products are two γ-ketols (or their hemiketal cyclic forms) and a ketone resulting from their decomposition.

Reduction of 6-Methoxy-1,9,10,10a-tetrahydro-3(2*H*)-phenanthrone (7). The reduction of 2.5 g of the racemic ketone (±)-**7** at pH 6 (−1.4 V) gave 1.6 g of a pure crystallized diol, (±)-t.t.t. isomer. (±)-Trans-threo-trans isomer (tentative structure): mp 140 °C dec; IR (KBr) ν_{OH} 3410 cm^{-1}; NMR (Me_2SO + $CDCl_3$) δCH(4) = 6.47 ppm, δOH = 4.33 ppm, δCH_3 = 3.57 ppm.

From the solution we obtained two fractions: 300 mg of a pure γ-ketol [mp = 160 °C; ν_{OH} 3650 and 3490, $\nu_{C=O}$ 1715 cm^{-1} (KBr); NMR ($CDCl_3$ + Me_2SO) δCH(4) = 6.32 ppm, δCH_3 = 3.77 and 3.80 ppm, δOH = 3.60 ppm] and 400 mg of a mixture of the t.t.t. diol (100 mg of which was separated by crystallization in ether) and two ketols in an 8:2 ratio, characterized by their NMR spectra (δCH = 5.58 ppm, δOH = 3.93 ppm and δCH = 6.20 ppm, δOH = 3.62 ppm, respectively).

Reduction of 7-Methoxy-4-methyl-1,9,10,10a-tetrahydro-3(2*H*)-phenanthrone (8). Racemic Ketone (±)-8, pH 6. The reduction of 2.5 g of the racemic ketone (±)-**8** at pH 6 (−1.5 V) gave 1.1 g of a crystallized mixture of the two diols (±)-t.t.t. (tentative structure) (δOH = 4.53 ppm) and (±)-c.t.t. (δOH = 5.07 and 4.73 ppm) in a 13:7 ratio. From the mother solution, we obtained by TLC 1 g of a mixture of saturated ketones, 190 mg of (±)-t.t.t. and (±)-c.t.c. diols in a 11:9 ratio, and 50 mg of a complicated mixture.

Racemic Ketone (±)-8, pH 11. The reduction of 2.7 g of the racemic ketone (±)-**8** at pH 11 (−1.7 V) gave a mixture of two insoluble diols (2 g), (±)-t.t.t. and (±)-c.t.t. (tentative structures), in a 9:11 ratio. By TLC of the residue, we separated 240 mg of a mixture of saturated ketones and three fractions (140, 50, and 240 mg) containing ketonic products (IR). By crystallization, we obtained 70 mg of the (±)-t.t.t. diol (mp = 203 °C dec; ν_{OH} (KBr) 3520 and 3370 cm^{-1}) and 120 mg of another symmetric diol (mp = 174 °C dec; ν_{OH} 3525 and 3510 cm^{-1}; δOH = 3.97 ppm, δCH_3(OMe) = 3.7 ppm, δCH_3(4) = 2 ppm).

Registry No.—(±)-**2**, 63783-22-2; (+)-**2** pinacol deriv., t.t.t. isomer, 68782-29-6; (+)-**2** pinacol deriv., c.e.t. isomer, 68832-55-3; (±)-**2** pinacol deriv., t.t.t. isomer, 68832-56-4; (±)-**2** pinacol deriv., c.t.t. isomer, 68832-57-5; (±)-**2** pinacol deriv., t.e.t. isomer, 68832-58-6; (±)-**2** pinacol deriv., c.e.t. isomer, 68832-59-7; (±)-**3**, 68782-30-9; (±)-**3** pinacol deriv., t.t.t. isomer, 68782-31-0; (±)-**3** pinacol deriv., c.t.c. isomer, 68832-60-0; (±)-**3** pinacol deriv., c.t.t. isomer, 68832-61-1; (±)-**3** pinacol deriv., c.e.t. isomer, 68832-62-2; (±)-**3** pinacol deriv., t.e.t. isomer, 68832-63-3; (±)-**4**, 68782-32-1; (+)-**4** pinacol deriv., t.t.t. isomer, 68782-33-2; (+)-**4** pinacol deriv., c.e.t. isomer, 68832-64-4; (+)-**4** pinacol deriv., c.t.c. isomer, 68832-65-5; (±)-**4** pinacol deriv., t.t.t. isomer, 68832-66-6; (±)-**4** pinacol deriv., c.t.t. isomer, 68832-67-7; (±)-**4** pinacol deriv., c.t.c. isomer, 68832-68-8; (±)-**4** pinacol deriv., c.e.c. isomer, 68832-69-9; (±)-**4** pinacol deriv., c.e.t. isomer, 68832-70-2; (±)-**4** pinacol deriv., t.e.t. isomer, 68832-71-3; (±)-**6** pinacol deriv., t.t.t. isomer, 68782-34-3; (±)-**7** pinacol deriv., t.t.t. isomer, 68813-13-8; (±)-**8** pinacol deriv., t.t.t. isomer, 68782-35-4; (±)-**8** pinacol deriv., c.t.t. isomer, 68832-72-4; (±)-**8** pinacol deriv., c.t.c. isomer, 68832-73-5; 1,2,3,4,4a,9,10,10a-octahydro-10a-methyl-3-phenanthrenone, 68782-36-5; 1,2,3,4,4a,9,10,10a-octahydro-4-methyl-3-phenanthrenone, 68782-37-6; 1,2,3,4,4a,9,10,10a-octahydro-4,10a-dimethyl-3-phenanthrenone, 68782-38-7; 1,1′,2,3,9,9′,10,10′,10a,10a′-decahydro-3-hydroxy-6,6′-dimethoxy[3,4a′(2′*H*)-biphenanthren]-3′(4′-*H*)-one, 68782-39-8; 1,2,3,4,4a,9,10,10a-octahydro-4-methyl-7-methoxy-3-phenanthrenone, 68782-40-1.

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Synthetic Electrochemical Studies on Nucleosides. 1. Novel Method for the Synthesis of 2′,3′-Unsaturated Nucleosides via Electrolysis

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A novel method for the synthesis of 2′,3′-unsaturated nucleosides via electrochemical reductions of 2′(3′)-*O*-acyl-3′(2′)-deoxyhalonucleosides is described. Electrolysis of 9-(2,5-di-*O*-acetyl-3-bromo-3-deoxy-β-D-xylofuranosyl)adenine (**1a**) at −1.3 V vs. SCE in MeOH–AcONa (0.25 M) gave 9-(5-*O*-acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine (**2a**) in 76% yield. The compound **2a** was also obtained in 74% yield via electrolysis of a positional isomer **1b**, 9-(3,5-di-*O*-acetyl-2-bromo-2-deoxy-β-D-arabinofuranosyl)adenine, under the same conditions. This electrochemical method could be extended to the synthesis of pyrimidine nucleosides (**2b** and **2c**) using tetraethylammonium tosylate as an electrolyte in DMF solution. In the electrolysis of **1f** in MeOH–AcONa (0.25 M), however, the extensive glycosidic cleavage followed by the formation of methyl 5-*O*-propionyl-2,3-dideoxy-D-*glycero*-pent-2-enofuranoside (**6**), furfuryl propionate (**7**), and uracil was observed, and **2c** was obtained in only 38% yield. This glycosidic cleavage provides the first example of an electrochemical elimination of a halogen and an adjacent substituent bonded via a nitrogen atom. 3′-Deoxyadenosine (cordycepin) was obtained in 14% yield together with **3a** (29%) and adenine (55%) via the electrolysis of 9-(3-deoxy-3-iodo-β-D-xylofuranosyl)adenine (**1d**) in MeOH–AcONa (0.25 M).

Electrochemical studies on nucleosides and nucleotides have been reported by a number of investigators.[1] These studies have been almost exclusively focused on reduction or oxidation of the nucleic acid bases by using polarography and related techniques, e.g., cyclic voltammetry,[1b,h] alternating current polarography,[1a,f] and oscillographic polarography,[1a] and little attention has been paid to the synthetic application of electrochemical techniques to the nucleoside field except in a few instances.[2] Electrolysis can be carried out in neutral media (protic or aprotic) at temperatures ranging from ambient or higher to well below 0 °C, and controlled potential electrolysis makes possible selective reaction of very similar

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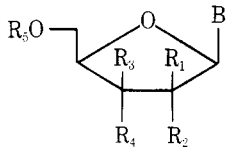
Table I. Polarographic Half-Wave Potentials



1a-i

compd	B	R_1	R_2	R_3	R_4	R_5	$E_{1/2}$, V vs. SCE
1a	Ad[a]	H	AcO	Br	H	Ac	−1.3
1b	Ad	Br	H	H	AcO	Ac	−1.4
1c	Ad	H	HO	Br	H	H	−1.6
1d	Ad	H	HO	I	H	H	−1.2
1e	Ac-Cy[b]	H	AcO	Br	H	Ac	−1.4
1f	Ur[c]	H	Br	H	$EtCO_2$	EtCO	−1.3
1g	Ur	H	Br	H	HO	H	−1.5
1h	Ur	H	Cl	H	AcO	Ac	−2.1
1i	Ur	H	Cl	H	HO	H	−2.1

[a] Adenine. [b] N^4-Acetylcytosine. [c] Uracil.

functional groups. In view of these merits, this technique should be a useful method in nucleoside synthesis, especially for structural transformations of the sugar moiety.

During the synthetic studies of 5′-amino-2′,3′,5′-trideoxy-β-D-*glycero*-pent-2′-enofuranosyl nucleosides,[3] we were faced with the problem of effective introduction of olefinic functionality into the 2′,3′ position. Synthetic routes to 2′,3′-unsaturated nucleosides have generally involved base-catalyzed elimination reactions of either 3′-*O*-methanesulfonyl or *O*2,3′-anhydro derivatives of 2′-deoxy nucleosides.[4] Treatment of 5′-*O*-trityluridine 2′,3′-thionocarbonate with Raney nickel has been shown to give the corresponding 2′,3′-unsaturated nucleoside in low yield.[5] The preparation of 1-(5-*O*-acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)uracil through the 2′,3′-episulfide has been reported by Ueda.[6] However, these are disadvantageous for large scale preparation because of multistep reactions, low overall yields, and the need of chromatographic separation of the products. Two efficient preparations starting from the more readily available ribonucleosides have recently been reported by Moffatt's[7a] and Robins' groups.[7b] Moffatt and his co-workers[7a] applied the chromous amine complex procedure to 2′,3′-*trans*-*O*-acetyldeoxyhalonucleosides and obtained the corresponding 2′,3′-unsaturated nucleosides in fairly good yields. However, the side reactions (concomitant formation of the dehalogenated product and glycosidic cleavage) and the special care required for the preparation of the reagent seem to reduce its practical utility. Robins' group[7b] developed a convenient route to 9-(2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine (**3a**) starting from adenosine. This route still has drawbacks in necessitating chromatographic purification of the intermediate, 6-*N*-pivalamido-9-[3-iodo-3-deoxy-2-*O*-(4,4-dimethyl-3-pivaloxypent-2-enoyl)-5-*O*-pivalyl-β-D-xylofuranosyl]purine, and in the limited applicability to purine nucleosides.

In this paper we describe[8] an efficient and versatile method for the synthesis of 2′,3′-unsaturated nucleosides via electrochemical reduction of 2′(3′)-*O*-acyl-3′(2′)-deoxyhalonucleosides, which are obtained by a single-step reaction from ribonucleosides.

The electrochemical elimination reactions of vicinal dihalides,[9] halohydrins,[10] and halo esters[11] have been demonstrated to form olefinic functionality. The electrolysis of vicinal dihalides has been extensively studied with regard to stereochemistry of the reaction process.[9b] However, little attention has been paid to its synthetic utility in the preparation of olefins since the product olefin is usually the starting point for the preparation of dihalides. Selective removal of a 2,2,2-trihaloethyl group, which is useful for protection of hydroxy, amino, and carboxy units, has been achieved by using controlled potential electrolysis.[11a] Similar electrochemical elimination has been exploited in our laboratory[12] in the synthesis of armentomycin, a unique halogen-containing amino acid. Recently, electrochemical reduction of 2,2,2-trichloroethanols has been found to give the 1,1-dichloroolefins in good yields.[10]

In addition, the unexpected formation of 2′,3′-dideoxynucleosides during catalytic hydrogenolysis of the 2′(3′)-*O*-acyl-3′(2′)-deoxyhalonucleosides over palladium carbon has been reported.[13] This phenomenon has been explained via a palladium-catalyzed elimination of the acetate group, giving a 2′,3′-olefin, followed by concomitant hydrogenation. These electrochemical and chemical data suggested that 2′(3′)-*O*-acyl-3′(2′)-deoxyhalonucleosides might be suitable substrates for the electrochemical olefin formation.

Polarography. First, polarographic half-wave potentials of several halo sugar nucleosides (**1a–i**) in dimethylformamide solution were determined in order to examine their reducibilities. The polarograms exhibited severe polarographic maxima. The reduction potentials observed can be attributed to electron transfer to the sugar moiety since the bases are known to be reduced at more cathodic potentials in nonaqueous solutions.[1b,h,i] The half-wave potentials of the halo sugar nucleosides exhibited markedly less cathodic potentials than those of simple alkyl halides, suggesting an electrochemical process similar to that in the case of vicinal halides.[14] Microcoulometry indicated that the reduction proceeded via a two-electron transfer. The polarographic data show that the ease of the reduction is very sensitive to the identity of the halogen atom and is influenced to some extent by both the vicinal substituent and its steric relationship. From Table I it is clear that the order of reducibility of the halo sugar nucleosides is iodo- > bromo- > chloronucleoside, and the vicinal halo esters are generally more reducible than the corresponding vicinal halohydrins. A small but appreciable difference in the half-wave potential between **1a** and **1b** would be reflective of the vicinal dihedral angle as shown in the case of vicinal dihalides[9b] and differences in the electronegativity of C-2′ and C-3′.

Results and Discussion

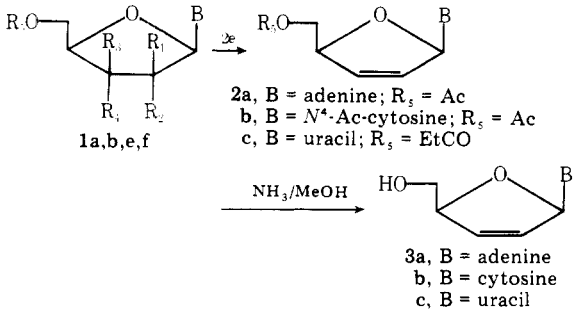
In view of the ready availability of materials, the vicinal bromo esters were chosen as substrates for the electrolysis. Macroscale electrolysis was first attempted using **1a**, which was readily prepared in a single-step reaction from adenosine according to our method.[15] Cathodic reduction of **1a** was

Table II. Electrolysis of Halo Sugar Nucleosides

run	substrate	solvent	electrolyte	cathode potential, V vs. SCE	product	yield, %
1	**1a**	DMF	TBA·Br[a]	−1.45	**2a**	77
2	**1a**	50% THF	HCl	−1.30	**2a**	46
3	**1a**	DMF	TEA·Ts[b]	−1.45	**2a**	81
4	**1a**	MeOH	NaOAc	−1.30	**2a**	76
5	**1b**	MeOH	NaOAc	−1.30	**2a**	74
6	**1e**	DMF	TEA·Ts	−1.45	**2b**	73
7	**1e**	MeCN	TEA·Ts	−1.45	**2b**	77
8	**1e**	MeOH	TEA·Ts	−1.45	**2b**	*c*
9	**1f**	DMF	TEA·Ts	−1.40	**2c**	70
10	**1f**	MeOH	TEA·Ts	−1.40	**2c**	78
11	**1f**	Me_2SO	$LiClO_4$	−1.30	**2c**	46
12	**1f**	MeOH	NaOAc	−1.40	**2c**	38

[a] Tetrabutylammonium bromide. [b] Tetraethylammonium tosylate. [c] Isolation of **2b** was not attempted because extensive reduction of the cytosine moiety took place.

carried out at −1.45 V vs. SCE in dimethylformamide using tetrabutylammonium bromide (TBA·Br) as a supporting electrolyte to give the desired 2′,3′-unsaturated nucleoside **2a**, 9-(5-*O*-acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine, in 77% yield. The structure of **2a** was unequivocal from an examination of its NMR spectrum and its elemental

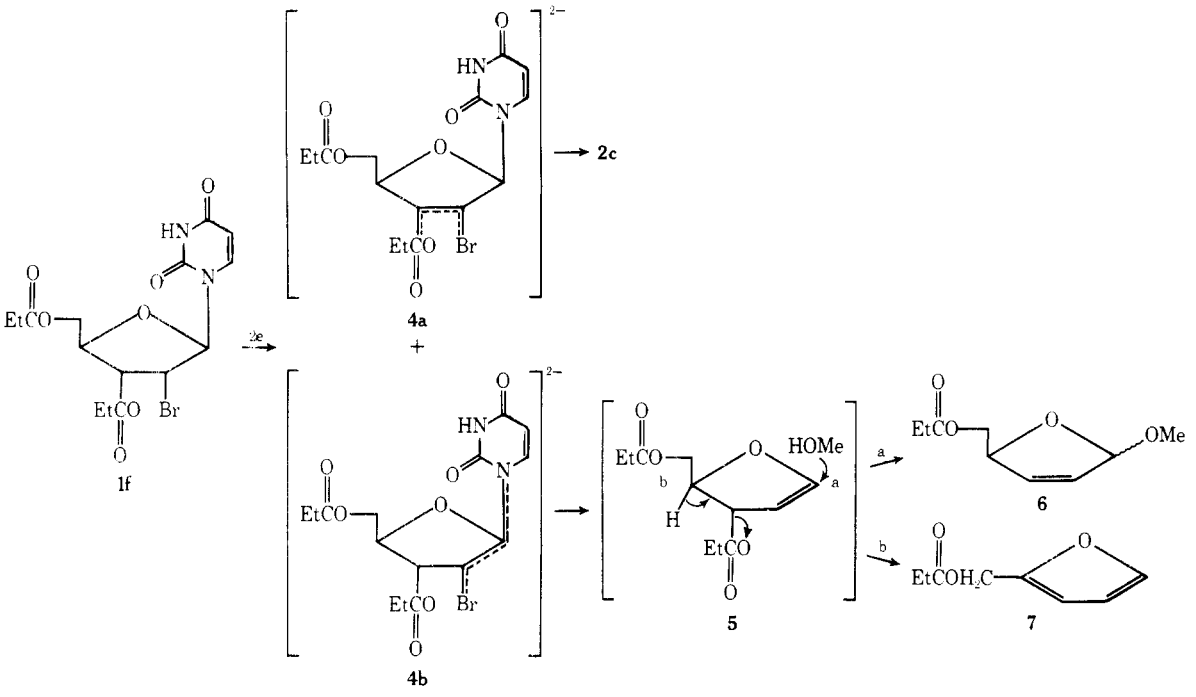


analysis. No formation of appreciable amounts of other products was detected by thin-layer chromatography (TLC) in the reaction mixture. In this case, however, chromatographic purification was necessary for the isolation of **2a** because its separation from the electrolyte was difficult by means of the usual extraction procedure. To improve this workup procedure, the use of several combinations of solvent and supporting electrolyte was examined (Table II). Electrolysis of **1a** at −1.30 V vs. SCE in aqueous tetrahydrofuran using dilute hydrochloric acid as an electrolyte afforded **2a** in 46% yield by direct crystallization of the crude product. However, this electrolysis condition caused considerable glycosidic cleavage with release of adenine probably due to the acidic media. The most suitable electrolyte was found to be tetraethylammonium tosylate (TEA·Ts), which could easily be removed from the reaction mixture by simple extraction with water. Thus, by using TEA·Ts, **2a** was obtained in 81% yield without chromatographic separation. A combination of methanol and sodium acetate (0.25 M) could also be employed as a catholyte of practical use. In this case, methanol containing 10% of concentrated hydrochloric acid was used as an anolyte.

In order to investigate stereochemical influence on the electrochemical elimination, electrolysis of 9-(2-bromo-2-deoxy-3,5-di-*O*-acetyl-β-D-arabinofuranosyl)adenine (**1b**), a positional isomer of **1a** with inverted stereochemistry, was carried out at −1.30 V vs. SCE in methanol–sodium acetate (0.25 M). From this electrolysis the crystalline 2′-olefin **2a** was isolated in almost the same yield (74%) as from **1a**.

Moffatt and co-workers have reported that the reaction of 5′-*O*-(2-acetoxyisobutyryl)-3′-*O*-acetyl-2′-bromo-2′-deoxyuridine with chromous acetate led to extensive glycosidic cleavage with release of uracil, and the corresponding 2′-olefin was obtained in 33% yield.[7a] Therefore, it is of interest to examine if our electrochemical method can be extended to the pyrimidine series. Electrolysis of 3′,5′-di-*O*-propionyl-2′-bromo-2′-deoxyuridine (**1f**) was attempted under a variety of conditions. Electrolysis of **1f** employing TEA·Ts as an electrolyte in dimethylformamide or in methanol afford the expected 2′-olefin, 1-(5-*O*-propionyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)uracil (**2c**), in over 70% yield. However, appreciable glycosidic cleavage leading to uracil (~25%) was observed in the case of methanol–sodium acetate (0.25 M) or dimethyl sulfoxide–lithium perchlorate, and **2c** was obtained in rather low yields. In addition, the interesting products **6** and **7** were isolated by chromatographic separation of the reaction products in yields of 22 and 3%, respectively. The structure of **7** was rigorously confirmed by a direct comparison of the spectral data (IR and NMR) with those of an authentic sample prepared according to Zanetti.[16] The structure of **6** was convincingly confirmed by its NMR spectrum in deuteriochloroform (see Experimental Section). Elemental analysis of **6** purified by column chromatography did not give good results. An attempted purification of **6** by vacuum distillation resulted in partial decomposition to **7**. A similar type of decomposition has been observed by Bischofberger[17] with related sugars. Since it was confirmed by a comparative experiment that both **1f** and **2c** were stable in methanol–sodium acetate (0.25 M) under nonelectrolytic conditions, it is apparent that **6** and **7** would arise from an electrolytic glycosidic cleavage. To our knowledge, this provides the first example of electrochemical elimination of a halogen and an adjacent substituent bonded via a nitrogen atom.

The exact mechanism of the electrolysis of the vicinal halo acylate has not been elucidated yet. However, the absence of the 2′-deoxy nucleoside in spite of the protic conditions and the low half-wave potential of **1f** compared to simple alkyl bromides strongly suggest that both the 2′-olefin formation and the glycosidic cleavage proceed in the concerted reduction mechanism which has generally been accepted for the electrolysis of vicinal dihalides.[14] Thus, it would appear that two energetically close transitions (**4a** and **4b**), which lead to the formation of the 2′-olefin **2c** and the glycosidic cleavage, respectively, are formed via concerted electron transfer. The glycosidic cleavage should afford initially a furanoid glycal **5** which is known to react with methanol,[18] giving **6**. The furan **7** may be derived from the transient glycal **5** and the furanoid **6**. However, route b from the glycal **5** via β-elimination would be more likely since the furanoid **6** was stable at ambient



temperature in the same solvent system as that for the electrolysis. It is not clear at present why the glycosidic cleavage was suppressed in the electrolysis using TEA·Ts. The electrolyte would exert some influences in combination with the solvent on the conformation of the substrate within the electrical double layer, and hence the transition **4a** would preferentially be formed.

It is very difficult to explain the exclusive formation of **2a** in the electrolysis of **1b** in methanol–sodium acetate (0.25 M). Possible contributing factors would be differences in the nature of the base moiety and in the relative configuration of the 1′,2′ substituents. It has been suggested by Casanova and Rogers[9a] that elimination from the trans periplanar conformation is strongly preferred in the electrolysis of vicinal dibromides. A trans configuration of the 1′,2′ substituents in **1f** would be more favorable for elimination than the cis configuration of the 2′,3′ substituents, provided that the electrolysis of 2′(3′)-*O*-acyl-3′(2′)-deoxyhalonucleosides proceeds by the same mechanism as that of vicinal dibromides. On the contrary, the relation between the 1′,2′ and 2′,3′ relative configurations in **1b** is reversed, and therefore it is likely that the 2′-olefin formation is exclusive.

Electrolysis of 1-(3-bromo-3-deoxy-2,5-di-*O*-acetyl-β-D-xylofuranosyl)-N^4-acetylcytosine (**1e**) was carried out using TEA·Ts as an electrolyte in aprotic solvents, and 1-(5-*O*-acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl-)-N^4-acetylcytosine (**2b**) was obtained in good yield without chromatographic purification. When the electrolysis was carried out in a protic solvent (methanol), extensive reduction of the base moiety was suggested by TLC examination of the reaction mixture. Thus, as the electrolysis proceeded, the UV positive spots on TLC faded. Deacylation of 2′-olefins **2a–c** by treatment with saturated methanolic ammonia led to the corresponding known compounds **3a–c** in high yields.

In order to examine the influence of vicinal leaving groups on the electrochemical elimination, electrolysis of the iodohydrin **1d** was investigated. The electrolysis was performed at −1.3 V vs. SCE in methanol–sodium acetate (0.25 M). Chromatographic purification on silica gel afforded **3a** in 29% yield along with cordycepin (14%) and adenine (55%). The formation of cordycepin is presumably a consequence of protonation of the 3′-carbanion which was formed via electrochemical reduction of the 3′-iodo group. It is apparent that the glycosidic cleavage leading to adenine occurred in the electrochemical process since it was confirmed experimentally that **1d**, cordycepin, and **2a** are stable in methanol–sodium acetate (0.25 M) on stirred mercury at the temperature of the electrolysis. The mechanism of this electrochemical glycosidic cleavage is not clear at present and awaits further detailed study.

The electrochemical method described here would provide potential utility in the synthesis of 2′,3′-unsaturated nucleosides. Wide applicability of the method has very recently been proven by Mengel[19] in the preparation of 2′,3′-unsaturated formycin and tubercidin.

Experimental Section

Melting points were measured using a Yamato melting point apparatus and are uncorrected. NMR spectra were recorded on a Hitachi Perkin-Elmer R-20A spectrometer and are reported in parts per million downfield from an internal standard of tetramethylsilane. UV spectra were measured on a Hitachi EPS-3T spectrometer. IR spectra were recorded on a Shimadzu IR-27G infrared spectrophotometer. Optical rotations were measured with a JASCO DIP-4 automatic polarimeter. Polarograms were taken at 20 °C by use of three electrodes with a Yanako P-8 polarograph attached to a Yanaco 101 recorder. The dropping mercury electrode had the following characteristics on open circuit: at h = 70.0 cm, t = 5.2 s drop^{-1}, and m = 1.27 mg s^{-1} in DMF–0.1 M tetraethylammonium chloride saturated with nitrogen. The electrolyses were carried out by use of a Hokuto potentio-galvanostat HA-104 (1A-55V) attached to a Hokuto HF-108A coulomb meter. Thin-layer chromatography (TLC) was performed on Merck silica gel GF_{254}. Spots were determined by UV examination. Column chromatography was done using Merck silica gel 60.

Dimethylformamide was dried over sodium sulfate for 3 days and distilled (bp 152–153 °C). Acetonitrile was dried in a similar manner as above and distilled after refluxing with phosphorus pentoxide (bp 80–81 °C). Tetraethylammonium chloride was dried over phosphorus pentoxide under reduced pressure for 3 days. Tetrabutylammonium bromide and tetraethylammonium tosylate were recrystallized twice from ethyl acetate and ethanol, respectively. Sodium acetate, lithium perchlorate, dimethyl sulfoxide, and methanol were the highest purity commercially available and were obtained from Katayama Kagaku Co., Ltd.

General Procedure for Electrolysis. Mercury was used as a cathode, and platinum foil or a carbon rod was employed as an anode. The electrolysis cell used was an ordinary beaker which was 5 cm in diameter and 10 cm in height. A cylindrical tube with a ~2-cm diameter and a fine-porosity glass frit at the bottom was used as an anodic compartment and fixed ~1 cm above the mercury cathode. A

saturated calomel electrode (SCE) was always adopted as a reference electrode. The salt bridge of the electrode was fixed ~3 mm above the cathode. The anolyte was placed in the anodic compartment so as to make its height identical with that of the catholyte. Nitrogen gas was bubbled through the catholyte for at least 15 min before electrolysis. The preelectrolysis procedure was always utilized to remove impurities in the catholyte. Electrolysis was carried out at the indicated cathode potentials below 10 °C under dry nitrogen gas. The substrate (1 mmol) was added by portions to the catholyte (20 mL) to maintain a current of 50–200 mA, and the electrolysis was continued until the current reached the back current. The electrolysis was usually completed within 2 h. When the anolyte migrated into the catholyte during the reaction, additional electrolyte was added to the anolyte. After the reaction, the catholyte that separated from mercury was treated as described below.

9-(5-*O*-Acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine (2a). (a) Using Tetrabutylammonium Bromide as a Supporting Electrolyte. Electrolysis was carried out as above at −1.45 V vs. SCE using **1a** (414 mg, 1 mmol) and DMF–0.25 M tetrabutylammonium bromide (TBA·Br). The catholyte was evaporated to dryness in vacuo. The residue was dissolved in 40 mL of AcOEt and stored overnight in a refrigerator. The resulting precipitate (TBA·Br) was removed by filtration, and the filtrate was evaporated to dryness. Then the residue was applied to a column of silica gel (30 g). Elution with $CHCl_3$–MeOH (95:5) gave 25 mg (6%) of the starting material **1a** as the first fraction and 235 mg (77%) of **2a** with mp 81–83 °C dec after crystallization with *i*-PrOH in the second fraction. An analytical sample of **2a** from *i*-PrOH had mp 83–85 °C dec solvated with 1 mol of *i*-PrOH: λ_{max} (MeOH) 260 nm (ε 15 530); ν_{max} (Nujol) 1740 cm^{-1}; $[\alpha]^{27}_D$ −40.7° (*c* 0.5, MeOH); NMR (Me_2SO-d_6) δ 1.05 (d, *J* = 6 Hz, 6, Me_2CHOH), 2.01 (s, 3, OAc), 3.45–4.1 (m, 1, Me_2CHOH), 4.21 (d, *J* = 5 Hz, 2, $C_{5'}$ H_2), 4.33 (d, *J* = 4 Hz, 1, Me_2CHOH), 4.95–5.3 (m, 1, $C_{4'}$ H), 6.15–6.4 (m, 1, $C_{3'}$ H), 6.4–6.65 (m, 1, $C_{2'}$ H), 6.9–7.1 (m, 1, $C_{1'}$ H), 7.3 (br s, 2, NH_2), 8.1 (s, 1, C_2 or C_8 H), 8.21 (s, 1, C_2 or C_8 H). Anal. Calcd for $C_{12}H_{13}N_5O_3$ (335.35): C, 53.72; H, 6.31; N, 20.88. Found: C, 53.57; H, 6.40; N, 20.94.

1-(5-*O*-Acetyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)-N^4-acetylcytosine (2b). Electrolysis of **1e** (432 mg, 1 mmol) was carried out at −1.45 V vs. SCE using DMF–TEA·Ts (0.25 M). After the reaction, the catholyte was evaporated to dryness in vacuo below 50 °C. The residue was dissolved in H_2O (10 mL) and extracted with $CHCl_3$ (3 × 10 mL). The extract was dried ($MgSO_4$) and evaporated to dryness. The residue was crystallized with *i*-PrOH to give 217 mg (74%) of **2b** with mp >280 °C. By recrystallization from MeOH, an analytical sample was obtained as colorless needles: mp >280 °C; λ_{max} (MeOH) 248.5 nm (ε 14 360), 299 (5660); ν_{max} (Nujol) 1713, 1743 cm^{-1}; NMR (Me_2SO-d_6) δ 2.02 (s, 3, Ac), 2.12 (s, 3, Ac), 4.2 (d, *J* = 4.2 Hz, 2, $C_{5'}$ H_2), 4.9–5.25 (m, 1, $C_{4'}$ H), 5.98–6.2 (m, 1, $C_{3'}$ H), 6.32–6.52 (m, 1, $C_{2'}$ H), 6.8–7.0 (m, 1, $C_{1'}$ H), 7.2 (d, *J* = 7.8 Hz, 1, C_5 H), 7.92 (d, *J* = 7.8 Hz, 1, C_6 H), 10.8–11.0 (br s, 1, NH). Anal. Calcd for $C_{13}H_{15}N_3O_5$ (293.27): C, 53.24; H, 5.16; N, 14.33. Found: C, 53.01; H, 5.24; N, 14.16.

Electrolysis of **1e** in MeCN–TEA·Ts (0.25 M) afforded **2b** in 77% yield. However, resinous substances deposited in the anolyte during electrolysis, probably due to polymerization of MeCN.

1-(5-*O*-Propionyl-2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)uracil (2c). (a) Using TEA·Ts. Electrolysis of **1f** was carried out at −1.4 V vs. SCE in MeOH–TEA·Ts (0.25 M). The separated catholyte was treated in the manner described above to give 210 mg (79%) of **2c** with mp 128–130 °C. An analytical sample was obtained by recrystallization from *i*-PrOH as colorless needles: mp 130–132 °C; λ_{max} (MeOH) 260 nm (ε 9540); ν_{max} (Nujol) 1712, 1740 cm^{-1}; $[\alpha]^{27}_D$ −78° (*c* 0.925, MeOH); NMR ($CDCl_3$) δ 1.15 (t, *J* = 7.2 Hz, 3, $-CH_2CH_3$), 2.34 (q, *J* = 7.2 Hz, 2, $-CH_2CH_3$), 4.31 (t, *J* = 3 Hz, 2, $C_{5'}$ H_2), 4.9–5.25 (m, 1, $C_{4'}$ H), 5.72 (d, *J* = 7.8 Hz, 1, C_5 H), 5.8–6.05 (m, 1, $C_{3'}$ H), 6.2–6.4 (m, 1, $C_{2'}$ H), 6.9–7.1 (m, 1, $C_{1'}$ H), 7.2–7.8 (m, 1, NH), 7.48 (d, *J* = 7.8 Hz, 1, C_6 H). Anal. Calcd for $C_{12}H_{14}N_2O_5$ (266.25): C, 54.13; H, 5.30; N, 10.53. Found: C, 54.29; H, 5.62; N, 10.39.

(b) Using Sodium Acetate. Electrolysis of **1f** (4.19 g, 10 mmol) was carried out at −1.4 V vs. SCE in MeOH–NaOAc (0.25 M) solution (200 mL) for 9 h using a beaker 7 cm in diameter and 15 cm in height for the cathodic compartment. The separated catholyte was evaporated to dryness, and the residue was extracted with hot $CHCl_3$ (3 × 50 mL) to leave an insoluble substance. This substance was dissolved in H_2O (20 mL) and acidified with dilute hydrochloric acid to give 0.27 g (24%) of uracil with mp > 300 °C. Then the above extract was dried ($MgSO_4$), concentrated, and applied to a chromatography column of silica gel (100 g). Elution with $CHCl_3$ gave 0.05 g (3%) of furfuryl propionate (**7**), which was identical (IR, NMR) with an authentic sample.[16] The second fraction contained 0.41 g (22%) of methyl 5-*O*-propionyl-2,3-dideoxy-D-*glycero*-pent-2-enofuranoside (**6**): NMR (CCl_4) δ 1.11 (t, *J* = 7.5 Hz, 3, $-CH_2CH_3$), 2.28 (q, *J* = 7.5 Hz, 2, $-CH_2CH_3$), 3.28 and 3.32 (two singlets totaling three protons, OCH_3), 4.05 (deformed d, 2, C_5 H_2), 4.55–5.1 (m, 1, C_4 H), 5.47–5.9 (m, 2, C_2 H, C_3 H), 6.03 (deformed d, 1, C_1 H). The NMR spectrum of **6** showed a pattern similar to that of methyl 5-*O*-benzoyl-2,3-dideoxy-D-*glycero*-pent-2-enofuranoside,[18] and the two signals for the methoxyl suggested that **6** is an anomeric mixture (~3:2). Subsequent elution with $CHCl_3$–MeOH (95:5) gave 0.87 g (21%) of the starting material (**1f**) and 1.02 g (38%) of **2c** with mp 128–130 °C.

Electrolysis of 9-(3-Deoxy-3-iodo-β-D-xylofuranosyl)adenine (1d). Electrolysis of **1d** was carried out at −1.3 V vs. SCE in MeOH–NaOAc (0.25 M). In this case, the current reached 300–400 mA by addition of **1d** and the reaction was completed in 30 min. The separated catholyte was concentrated and applied to a chromatography column of silica gel (60 g). Elution with $CHCl_3$–MeOH (9:1) gave 60 mg (29%) of **3a** with mp 189–191 °C, 35 mg (14%) of cordycepin with mp 222–224 °C, and 74 mg (55%) of adenine, all identical (TLC, IR) with authentic samples.

Deacylation of 2'-Olefins (2a–c). A solution of **2** (10 mmol) in saturated methanolic ammonia (50 mL) was stirred overnight at room temperature and evaporated to dryness in vacuo. After repeated coevaporation with EtOH, the residue was recrystallized from the solvent described below to give **3** in high yields. Analytical data are as follows.

Compound **3a** (recrystallized from MeOH, 89% yield): mp 196–197 °C (lit. mp 194–195[7a] and 196–200 °C[7b]); λ_{max} (MeOH) 260 nm (ε 15 400); $[\alpha]^{27}_D$ +24.3° (*c* 0.23, MeOH). Anal. Calcd for $C_{10}H_{11}N_5O_2$ (233.23): C, 51.49; H, 4.75; N, 30.03. Found: C, 51.41; H, 4.86; N, 29.90.

Compound **3b** (EtOH, 87% yield): mp 168–169 °C (lit.[20] mp 168–169 °C); λ_{max} (MeOH) 272 nm (ε 8440); $[\alpha]^{27}_D$ +68.7° (*c* 0.15, EtOH). Anal. Calcd for $C_9H_{11}N_3O_3$ (209.20): C, 51.67; H, 5.30; N, 20.09. Found: C, 51.54; H, 5.40; N, 20.07.

Compound **3c** (EtOH, 86% yield): mp 155–156 °C (lit. mp 153–154[4a] and 154.5–155.5 °C[7a]); λ_{max} (H_2O) 261 nm (ε 10 050); $[\alpha]^{27}_D$ −91.7° (*c* 0.3, H_2O). Anal. Calcd for $C_9H_{10}N_2O_4$ (210.19): C, 51.42; H, 4.80; N, 13.33. Found: C, 51.28; H, 4.89; N, 13.36.

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Registry No.—**1a,** 62805-48-5; **1b,** 62805-49-6; **1c,** 37731-73-0; **1d,** 54937-38-1; **1e,** 52482-84-5; **1f,** 29171-87-7; **1g,** 4753-02-0; **1h,** 10190-39-3; **1i,** 4753-04-2; **2a,** 62805-50-9; **2b,** 62805-52-1; **2c,** 62805-51-0; **3a,** 7057-48-9; **3b,** 7481-88-1; **3c,** 5974-93-6; **6,** 68525-57-5; **7,** 623-19-8; uracil, 66-22-8; cordycepin, 73-03-0.

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Preparation of 2-Substituted Arsabenzenes[1,2]

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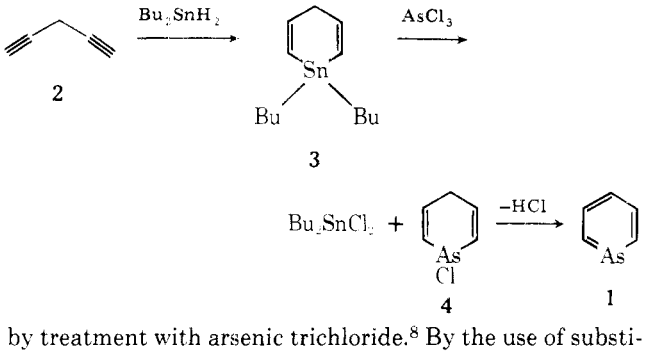
A variety of 1,4-diynes react with dibutyltin hydride to give predominately 2-alkyl-1,1-dibutyl-1,4-dihydrostannabenzenes. These may be readily converted to 2-alkylarsabenzenes by treatment with arsenic trichloride. In this manner, 6-acetoxy-1,4-hexadiyne has been converted to 2-arsabenzyl acetate and hence to a number of 2-functionalized arsabenzenes.

Spectroscopic studies of arsabenzene (arsenin, **1**) clearly show that this new heterocycle closely resembles its more familiar benzocyclic relatives.[3] For example, arsabenzene has a planar ring with normal aromatic C–C bond distances of 1.395 Å.[4] Its proton NMR spectrum shows low field signals indicative of a diamagnetic ring current.[5] Similarly, UV photoelectron spectral studies supported by several MO calculations further demonstrate this aromaticity.[6]

On the other hand, exploration of the chemistry of arsabenzene has been more modest. To some extent these chemical studies have been hampered by the lack of general methods for placing substituents on the arsabenzene ring. However, the parent system is easily prepared by a two-step synthesis. Thus, 1,4-pentadiyne (**2**) may be hydrostannated with dibutyltin dihydride to give 1,4-dihydro-1,1-dibutylstannabenzene (**3**),[7] which is readily converted to arsabenzene



by treatment with arsenic trichloride.[8] By the use of substituted 1,4-diynes in place of **2**, this synthesis appears to offer potential for the preparation of substituted arsabenzenes. In fact, this approach has been used to prepare several 4-functionalized arsabenzenes.[9,10] We now wish to report further on our synthesis of arsabenzene and its extension to the synthesis of 2-substituted arsabenzenes.

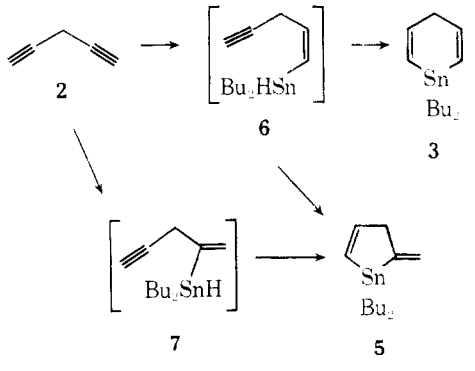
Results and Discussion

While the reactions of most diacetylenes with tin dihydrides give largely oligomeric products,[11] the hydrostannation of 1,4-pentadiyne with an equivalent of dibutyltin dihydride in refluxing heptane affords a 42% yield of 1,4-dihydro-1,1-dibutylstannabenzene (**3**). This 1:1 adduct is easily distilled from the apparently polymeric viscous residue. The characteristic AB pattern in the vinyl region of the ^{1}H NMR spectrum suggests structure **3** (Table I). A careful examination of the product revealed a minor isomer (5%) in addition to **3**. This material could be separated by GLC. Its IR spectrum showed bands assigned to a terminal methylene [905 cm^{-1} $(CS)_2$], while the ^{1}H NMR spectrum was consistent with formulation **5** (Table II). It might be noted that the five-membered ring has a characteristically smaller value for the coupling constants for vicinal vinyl ring protons, while the β-vinyl ring proton showed a lower field signal than those for **2**.

This structural assignment can be made ironclad by the use of the facile and stereospecific cleavage of vinylstannanes by acetic acid.[12] Both isomers give 1,4-pentadiene and dibutyltin acetate in near quantitative yield. However, the reaction of **3** with acetic-d_1 acid gave *cis,cis*-1,4-pentadiene-*1,5*-d_2 while **5** gave 1,4-pentadiene-*1,4*-d_2.

The presence of small quantities of the five-membered ring isomer in **3** is preparatively unimportant. Compound **3** is readily converted to arsabenzene by the exchange reaction with arsenic trihalide followed by gentle warming and treatment with base to remove hydrogen halide from intermediate **4**. Although air-sensitive, arsabenzene is a stable distillable liquid, easily handled under an inert atmosphere.

The hydrostannation of nonpolar substituted acetylenes is known to be a homolytic addition reaction.[13,14] To some extent the relatively larger yield of **3** vs. **5** rests on the known preference of stannyl radicals for terminal addition to acetylenes.[15] Thus, production of **3** must involve two terminal additions (**2** → **6** → **3**) while a single nonterminal addition (**2** → **7** → **5** or **2** → **6** → **5**) can only give the five-membered ring adduct.



We had feared that the regioselectivity which led to the desired six-membered ring might be compromised by the use of substituted acetylenes. Unfortunately, this proved to be the case as 2,5-heptadiyne (**8a**) reacted with dibutyltin dihydride to give a 58% yield of two adducts in a ratio of 3:1. Acetic acid cleavage afforded only *trans,trans*-2,5-heptadiene. The two

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