII, Pd^0 is eliminated from intermediate ix to give π complex x. Oxidative addition can then occur to give π-allyl complex xi. If this is the pathway, then how can elimination occur under such mild conditions to give the diene **23**? Unlike other reported instances[23,24] where π-allyl complexes are believed to be direct precursors to dienes, the proton to be eliminated here is not particularly acidic. On the other hand, the ability of 5-allyldeoxyuridines to support a positive charge on the α-carbon of the side chain suggests that a late transition state (C–Pd

(19) Mesnard, P.; Bertucat, M. *Bull. Soc. Pharm. Bordeaux*, **1956**, *95*, 25–7.
(20) Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083.
(21) Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, 2301–4.
(22) Tsuji, J.; Tamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.* **1978**, 2075–8.
(23) Susuki, T.; Tsuji, J. *Bull. Chem. Soc. Jpn* **1973**, *46*, 655–6.
(24) Harrison, I. T.; Kimura, E.; Bohme, E.; Fried, J. H. *Tetrahedron Lett.* **1969**, 1588.
(25) Bergstrom, D. E.; Ruth, J. L. *J. Carbohydr., Nucleosides, Nucleotides* **1977**, *4*, 257.
(26) "Organic Intermediates"; Research Organic/Inorganic Chemical Corp.: Sun Valley, CA, 1972; p 41.

bond cleavage nearly complete) is possible and that elimination of H^+ to give the diene is greatly facilitated.

Conclusion

The purpose of this study was to lay the groundwork and establish methodology for attaching functionalized side chains to the C-5 positions of pyrimidine and pyrrolo[2,3-*d*]pyrimidine nucleosides. Modification at the nucleoside, nucleotide, and polynucleotide level could produce a wide array of useful nucleic acid–base-derived biological probes. Furthermore, spacers for attaching analogues to affinity columns or irreversibly binding to enzymes could be introduced into coenzyme analogues. Finding a short direct route to introduce C-5 substituents into molecules as complex as nucleosides and nucleotides presented a formidable challenge. The relative ease with which mercury can be linked covalently at the C-5 position of pyrimidine and pyrrolo[2,3-*d*]pyrimidine nucleosides, nucleotides, mono-, di-, and triphosphates, and polynucleotides provided the impetus for our study of the organopalladium coupling reaction. Of the types of readily available olefins which are known to couple to arylpalladium intermediates, allylic chlorides initially looked the most promising. In the present study we examined the reaction of 5-(chloromercuri)-2′-deoxyuridine with methanolic Li_2PdCl_4 and allylic chlorides, alcohols, and acetates. From the standpoint of preparative chemistry the results are very clear. Allylic chlorides are unquestionably superior. Allylic chlorides of the structure $CH_2{=}CHC(R)Cl(CH_2)_nR'$ (n = 0, R = CH_3, R′ = CH_3; n = 1, R = H, R′ = CN; n = 0, R = H, R′ = CH_3) coupled in good yield only at the terminal carbon. When R′ was CH_3 and R was H or CH_3, the single major products in each instance were the *E* isomers, **14** and **16**. The cyano group at the opposite terminus of the allylic chloride led on coupling to both *E* and *Z* isomers, **17a,b**. If more complex side chains are to be attached via functionalized allylic chlorides, the problem of *E*/*Z* isomer formation should be clearly resolved. Our continuing studies should eventually establish both what kind of functional group and how its location on the chain affect the *E*/*Z* isomer ratio.

Finally, the problem of allylic chloride synthesis may well be the principal limitation of our synthetic approach. In the past allylic chlorides have typically been synthesized from the corresponding alcohol which frequently led to allylic rearrangement and ambiquity in regiospecificity. The reagent systems carbon tetrachloride–triphenylphosphine[9,10] and hexachloroacetone–triphenylphosphine[8] have largely solved this problem for the synthesis of aliphatic allylic chlorides. For more complex structures substituted by functional groups sensitive to these reagents, alternate procedures such as the reaction of hypochlorous acid with olefins may be suitable.[27]

The methodology developed here extends far beyond nucleosides and may find general application to organopalladium intermediates derived from aryl and vinyl mercurials.

Experimental Section

^1H nuclear magnetic resonance (NMR) spectra were recorded on Varian EM-360 (60 MHz), JEOL-100 (100 MHz) Fourier transform, and Nicolet NT-360 Fourier transform NMR spectrometers. ^{13}C NMR spectra were recorded on the JEOL-100 Fourier transform NMR spectrometer and were completely decoupled from proton resonances. ^1H NMR spectra in various deuterated organic solvents were run against tetramethylsilane as an internal standard while those in D_2O were run against internal sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate. Quantitative ultraviolet (UV) spectra were recorded to ±0.5 nm by using a Cary 17 spectrophotometer in H_2O, and the pH extremes were obtained by diluting 20.00 mL of the stock neutral solution to 23.00 mL with 1.0 N HCl or 1.0 N NaOH (final pH approximately 1.2 or 12.6, respectively). Infrared (IR) spectra of KBr pellets were recorded on a Beckman IR-8 and calibrated to the polystyrene absorption at 1601 cm^{-1}. Melting points were determined on a Büchi 510 programmable melting point apparatus and are uncorrected. Elemental analyses were determined by the Analytical Laboratory at the University of California, Berkeley, Chemalytics, Inc., or Galbraith Laboratories, Inc. Thin-layer chromatography (TLC) was carried out with 3.5 × 10 cm E. Merck 60F-254 chromatogram sheets (0.25 mm, silica gel) in 5 × 5 × 12 cm chambers lined with 11-cm Whatman filter paper. Three different solvent systems were used (relative proportions are v/v): system A, $CH_3OH/CHCl_3$ (1:3); system B, MeOH/EtOAC (3:2); system C, CH_3CN/*n*-BuOH/0.10 M NH_4OAc/concentrated NH_4OH (10:60:20:10). Analytical gas–liquid chromatography (GLC) was done by using a Varian Model 940 gas chromatograph. The columns used were as follows: (1) 6 ft × $^1/_8$ in., 10% Carbowax on Chrom G; (2) 6 ft × $^1/_8$ in., 10% QF-1 on Chrom Q; (3) 6 ft × $^1/_8$ in., 10% SE-30 on Chrom Q; (4) 6 ft × $^1/_8$ in., 10% UCW 98 on Chrom G. Preparative GLC was done with an Aerograph manual temperature programmed gas chromatograph (Model A-90-P3 with a 6 ft × $^1/_4$ in., 10% SE-30 on Chrom Q column).

Preparative liquid chromatography was accomplished on Bio-Gel P-2 eluted with doubly distilled water and E. Merck silica gel 60 (60–230 mesh) eluted with methanol–chloroform.

Allylic Chlorides. Allylic chlorides were prepared from the corresponding alcohols by following the procedure of Magid et al.[8] Only 4-chlorohex-3-enenitrile has not been previously described. It was prepared from 4-hydroxyhex-5-enenitrile by the same procedure to give a crude product which was distilled at 0.3 torr and 40–55 °C in a Kugelrohr apparatus. The product purified by this procedure still contained a high percentage of hexachloroacetone but was suitable for organopalladium coupling reactions: IR (CCl_4) 2245 cm^{-1} (C≡N); ^1H NMR (hexachloroacetone) δ 2.32 (t, 2 H), 2.64 (q, 2 H), 4.63 (q, 1 H), 5.3–6.3 (m, 3 H).

Allyl Acetates. Allyl acetates were prepared from the corresponding allyl alcohols and acetic anhydride in pyridine.[19] Their purity was established by GLC (system 1) and their identity by ^1H NMR and IR spectra.

3-Acetoxy-1-butene was prepared from 3-buten-2-ol: 65% yield; bp 100 °C (760 mm); ^1H NMR (CCl_4) δ 1.27 (d, 3 H, J = 7 Hz), 1.74 (s, 3 H), 4.9–5.4 (m, 1 H), 5.03 (m, 1 H), 5.18 (m, 1 H), 5.84 (m, 1 H).

3-Acetoxy-4-methyl-1-pentene was prepared from 4-methyl-1-penten-3-ol: 86% yield; bp 130 °C (25 mm); ^1H NMR ($CDCl_3$) δ 0.91 (d, 6 H, J = 7 Hz), 1.87 (m, 1 H, J = 7 Hz), 2.05 (s, 3 H), 5.0–5.3 (m, 2 H), 5.6–5.9 (m, 1 H); IR 3090, 2980, 1640, 1380, 1370, 1250, 1020, 999, 930 cm^{-1}.

3-Acetoxy-3-methyl-1-butene was prepared from 2-methyl-3-buten-2-ol in 64% yield by a modification of the Mesnard–Bertucat procedure in which the reaction mixture was heated at 105 °C for 40 h. The product was distilled through a Kugelrohr apparatus: bp 100–105 °C (25 mm); ^1H NMR (CCl_4) δ 6.20 (dd, 1 H, J_1 = 17 Hz, J_2 = 10 Hz), 5.21 (dd, 1 H, J_1 = 17 Hz, J_2 = 2 Hz), 5.08 (dd, 1 H, J_1 = 11 Hz, J_2 = 2 Hz), 1.96 (s, 3 H), 1.57 (s, 6 H); IR (CCl_4) 3090, 2780, 2740, 1720, 1630, 1405, 1360, 1230, 1120, 1000, 935 cm^{-1}.

4-Acetoxyhex-5-enenitrile. The synthesis was accomplished in three steps (a–c) from β-cyanopropionaldehyde dimethyl acetal[26] (β-CPAA).

(a) H_2SO_4 (1 M, 250 mL) was added to 50.0 g (0.602 mol) of β-CPAA, and the mixture was refluxed gently for 35 min. The progress of the reaction was monitored by GLC (system 4). The cooled mixture was diluted with 100 mL of H_2O, treated with 200 mL of saturated $NaHCO_3$, extracted with 6 × 250 mL of CH_2Cl_2, dried over $MgSO_4$ for $^1/_2$ h, filtered, evaporated, and vacuum distilled [80 °C air temperature (0.5 mmHg)] by using a Kugelrohr apparatus to give β-cyanopropionaldehyde (β-CPA): 58–65%

(27) Hegde, S. G.; Vogel, M. K.; Saddler, J.; Hrinyo, T.; Rockwell, N.; Haynes, R.; Oliver, M.; Wolinsky, J. *Tetrahedron Lett.* **1980**, 441–4.

yield; ^{1}H NMR δ 9.4 (s, 1 H), 2.5 (br m, 4 H). The purity was established by GLC (system 4).

(b) Vinylmagnesium bromide was prepared by using the method of Fuson and Mon.[28] β-CPA (5.0 g, 0.060 mol) was added to 60 mL of dry (distilled from $LiAlH_4$) THF under a N_2 atmosphere, in a two-necked, 250-mL, round-bottomed flask. Then, vinylmagnesium bromide (0.061 mol) in 50.0 mL of dry THF was added dropwise to the β-CPA with vigorous stirring at −40 °C by use of a dry ice/acetonitrile cooling bath. After the addition the ice bath was removed and stirring continued at room temperature for 6 to 8 h to give a pale yellow-green solution with much light green precipitate. The mixture was hydrolyzed with a mixture of 100 g of chipped ice, 16.7 mL of concentrated H_2SO_4, and 85 mL of ice-cold H_2O and stirred vigorously for $^1/_2$ h. This was extracted with 4 × 200 mL of ethyl acetate, washed with 50 mL of saturated $NaHSO_3$ and 80 mL of saturated $NaHCO_3$, dried over $MgSO_4$, filtered, evaporated, and distilled at 100 °C (0.5 mmHg) by using Kugelrohr apparatus: yield 30–65%; ^{1}H NMR (neat) δ 5.85 (m, 1 H, J_1 = 17 Hz, J_2 = 10 Hz, J_3 = 6.5 Hz), 5.29 (dd, 1 H, J_1 = 17 Hz, J_2 = 2 Hz), 5.15 (dd, 1 H, J_1 = 10 Hz, J_2 = 2 Hz), 4.18 (m, 1 H), 4.08 (s, 1 H), 2.47 (t, 2 H, J = 7 Hz), 1.83 (m, 2); IR (neat) 3460, 3095, 2950, 2260, 1730, 1640, 1420, 1128, 1060, 990, 930 cm^{-1}. The purity was established by GLC (system 1).

(c) Finally, 4-acetoxyhex-5-enenitrile was obtained from 4-hydroxyhex-5-enenitrile in 60% yield by following the procedure of Mesnard and Bertucat:[19] ^{1}H NMR ($CDCl_3$) δ 1.98 (m, 2 H), 2.04 (s, 3 H), 2.35 (m, 2 H), 5.1–5.3 (m, 2 H), 5.7 (m, 1 H); IR (neat) 3100, 2950, 2250, 1730, 1640, 1425, 1370, 1230, 1110, 1030, 990, 910 cm^{-1}.

(*E*)-5-[3-(2′-Deoxyuridylin-5-yl)-1-propen-1-yl]-2′-deoxyuridine (5). The reaction of **1** with allyl chloride and Li_2PdCl_4 in methanol was carried out as described previously.[1] The minor product eluted from silica gel columns with 20% methanol–chloroform (v/v) was rechromatographed on Bio-Gel P-2 to give two UV-absorbing products in approximately equal amounts. Recovery of the material from several reaction runs gave a combined average yield of 12%. The slower eluting product was isolated and recrystallized from water to give white crystals identified as **5**: mp 231–231.5 °C; ^{1}H NMR δ 7.92 (s, 1 H), 7.69 (s, 1 H), 6.33 (m, 4 H), 4.5 (m, 2 H), 4.1 (m, 2 H), 3.90 (m, 4 H), 3.23 (d, 2 H, J = 5 Hz), 2.44 (dd, 4 H, J_1 = 5.5 Hz, J_2 = 6.5 Hz), UV (H_2O) λ_{max} 271, 244, λ_{min} 263, 226; TLC R_f 0.28 (A), 0.61 (B), 0.20 (C); IR 3470, 3210, 3060, 1685, 1655, 1475, 1380, 1095, 1045, 970 cm^{-1}; ^{13}C NMR (Me_2SO) 162.5, 161.6 (both C-4), 150.7, 149.8 (both C-2), 136.6 (C-6), 126.9 (C-2 of propenyl), 122.6 (C-1 of propenyl), 111.3, 110.4 (both C-5), 87.2 (C-1′), 84.1 (C-4′), 70.3 (C-3′), 61.2 (C-5′), 38.7 ppm (C-3 of propenyl). Anal. Calcd for $C_{21}H_{26}N_4O_{10}$: C, 51.01; H, 5.30; N, 11.33. Found: C, 51.32; H, 5.25; N, 11.51. The second component could not be effectively purified but was tentatively identified as **6** on the basis of ^{1}H NMR spectra: ^{1}H NMR (D_2O) δ 7.93 (s, 1 H), 7.74 (s, 1 H), 6.33 (m, 2 H), 4.59 (m, 2 H), 4.12 (m, 1 H), 3.90 (narrow m, 2 H), 3.32 (s, 3 H), 2.43 (m, 6 H), 2.04 (m, 2 H).

5-(2-Buten-1-yl)-2′-deoxyuridines 9 and 10. (a) From 3-Chloro-1-butene. A suspension of 1.222 g (2.63 mmol) of 5-(chloromercuri)-2′-deoxyuridine[25] (**2**) in 35 mL of methanol was stirred at room temperature. 3-Chloro-1-butene (3.0 mL, 2.91 mmol) was added followed by 8.0 mL (0.8 mmol, 0.30 equiv) of 0.10 M Li_2PdCl_4 in methanol. The yellow-white suspension dissolved within 4 min. After 1.5 h, hydrogen sulfide was bubbled through for 30 s, and the mixture was filtered through Celite to remove metal sulfides. Evaporation of the filtrate and chromatography on a column of 85 g of silica gel (2.0 × 66 cm) eluted with an increasing volume percent of methanol in chloroform (5–18%) gave one major UV-absorbing product. Rotary evaporation gave a white solid (528 mg, 71%) which was indicated by ^{1}H NMR to be a 9:1 mixture of 5-(2-buten-1-yl)-2′-deoxyuridines **9** and **10** and 5-(1-buten-3-yl)-2′-deoxyuridine (**11**), respectively. Nucleoside **11** was not isolated or characterized but was considered the best fit on the basis of the doublet (J = 7 Hz) at 1.13 ppm. Further purification by chromatography on a column of Bio-Gel P-2 (2.0 × 138 cm) eluted with water and then recrystallization from ethyl acetate gave white crystals identified as 5-(2-buten-1-yl)-2′-deoxyuridine: mp 136.0–137.0 °C; ^{1}H NMR (100 MHz, Me_2SO-d_6) δ 7.63 (s, 1 H), 6.17 (t, 1 H, J = 7 Hz), 5.45 (m, 2 H), 4.22 (m, 1 H), 3.77 (m, 1 H), 3.60 (m, 2 H), 2.90 (m, 2 H), 2.08 (m, 2 H), 1.62 (d, 3 H, J = 4.5 Hz); ^{13}C NMR (Me_2SO-d_6) 168.98 (C-4), 150.64 (C-2), 136.68 (C-6), 128.27, 127.24, 125.83 (CH_2C-H=$CHCH_3$), 112.15 (C-5), 87.75 (C-4′), 84.46 (C-1′), 70.87 (C-3′), 61.73 (C-5′), 37.48 (C-2′), 35.10, 29.62 (ratios 3:1, CH_2CH=$CHCH_3$), 24.21, 18.09 ppm (CH_2CH=$CHCH_3$); UV (MeOH) λ_{max} 267, λ_{min} 235; TLC R_f 0.55 (A), 0.71 (B), 0.51 (C); IR 3440, 3180, 3040, 1675, 1465, 1280, 1100, 970, 875, 760 cm^{-1}; mass spectrum, m/e 282 (M), 166 [5-(2-butenyl)uracil]. Anal. Calcd for $C_{13}H_{18}N_2O_5$: C, 53.31; H, 6.43; N, 9.92. Found: C, 53.31; H, 6.11; N, 9.77.

(b) From 3-Acetoxy-1-butene. To a stirring suspension of 92.6 mg (2.0 mmol) of 5-(chloromercuri)-2′-deoxyuridine in 60 mL of methanol were consecutively added 1.60 g (14.0 mmol) of 3-acetoxy-1-butene and 22.0 mL (2.2 mmol) of 0.1 M Li_2PdCl_4 in methanol. After being stirred overnight (19 h) at room temperature, the reaction mixture was treated with H_2S gas for 1.0 min, filtered with CH_3OH washes (3 × 50 mL), evaporated to a clear glass, extracted with hot water (3 × 5.0 mL), and applied to a 2.3 × 138 cm, Bio-Gel P-2 column. Three major UV-absorbing fractions were obtained. The middle-eluting fractions were evaporated to give 140 mg of glassy material. Preparative TLC using 0.5 × 20 × 20 cm silica gel 60 F-254 plates with 25% MeOH/75% $CHCl_3$ as solvent gave 12.2 mg (24%) of (*E*)- and (*Z*)-5-(2-butenyl-1-yl)-2′-deoxyuridines **9** and **10**. The product was spectroscopically identical with that produced in the 3-chloro-1-butene reaction: TLC R_f 0.50 (A), 0.52 (C). Anal. Calcd for $C_{13}H_{18}N_2O_5 \cdot {}^1/_2H_2O$: C, 53.60; H, 6.53; N, 9.62. Found: C, 53.54; H, 6.40; N, 9.46.

The first and last peaks from the Bio–Gel P-2 column were further purified by preparative TLC with elution with 25% MeOH/75% $CHCl_3$ but could not be further resolved. Both fractions consisted of a number of products tentatively identified by ^{1}H NMR. Among these were 5-(1-methoxy-3-hydroxybutyl)-2′-deoxyuridine, 5-(1-methoxybutyl)-2′-deoxyuridine, 5-(2,3-dihydroxybutyl)-2′-deoxyuridine, and a dimeric product.

5-(2-Buten-1-yl)cytidine (12a,b). To a stirred suspension of 1.036 g (2.17 mmol) of 5-(chloromercuri)cytidine[25] in 20 mL of methanol were added copper(II) chloride (350 mg, 2.6 mmol), 2.2 mL of (22 mmol) 3-chloro-1-butene, and 5.0 mL (0.50 mmol. 0.23 equiv) of 0.10 M Li_2PdCl_4 in methanol. Within 45 min, all solid starting material had dissolved, leaving a clear brown solution. After 2 h, treatment with hydrogen sulfide, filtration through Celite, and concentration to a solid, the crude product was chromatographed on a column of 80 g of silica gel (2.0 × 62 cm) eluted with an increasing volume percent of methanol in chloroform (10–30%). One major UV-absorbing product was eluted, giving 495 mg (77%) of white solid after evaporation. The ^{1}H NMR in D_2O indicated the solid to be principally 5-(2-buten-1-yl)cytidine (**12**) with a trace (4.5%) of 5-(1-buten-3-yl)cytidine (**13**). The product was further purified by a second silica gel column, by preparative TLC on silica gel plates eluted with ethyl acetate/methanol/acetonitrile (75:15:10 v/v), and by chromatography on a 2.0 × 58 cm column of Bio-Gel P-2 eluted with water. It would not recrystallize from acetonitrile, water, ethanol, or ethyl acetate. The white solid product was identified as 5-(2-buten-1-yl)cytidine (**12**): mp 93–99 °C; ^{1}H NMR (D_2O, external Me_4Si) δ 7.69 (s, 1 H), 5.91 (narrow m, 1 H), 5.5–5.6 (m, 2 H), 4.2 (complex m, 3 H), 3.88 (narrow m, 2 H), 2.92 (narrow m, 2 H), 1.62 (d, 3 H, J = 4.5 Hz); UV (MeOH) λ_{max} 278, λ_{min} 254; TLC R_f 0.22 (A), 0.56 (B), 0.42 (D). Anal. Calcd for $C_{13}H_{19}N_3O_5 \cdot {}^1/_2H_2O$: C, 50.93; H, 6.25; N, 13.71. Found: C, 51.18; H, 6.16; N, 13.61.

A similar reaction with 5-(acetoxymercuri)cytidine[25] and 0.02 equiv of Li_2PdCl_4 gave **12** in 47% yield with equal purity.

(*E*)-5-(2-Penten-1-yl)-2′-deoxyuridine (14). To a stirring suspension of 5-(chloromercuri)-2′-deoxyuridine (**1**; 463 mg, 1.0 mmol) in 14.0 mL of MeOH were added 3-chloro-1-pentene (0.80 g, 7.66 mmol) and 0.1 M Li_2PdCl_4 (3.0 mL, 0.3 mmol) in methanol. The reaction mixture was stirred for 2 h at room temperature and worked up by H_2S treatment and filtration through Celite. Chromatography of the residue, from evaporation of the filtrate, on silica gel with elution with 15% methanol–chloroform (v/v) gave a single major product as determined by TLC: R_f 0.50 (A),

(28) Fuson, R. C.; Mon, M. T. *J. Org. Chem.* **1961**, *26*, 756–8.
(29) "Sadtler Standard C-13 NMR Spectra"; Sadtler Research Laboratories: Philadelphia, 1976; Vol. 2, No. 335C.

0.52 (C). The compound was recrystallized from ethyl acetate to give 148 mg (50% yield) of white crystals identified as (*E*)-5-(2-penten-1-yl)-2′-deoxyuridine (**14**): ^{1}H NMR (Me_2SO-d_6) δ 7.60 (s, 1 H), 6.21 (t, 1 H, J = 7 Hz), 5.49 (m, 1 H), 5.09 (m, 1 H), 4.23 (m, 1 H), 3.76 (m, 1 H), 3.55 (m, 2 H), 2.88 (m, 2 H), 2.04 (m, 2 H), 0.95 (t, 3 H, J = 7 Hz); ^{13}C NMR (Me_2SO-d_6) 167.2 (C-4), 151.0 (C-2), 136.1 (C-6), 133.5 (CH_2CH=$CHCH_2CH_3$), 125.3 (CH_2CH=$CHCH_2CH_3$), 112.7 (C-5), 87.15 (C-4′), 83.94 (C-1′), 70.30 (C-3′), 61.15 (C-5′), 37.62 (C-2′), 28.98 (CH_2CH=$CHCH_2CH_3$), 24.78 (CH_2CH=$CHCH_2CH_3$), 13.44 ppm (CH_2CH=$CHCH_2CH_3$); the compound did not melt but softens at 94–97 °C and decomposes >180 °C. Anal. Calcd for $C_{14}H_{20}N_2O_5 \cdot 0.7H_2O$: C, 54.45; H, 6.93; N, 9.07. Found: C, 54.13; H, 6.51; N, 8.96.

(*E*)-5-(2-Penten-1-yl)-2′-deoxycytidine (15). To a stirred suspension of 5-(chloromercuri)-2′-deoxycytidine (463 mg, 1.0 mmol) in 10 mL of MeOH were added consecutively $CuCl_2$ (162 mg, 1.2 mmol), 3-chloro-1-pentene (0.58 g, 5.7 mmol), and 0.1 M Li_2PdCl_4 (2.3 mL, 0.23 mmol) in methanol. Workup and chromatography on silica gel (elution with 25:75 MeOH–$CHCl_3$ (v/v)) gave a single major product as determined by TLC [R_f 0.28 (A), 0.44 (B)]: ^{1}H NMR (Me_2SO-d_6) δ 7.74 (s, 1 H), 6.25 (t, 1 H, J = 7 Hz), 5.58 (m, 2 H), 4.29 (m, 1 H), 3.83 (m, 1 H), 3.64 (m, 2 H, superimposed on HOD peak), 3.00 (m, 2 H), 2.04 (br m, 4 H), 0.99 (t, 3 H, J = 7 Hz); ^{13}C NMR (Me_2SO-d_6) 166.3 (C-4), 155.0 (C-2), 138.3 (C-6), 133.7 (CH_2CH=$CHCH_2CH_3$), 125.2 (CH_2CH=$CHCH_2CH_3$), 104.8 (C-5), 87.15 (C-4′), 84.82 (C-1′), 70.26 (C-3′), 61.18 (C-5′), 36.87 (C-2′), 29.55 (CH_2CH=$CHCH_2CH_3$), 24.80 (CH_2CH=$CHCH_2CH_3$), 13.50 ppm (CH_2CH=$CHCH_2CH_3$); the compound does not melt but softens at 60–67 °C and decomposes at >180 °C. Anal. Calcd for $C_{14}H_{21}N_3O_4 \cdot 0.6H_2O$: C, 54.93; H, 7.26; N, 13.73. Found: C, 54.78; H, 7.10; N, 13.51.

(*E*)-5-(4-Methyl-2-penten-1-yl)-2′-deoxyuridine (16). 5-(Chloromercuri)-2′-deoxyuridine (324.1 mg, 0.7 mmol), 4-methyl-3-chloro-1-pentene (0.35 g, 2.95 mmol), and 0.1 M Li_2PdCl_4 (1.75 mL) were combined in 14 mL of MeOH, and the reaction mixture was stirred at room temperature for 20 h. Workup via H_2S precipitation of mercuric and palladium sulfides followed by chromatography on silica gel eluted with 15% MeOH/$CHCl_3$ gave **16** as the sole major product. ^{1}H and ^{13}C NMR spectra were identical with those of material obtained from the reaction of 4-methyl-1-penten-3-ol with **1** (see below).

5-(5-Cyano-2-penten-1-yl)-2′-deoxyuridine (17). (a) From 4-Chlorohex-5-enenitrile. 5-(Chloromercuri)-2′-deoxyuridine (463 mg, 1.0 mmol), 4-chlorohex-5-enenitrile (6.0 mmol), and 0.1 M Li_2PdCl_4 in MeOH (3.5 mL) were combined in 20.0 mL of MeOH and stirred at room temperature for 3 h. Workup via H_2S precipitation of mercuric and palladium sulfides followed by chromatography on silica gel eluted with 15% MeOH/$CHCl_3$ and then chromatography on Bio-Gel P-2 eluted with water gave 123 mg (38.3% yield) of **17** whose spectroscopic properties were identical with those of **17** obtained from the reaction of **1** with 4-acetoxyhex-5-enenitrile. Anal. Calcd for $C_{15}H_{19}O_5N_3$: C, 56.07; H, 5.92; N, 13.08. Found: C, 55.74; H, 6.21; N, 12.83.

(b) From 4-Acetoxyhex-5-enenitrile. 4-Acetoxyhex-5-enenitrile (1.224 g, 8.0 mmol) and 5-(chloromercuri)-2′-deoxyuridine (0.463 g, 1.0 mmol) in 40 mL of acetonitrile were mixed with 10.5 mL (1.05 mmol) of 0.1 M $LiPdCl_3$ in acetonitrile. The reaction mixture, which turned greenish black within 0.5 h, was heated to 60 °C for 4 h and cooled, 40 mL of CH_3OH was added, and the resulting mixture was treated with H_2S gas for 30 s, filtered with CH_3OH washes (4 × 20 mL), evaporated, extracted with hot H_2O (3 × 5 mL), and chromatographed on a 120 × 2.3 cm Bio-Gel P-2 column to give two UV-absorbing fractions. The later eluting, minor peak was not identified. The earlier eluting peak was evaporated and applied to a 110 × 2.3 cm, G-10, Sephadex column, giving two major UV-absorbing peaks. The earlier eluting peak was a mixture of 2′-deoxyuridine and other minor components.

The later eluting peak (50 mg 15.6% yield) was identified as 5-(5-cyano-2-penten-1-yl)-2′-deoxyuridine (**17**). It was further purified by preparative TLC using 0.5 mm thickness silica gel 60 F-254 plates (20 × 20 cm) with 25% MeOH/75% $CHCl_3$ as solvent: analytical TLC R_f 0.46, (A), 0.42 (C). ^{13}C and ^{1}H NMR showed the presence (2:1 ratio) of (*E*)- and (*Z*)-5-(cyano-2-penten-1-yl)-2′-deoxyuridines: ^{1}H NMR (360 MHz) (D_2O) δ 7.43 (s, 0.67 H), 7.42 (s, 1.33 H), 6.12 (t, 2 H, J = 7 Hz), ~5.5 (m, 4 H), 4.18 (dd, 2 H, J_1 = 6 Hz, J_2 = 5 Hz), 3.86 (dd, 2 H, J_1 = 5 Hz, J_2 = 4 Hz), 3.65 (m, 2 H), 3.58 (m, 2 H), 2.93 (d, 1.33 H, J = 6 Hz), 2.87 (d, 2.67 H, J = 6 Hz), 2.39 (m, 4 H), 2.27 (q, 2 H, J = 6 Hz), ~2.19 (m, 6 H); ^{13}C NMR (D_2O) 169.0 (C-4), 150.64 (C-2), 136.80 (C-6), 129.43, 129.06, 128.0 (CH_2CH=$CHCH_2CH_2CN$), 120.77 (C≡N), 112.79 (C-5), 87.75 (C-4′), 84.46 (C-1′), 70.81 (C-3′), 61.73 (C-5′), 37.48 (C-2′), 29.49, 28.02 (ratio 2:1, CH_2CH=$CHCH_2CH_2CN$), 24.74, 23.10 (CH_2CH=$CHCH_2CH_2CN$), 16.82 ppm (CH_2CH=$CHCH_2CH_2CN$).

5-(2-Methyl-2-propenyl)-2′-deoxyuridine (18) and 5-(2-Hydroxy-2-methylpropyl)-2′-deoxyuridine (19). To a stirred suspension of **1** (0.966 g, 2.08 mmol) in methanol (20 mL) were added 3-chloro-2-methylpropene (2.5 mL, 26 mmol), copper(II) chloride (0.30 g, 2.2 mmol), and 1.0 mL of 0.1 M Li_2PdCl_4 (0.10 mmol) in methanol. All of the solid dissolved within 1.5 h.

(a) Sodium Borohydride Workup. $NaBH_4$ (100 mg) was slowly added to the reaction mixture in small portions. The black precipitate was removed by filtration and the filtrate stirred overnight open to the atmosphere to allow oxidation of Cu^I to Cu^{II}. The green solution was treated with $NaBH_4$ (50 mg), filtered, and chromatographed on silica gel eluted with 10% MeOH/$CHCl_3$ to give a single major product with R_f 0.47 in 15% MeOH/$CHCl_3$. The material was a viscous oil which could not be induced to crystallize: ^{1}H NMR (D_2O) δ 7.75 (s, 1 H), 6.31 (t, 1 H), 4.80 (m, 2 H), 4.49 (m, 1 H), 4.05 (m, 1 H), 3.80 (narrow m, 2 H), 3.01 (s, 2 H), 2.36 (dd, 2 H), 1.72 (s, 3 H); ^{13}C NMR (D_2O) 23.75 (CH_3), 36.12 ($CH_2C(CH_3)$=CH_2), 41.56 (C-2′), 63.30 (C-5′), 72.62 (C-3′), 87.55 (C-1′), 88.83 (C-4′), 113.76 ($CH_2C(CH_3)$=CH_2), 115.21 (C-5), 140.93 (C-6), 145.87 ($CH_2C(CH_3)$=CH_2), 153.52 (C-2), 167.66 ppm (C-4).

(b) H_2S-Celite Workup. Treatment with H_2S, filtration through Celite, and chromatography of the filtrate residue on Bio-Gel P-2 (2.0 × 135 cm column) eluted with water gave two separated UV-absorbing fractions. The faster eluting product was lyophilized and dried to give 260 mg (42%) of a white solid identified as 5-(2-hydroxy-2-methylpropyl)-2′-deoxyuridine (**19**): ^{1}H NMR δ 7.81 (s, 1 H), 6.33 (t, 1 H, J = 6.5 Hz), 4.51 (m, 1 H), 4.10 (m, 1 H), 3.86 (m, 2 H), 2.52 (s, 2 H), 2.40 (dd, 2 H, J = 5.5 Hz, J_2 = 6.5 Hz), 1.23 (s, 6 H); UV (MeOH) λ_{max} 268, λ_{min} 235 nm. Anal. Calcd for $C_{13}H_{20}N_2O_6$: C, 51.94; H, 6.71; N, 9.33. Found: C, 51.56; H, 6.52; N, 9.09.

The slower eluting product was lyophilized to dryness to leave 140 mg of a white solid: UV λ_{max} 270, λ_{min} 245 nm; ^{1}H NMR showed a mixture of products.

(*E*)-5-(4-Methyl-2-penten-1-yl)-2′-deoxyuridine (16) and 5-(4-Methyl-3-oxopentyl)-2′-deoxyuridine (20). To a stirred suspension of **1** (881 mg, 1.90 mmol) in methanol (25 mL) were added 4-methyl-1-penten-3-ol (2.5 mL, 22 mmol), 0.10 M Li_2PdCl_4 (4.0 mL, 0.40 mmol) in methanol, and cupric chloride (310 mg, 1.8 mmol). After 6.5 h the black suspension was filtered, and the filtrate was treated with hydrogen sulfide and refiltered through Celite. Chromatography of the resulting oil on silica gel eluted with methanol–chloroform (5–17% v/v methanol) gave a single, major, UV-absorbing product as a white solid (408 mg) after evaporation. Column chromatography on Bio-Gel P-2 (2.0 × 135 cm) gave two compounds. The earlier eluting product was evaporated to a white solid (150 mg, 24%) identified as 5-(4-methyl-3-oxopentyl)-2′-deoxyuridine (**20**): mp 172–173 °C dec (browns at 166 °C); ^{1}H NMR δ 7.66 (s, 1 H), 6.32 (t, 1 H, J = 7 Hz), 4.52 (m, 1 H), 4.05 (m, 1 H), 3.89 (m, 2 H), 2.9–2.2 (br m, 7 H), 1.08 (d, 6 H, J = 6.5 Hz); UV λ_{max} 267, λ_{min} 235; TLC R_f 0.59 (A), 0.70 (B), 0.46 (C); mass spectrum, m/e 326 (M), 210 [5-(4-methyl-3-oxopentyl)uracil]. Anal. Calcd for $C_{15}H_{22}N_2O_6$: C, 55.21; H, 6.80; N, 8.58. Found: C, 55.32, H, 6.64; N, 8.43. The later eluting product from chromatography on Bio-Gel P-2 was a white solid (95 mg, 16%) identified as 5-(4-methyl-2-penten-1-yl)-2′-deoxyuridine (**16**): mp 111–113 °C dec; ^{1}H NMR (acetone-d_6) δ 7.76 (s, 1 H), 6.35 (t, 1 H, J = 7 Hz), 5.55 (narrow m, 2 H), 4.50 (m, 1 H), 3.98 (m, 1 H), 3.88 (narrow m, 2 H), 2.97 (d, 2 H, J = 4.5 Hz), 2.25 (dd, 2 H, J_1 = 7 Hz, J_2 = 5 Hz), 2.1 (m, 1 H), 0.95 (d, 6 H, J = 7 Hz); UV λ_{max} 267, λ_{min} 235; TLC R_f 0.60 (A), 0.72 (B), 0.53 (C); mass spectrum, m/e 310 (M), 194 [5-(4-methyl-2-penten-1-yl)uracil].

5-(3-Methyl-2-buten-1-yl)-2′-deoxyuridine (21) and 5-(1-Methoxy-3-hydroxy-3-methylbutyl)-2′-deoxyuridine (22). The same procedure outlined above for preparation of nucleosides **16** and **20** was followed with the alcohol 3-hydroxy-3-methyl-1-

butene, except that 1.10 equiv of Li_2PdCl_4 was employed and $CuCl_2$ was omitted. After silica gel and Bio-Gel P-2 chromatography the major product was a white solid (159 mg, 16%) identified as 5-(1-methoxy-3-hydroxy-3-methylbutyl)-2′-deoxyuridine (**22**): mp 69–72 °C; ^1H NMR δ 7.90 (s, 1 H), 6.31 (t, 1 H, J = 6.5 Hz), 4.45 (m, 2 H), 4.07 (m, 1 H), 3.87 (narrow m, 2 H), 3.29 (s, 3 H), 2.40 (dd, 2 H, J_1 = 5.5 Hz, J_2 = 6.5 Hz), 1.90 (d, 2 H, J = 5 Hz), 1.27 (s, 6 H); UV λ_{max} 266, λ_{min} 234; TLC R_f 0.54 (A), 0.68 (B), 0.40 (C). Anal. Calcd for $C_{15}H_{24}N_2O_7$: C, 52.32; H, 7.03; N, 8.13. Found: C, 52.33; H, 7.02; N, 7.92.

Nucleoside **21** from this experiment was identified on the basis of thin-layer chromatographic comparison to **21** prepared from 3-acetoxy-3-methylbutene and the ^1H NMR spectrum in D_2O: 7.46 (s, 1 H), 6.22 (t, 1 H, J = 6 Hz), 5.28 (m, 1 H), 4.44 (m, 1 H), 3.97 (m, 1 H), 3.75 (narrow m, 2 H), 2.92 (d, 2 H, J = 7 Hz), 2.31 (dd, 2 H), 1.72 (s, 3 H), 1.64 (s, 3 H). The yield (5%) was estimated by comparing peak areas in the ^1H NMR spectrum of the crude mixture of **21** and **22**.

(*E*)-5-(4-Methyl-1,3-pentadien-1-yl)-2′-deoxyuridine (23). To 1.37 g (9.6 mmol) of 4-methyl-3-acetoxy-1-pentene in 30 mL of methanol were added 0.556 g (1.2 mmol) of 5-(chloromercuri)-2′-deoxyuridine and 12.6 mL (1.26 mmol, 5% excess) of 0.1 M Li_2PdCl_4 in methanol. The reaction turned black immediately. It was stirred overnight (19 h) at room temperature, treated with H_2S gas for 1.0 min, filtered through Whatman no. 1 filter paper, and evaporated to give a greenish paste. The paste was dissolved in hot, distilled water (3 × 5.0 mL), applied to a 2.3 × 138 cm Bio-Gel P-2 column, and eluted with H_2O to give two major UV-absorbing peaks. The earlier eluting peak gave 20 mg (5.2% yield) of white powder. ^1H NMR indicated the product to be 5-(4-methyl-2-penten-1-yl)-2′-deoxyuridine (**16**).

The later eluting, major, product from Bio-Gel P-2 chromatography was obtained as a yellow powder (48 mg, 13%) which recrystallized from hot water to give 36 mg of fluffy yellow crystals which begin to decompose at 180 °C: TLC R_f 0.53 (A), 0.52 (C); ^1H NMR (acetone-d_6) δ 8.02 (s, 1 H), 7.23 (dd, 1 H, J_1 = 17 Hz, J_2 = 10 Hz), 6.19 (t, 1 H, J = 7 Hz), 6.00 (d, 1 H, J = 15 Hz), 5.72 (d, 1 H, J = 10.5 Hz), 4.33 (m, 1 H), 3.82 (m, 1 H), 3.71 (m, 2 H), 2.17 (dd, 2 H, J_1 = 7 Hz, J_2 = 5.5 Hz), 1.65 (s, 6 H); ^{13}C NMR (Me_2SO-d_6) 162.4 (C-4), 149.4 (C-2), 136.2 (C-6), 135.0 (C-1″), 126.0 (C-2″), 125.35 (C-3″), 121.4 (C-4″), 111.4 (C-5), 87.51 (C-4′), 84.40 (C-1′), 70.0 (C-3′), 61.1 (C-5′), 37.04 (C-2′), 25.87 (C-6″), 18.46 ppm (C-5″); IR (KBr) 3600–3200, 3090, 2980–2900, 1700, 1645, 1380, 1370, 1090 cm^{-1}. Anal. Calcd for $C_{15}H_{20}N_2O_5 \cdot H_2O$: C, 55.21; H, 6.75; N, 8.59. Found: C, 55.19; H, 6.71; N, 8.73.

5-(3-Methyl-2-buten-1-yl)-2′-deoxyuridine (21) and 5-(3-Hydroxy-3-methyl-1-butyl)-2′-deoxyuridine (24) from the Reaction of 1 with 3-Acetoxy-3-methyl-1-butene. 5-(Chloromercuri)-2′-deoxyuridine (695 mg, 1.5 mmol) and 3-acetoxy-3-methyl-1-butene were reacted as outlined above in the preparation of **23**. Chromatography on Sephadex G-10 (110 × 2.3 cm) eluted with water gave two major UV-absorbing peaks. Fractions from the latter peak were lyophilized to give 5-(3-methyl-2-buten-1-yl)-2′-deoxyuridine (**21**): 65 mg (14.6% yield); ^1H NMR (100 MHz, acetone-d_6) δ 7.75 (s, 1 H), 6.36 (t, 1 H, J = 7 Hz), 5.26 (m, 1 H), 4.52 (m, 1 H), 3.99 (dd, 1 H), 3.79 (m, 2 H), 2.98 (d, 2 H, J = 9.7 Hz), 2.30 (dd, 2 H, J_1 = 7.3 Hz, J_2 = 6 Hz), 1.74 (s, 3 H), 1.68 (s, 3 H); the compound did not melt but softened at 104–105 °C and decomposed at over 180 °C; TLC R_f 0.50 (A), 0.52 (C). Anal. Calcd for $C_{14}H_{20}O_5N_2 \cdot H_2O$: C, 53.50; H, 7.01; N, 8.92. Found: C, 53.46; H, 6.45; N, 8.93.

The earlier eluting peak from G-10 Sephadex chromatography was evaporated to 10 mL and chromatographed on Bio-Gel P-2, giving two major UV-absorbing fractions. The earlier eluting fraction gave 60 mg of solid which was still a mixture of at least two compounds by TLC in systems A and C. Tentative structure assignments on the basis of ^1H NMR (100 MHz) of the mixture are 5-(1-methoxy-3-hydroxy-3-methyl-1-butyl)-2′-deoxyuridine and 5-(1-methoxy-3-acetoxy-3-methyl-1-butyl)-2′-deoxyuridine.

The second peak off the Bio-Gel P-2 column gave 120 mg of impure product further purified by two successive runs on preparative thin-layer plates (0.5 × 20 × 20 cm, silica gel 60 F-254) eluted with 1:3 methanol–chloroform (v/v).

A second chromatography on Bio-Gel P-2 resulted in partial separation of two UV-absorbing peaks. The earlier eluting fraction (TLC R_f 0.34 (C)) was not identified. The later eluting fraction (TLC R_f 0.42 (C)) was evaporated to give 5-(3-hydroxy-3-methyl-1-butyl)-2′-deoxyuridine (**24**): 45 mg (9.6% yield); ^1H NMR (100 MHz, D_2O) δ 7.70 (s, 1 H), 6.35 (t, 1 H, J = 7 Hz), 4.46 (m, 1 H), 4.01 (m, 1 H), 3.83 (m, 2 H), 2.39 (m, 4 H), 1.70 (m, 2 H), 1.25 (s, 6 H); on being heated **24** softened at 80–85 °C and decomposed above 180 °C.

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Registry No. **1**, 65505-76-2; **3**, 73-39-2; **5**, 76334-41-3; **6**, 76334-42-4; **9**, 76334-43-5; **10**, 76334-44-6; **11**, 76334-45-7; **12a**, 76334-46-8; **12b**, 76334-47-9; **13**, 76334-48-0; **14**, 76334-49-1; **15**, 76334-50-4; **16**, 76334-51-5; **17a**, 76334-52-6; **17b**, 76334-53-7; **18**, 76334-54-8; **19**, 76334-55-9; **20**, 76334-56-0; **21**, 76334-57-1; **22**, 76334-58-2; **23**, 76334-59-3; **24**, 76334-60-6; 5-allylcitidine, 66270-30-2; 5-(1-methoxy-3-hydroxybutyl)-2′-deoxyuridine, 76334-61-7; 5-(1-methoxybutyl)-2′-deoxyuridine, 76334-62-8; 5-(2,3-dihydroxybutyl)-2′-deoxyuridine, 76334-63-9; 5-(1-methoxy-3-acetoxy-3-methyl-1-butyl)-2′-deoxyuridine, 76334-64-0; 5-(2,2-dimethoxy-1-methylethyl)-2′-deoxyuridine, 76334-65-1; 5-(HgCl)C, 65523-07-1; 5-(HgCl)dC, 65523-09-3; 4-chlorohex-3-enenitrile, 76334-66-2; 3-acetoxy-1-butene, 6737-11-7; 3-acetoxy-4-methyl-1-pentene, 1115-38-4; 3-acetoxy-3-methyl-1-butene, 24509-88-4; 4-acetoxyhex-5-enenitrile, 76334-67-3; 3-chloro-1-butene, 563-52-0; 3-chloro-1-pentene, 24356-00-1; 4-methyl-3-chloro-1-pentene, 68317-98-6; 4-chlorohex-5-enenitrile, 72335-20-7; 3-chloro-2-methylpropene, 563-47-3; 4-methyl-1-penten-3-ol, 4798-45-2; 3-hydroxy-3-methyl-1-butene, 115-18-4; 3-buten-2-ol, 598-32-3; β-CPAA, 14618-78-1; β-CPA, 3515-93-3; 4-hydroxyhex-5-enenitrile, 76334-68-4; ethyl allyl ether, 557-31-3; allyl chloride, 107-05-1; allyl alcohol, 107-18-6.