Molecular Design by Cycloaddition Reactions. XVII.[1] Oxymercuration of Polycyclic Olefins

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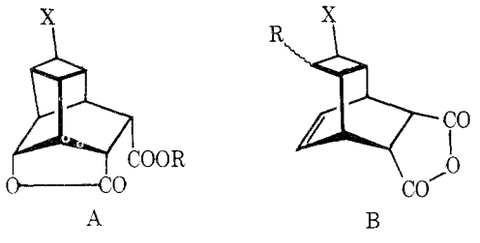
Reactions of tricyclo[4.2.2.0^{2,5}]deca-3,7-diene and related derivatives with mercuric acetate have been investigated. Structural effects for these reactions are also discussed.

We have previously reported the transannular cross cyclization reaction of cyclooctatetraene–maleic anhydride adduct (1) having both cyclobutene and bicyclohexene moieties with electrophiles such as bromine, iodine chloride, and *tert*-butyl hypochlorite.[2] However, similar reaction of 1 with iodine azide afforded only a 1:1 adduct B instead of the expected transannular cyclization products A (Chart I).

Chart I



A question whether the transannular cross bonding of the proximal π bonds *via* an intermediacy of bridged halonium ion is general or not led us to examine the transannular cross cyclization of these systems with an electrophilic reagent such as mercuric acetate.[3]

In this paper we have described the reactions of tricyclo[4.2.2.0^{2,5}]deca-3,7-diene derivatives and related compounds with mercuric acetate.

Results

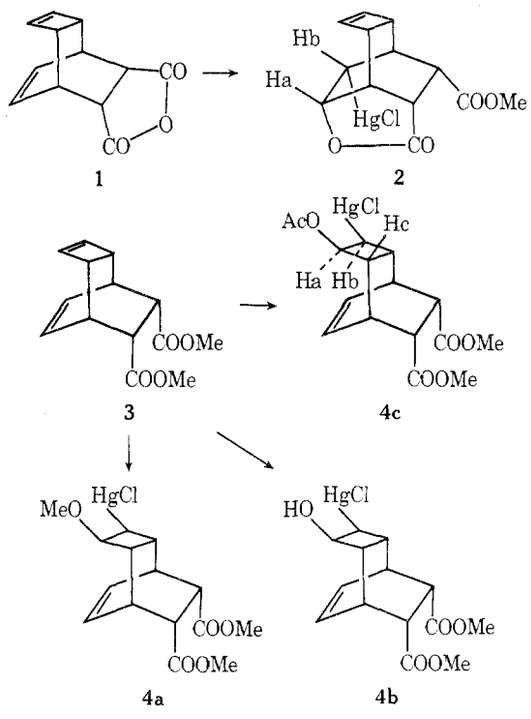
Additions of Mercuric Acetate to the Adducts 1 and 3. Addition of equimolar mercuric acetate to the adduct 1 (a 1:1 adduct of cyclooctatetraene and maleic anhydride) in absolute methanol followed by treatment of aqueous sodium chloride gave a product **2** in 40% yield. The ir absorption of **2** at 1780 cm^{-1} suggests the presence of a five-membered ring lactone moiety. The nmr spectrum of **2** exhibits characteristic two olefinic proton signals at δ 6.26 (d) and 6.07 (d), a methine proton signal adjacent to the lactone moiety at δ 4.60 (dd), and one methoxy group at δ 3.70 (3 H, s) (Table I). This appearance of two olefinic proton signals suggested the survival of the cyclobutene moiety.

On the other hand, the presence of a coupling between Ha and Hb indicated the chloromercury group of endo configuration rather than exo, in which the dihedral angle between Ha and Hb was approximately 90°.

On the basis of the above spectral data, the structure of the product **2** was established as shown in Scheme I.

Similar addition of equimolar mercuric acetate to compound **3** in absolute methanol, aqueous acetone, and acetic acid followed by treatment of aqueous sodium chloride gave compounds **4a, 4b,** and **4c,** respectively. The ir spectra of these compounds (**4a–c**) show common characteristic ester carbonyl bands at 1740–1745 cm^{-1}. The nmr spectra of these compounds exhibit two equivalent olefinic proton

Scheme I



signals as shown in Table I, which suggests the presence of a bicyclic cyclohexene moiety.[3b]

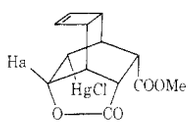
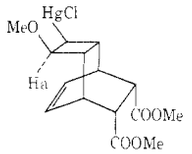
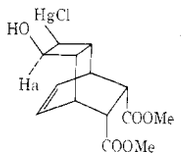
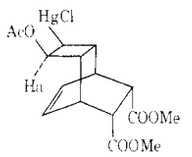
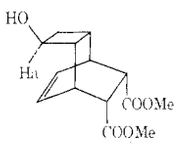
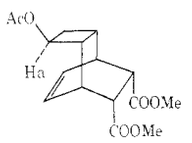
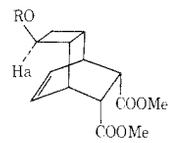
The exo-cis configuration of the products **4a–c** was accomplished by the chemical degradation and spectral analyses.

Compounds **4a** and **4c** were obtained by treatment of **4b** with diazomethane in the presence of boron trifluoride and acetic anhydride in pyridine, respectively. Reduction of **4c** with sodium borohydride in methanol gave **6** together with **5.** Further treatment of **5** with acetic anhydride and *p*-nitrobenzoyl chloride in pyridine gave **6** and **7,** respectively. As can be seen in Table I, the nmr spectrum of **4c** shows Ha at δ 4.50 as a double doublet (J_{ab} = 4 Hz, J_{ac} = 6.75 Hz). Appearance of a new coupling of 7.0 Hz was caused by replacing mercury with the proton, indicating the trans coupling in the cyclobutane system. Treatment of equimolar mercuric acetate with **8** in absolute methanol also gave **2.**

By contrast, similar addition of equimolar mercuric acetate to **9** in absolute methanol or acetic acid gave white solids, the ir spectra of which shows carbonyl absorptions at 1650, 1560, and 1400 cm^{-1}. Further treatment of the solids with hydrochloric acid recovered **9,** suggesting only the salt formation of mercuric acetate and **9** during the course of the reaction.

From the above results, it is pointed out that the reaction of mercuric acetate with tricyclo[4.2.2.0^{2,5}]deca-3,7-diene derivatives is influenced by the functional groups

Table I
Nmr Data for Products

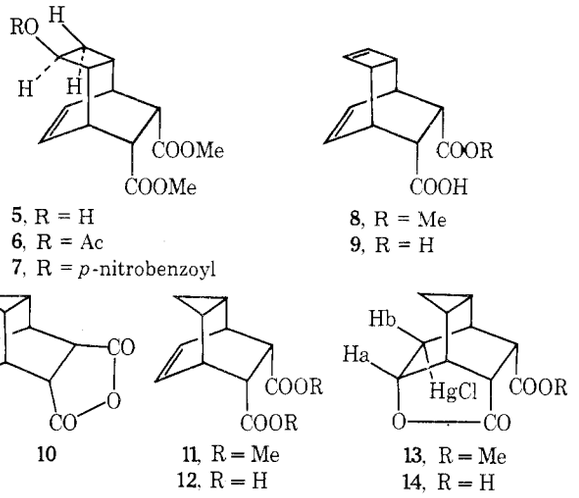
Compd no.	Structure	Chemical Shifts, δ (*J*, Hz)
2		6.26 (d, *J* = 3.0, 1 H, olefin), 6.07 (d, *J* = 3.0, 1 H, olefin), 4.60 (dd, *J* = 6.0, 4.0, 1 H, Ha), 3.70 (s, 3 H, COOMe), 3.5–2.5 (m, 7 H)
4a		6.63 (t, *J* = 4.0, 2 H, olefins), 3.60 (s, 6 H, COOMe × 2), 3.50 (m, 1 H, Ha), 3.20 (s, 3 H, OMe), 3.2–2.5 (m, 7 H)
4b		6.60 (t, *J* = 4.0, 2 H, olefins), 3.90 (m, 1 H, Ha; dd, *J* = 3.0, 6.0 exchanged by D_2O at δ 1.86), 3.58 (s, 6 H, COOMe × 2), 3.3–2.5(m, 7 H), 1.86 (br s, 1 H, OH, exchangeable by D_2O)
4c		6.66 (t, *J* = 4.0, 2 H, olefins), 4.50 (dd, *J* = 4.0, 6.75, 1 H, Ha), 3.62 (s, 6 H, COOMe × 2), 3.4–2.5 (m, 7 H), 2.03 (s, 3 H, OAc)
5		6.25 (t, *J* = 4.0, 2 H, olefins), 3.78 (m, 1 H, Ha), 3.50 (s, 6 H, COOMe × 2), 3.2–2.6 (m, 4 H), 2.5–2.2 (m, 3 H, 1 H exchangeable by D_2O), 2.0–7 (m, 2 H)
6		6.47 (t, *J* = 4.0, 2 H, olefins), 4.38 (*J* = 4.0, 6.75, 7.0, 1 H, Ha), 3.60 (s, 6 H, COOMe × 2), 3.3–2.3 (m, 8 H), 1.99 (s, 3 H, OAc)
7	 R = *p*-nitrobenzoyl	8.13 (s, 4 H, aromatic), 6.47 (t, *J* = 4.0, 2 H, olefins), 4.67 (m, 1 H, Ha), 3.53 (s, 6 H, COOMe 2), 3.23 (m, 1 H), 2.97 (m, 1 H), 2.83 (s, 2 H), 2.60 (m, 2 H), 2.20 (m, 2 H)

such an anhydride, dialkoxycarbonyl ester, and dicarboxylic acid moieties.

With a view of obtaining further information on the above reaction with polycyclic olefins, addition reactions of mercuric acetate with tricyclo[3.2.2.0^{2,4}]nona-6-ene derivatives (**10, 11, 12**) and bicyclo[2.2.1]hepta-2-ene derivatives (**15, 16, 17**) were also investigated.

Addition of equimolar mercuric acetate to **10** in absolute methanol followed by treatment of aqueous sodium chloride gave **13.** The ir absorption at 1770 cm^{-1} in **13** suggests the presence of a five-membered ring lactone moiety. Elemental analysis shows the product to be $[C_{12}H_{13}O_4HgCl]_n$. The nmr spectrum of **13** exhibits a methine proton signal (δ 4.47, dd) adjacent to a lactone moiety and one methoxy group (δ 3.77, 3 H, s), but no olefinic proton signals were observed. Similar to **2,** the presence of a coupling between Ha and Hb suggested the mercury group was endo. From these analyses, the structure **13** was established as depicted in Chart III.

Chart II



5, R = H
6, R = Ac
7, R = *p*-nitrobenzoyl

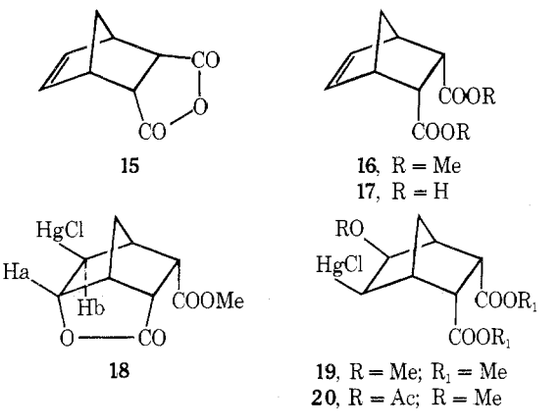
8, R = Me
9, R = H

10

11, R = Me
12, R = H

13, R = Me
14, R = H

Chart III



15

16, R = Me
17, R = H

18

19, R = Me; R_1 = Me
20, R = Ac; R = Me

Reaction of **11** with mercuric acetate in aqueous acetone gave also **13,** but in absolute methanol or acetic acid the reaction did not proceed.

Similar addition of mercuric acetate to **12** in absolute methanol gave **14** which was also obtained by hydrolysis of **13.** On the other hand, reaction of mercuric acetate with **12** in acetic acid gave white solids. Further treatment of the solids with hydrochloric acid gave only starting material **12.**

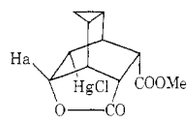
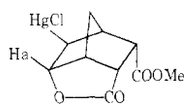
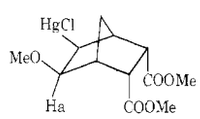
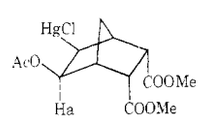
Treatment of mercuric acetate with **15** in absolute methanol gave **18.** The ir spectrum of **18** shows carbonyl absorptions at 1740 and 1760 cm^{-1}. Elemental analysis shows the product to be $[C_{10}H_{11}O_4HgCl]_n$. The nmr spectrum of **18** exhibits a methine proton signal adjacent to the lactone moiety at δ 5.27 (d). The absence of an appreciable coupling between Ha and Hb indicated the mercury group to be exo.[3b]

Similar treatment of mercuric acetate with **16** in absolute methanol, acetic acid, and 25% aqueous acetone gave **19, 20,** and **18,** respectively. The nmr spectrum of **19** shows the presence of one methoxy group and two carbomethoxy groups but the absence of a lactone group; the doublet signal at δ 3.83 with a coupling of 7.0 Hz suggested the exo-cis addition.[3b]

On the other hand, the nmr spectrum of **20** exhibits the doublet signal at δ 5.13 with a coupling of 7.5 Hz suggesting also the exo-cis addition.

By contrast, any attempted reaction of **17** with mercuric acetate was unsuccessful, even with absolute methanol or

Table II
Nmr Data for Products

Compd no.	Structure	Chemical Shifts, δ (J, Hz)
13		4.47 (dd, J = 6.0, 8.0, 1 H, Ha), 3.77 (s, 3 H, COOMe), 3.3–2.5 (m, 4 H), 1.60 (s, 1 H), 1.20 (m, 2 H), 0.60 (m, 2 H)
18		5.27 (d, J = 6.0, 1 H, Ha), 3.48 (s, 3 H, COOMe), 3.20 (m, 2 H), 2.84–2.40 (m, 4 H), 1.99 (m, 1 H), 1.27 (m, 1 H)
19		3.83 (d, J = 7.0, 1 H, Ha), 3.77 (s, 6 H, COOMe × 2), 3.77 (m, 1 H), 3.30 (s, 4 H, OMe and one methine), 3.03 (m, 2 H), 2.87 (m, 2 H), 1.80 (m, 1 H), 1.27 (m, 1 H)
20		5.13 (d, J = 7.5, 1 H, Ha), 3.67 (s, 3 H, COOMe), 3.60 (s, 3 H, COOMe), 3.20–2.67 (m, 5 H), 2.00 (s, 3 H, OAc), 1.80 (m, 1 H), 1.34 (m, 1 H)

[a] 100 MHz.

acetic acid, and only resulted in the recovery of **17**. The results are summarized in Chart III and Table II.

Discussion

Several explanations involving factors such as torsional effects, twist-strain effects, and structural effects (steric and neighboring group effects)[3b] have been proffered for the electrophilic additions to strained olefins.

The results of the addition reactions of mercuric acetate to bicyclo[2.2.1]heptenyl system are compatible with that of more simple norbornene;[3b] the initial mercuric ion could proceed to attack on the endo side.

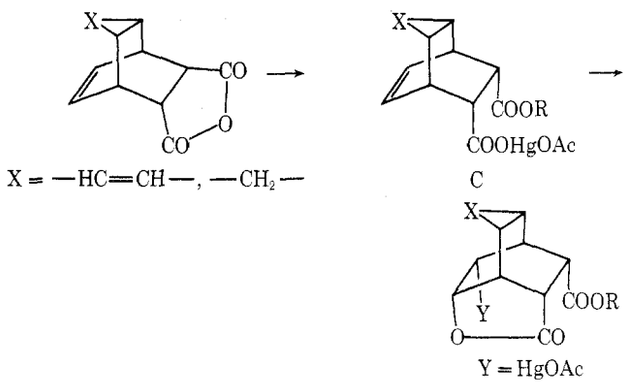
Whereas mercuric salts add to norbornenes on the cis-exo side in the absence of effective neighboring groups, the presence of effective ones such as an anhydride moiety causes lactonization as shown in Chart III.

By contrast, in the case of tricyclo[4.2.2.$0^{2,5}$]deca-3,7-dienes and tricyclo[3.2.2.$0^{2,4}$]nonenes having cyclobutene and/or cyclopropane moieties and a sterically hindered cyclohexene moiety, the reactions proceed with more complexity. Under preferable conditions, the reactivity to the salts might decrease in the order of anhydride > cyclobutene > cyclohexene moieties.

It seems likely that there are two active functional groups such as double bonds and anhydride groups in the molecules. The oxymercurations to the anhydrides **1** and **10** resulted in the formation of the lactonization products **2** and **13** respectively. Actually, no transannular cyclization products in the case of **1** with mercuric acetate were obtained in comparison with that of **1** with a halogeno reagent.[2] By contrast, the exclusive formation of saturated products from the oxymercuration of 9,10-benzotricyclo[4.2.2.$2^{2,5}$]dodeca-3,7,9-diene in acetic acid indicates that the participation of two π systems is even more extensive than those in norbornadiene.[3c] However, the reasons underlying these different pathways in changing electrophiles are not fully dissolved at the present stage.

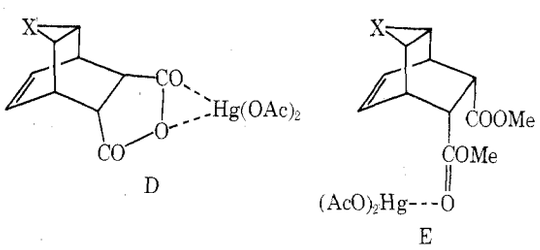
Anyway, the mechanistic speculation leads to consideration of a plausible pathway; an initial attack of the mercury on the anhydride moiety would proceed by a concerted attack of methanol to give a salt C followed by intramolecular cyclization as shown in Scheme II. This mechanism was also in agreement with the reaction pathway in the oxymercuration of **8** (*cf.* C).

Scheme II



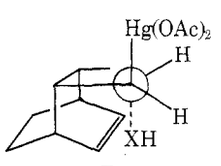
As was shown in Scheme I, the fact that the oxymercuration of the dimethyl ester (**3**) occurred only in the sterically unhindered olefin on the cyclobutene moiety supports the above speculation, but denies the other possibility of the formation of Lewis acid–base complexes D and E;[4] if the Lewis acid–base complexes are formed, the esters **3** and **11** should give **2** and **13**, respectively, by the endo attack of mercury. This was also explained for the oxymercuration of the dimethyl ester **11**, which did not proceed using absolute methanol or acetic acid. However, when 25% aqueous acetone was employed, the lactonization product **13** was obtained; an initial hydrolysis of the dimethyl ester would give a monoester, which reacts with mercuric acetate to give C followed by an intramolecular cyclization.

Chart IV



It is to be noted that cis addition of mercury on the cyclobutene moiety can be explained by examination of the transition state according to the twist strain theory.[3a] Because of the highly strained anticoplanar transition state F, the addition occurs preferentially at syn[5] as depicted in Chart V.

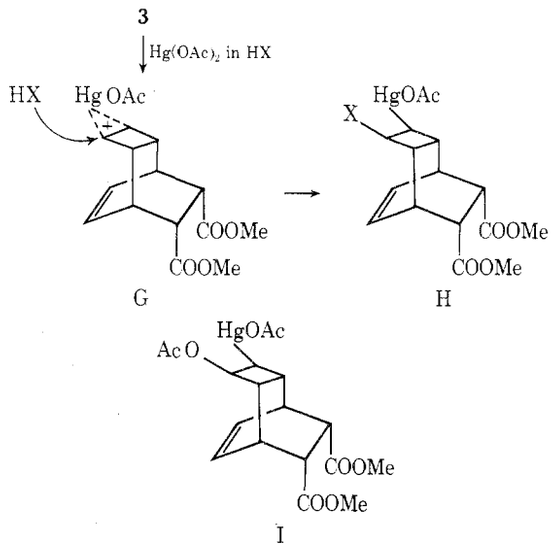
Chart V



The formation mechanism by the molecular addition for **4** could not explain these facts; this mechanism might give rise to the formation of I even in the nucleophilic solvents

such as water and methanol. However, the oxymercuration of **3** is found to proceed by an attack of nucleophilic solvents such as water, methanol, or acetic acid to the intermediacy of G to give H as shown in Scheme III.

Scheme III



It is apparent that the presence of two carboxylic acid groups in polycyclic olefins plays an important role in the oxymercuration.[3b] Indeed, the addition reactions of mercuric acetate to the solution (absolute methanol or acetic acid) of the dicarboxylic acid derivatives (**9–17** except for **12** in absolute methanol) resulted in the salt formation of the dicarboxylic acid and mercuric acetate, although it was difficult to purify them; these solids show carbonyl absorptions at 1650–1550 cm^{-1} and 1400 cm^{-1} and have high melting points (>300°).

Experimental Section

The melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed on a Perkin-Elmer 240 elemental analyzer. The nmr spectra were taken with a JEOL C-60-XL recording spectrometer with tetramethylsilane as an internal standard and the chemical shifts are expressed in δ values. The ir spectra were taken with a JASCO Model IRA-1 grating infrared spectrophotometer.

General Procedure for Oxymercuration Reactions. A solution of olefin and mercuric acetate in a solvent was stirred for 6 hr at room temperature. After evaporation of the solvent under reduced pressure, the residue was treated with excess aqueous sodium chloride. Then the precipitated material was filtered and washed with water. It was purified by silica gel chromatography and/or recrystallization.

Oxymercuration of 1. A solution of **1** (300 mg) and mercuric acetate (480 mg) in methanol (20 ml) was stirred. Then work-up gave **2** (300 mg): mp 210–212° (from acetone); ir (KBr) 1780, 1700 cm^{-1}.

Anal. Calcd for $C_{13}H_{13}O_4HgCl$: C, 33.27; H, 2.79. Found: C, 33.52; H, 2.73.

Oxymercuration of 3. A. In Methanol. A solution of (290 mg) and mercuric acetate (370 mg) in methanol (20 ml) was stirred. Work-up gave **4a** (600 mg): mp 200–202° (from MeOH); ir (KBr) 1740 cm^{-1}.

Anal. Calcd for $C_{15}H_{19}O_5HgCl$: C, 34.95; H, 3.71. Found: C, 34.89; H, 3.69.

B. In 25% Aqueous Acetone. A solution of **3** (250 mg) and mercuric acetate (330 mg) in 25% aqueous acetone (20 ml) was stirred. Work-up gave **4b** (60 mg): mp 154–156° (from acetone–*n*-hexane); ir (KBr) 3400, 1740 cm^{-1}.

Anal. Calcd for $C_{14}H_{17}O_5HgCl$: C, 33.54; H, 3.42. Found: C, 33.59; H, 3.40.

C. In Acetic Acid. A solution of **3** (700 mg) and mercuric acetate (900 mg) in acetic acid (10 ml) was stirred for 12 hr. Work-up gave **4c** (1.16 g): mp 187–189° (from MeOH); ir (KBr) 1745, 1705 cm^{-1}.

Anal. Calcd for $C_{16}H_{19}O_6HgCl$: C, 34.60; H, 3.43. Found: C, 34.81; H, 3.49.

Reaction of 4b with Diazomethane. A solution of **4b** (100 mg) and excess ethereal diazomethane in the presence of boron trifluoride etherate (30 mg) was stirred. After evaporation of the solvent, the residue was added with water and then extracted with chloroform. The extract was dried with sodium sulfate and was evaporated under reduced pressure. The residue was recrystallized from methanol to give **4a** (20 mg).

Acetylation of 4b. A solution of **4b** (30 mg), pyridine (10 ml), and acetic anhydride (2 ml) was stirred for 2 days. The solution was then added with water and was extracted with chloroform. The extract was evaporated under reduced pressure to give **4c** (30 mg).

Reduction of 4c. To a solution of **4c** (1.0 g) in methanol (50 ml) sodium borohydride (500 mg) was added. The reaction mixture was then added with water and extracted with chloroform. After evaporation of the extract under reduced pressure, the residue was subjected to silica gel chromatography using chloroform. **6** had mp 50° (80 mg): ir (neat) 1745, 1720 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.30; H, 6.60.

5 had $n^{20}D$ 1.5079 (360 mg): ir (neat) 3400, 1740 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.62; H, 6.10. Found: C, 63.70; H, 6.15.

Acetylation of 5. A mixture of **5** (30 mg) in pyridine (10 ml) and acetic anhydride (2 ml) was stirred for 1 day. The solution was added to water and extracted with chloroform. The extract was then treated with hydrochloric acid. The chloroform layer was evaporated under reduced pressure to give **6** (25 mg).

***p*-Nitrobenzoylation of 5.** A solution of **5** (160 mg) and *p*-nitrobenzoyl chloride in pyridine (10 ml) was stirred for 1 day. Work-up as described above gave **7** (180 mg): mp 161–162° (from benzene-*n*-hexane); ir (KBr) 1745, 1700, 1530, and 1355 cm^{-1}.

Anal. Calcd for $C_{21}H_{21}NO_8$: C, 60.72; H, 5.10; N, 3.37. Found: C, 60.75; H, 5.15; N, 3.40.

Oxymercuration of 8. A solution of **8** (230 mg) and mercuric acetate (320 mg) in methanol (20 ml) was stirred. Then work-up gave **2** (160 mg).

Oxymercuration of 9. A. In Methanol. To a solution of **9** (300 mg) in methanol (20 ml) mercuric acetate (434 mg) was added. Then the precipitated material was filtered which showed carbonyl absorptions at 1650, 1555, and 1400 cm^{-1}. The solid was treated with an excess of aqueous sodium chloride followed by addition of hydrochloric acid (1 ml). The solution was extracted with ether to give **9** (280 mg).

B. In Acetic Acid. To a solution of **9** (300 mg) in acetic acid (10 ml) mercuric acetate (434 mg) was added. Work-up gave **9** (290 mg).

Oxymercuration of 10. A solution of **10** (300 mg) and mercuric acetate (500 mg) in methanol (20 ml) was stirred. Work-up gave **13** (450 mg): mp 200–202° (from acetone); ir (KBr) 1770, 1700 cm^{-1}.

Anal. Calcd for $C_{12}H_{13}O_4HgCl$: C, 31.52; H, 2.87. Found: C, 31.67; H, 2.87.

Oxymercuration of 11. A solution of **11** (700 mg) and mercuric acetate (945 mg) in 25% aqueous acetone (20 ml) was stirred. Work-up gave **13** (944 mg).

Oxymercuration of 12. A solution of **12** (210 mg) and mercuric acetate (320 mg) in methanol (20 ml) was stirred. Work-up gave **14** (170 mg): mp 199–201° (from acetone–methanol); ir (KBr) 1765, 1690 cm^{-1}.

Anal. Calcd for $C_{11}H_{11}O_4HgCl$: C, 29.88; H, 2.28. Found: C, 29.92; H, 2.55.

Hydrolysis of 13. A mixture of 10% aqueous sodium hydroxide (20 ml) and **13** (100 mg) was stirred for 12 hr. The solution was treated with diluted hydrochloric acid and was extracted with chloroform to give **14** (60 mg).

Oxymercuration of 12. A solution of **12** (100 mg) and mercuric acetate (160 mg) in acetic acid (10 ml) was stirred for 12 hr. Work-up as described above gave **12** in quantitative yield.

Oxymercuration of 15. A solution of **15** (500 mg) and mercuric acetate (980 mg) in methanol (20 ml) was stirred. Work-up gave **18** (1.1 g): mp 226–228° (from acetone); ir (CBr) 1760, 1745 cm^{-1}.

Anal. Calcd for $C_{10}H_{11}O_4HgCl$: C, 27.85; H, 2.57. Found: C, 27.77; H, 2.49.

Oxymercuration of 16. A. In Aqueous Acetone. A solution of **16** (315 mg) and mercuric acetate (477 mg) in 25% aqueous acetone (20 ml) was stirred. Work-up gave **18** (500 mg).

B. In Methanol. A solution of **16** (315 mg) and mercuric acetate (477 mg) in methanol (20 ml) was stirred. Work-up gave **19** (455 mg): mp 132–134° (from MeOH); ir (KBr) 1740 cm^{-1}.

Anal. Calcd for $C_{12}H_{17}O_5HgCl$: C, 30.20; H, 3.59. Found: C, 30.18; H, 3.44.

C. In Acetic Acid. A solution of **16** (315 mg) and mercuric acetate (477 mg) in acetic acid (10 ml) was stirred. Work-up gave **20** (650 mg): mp 176–178° (from acetone); ir (KBr) 1745, 1720 cm^{-1}.

Anal. Calcd for $C_{13}H_{17}O_6HgCl$: C, 30.90; H, 3.39. Found: C, 30.80; H, 3.39.

Oxymercuration of 17. A. In Methanol. A solution of **17** (300 mg) and mercuric acetate (530 mg) in methanol (20 ml) was stirred. Work-up gave **17** in quantitative yield.

B. In Acetic Acid. A solution of **17** (300 mg) and mercuric acetate (530 mg) in acetic acid (10 ml) was stirred. Work-up gave **17** (280 mg).

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Registry No.—**1,** 51447-09-7; **2,** 52730-88-8; **3,** 35211-83-7; **4a,** 52730-89-9; **4b,** 52730-90-2; **4c,** 52827-09-5; **5,** 52748-22-8; **6,** 52748-23-9; **7,** 52748-24-0; **8,** 52748-25-1; **9,** 52746-59-5; **10,** 944-41-2; **11,** 956-36-5; **12,** 52746-60-8; **13,** 52730-91-3; **14,** 52730-92-4; **15,** 129-64-6; **16,** 39589-98-5; **17,** 3753-88-1; **18,** 26097-22-3; **19,** 52730-93-5; **20,** 52730-94-6; mercuric acetate, 1600-27-7; diazomethane, 334-88-3; acetic anhydride, 108-24-7; *p*-nitrobenzoyl chloride, 122-04-3.

References and Notes

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(5) This is not in conflict with the fact that oxymercuration of cyclobutene occurs at trans; see ref 3a.

Halo Sugar Nucleosides. IV.[1] Synthesis of Some 4′,5′-Unsaturated Pyrimidine Nucleosides

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Syntheses are described for the 1-(5-deoxypent-4-enofuranosyl) nucleosides derived from uridine, thymidine, cytidine, and 2′-deoxycytidine. These compounds were prepared *via* dehydrohalogenation of the appropriately acylated 5′-iodo-5′-deoxy nucleosides using either silver fluoride in pyridine or bases such as 1,5-diazabicyclo-[4.3.0]non-5-ene. The nucleoside diene 2-methylene-5-(*R*)-(thymin-1-yl)-2,5-dihydrofuran (**10**) could also be prepared either by treatment of 3′,5′-dideoxy-3′,5′-diiodothymidine with silver fluoride in pyridine or by base-catalyzed elimination of iodide from the 5′-iodo-2′,3′-unsaturated nucleoside **11b**. Catalytic reduction of N^4-acetyl-5′-deoxy-5′-iodo-2′,3′-*O*-isopropylidenecytidine followed by hydrolysis of the protecting groups gave the previously unknown 5′-deoxycytidine.

Previous work in this series has described the development of synthetic routes for the replacement of specific hydroxyl groups in both purine and pyrimidine nucleosides by iodo,[2] bromo,[1] or chloro[1] functions. In addition, other methods have been devised for the specific conversion of cis vicinal diols into vicinal chloro or bromo acetates.[3] The resulting halo sugar nucleosides are versatile starting materials for the preparation of unusual deoxy nucleosides,[2b,3b,3c] unsaturated nucleosides,[4] anhydro nucleosides,[3] etc.

Nucleosides containing unsaturated sugars have, in recent years, been the targets of considerable synthetic effort.[5] This is due both to the potential biological activity of these compounds, and to the possibility of using them as intermediates for the synthesis of other compounds, as in, *e.g.*, the synthesis of the antibiotic nucleocidin.[4a] We have been particularly interested in the synthesis of 4′,5′-unsaturated nucleosides since this structural feature is present in the nucleoside antibiotic Angustmycin A,[6] a compound that has been prepared both by modification of the antibiotic psicofuranine[7] and by total synthesis,[8] and in the products from treatment of coenzyme B_{12} with alkali.[9] In the present paper we describe the preparation of the 4′,5′-unsaturated nucleosides derived from the pyrimidine nucleosides uridine, thymidine, cytidine, and deoxycytidine. A part of this work has previously been briefly described.[10]

The early work of Helferich, *et al.*, has shown that 6-deoxyhex-5-enopyranosides can be prepared by treatment of the related 6-deoxy-6-halohexopyranose derivatives with silver fluoride in pyridine.[11] It was not until 1966, however, that this method was extended to the preparation of 5-deoxypent-4-enofuranose systems by Hough and Otter,[12] working with furanose sugars, and by our own preliminary work in the uridine series.[10]

The most readily available starting material for explorative studies on the dehydrohalogenation of 5′-halo-5′-deoxy nucleosides was 5′-deoxy-5′-iodo-2′,3′-*O*-isopropylideneuridine (**1a**),[2a] but, to our disappointment, we found that treatment of **1a** with a suspension of finely divided silver fluoride in pyridine at room temperature for several days led to three products, only a minor one being the desired 1-(5-deoxy-2,3-*O*-isopropylidene-β-D-*erythro*-pent-4-enofuranosyl)uracil (**2**). The major product, which was readily isolated owing to its solubility in water, was readily shown to be 2,5′-anhydro-2′,3′-*O*-isopropylideneuridine (**3**)[13] by comparison with an authentic sample.[2a] The organic solvent soluble products (20–35%) ran as a single spot upon tlc in a variety of systems, but examination of the nmr spectrum clearly showed this material to be a 3:1 mixture of 5′-deoxy-5′-fluoro-2′,3′-*O*-isopropylideneuridine (**1b**)[14] and the desired **2**. By subtraction of the resonances attributable to **2**, the characteristic spectrum of **1b** with large fluorine couplings ($J_{5'\text{-}F}$ = 46 Hz, $J_{4'\text{-}F}$ = 25 Hz) was readily apparent and was compared with that of an authentic sample.[14] The preferential formation of the cyclonucleoside (**3**) is presumably a consequence of the tendency of 2′,3′-*O*-iso-