Iodo Enol Lactone Formation and Hydrolysis

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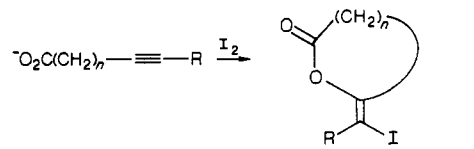
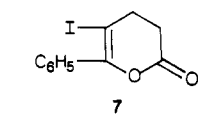
Received October 13, 1988

Introduction

Iodo enol lactones are formed by the iodolactonization of alkynoic acids. Our interest in this subject stems from the investigation of another iodocyclization reaction, in which the cyclic sulfonium salts are formed from alkenyl thioethers and in which the addition of iodine to the double bond induces participation by the neighboring thioether group.[1] Iodolactonization of alkenoic acids is widely used to gain stereocontrol in the construction of precursors and subunits of many macrolide natural products[2] while iodolactonization of alkynoic acids produces halo enol lactones that have value as inactivators of serine proteases.[3] While the iodolactonization of alkenoic acids is carried out in aqueous solutions with iodine, a bicarbonate salt, and potassium iodide, much in the original fashion of Bougault, the preferred method of iodolactonization of alkynoic acids uses *N*-iodosuccinimide and a phase-transfer system or dry acetonitrile.[3] Additionally, Staninets and Shilov[4] have reported kinetic data on the aqueous iodolactonization of many alkenoic acids, but only two of the alkynoic acids, 4-pentynoic acid (**1**) and 2-propynylmalonate, both of which form tetrahydrofuran-2-ones (γ-butyrolactones). We thought that it would be of interest to determine if a tetrahydropyran-2-one (a δ-valerolactone) can be formed by aqueous iodolactonization of 5-hexynoic acid (**2**), and to determine the effect of a terminal phenyl group on the rates and products of aqueous iodolactonization by comparing the reactions of 5-phenyl-4-pentynoic acid (**3**), to the reactions of **1**.



1: $n = 2$, R = H
2: $n = 3$, R = H
3: $n = 2$, R = C_6H_5
4: $n = 2$, R = H
5: $n = 3$, R = H
6: $n = 2$, R = C_6H_5



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Experimental Section

Equipment and Chemicals. The following instruments were used: General Electric Company Model QE 300 or Varian Model EM390 NMR spectrometers, Beckman DU spectrophotometer with a Gilford Update, IBM IR32 infrared spectrometer, Radiometer Copenhagen PHM 82 standard pH meter, Varian Model 5020 gradient liquid chromatograph with an analytical silica gel column and an eluent of 90–99% CH_2Cl_2 and 10–1% CH_3CN, EM Reagents silica gel 60 F254 precoated TLC sheets with mixtures of ethanol in chloroform, ZAB-HS-2F Model high resolution mass spectrometer (VG Analytical, Wythenshawe, U. K.), Trio-2 (VG Masslab, Altrincham, U. K) or Hewlett-Packard 5890GC-5970MSD low resolution mass spectrometer. The mass spectra on the two VG instruments were obtained at the Facility for Advanced Instrumentation at UCD. 4-Pentenoic and 4-pentynoic acids were purchased from Aldrich Chemical Co. and recrystallized from benzene–petroleum ether. Separate lots of 5-hexyn-1-ol were purchased from Aldrich Chemical Co. and from Fairfield Chemical Co., Inc.

Kinetics. Iodolactonization. The triiodide concentration was monitored spectrophotometrically at 353 nm under conditions of invarient pH, concentration of alkynoic acid, concentration of iodide, and temperature. The method has been described previously.[1]

Iodo Enol Lactone Hydrolysis. A modification of the method of Daniels et al.[3b] was used. Solutions of 0.005 M iodo enol lactone were prepared by dissolving the iodo enol lactone in 0.40 mL of acetonitrile and adding 9.60 mL of 26 °C, pH 6.5, 0.10 M sodium phosphate buffer. The mixture was returned to the thermostated bath and 0.50-mL aliquots were removed, extracted in a centrifuge tube with 1.0 mL of methylene chloride containing 10 μL of a 0.0010 M solution of diphenylacetylene in acetonitrile, and extracted twice more with 1.0-mL portions of methylene chloride. The organic layers were combined, dried over Na_2SO_4, and analyzed by HPLC. Plots of ln (% remaining iodo enol lactone) versus time were linear and had correlation coefficients of 0.987–0.996 to >60% completion. The values reported are averages of two determinations.

Synthesis. Preparation of 3. Compound **3** was prepared from 4-benzoylbutryic acid (Aldrich Chemical Co.) via pyrolysis of 3-(4-phenyl-1,2,3-selenadiazol-5-yl)propanoic acid.[5] Compound **3** was purified by column chromatography (Baker 60 × 200-mesh silica gel, 5% ethanol in chloroform) and recrystallization from water; mp 100 °C (lit.[5] mp 99–100 °C); ^1H NMR ($CDCl_3$) δ 7.2 (m, 5), 2.6 (m, 4).

Preparation of the Mixture of 1 and 2. 5-Hexyn-1-ol (2.5 g, 0.0255 mol, single peak by GC/MS, $m/e = 97$ (M − 1)) in acetone was added slowly to a solution of chromium trioxide (5.12 g, 0.0512 mol) in 5 M sulfuric acid.[6] Using the literature workup, the crude product (1.87 g) was distilled at 64 °C (1–2 Torr) (lit.[6b] **1**, crystalline plates, mp 53–55 °C, **2**, crystaline plates, mp 41–43.5 °C, bp 106 °C/9 Torr). When the product was analyzed by GC/MS, it was found to be a mixture of **1** ($m/e = 97$ (M − 1) and **2** ($m/e = 111$ (M − 1)) in the ratio 12:88.

Iodolactonization. Method 1. Aqueous Solution.[2] The organic acid (0.3–0.5 g) was dissolved in 10 mL of water containing sufficient phosphate buffer or bicarbonate to adjust the pH to 6.5. A stoichiometric amount of the solution containing 0.096 M iodine and 0.2 M potassium iodide was added, in portions, to the foil-wrapped reaction flask, with stirring, until the solution was colorless or up to 24 h. Residual iodine was destroyed with a 5% sodium thiosulfate solution and the mixture extracted with methylene chloride (2–20 mL). The organic layer was washed with 5% sodium bicarbonate and dried over sodium sulfate. Removal of the solvent under reduced pressure gave the lactones.

Method 2. Two Phase. The reaction was carried out as above with the exception that a 20-mL layer of methylene chloride was added to the reaction mixture at the beginning of the reaction.

All of the iodo enol lactones are light and temperature sensitive and must be stored in foil-wrapped containers in the freezer.

Iodolactonization of 3. By method 2, **3** (0.087 g, 5.0×10^{-4} mol) was converted quantitatively to 5-(phenyliodomethylene)-tetrahydrofuran-2-one (**6**) in 9 h: IR 1807 cm^{-1}; ^1H NMR ($CDCl_3$)

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0022-3263/89/1954-2764$01.50/0

Table I. Constants for Reaction of Aqueous Iodine with 3[a]

run	10^3[3]	10^3[KI]	$10^2 \times$ buffer	pH	$10^4 k_1$, s^{-1}	k_2, M^{-1} s^{-1}
1	1.00	50.0	5.00	5.0[b]	0.325 ± 0.008	0.033
2	1.00	25.0	5.00	5.0[b]	0.667 ± 0.003	0.0667
3	1.00	12.5	5.00	5.0[b]	0.895 ± .01	0.090
4	1.00	6.25	5.00	5.0[b]	1.45 ± <.01	0.145
5	1.00	3.13	5.00	5.0[b]	2.9 ± 0.1	0.29
6	1.00	3.13	3.34	5.0[b]	2.27 ± 0.07	0.227
7	1.00	3.13	1.67	5.0[b]	1.98 ± 0.12	0.198
8	1.00	3.13	5.00	2.7[c]	0.155 ± 0.006	0.0155
9	1.00	3.13	5.00	3.8[c]	0.976 ± 0.005	0.0976
10	1.00	3.13	5.00	6.0[b]	3.0 ± 0.2	0.30
11	0.33	3.13	5.00	5.0[b]	1.31 ± 0.18	0.40
12	0.67	3.13	5.00	5.0[b]	1.8 ± 0.3	0.27

[a] 26.0 °C, all concentrations in molarity, $[I_3^-] = (3–9) \times 10^{-5}$ M, [KI] + [KCl] = 1.0 M. Error determined from replicate runs. [b] Acetate buffer. [c] Chloroacetate buffer.

δ 2.8 (m, 2), 3.1 (m, 2), 7.3 (m, 3), 7.5 (m, 2); ^{13}C NMR ($CDCl_3$) δ 28.36, 43.42, 105.00, 124.8, 128.11, 129.67, 148.65, 174.69; single peak in HPLC; single spot on TLC, R_f = 0.74 (5% ethanol in chloroform); high resolution GC/MS, m/e = 299.89636 ($C_{11}H_9O_2I$).

Iodolactonization of 1. By method 1, 5(*E*)-(iodomethylene)tetrahydrofuran-2-one (**4**)[3a] precipitated from the reaction mixture during the reaction between the aqueous iodine and 1 in 98% yield: IR 1808 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ 5.8 (t, 1 H), 2.8 (m, 4 H).

Iodolactonization of the Mixture of 1 and 2. By method 1: the reaction of aqueous iodine and the mixture of 1 and 2 (0.409 g, 3.71×10^{-3} mol) yielded a yellow solid, CHI_3 (0.17 g, 4.3×10^{-4} mol); ^{1}H NMR ($CDCl_3$) δ 5.4 (s). The GC/MS analysis of the total product obtained by extraction with methylene chloride contained three major peaks, the retention times, the base peaks, and identification are listed: 5.3–6.0 min, m/e = 267 (CHI_3 – 127); 5.9 min, m/e = 224 (**4**); 7.7 min, m/e = 238 (**5**). The three major peaks were also separable on the HPLC analytical column.

By method 2: The reaction of aqueous iodine and the mixture (0.30 g, 2.7×10^{-3} mol) yielded 0.304 g of product. The GC/MS analysis of the product contained two major peaks, which were identical to **4** and **5** and had ratios of area of 18:82. The sample had two vinyl protons with ^{1}H NMR shifts of δ 5.8 of **4** and δ 5.9 of **5**. No CHI_3 was detected.

Pure **5** (single peak by GC/MS) was prepared by reacting the mixture of acids by using method 2. To the mixture (0.60 g, 5.4×10^{-3} mol) was added 0.5 equiv of iodine. After 23 h, the methylene chloride layer containing a mixture of **4** and **5** was removed. A portion of fresh methylene chloride and 0.5 equiv of the aqueous iodine solution were added, and the reaction was stirred for 32 h. The regular workup of the second organic layer yielded of pure **5** (0.49 g, 2.0×10^{-3} mol).

With *N*-iodosuccinimide. Following the literature procedure,[3a] a mixture of **4** and **5** with ratios of GC/MS areas of 13:87 was obtained. No CHI_3 was detected. The ratio of iodo enol lactones was 11:89 as determined from integration of the two vinyl proton signals at δ 5.9 (**4**) and δ 6.0 (**5**).

Results

Compound **3** is converted quantitatively to a single product, **6**, in 9 h. The stereochemistry (*E* or *Z*) was not determined since there is no diagnostic alkene proton for ^{1}H NMR analysis and suitable crystals could not be grown for a structural determination. The rates of the reaction of the alkynoic acids with iodine were monitored spectrophotometrically by using the triiodide absorbance at 353 nm of the samples in thermostated cells under conditions of limiting amounts of triiodide, and invariant, high concentrations of buffers, iodid, and alkynoic acid, HA. Under these conditions the reaction is pseudo first order in triiodide, and through more than 2 half-lives, the coefficient of correlation is greater than 0.997. The pseudo-first-order rate constants, k_1, for the reaction of **3** are listed in Table I. The reaction is first order in **3** (runs 5, 11, and 1, the average k_2 is 0.32 ± 0.05 M^{-1} s^{-1} with no trend), and the second-order rate constants, k_2, which are listed in Table I, were calculated as $k_1/[HA]$. The rate is inversely proportional to the iodide ion concentration (runs 1–5) as shown by the plot of 4 + log k_1 versus log [KI] (Figure 1), where the value of the equilibrium constant for the formation of triiodide, K_I, is 723. At a given pH and iodide, the kinetics follow the rate law

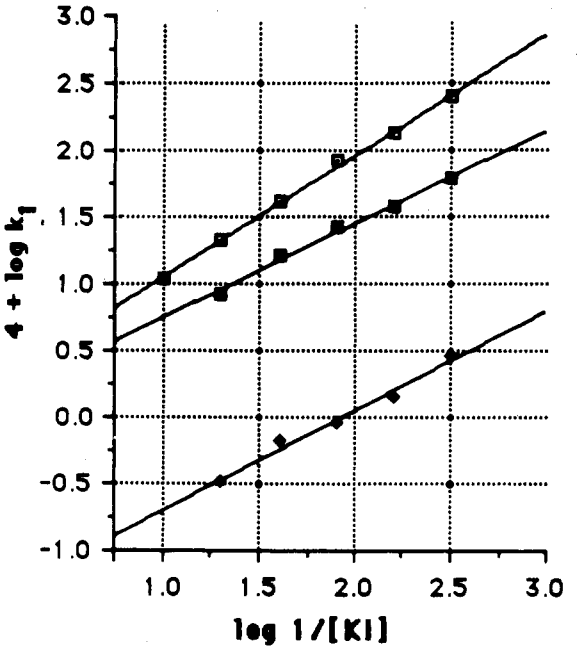


Figure 1. Plots of the log of the pseudo-first-order rate constants in s^{-1} versus the log {1/[KI]} for the iodolactonization of unsaturated acids in acetate buffer, pH 5.0, at 26.0 °C, [KI] + [KCl] = 1.0 M. (□) 4-Pentenoic acid, $y = 0.151 + 0.91x$, R = 1.00; (◆) **3**, $y = -1.43 + 0.744x$, R = 0.99; (■) **1**, $y = 0.0624 + 0.695x$, R = 0.99.

$$d[I_3^-]/dt = d[HA]/dt = -k_2[I_3^-][HA]$$

The value of k_2 is inversely proportional to $[I^-]$

$$d[HA]/dt = -[k_2'/[I^-]][I_3^-][HA] \quad (1)$$

$$[I_3^-] = K_I[I_2][I^-]$$

$$d[HA]/dt = -k_2'K_I[I_2][HA]$$

There is a variation with the concentration of acetate buffer (runs 5–7, average k_2 is 0.24 ± 0.03 M^{-1} s^{-1}) and the rate constant appears to increase by 14% with each 0.010 M increase in acetate buffer. However, the variation may be due to reproducibility error. The dependence on hydronium ion (runs 5 and 8–10) shows that $[k_2'K_I]$ is proportional to $K_{HA}/[[H_3O^+] + K_{HA}]$ when K_{HA} has the value 7×10^{-5}. Thus, the final rate expression is

$$d[HA]/dt = -k_2''[I_2][HA][K_{HA}/\{[H_3O^+] + K_{HA}\}] = -k_2''[I_2][A^-] \quad (2)$$

The aqueous iodolactonization of the next two compounds has been discussed in the literature[4b] but we were unable to determine the pH or the concentrations of iodide under which the reported data were obtained. In order to compare the rates of our compound, under the same set of solutions, we obtained our own kinetic values for **1** and for 4-pentenoic acid. At pH 5.0 the rates are inversely proportional to the concentration of the iodide ion as shown in Figure 1.

The inverse addition of commercial 5-hexyn-1-ol to chromium trioxide[6a] should produce **2**. In our hands, the

acid produced from the oxidation of commercial 5-hexyn-1-ol is a mixture of **1** and **2**, in the ratio 12:88 as verified by GC/MS. The same ratio of the corresponding lactones **4** and **5** was produced by use of *N*-iodosuccinimide.[3a]

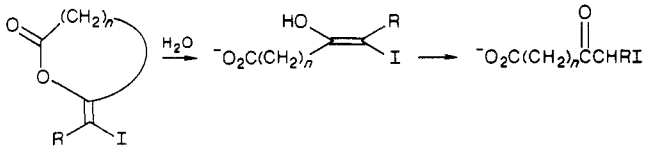
When the mixture of **1** and **2** was treated with aqueous triiodide according to method 1, at either pH 4.5 or 6, the product was a mixture of iodoform, **4**, and **5**. The mixture was analyzed by GC/MS, HPLC, and ^{1}H NMR. Indeed, during the iodolactonization product runs, we observed the precipitation of iodoform from the mixture within 2 h at pH 5.6. Since the iodoform reaction of the iodomethyl keto acid consumes triiodide, it would be difficult to obtain the simple rate of iodolactonization of **2**. For that reason, we did not seek another method for the preparation of **2**, but instead, we studied the competitive rates[7] of the consumption of aqueous triiodide by known mixtures of **1** and **2** using method 2 to avoid iodolactone hydrolysis. We did not observe hydrolysis of **4** during the aqueous iodolactonization of **1** alone.

When a small, limiting amount of iodine reacts with a mixture of **1** and **2**, the rate constants for the two alkynoic acids, k_1:k_2, can be determined by use of the equation

$$k_1{:}k_2 = [[\mathbf{4}]/[\mathbf{5}]][[\mathbf{2}]_0/[\mathbf{1}]_0]$$

in which k_1:k_2 is the ratio of the rate of iodine consumption by **1** to the rate of iodine consumption by **2**, [**4**] is the concentration of product formed from **1** and [**5**] is the concentration of product formed from **2** after 5% of the stoichiometric amount of iodine has been added, and $[\mathbf{2}]_0/[\mathbf{1}]_0$ is the ratio of the initial concentrations of **2** and **1**. When $[\mathbf{2}]_0/[\mathbf{1}]_0$ equals 88:12 [**4**]/[**5**] equals 71:29, and in a second experiment, when $[\mathbf{2}]_0/[\mathbf{1}]_0$ equals 43:57, [**4**]/[**5**] equals 92.3:7.7. Thus, the value of k_1:k_2 is equal to 17 ± 2.

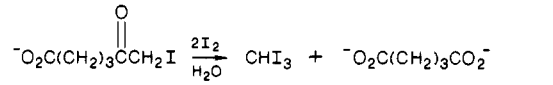
In order to show that hydrolysis can be competitive with iodolactonization of **2** and not with **1**, we determined that compound **5** hydrolyzes with a rate constant of (2.5 ± 0.2) × 10^{-5} s^{-1} and **4** hydrolyzes with a rate constant of (1.8 ± 0.2) × 10^{-5} s^{-1} in 0.1 M, pH 6.5 phosphate buffer in 4% aqueous acetonitrile at 26 °C.



Discussion

Product Formation. Compound **3** is converted quantitatively to a single isomer of **6**, which is the kinetically controlled product by *5-Exo-Trig* cyclization.[8a] Although *6-Endo-Trig* cyclization to **7** is permitted[8a] and has been observed by Yamamoto in the Hg(II) cyclizations of **3**,[8b] it did not occur with iodine. Similarly, iodination of the alkene, *cis*-5-phenyl-4-pentenoic acid yields only the corresponding γ-butyrolactone.[9] However, *trans*-5-phenyl-4-pentenoic acid yields a mixture of the γ-butyrolactone and the δ-valerolactone and methyl 2-(2-phenylethynyl)-benzoate cyclized in the *6-Endo-Trig* manner to the δ-valerolactone with lithium bromide and bromine in acetic acid.[10] In the latter case, the reaction is thought to involve a bridged bromonium ion that is stabilized by the electron-donating phenyl group on carbon 1 of the ethynyl group. In the present case, the reaction involves cyclization at the iodine-complexed alkyne bond, and, apparently, stabilization of a positive charge by the phenyl group is not as important.

The iodo enol lactones are the sole organic products of the reactions of **3** and **1**. The product of the slow iodolactonization of **2** is **5**, which, if it left in the aqueous solution during the course of the cyclization reaction, hydrolyzes to the iodomethyl ketone. The hydrolysis product reacts further with iodine to produce iodoform. However,



if a second phase of methylene chloride is present to extract out **5** as it is formed, a reasonably high yield is obtained, even after 30 h in the dark.

Iodolactonization Kinetics. The rate expression for the reaction of **3** is given in eq 1 where HA is **3**. The dependence of the rate on the inverse of iodide ion concentration in eq 1 indicates that the electrophilic species is iodine, as shown in Scheme I and in eq 2. The same iodide dependence has been observed in all iodolactonization reported in the literature.[4a] The data for the 4-pentynoic acids were not as well-correlated as those for 4-pentenoic acid. The same set of triiodide solutions was used for all the data shown in Figure 1. Since the rate constants will be used in conjunction with a discussion of iodolactonization in preparative solutions, the *y* axis in Figure 1 has been drawn at a value corresponding to 0.18 M KI, which is about the average concentration of KI in these mixtures. The lines in Figure 1 are not parallel, but no reasonable interpretation could be made for the smaller inverse dependence (between 0 and −1); however, the same dependence was observed in the instance where the neighboring group was a thioether group.[1]

The pH dependence shown in eq 2 indicates that it is the conjugate base of the acid (K_{HA} = 7 × 10^{-5}) that reacts rapidly with iodine and in the rate-determining step, the carboxylate can act as the nucleophile to form the iodo lactone, as shown in Scheme I. This iodocyclization mechanism was proposed by Shilov[4a] for alkenoic and other alkynoic acids. The maximum rate of formation of iodo lactone will occur in solutions of pH 6.5 and there is no value in using solutions of higher pH.

The kinetics of the iodocyclization reaction differ from those of the iodination of α,β-unsaturated alkynoic acids, propiolic and phenylpropiolic acids,[11] which have k_{HA}:k_A ratios of 1.6 and ca. 0.5, and thus both the acid or anion consume iodine. Although the α,β-unsaturated alkynoic acids have multiterm rate laws, one of the terms corresponds to attack of the electrophile (iodine) and nucleophile (iodide) in the rate-determining step, analogous to the process in iodolactonization that involves attack of iodine and the anion of the carboxylic acid.

The relative reactivities of the three alkynoic acids examined in this work are **1**:**3**:**2** = 17:6:1. On the same scale, the relative reactivities of the alkenoic acids are 4-pentenoic:5-phenyl-4-pentenoic:5-hexenoic = 850:620:110. Thus, chain length and substitution have similar effects in both series of unsaturated acids. There has been some interest, recently, in the relative reactivities of C–C double and triple bonds toward electrophiles.[12] Neither physical

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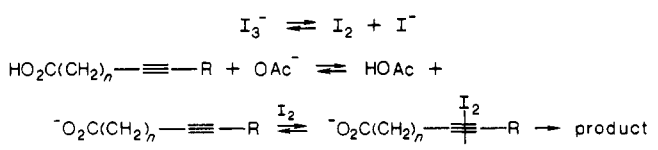
(9) Julia, M.; Guy-Rousault, A. *Compt. Rend.* **1964**, *258*, 3728.
(10) Oliver, M. A.; Gandour, R. D. *J. Org. Chem.* **1984**, *49*, 558.
(11) Mauger, E.; Berliner, E. *J. Am. Chem. Soc.* **1972**, *94*, 194 and earlier papers.

Scheme I



nor kinetic measures is self-consistent. Bromine reacts more rapidly with alkenes than with alkynes. For styrene:phenylacetylene the ratio is 400, whereas for 1-hexene:1-hexyne, the ratio is 1.7×10^6. The wide variation in the ratios has been interpreted in terms of the type of cationic intermediate that is formed, and the ratios are smaller when the intermediate is bridged rather than open, and when the solvent is more nucleophilic in nature. No ratios have been determined for iodine addition since iodine does not react readily with isolated double or triple bonds. In our iodolactonization reactions the alkenoic acids react only 50–100 times faster than the alkynoic acids, and the value depends on the concentration of KI (see Figure 1). The small and constant ratios are consistent with the postulated π-complex formation with both alkenes and alkynes[13] and the prominence of the neighboring carboxylate anion in these reactions.

Hydrolysis. For the corresponding 3-phenyl-substituted iodo enol lactones,[3b] it has been observed that 3-phenyl-6-(iodomethylene)tetrahydrofuran-2-one hydrolyzes 5.7 times more slowly than 3-phenyl-5-(iodomethylene)-tetrahydrofuran-2-one at pH 7.2. Compound **5** is formed 17 times more slowly than **4**, but if **5** also hydrolyzes more slowly than **4**, we should have observed hydrolysis of both compounds. For this reason we determined the rates of hydrolysis of **5** and **4** at pH 6.5 and found that they hydrolyze at approximately the same rate. There is precedent for the similar rates of hydrolysis of **5** and **4** since they are geometrically similar to anhydrides and it has been observed that succinic anhydride hydrolyzes at about the same rate as glutaric anhydride in neutral solution.[14] Thus, we can extrapolate the rates of iodo enol lactone formation to 0.2 M KI and compare the rates of iodo lactone formation (extrapolated from values at pH 5 in Figure 1–at pH 6.5 they would be slightly faster) and hydrolysis (see Results) under preparative conditions: for **5**, these rates are approximately 1:2.5, whereas for **4** the rates are approximately 10:1. Compound **5** is capable of hydrolyzing as soon as it is formed, while **4** is formed considerably more rapidly than it is hydrolyzed. For this reason 5-(iodomethylene)furan-2-ones such as **4** may be formed with aqueous iodine, but the 6-(iodomethylene)-pyran-2-ones such as **5** may be prepared only with concurrent extraction from the aqueous solution.

Acknowledgment. We thank the University of California for a President's Undergraduate Fellowship to G. W.L.

Registry No. **1**, 6089-09-4; **2**, 53293-00-8; **3**, 3350-92-3; **4**, 120205-37-0; **5**, 120205-38-1; **6**, 120205-39-2; 4-benzoylbutyric acid, 1501-05-9; 3-(4-phenyl-1,2,3-selenadiazoyl-5-yl)propanoic acid, 49769-22-4; 5-hexyn-1-ol, 928-90-5; iodine, 7553-56-2.

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Synthesis of Pyrimidine 3′-Allyl-2′,3′-dideoxyribonucleosides by Free-Radical Coupling

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Received November 17, 1988

Since 3′-azido-2′,3′-dideoxythymidine (AZT) has been reported[1] as a potent antiviral agent against human immunodeficiency virus (HIV), a number of 3′-azido- and 2′,3′-dideoxynucleosides have been synthesized and evaluated against the virus in order to determine the structure–activity relationships.[2-8] These studies suggest that any modification of the 5-position of AZT decreases the anti-HIV activity.[7] Therefore, modification of the ribose moiety seemed to be a logical extension of the above findings. From the X-ray crystallographic studies of AZT, Camerman et al.[9] proposed that the 3′-azido group plays a significant role in binding to the reverse transcriptase of HIV. As a part of our continuing efforts to study the structure–activity relationships of pyrimidine nucleosides as potential antiviral agents against HIV, it was of interest to synthesize 3′-allyl-substituted pyrimidine nucleosides **7** and **8** as nonpolar analogues of AZT and 3′-azido-2′,3′-dideoxyuridine (CS-87, AzddU),[10,11] which is expected to undergo clinical trials in the near future.

Results and Discussion

Our initial approach for the introduction of an allyl group at the 3′-position of pyrimidine nucleosides was to utilize 3′-ketonucleosides,[10-12] to which appropriate Grignard reagents could be added to obtain the corresponding 3′-alcohols (3′-up configuration).[12,14] In order to obtain the 3′-deoxygenated nucleosides **5** and **6** from the above-mentioned alcohols, various methods of deoxygenation were tried. Direct deoxygenation of the alcohols with arylalkylsilane–borontrifluoride[13] failed to give the desired products. Other deoxygenation methods such as reduction of 3′-oxalate[11] or 3′-xanthate[14] with tributyltin hydride were also unsuccessful, producing only complex mixtures.

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