Electroreduction of α,β-Unsaturated Esters. I. A Simple Synthesis of *rac*-Deoxypicropodophyllin by Intramolecular Diels–Alder Reaction Plus Trans Addition of Hydrogen[1a,b]

L. H. KLEMM,* D. R. OLSON,[1c] AND D. V. WHITE[1d]

Department of Chemistry, University of Oregon, Eugene, Oregon 97403

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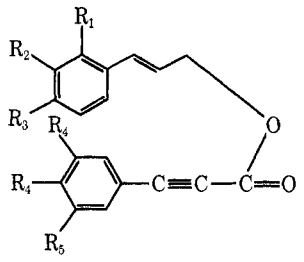
A one-step synthesis of dihydrocyclolignan lactones (including γ-apopicropodophyllin, **2c**) from *trans*-cinnamyl chlorides and sodium phenylpropiolates is described. Studies on polarographic and macroscale electroreductions of model α,β-unsaturated esters in the solvent–electrolyte acetonitrile–tetraethylammonium bromide are presented. In particular, electroreduction of **2c** at controlled cathode potential gives *rac*-deoxypicropodophyllin (**3**) by trans addition of hydrogen to the conjugated carbon–carbon double bond.

In previous papers[2-4] we reported syntheses of cyclolignan lactones **2** by means of the intramolecular Diels–Alder reaction of *trans*-cinnamyl phenylpropiolates (**1**) in refluxing acetic anhydride. Formation of **1** from the corresponding phenylpropiolyl chloride and *trans*-cinnamyl alcohol, however, proved to be difficult or capricious in many cases.[5] We now report an alternative synthetic procedure for **2** wherein the ester **1** is formed (from the corresponding *trans*-cinnamyl chloride and sodium phenylpropiolate) in refluxing anhydrous dimethylformamide (DMF) and is cyclized *in situ*.[6] Thus, cyclolignans **2a–c** were obtained by this method in yields of 18–51% from the corresponding phenylpropiolic acids. At least in these three cases, the DMF method offers a more convenient, reliable route to **2**, as well as an overall yield of magnitude comparable to that found with use of acetic anhydride.



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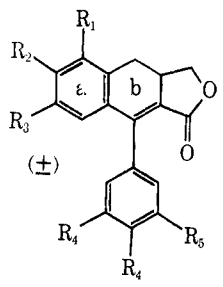
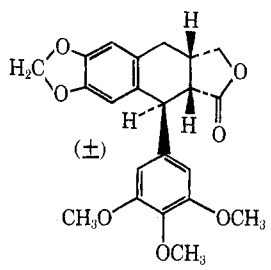


2



3

a, $R_1 = R_2 = R_3 = R_4 = R_5 = H$
b, $R_1 = R_5 = H$; $R_2 = R_3 = R_4 = OCH_3$
c, $R_1 = H$; $R_2R_3 = OCH_2O$; $R_4 = R_5 = OCH_3$
d, $R_1 = R_4 = R_5 = OCH_3$; $R_2R_3 = OCH_2O$

Reduction of the carbon–carbon double bond of **2** should lead to cyclolignans of the 1-phenyl-3-hydroxymethyl-1,2,3,4-tetrahydro-2-naphthoic acid lactone type. Catalytic hydrogenation of γ-apopicropodophyllin (**2c**) to the *cis,cis*-tetrahydrolactone, *rac*-isodeoxypicropodophyllin (**4**), in 19–37% yield has been described previously.[7] Particularly, when platinum oxide (in acetic acid) was used as a catalyst, the major product isolated (30% yield)[7] resulted from hydrogenation of ring a plus dehydrogenation of ring b. It seemed likely that electrochemical reduction of compounds of structure **2** at constant cathode potential should allow saturation of the lactone α,β-carbon–carbon double bond without attendant reaction elsewhere in the molecule. This has been accomplished on a synthetic scale by use of a mercury cathode and **2c** in an anhydrous mixture of acetonitrile (solvent), hydrogen bromide (proton source), and tetraethylammonium bromide (supporting electrolyte) to give crystalline *trans-cis*-tetrahydrolactone (**3**), *rac*-deoxypicropodophyllin. Assignment of stereochemistry to **3** is based on (a) the presence of a cis lactone band[7] at 1765 cm^{-1}; (b) identity of its infrared spectrum with that reported[7] for (+)-deoxypicropodophyllin; and (c) nonidentity of **3** and **4**.

Only limited information on the stereochemistry of electroreduction of α,β-unsaturated esters is available. Elving, *et al.*,[8] obtained diethyl fumarate from trans reduction of diethyl acetylenedicarboxylate at a mercury cathode in aqueous HCl–KCl containing some ethanol. Ono[9] obtained ethyl cinnamate (presumably trans) from reduction of ethyl phenylpropiolate at controlled cathode potential in aqueous acidic ethanol. The conversion of **2c** into **3** appears to be the first pertinent example of trans electroreduction of a carbon–carbon double bond which is conjugated with an ester function.

In order to facilitate the selection of experimental conditions of cathode potential and proton availability for use in syntheses, preliminary polarographic studies

(1) (a) This investigation was supported by Research Grant No. GM 12730 from the National Institute of General Medical Sciences, U. S. Public Health Service. Paper VII in the series on Intramolecular Diels–Alder Reactions. (b) For paper VI, see L. H. Klemm, R. A. Klemm, P. S. Santhanam, and D. V. White, *J. Org. Chem.*, **36**, 2169 (1971). (c) Research Assistant, 1968–present. (d) Research Associate, 1969–1970.

(2) L. H. Klemm, K. W. Gopinath, D. H. Lee, F. W. Kelly, E. Trod, and T. M. McGuire, *Tetrahedron*, **22**, 1797 (1966).

(3) L. H. Klemm, D. H. Lee, K. W. Gopinath, and C. E. Klopfenstein, *J. Org. Chem.*, **31**, 2376 (1966).

(4) L. H. Klemm and P. S. Santhanam, *ibid.*, **33**, 1268 (1968).

(5) L. H. Klemm, K. W. Gopinath, G. C. Karaboyas, G. L. Capp, and D. H. Lee, *Tetrahedron*, **20**, 871 (1964).

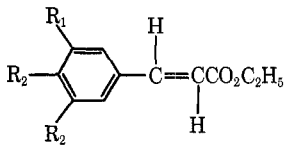
(6) The syntheses of phenylpropargyl and *trans*-cinnamyl propiolates in DMF have been described previously.[1b] These propiolates underwent intramolecular Diels–Alder reaction in acetic anhydride, but they gave unidentified reaction(s) in DMF.

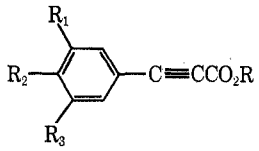
(7) A. W. Schrecker and J. L. Hartwell, *J. Amer. Chem. Soc.*, **75**, 5916 (1953).

(8) I. Rosenthal, J. R. Hayes, A. J. Martin, and P. J. Elving, *ibid.*, **80**, 3050 (1958).

(9) S. Ono, *Nippon Kagaku Zasshi*, **77**, 665 (1956); *Chem. Abstr.*, **52**, 9020 (1958).

were made on a series of seven β-aryl α,β-unsaturated esters (**2d**, **5**–**7**) which were available in our laboratory (Table I).





5a, $R_1 = H$; $R_2 = OCH_3$
b, $R_1 = R_2 = OCH_3$

7a, R = Et; $R_1 = R_2 = R_3 = H$
b, R = Et; $R_1 = R_3 = OCH_3$; $R_2 = H$
c, R = Me; $R_1 = H$; $R_2R_3 = OCH_2O$

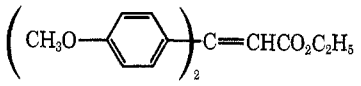


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TABLE I

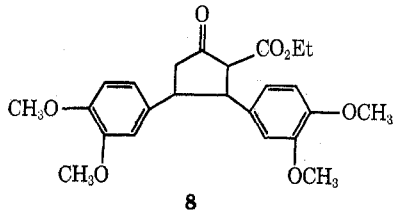
POLAROGRAPHIC HALF-WAVE REDUCTION POTENTIALS[a] FOR SOME β-ARYL α,β-UNSATURATED ESTERS

Substrate no.	Solvent–electrolyte[b]	First wave $-E_{1/2}$	Second wave $-E_{1/2}'$	Third wave $-E_{1/2}''$
2d	A	1.78[c]	2.00	
	B	1.69[d]		
5a	A	1.94[c]	2.26	
	B	1.83[e]	1.99	
	C	1.79[e]	1.93	
5b	A	1.87[c]	2.23	
	B	1.78[e]	1.93	
6	A	1.91[e]	2.06	
7a	A	1.94[f]	2.21	2.55
	B	~1.81[g]		
7b	A	1.91[f]	2.15	2.52
	B	~1.78[g]		
7c	A	1.97[f]	2.23	2.62
	B	1.82		
	D	1.74		

[a] In volts *vs.* the saturated aqueous calomel electrode. [b] A, 0.05 *M* Et_4NBr in anhydrous MeCN; B, solvent A diluted with 3.85 vol. % water; C, solvent A diluted with 7.7 vol. % water; D, 0.4 mg of phenol per ml of solvent B. [c] The first and second waves have approximately equal heights. [d] Wave height is twice that of the first wave in solvent A. [e] The first and second waves overlap but have nearly equal heights. [f] The three waves have unequal heights. [g] Irregular wave.

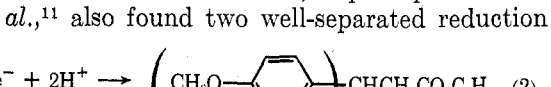
From the table one notes that the trans cinnamates **5**, as well as the β-arylcinnamates **2d** and **6**, show two reduction waves of approximately equal heights under conditions of low proton availability (anhydrous acetonitrile solvent). When water (a better proton source) is added to the solvent both waves are shifted to less negative potentials, though the second wave is moved further than the first one. That each of the two waves corresponds to the uptake of one electron is apparent from products obtained on macroscale syntheses. Thus, controlled reduction of **5a** under anhydrous conditions at a cathode potential of *ca.* −2.12 V (on the plateau of the first reduction wave) gave dimerization–cyclization to **8**, as per eq 1.[10] On the other hand, reduction of **6** at *ca.* −2.17 V (on the plateau of the second wave) gave simple hydrogenation of the conjugated carbon–carbon double bond, as per eq 2. Petrovich, *et al.*,[11] also found two well-separated reduction waves of equal heights on polarography of ethyl cinnamate in anhydrous DMF which contained tetraethylammonium perchlorate. Addition of water (1 *M*) shifted both waves to less negative potentials in the same manner as in MeCN. In neutral or acidic aqueous solution (containing as much as 50% ethanol or dioxane) methyl, ethyl, and benzyl cinnamates gave only one two-electron wave.[12,13] It was proposed[13] that in the pH range of 6–8 the protonated ester is the reducible species.

25a + $2e^-$ + H^+ ⟶



+ EtO^- (1)

8



(2)

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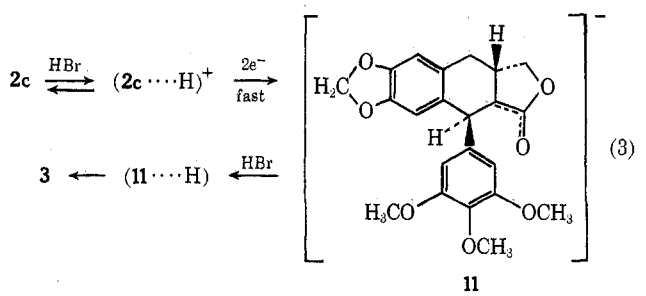
The phenylpropiolates **7** showed three waves of unequal heights on polarography under anhydrous conditions. When water or aqueous phenol (solvent–electrolyte D) was added to the acetonitrile in order to increase proton availability the three waves coalesced into a single (or nearly single) wave at a less negative $E_{1/2}$ value than for the first wave. When ethyl phenylpropiolate (**7a**) was electroreduced at *ca.* −2.06 *V* (plateau of the first wave) under anhydrous, low protic conditions only a small amount of the saturated compound ethyl β-phenylpropionate (**10**) was isolated. No ethyl cinnamate was found. This is not surprising in view of the fact that $E_{1/2}$ for ethyl cinnamate should be slightly less negative (perhaps at −1.91 V) than that for **5a** under these conditions. Macroscale reduction of **7a** at −2.06 V under anhydrous, high protic conditions (obtained by addition of a four molar quantity of anhydrous hydrogen bromide per mole of substrate) raised the yield of **10** to 55%. Compound **10** was also obtained by Ono[9] from electroreduction of **7a** in aqueous acidic ethanol at a cathode potential sufficiently negative as to lie on the plateau of the second wave (no third wave observed) present under his reaction conditions.

Equation 3 shows a plausible mechanism for the con-



(3)

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(10) To be described in paper II in this series; *cf.* J. P. Petrovich, M. M. Baizer, and M. R. Ort, *J. Electrochem. Soc.*, **116**, 749 (1969).

(11) J. P. Petrovich, M. M. Baizer, and M. R. Ort, *ibid.*, **116**, 743 (1969).

(12) S. Ono, *Nippon Kagaku Zasshi*, **76**, 631 (1955); *Chem. Abstr.*, **51**, 17525 (1957); S. Ono and M. Uehara, *Nippon Kagaku Zasshi*, **78**, 929 (1957); *Chem. Abstr.*, **54**, 4485 (1960); S. Ono and T. Hayashi, *Bull. Chem. Soc. Jap.*, **26**, 268 (1953).

(13) M. J. D. Brand and B. Fleet, *J. Electroanal. Chem.*, **16**, 341 (1968).

version of **2c** into **3** in electrosynthesis. Protonation of **2c** is presumed to occur in the substrate solution and thereby to produce a single reduction wave (*cf.* **2d**, Table I). On contact with the cathode this protonated species takes up two electrons rapidly to give the intermediate anion **11**. In **11** the added proton is placed on C-1, since this allows the remaining negative charge to reside partially on the carbonyl oxygen atom. The preferred transition state for the protonation at C-1 should have the aryl group trans (rather than cis) to the methylene group at C-3. Sites of protonation in $(\mathbf{2c}\cdots H)^+$ and $(\mathbf{11}\cdots H)$ are uncertain, but it is possible that the latter complex is the enol form of **3** which tautomerizes to give the thermodynamically preferred cis lactone and trans-1,2 configurations of **3**.

The difference in net electronic effect of a meta (electron withdrawing, as compared to hydrogen) and a para alkoxy substituent (electron donating) in the benzene ring is noted when one compares half-wave reduction potentials for the α,β-unsaturated ester systems in **5** and **7**. Thus, **7b** (two meta MeO groups) reduces more readily than the unsubstituted compound **7a**, while **7c** (OCH_2O group attached both meta and para) reduces less readily than **7a**. Likewise **5b** reduces more readily than **5a**. This effect is also observed in polarographic reduction of 3- and 4-substituted benzaldehydes[14] and in chemical and catalytic reductions of β,β-diarylitaconic acids.[15]

Experimental Section[16]

1-Phenyl-3-hydroxymethyl-3,4-dihydro-2-naphthoic Acid Lactone (2a).—A mixture of 5 g of phenylpropiolic acid (Aldrich), 2.88 g (equimolar amount) of anhydrous $NaHCO_3$, and 10 ml of MeOH was warmed until gas evolution (CO_2) ceased. Solvent was removed *in vacuo*. A mixture of the residual sodium phenylpropiolate, 5.2 g (equimolar amount) of *trans*-cinnamyl chloride, and 40 ml of anhydrous dimethylformamide was refluxed (nitrogen atmosphere) for 5 hr. The white precipitate (NaCl) which formed in the cooled mixture was removed by filtration. Cooling the filtrate to −20° gave 3.1 g (mp 190–191.5°) of **2a**, identified by direct comparison with an authentic sample.[3] Additional **2a** was obtained by evaporation of the mother liquor and addition of benzene–petroleum ether (bp 30–60°), total yield 4.6 g (51%), mp 185–191.5°.

1-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-3-hydroxymethyl-3,4-dihydro-2-naphthoic Acid Lactone (2b).—Sodium 3,4-dimethoxyphenylpropiolate was prepared in the preceding manner. *trans*-3,4-Dimethoxycinnamyl chloride was obtained by slow addition at 0° of a mixture of 1.2 ml (0.015 mol) of pyridine, 0.94 ml (0.013 mol) of thionyl chloride, and 20 ml of $CHCl_3$ to a solution of 2.1 g (0.011 mol) of *trans*-3,4-dimethoxycinnamyl alcohol[5] in 50 ml of $CHCl_3$. The mixture was refluxed for 1 hr, washed with water, dried (Na_2SO_4), and evaporated to yield the crude organic chloride. As for **2a**, these components were refluxed in DMF to form **2b**, isolated on addition of MeOH to the evaporated solution, yield 18%, mp 220.5–222° (lit.[2] 221–222°).

***rac*-γ-Apopicropodophyllin (2c).**—This was prepared in the foregoing manner from *trans*-3,4-methylenedioxycinnamyl alcohol[5] and 3,4,5-trimethoxyphenylpropiolic acid.[5] The residue from evaporation of the DMF solution was diluted with water and extracted with $CHCl_3$ (dried). Evaporation of the organic extract and addition of ether to the residue gave **2c** (29%), mp 243–246° (lit.[2] 252–253°).

Chemicals for Electroreductions.—In both polarography and electrosynthesis the solvent was anhydrous, spectral grade acetonitrile (used without further purification). The supporting electrolyte was tetraethylammonium bromide (originally 99% pure, recrystallized repeatedly from reagent grade 1-butanol, and stored in the dark *in vacuo* and in the presence of anhydrous $CaSO_4$). In polarography the concentration of Et_4NBr was 0.05 *M*; in synthesis it was 0.1 *M*. In some polarographic studies, water or aqueous phenol was added to the solvent to serve as a proton source (see Table I). In electrosynthesis anhydrous HBr was oftentimes used for this purpose. Without added H_2O or HBr, the MeCN itself is presumed to be the main proton source. Substrate molecules were available either commercially or from studies in our own laboratory.[1b,5,6,17]

Polarography.—The apparatus and the general procedure (but not the solvent–electrolyte) were the same as described previously.[18] Concentrations of each substrate were varied over the range of 2.2–5.8 × 10^{-4} *M*. Correction for *iR* drop was negligibly small. Reproducibility in $E_{1/2}$ values was ±0.01 V.

Electrosynthesis.—Macroscale electroreductions were conducted in a cell made from a 250-ml beaker which contained a mercury pool cathode and a horizontal silver disk anode (2.6 cm radius), separated from one another by means of a sintered-glass partition of medium porosity. The cathode potential was maintained constant by means of an American Instrument Co. Redox-O-Trol. The solvent–electrolyte (50 ml) was preelectrolyzed until the current fell to a small value (3–4 mA). During preelectrolysis and electrosynthesis purified nitrogen (>99.99%) was bubbled through the catholyte (stirred magnetically). For **6**, the neat substrate (a liquid) was added to the catholyte in one portion. For **2c**, a solution of the substrate, plus slightly more than a 2-*M* quantity of anhydrous HBr in MeCN was added to the catholyte during the course of the electroreduction. Addition of **7a**, with or without HBr, was portionwise. Electroreduction was continued until the current again became small. Combined solutions from anode and cathode compartments were evaporated to dryness and the residue was extracted with $CHCl_3$ (plus water). Evaporation of the dried (Na_2SO_4) organic layer gave the crude product.

***rac*-Deoxypicropodophyllin (3).**—A mixture of 178 mg (0.45 mmol) of **2c**, mp 245–246.5°, 1.1 mmol of anhydrous HBr, and 8 ml of MeCN was added to the catholyte (cathode potential −2.10 V) over a period of 10 min and electroreduction was continued for 5 min longer. Crude product was crystallized from 2-propanol, yield 121 mg (68%), mp 196–201°. Recrystallizations from 2-propanol and methanol gave needles: mp 210–211°, depressed to 186–196° on admixture with *rac*-isodeoxypicropodophyllin (**4**),[2] mp 203–204.5°; ir ($CHCl_3$) identical with that reported[7] for (+)-deoxypicropodophyllin but different from that of **4** in the range of 1000–1020 cm^{-1}; pmr ($CDCl_3$) δ 2.6–3.4 (m, 4, H-2, H-3, H-4), 3.80 (s, 3, CH_3O at C-4′) and 3.85 (s, 6, 2 CH_3O at C-3′ and C-5′) which overlap 3.7–4.2 (m, 10 total, including H-1), 4.2–4.6 (broad s, 2, $CH_2OC{=}O$), 5.96 (broadened s, 2, OCH_2O), 6.3–6.9 (m, 4, aromatic protons); mass spectrum *m/e* 398 (100, M^+).

Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.46; H, 5.52.

Ethyl β,β-Bis(4-methoxyphenyl)propionate (9).—Electroreduction of 778 mg of **6** [obtained by dehydration of ethyl β-hydroxy-β,β-bis(4-methoxyphenyl)propionate][17] over a period of 18 min and chromatography of the crude product by means of silica gel (4 g) and CH_2Cl_2 (to remove tar) gave 300 mg (39%) of crude **9**: ir 1720 cm^{-1}, identified by direct spectral comparison with an authentic sample of **9** [pmr (CCl_4) δ 1.01 (t, 3, J_{Et} = 7 Hz, CH_3), 2.89 (d, 2, $J_{\alpha,\beta}$ = 8 Hz, $CHCH_2C{=}O$), 3.57 (s, 6, 2 MeO), 3.93 (q, 2, CH_2CH_3), 4.43 (t, 1, $CHCH_2$), 6.91 (d of d, 8, J_{ortho} = 8.5 Hz, Δδ = 20.8 Hz, aromatic protons)][19] from catalytic hydrogenation of **6**[17] and by hydrolysis to β,β-bis(4-methoxyphenyl)propionic acid, mp 137–138° (from benzene–hexane), undepressed on admixture with an authentic sample.[17]

Electroreduction of Ethyl Phenylpropiolate (7a).—A solution

(14) P. Zuman, "Substituent Effects in Organic Polarography," Plenum Press, New York, N. Y., 1967, p 76.

(15) L. H. Klemm and C. D. Lind, *J. Org. Chem.*, **21**, 258 (1956), and references cited therein.

(16) Microanalyses were performed by M-H-W Laboratories, Garden City, Mich. Infrared spectra were determined on $CHCl_3$ solutions by means of Beckman IR-5A and Perkin-Elmer Model 700 spectrometers; mass spectra, by means of a CEC Model 21-110 instrument at 70 eV; pmr spectra, by means of a Varian A-60 spectrometer, with tetramethylsilane used as internal standard.

(17) L. H. Klemm and G. M. Bower, *J. Org. Chem.*, **23**, 344 (1958).

(18) L. H. Klemm, W. C. Solomon, and A. J. Kohlik, *ibid.*, **27**, 2777 (1962).

(19) L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1959, pp. 89–90.

of 1.12 g of **7a** in 25 ml of MeCN was added to the cell over a period of 60 min and reduction was continued for 100 min longer. Vpc (10% silicone rubber on Chromosorb W, 200°) of the $CHCl_3$-soluble product indicated the formation of ethyl β-phenylpropionate (**10**) (11%), identified by comparison with an authentic sample. Acidification of the aqueous layer to pH 1 and extraction with $CHCl_3$ gave 400 mg (43%) of phenylpropiolic acid.

Repetition of the procedure but with 2 equiv of anhydrous HBr added to the substrate solution raised the yield of **10** to 26%. With 4 equiv of HBr the yield of **10** was 55%.

Registry No.—**2a**, 31892-93-0; **2c**, 6258-32-8; **2d**, 31892-95-2; **3**, 31892-96-3; **5a**, 24393-65-5; **5b**, 31892-98-5; **6**, 31892-99-6; **7a**, 2216-94-6; **7b**, 29577-38-6; **7c**, 31893-02-4.

Nucleosides. XIV. Synthesis of 3′-Deoxyadenosine and 9-(3-Deoxy-α-L-*threo*-pentofuranosyl)adenine

K. L. NAGPAL AND JEROME P. HORWITZ*[1]

Detroit Institute of Cancer Research, Division of the Michigan Cancer Foundation, Detroit, Michigan 48201, and Department of Oncology, Wayne State University School of Medicine, Detroit, Michigan 48207

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Treatment of methyl 9-(2,3-*O*-isopropylideneribofuranosyluronate)adenine (**3**) with sodium isopropoxide at room temperature leads to isopropyl 3′-deoxy-3′-adenosinene 5′-carboxylate (**4**) in 70% yield. The latter on catalytic (Pd/C) hydrogenation affords a mixture of two (C-4′) epimeric esters **5** and **6**, one of which (**5**) on reduction with sodium bis(2-methoxyethoxy)aluminum hydride furnished 3′-deoxyadenosine (**7**, cordycepin). The other ester (**6**), subjected to the same conditions of reduction, gave 9-(3-deoxy-α-L-*threo*-pentofuranosyl)-adenine (**8**). Compounds **7** and **8** could also be obtained in a more efficacious manner by column chromatography (Dowex 1) of the mixture derived by performing the reductions consecutively without separation of the isomeric intermediates **5** and **6**.

Recent reports from this laboratory[2a-c] described the introduction of 3′,4′ unsaturation into both pyrimidine and purine 2′-deoxynucleosides *via* corresponding 2′-deoxy-β-D-*erythro*-pentofuranosyluronic acid derivatives. Concurrently, Jones and Moffatt[2d,e] and Howgate,[3] *et al.*, reported the facile conversion of 2′,3′-*O*-alkylidene ribonucleoside 5′-carboxaldehydes (**1**) into 3′,4′-unsaturated nucleosides (**2**) and derivatives thereof under relatively mild basic conditions. The present communication describes the application of the latter approach to methyl 9-(2,3-*O*-isopropylideneribofuranosyluronate)adenine (**3**) which led to a practical synthesis of the antibiotic 3′-deoxyadenosine (**7**, cordycepin) and its C-4′ epimer, 9-(3-deoxy-α-L-*threo*-pentofuranosyl)-adenine[4] (**8**). The fact that **7** is a strong inhibitor of RNA synthesis, which generally accounts for its cytostatic activity,[5] stimulated our interest in **8** (Scheme I).

The conversion of **1** to **2** has been effected with a relatively wide spectrum of bases[2d,e] ranging from sodium bicarbonate or sodium carbonate in DMF to alkali metal alkoxides in both protic and dipolar aprotic media. By contrast, **3** was recovered unchanged after prolonged treatment with sodium carbonate in DMF. Moreover, triethylamine in DMF, the system of choice for the conversion of ethyl 3′-*O*-methylsulfonylthymidine 5′-carboxylate[2b] into ethyl 3′-deoxy-3′-thymidinene 5′-carboxylate,[6] proved equally ineffective after 13 hr at 80°. The desired elimination was effected, along with transesterification, by the action of sodium isopropoxide[7] in 2-propanol to give isopropyl 3′-deoxy-3′-adenosinene 5′-carboxylate[6] (**4**) in 70% yield after 0.5 hr at ambient temperature. The structure of the olefinic ester **4** was readily deduced from its nmr spectrum which showed, *inter alia*, a doublet at τ 6.53 ppm characteristic of the C-3′ vinyl proton in the sugar moiety.[2b]

Jones and Moffatt[2d,e] reported the occurrence of epimerization at C-4′, along with elimination when nucleoside 5′-carboxaldehydes (**1**) were brought into contact with adsorbents such as silica gel. There was no evidence of epimerization in our experiments. However, a small amount of the corresponding 3′,4′-unsaturated acid was occasionally isolated along with the ester (**4**) which is apparently generated from **4** during the work-up of the reaction mixture.

It would appear that, with the exception of a need for a stronger base to effect the process of elimination in the case of **3** relative to the nucleoside 5′-carboxaldehyde, the two elimination reactions probably proceed *via* similar paths. However, the scope of the present study precludes any firm conclusion in regard to the exact mechanism(s).

Catalytic hydrogenation (Pd/C) of **4** yielded two saturated esters **5** and **6** in the ratio of 1.5:1 which were separated on preparative tlc. The faster moving component **5**, on reduction with sodium bis(2-methoxyethoxy)aluminum hydride in tetrahydrofuran, yielded 3′-deoxyadenosine (**7**) in 50% yield. The slower moving ester **6**, subjected to the same conditions of reduction, afforded the epimeric structure, 9-(3-deoxy-α-L-*threo*-pentofuranosyl)adenine (**8**), in virtually the same yield.

(1) To whom correspondence should be addressed: Detroit Institute of Cancer Research.

(2) (a) J. Zemlicka, R. Gasser, and J. P. Horwitz, Abstracts, 160th National Meeting of the American Chemical Society, Chicago, Ill., 1970, Abstract No. CARB 3; (b) *J. Amer. Chem. Soc.*, **92**, 4744 (1970); (c) Abstracts, Joint Conference Chemical Institute of Canada and American Chemical Society, Toronto, Canada, 1970, Abstract No. CARB 5; (d) G. H. Jones and J. G. Moffatt, Abstracts, 158th National Meeting of the American Chemical Society, New York, N. Y., 1969, Abstract No. CARB 15; (e) U. S. Patent 3,457,255 (1969); *Chem. Abstr.*, **72**, 3727 (1970).

(3) P. Howgate, A. S. Jones, and J. P. Tittensor, *Carbohyd. Res.*, **12**, 403 (1970).

(4) This compound has been described (*cf.* ref 2e), but corresponding physical constants have not been disclosed.

(5) For pertinent references, see R. J. Suhadolnik, "Nucleoside Antibiotics," Wiley, New York, N. Y., 1970, p 50.

(6) See J. P. Horwitz, J. Chua, M. A. Da Rooge, M. Noel, and J. T. Donatti, *J. Org. Chem.*, **31**, 205 (1966), for the basis of this nomenclature.

(7) This base system was chosen because the ester **3** was relatively insoluble in both methanol and ethanol.