solution. Further work is in progress on the Co(III)–DTPA system to determine whether other complexes or isomers are formed.[2]

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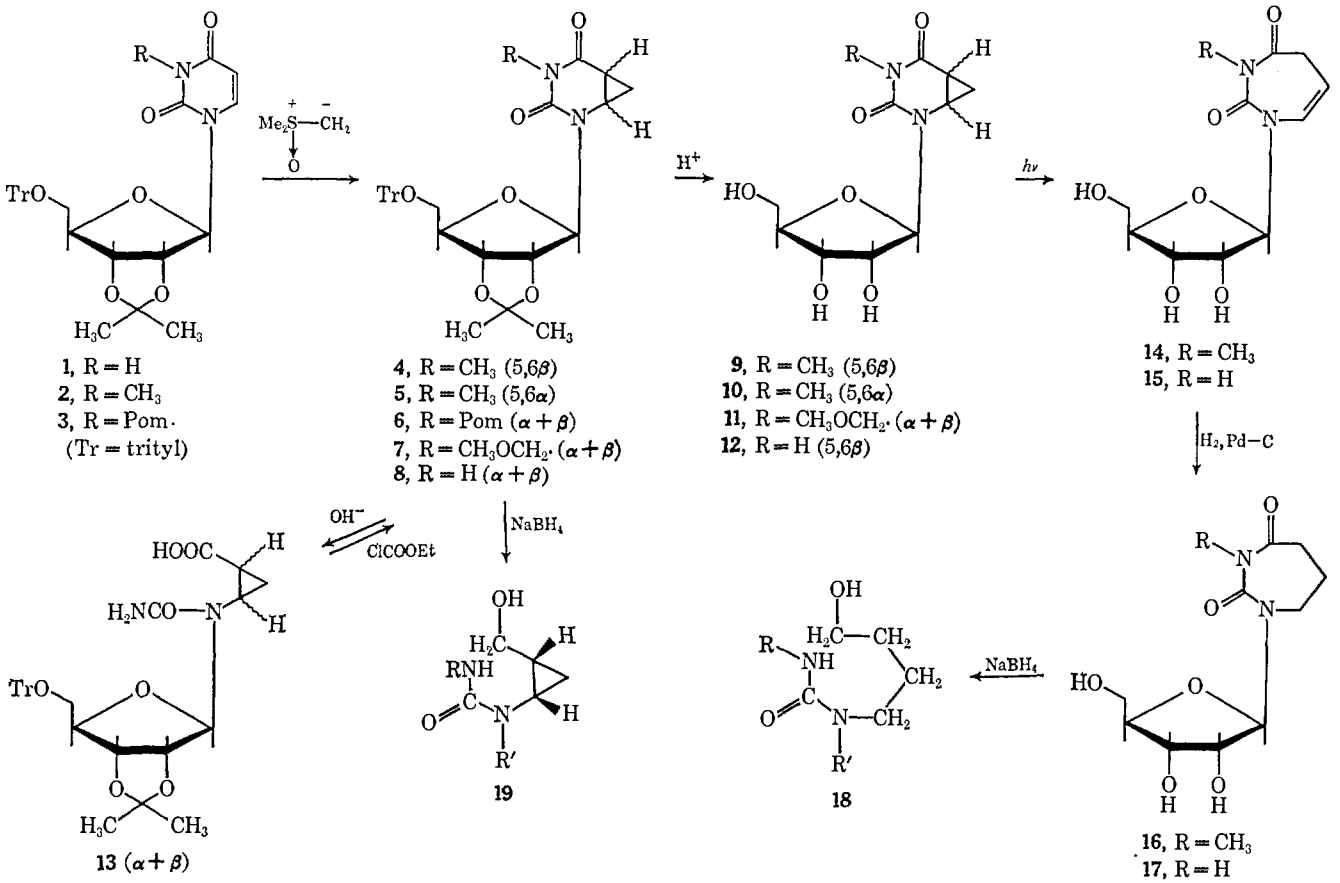
Preparation and Photochemistry of 5,6-Cyclopropyluridines and of Bicyclic Isomers of Thymines

Sir:

Template activity, photolesions and photodimerizations, ability to be incorporated into DNA or sRNA, and, therefore, potential cytotoxic, anticancer, and antiviral activities are intimately associated with the 5,6 unsaturation and substitution of pyrimidine nucleosides.[1,2] As possible intermediates between (dihydro) pyrimidines and 5-hydroxymethylpyrimidines, we have now prepared 5,6-cyclouracils and -thymines and pure diasteroisomers of cyclo-5-methyluridine in which the 5-methylgroup has become a 5,6α- or 5,6β-cyclopropane ring contributing to the uv chromophore of the bicyclic system ($\lambda_{max}^{H_2O}$ 245 sh mμ (ε ~1230)) which straddles the absorption of uridine ($\lambda_{max}^{H_2O}$ 262 mμ) and dihydrouridine (end absorption, $\lambda_{max}^{H_2O}$ 230 mμ at pH 9).

Excess dimethyloxosulfonium methylide,[3] in contrast to the Simmons–Smith reagent,[4] smoothly converted 1,3-dialkyluracils and -thymines into the novel cyclopropane derivatives 2,4-dialkyl- and 2,4,6-trialkyl-2,4-diazabicyclo[4.1.0]heptane-3,5-diones, which like dihydrouridine[5] or thymine photodimers[6] are easily hydrogenolyzed with $NaBH_4$ in quantitative yield to *cis*-1,2-disubstituted cyclopropanes **19**.

The difficulties of preparing 3-unsubstituted cyclo-5-methyluridines became apparent when 2′,3′-O-isopropylidene-5′-O-trityluridine (**1**) was allowed to react with excess methylide to yield the two diastereoisomeric 3-methyl-5,6-cyclopropyluridines **4** (25% yield; $[\alpha]^{25}D$ +2.6° (MeOH)) and **5** (10% yield; $[\alpha]^{25}D$ −46° (MeOH)) in addition to the methylation product **2** (20% yield; mp 195°; $[\alpha]^{25}D$ −5.5° ($CHCl_3$)), which could all be separated by careful chromatography on silica gel (benzene–acetone). The protected 3-methyluridine **2** gave the diastereoisomers **4** and **5** in 80% yield in a ratio of 7:3.[7]



Cation exchange resin (Bio-Rad, AG-50W (H^+), in aqueous MeOH) quantitatively removed the pro-

(1) *Cf.* B. R. Baker, "Design of Active-Site-Directed Irreversible Enzyme Inhibitors," John Wiley & Sons, Inc., New York, N. Y., 1967; A. Goldin, H. B. Wood, and R. R. Engle, *Cancer Chemother. Rept*, 1, Part 2, 1 (1968).
(2) *Cf.* B. Witkop, *Photochem. Photobiol.*, 7, 813 (1968).
(3) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
(4) H. E. Simmons and R. D. Smith, *ibid.*, **81**, 4256 (1959).
(5) P. Cerutti, Y. Kondo, W. R. Landis, and B. Witkop, *ibid.*, **90**, 771 (1968).
(6) T. Kunieda and B. Witkop, *ibid.*, **89**, 4243 (1967).
(7) The ratio was calculated from the nmr spectrum on the basis of the peaks at τ 4.0 due to the C_1' proton of the ribofuranosyl moiety.

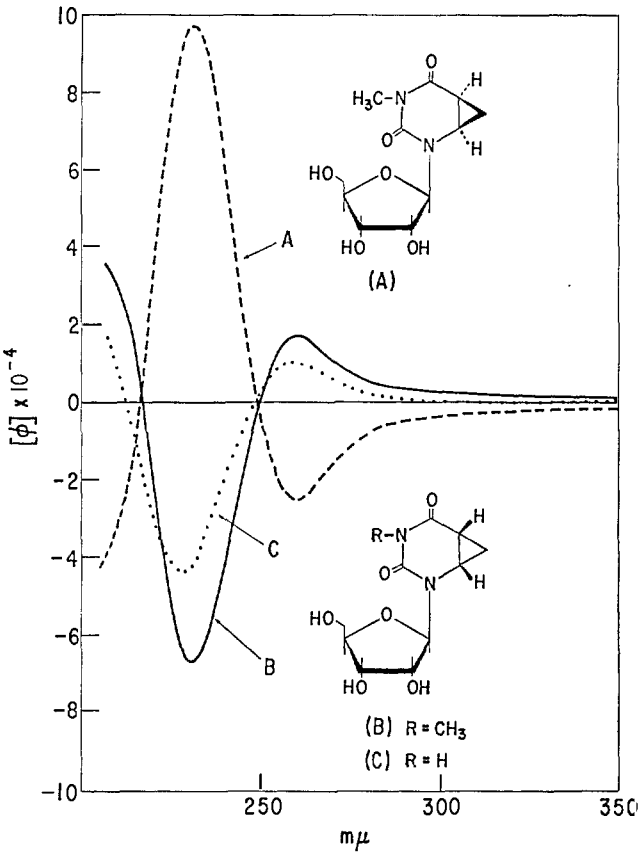


Figure 1. ORD curves of 1-β-D-ribofuranosyl-3-methyl-5,6α-(A) and 5,6-β-cyclothymine (B) and of 1-β-D-ribofuranosyl-5,6β-cyclothymine (C) in H_2O.

tecting groups of the sugar moiety to yield 1-β-D-ribofuranosyl-3-methylcyclothymines **9** ($[\alpha]^{25}D$ +20° (H_2O)) and **10** (mp 146°; $[\alpha]^{25}D$ −108° (H_2O)), whose ORD curves (Figure 1) show strongly positive and negative Cotton effects. On the basis of the abnormal contribution to the three-membered ring[8] and the positive Cotton effect of (*S*)-(−)-dihydrothymidine,[9] absolute configurations are assigned to **9** and **10** as shown in Figure 1.

Analogously, a 5:4 mixture[7] of diastereomeric 3-Pom-cyclomethyluridines[10] **6** was obtained in 20% yield in addition to N-methylnucleosides **2**, **4**, and **5** as a result of the lability of the Pom group to base.

Dowex 1 (OH^-) in MeOH converted **6** to the 3-methoxymethyl nucleoside **7**, which was hydrolyzed to 1-β-D-ribofuranosyl-3-(methoxymethyl)cyclothymine (**11**).

Starting material **3** and the cyclopropyl nucleoside **6** are not separable by chromatography; therefore **6** was hydrolyzed by alkali in aqueous dioxane to the ring-opened **13**, easily purified by chromatography and recyclized to the desired cyclothymine nucleosides **8** by the action of ethyl chloroformate (*not* DCC).

The residual blocking groups of **8** were removed by cautious acid treatment. Chromatography on silica gel (MeOH–$CHCl_3$) gave pure 1-β-D-ribofuranosyl-5,6β-cyclothymine (**12**; $[\alpha]^{25}D$ +15° (H_2O)) as a colorless microcrystalline powder. The ORD curve (Figure 1) with positive Cotton effect closely resembles that of **9**, indicative of the same absolute configurations at C_5 and C_6.

On uv irradiation **9**, **10**, and **12** gave the diazepine nucleosides **14** (τ_{D_2O} 3.57 (1 H, d, J = 7.0 Hz) and 4.10 (1 H, q, J = 7.0 Hz), olefinic protons) and **15** (τ_{D_2O} 3.58 (1 H, d, J = 7.5 Hz) and 4.19 (1 H, q, J = 7.5 Hz), olefinic protons), which were catalytically hydrogenated on Pd–C to 1-β-D-ribofuranosyl-3-methyltetrahydro-2H-1,3-diazepine-2,4(3H)-dione (**16**; mp 177°; $[\alpha]^{25}D$ −78.3° (H_2O)) and 1-β-D-ribofuranosyltetrahydro-2H-1,3-diazepine-2,4-(3H)-dione (**17**; mp 161°, $[\alpha]^{25}D$ −57.5° (H_2O)), which showed negative plain ORD curves in contrast to that of dihydrouridine.[9] Tetrahydrodiazepinediones of type **16** and **17** are easily opened by $NaBH_4$ to 4-ureido-1-butanols **18**.

The evaluation of the biological activities of these novel cyclothymine nucleosides and their photoproducts *in vitro* and *in vivo*[11] is in progress.

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(10) Pom = pivaloyloxymethyl: M. Rasmussen and N. J. Leonard, *ibid.*, 89, 5439 (1967).

(11) We are indebted to Dr. G. A. LePage, Stanford Research Institute, for some of the preliminary tests by his microassay procedure; *cf.* K. J. Pierre and G. A. LePage, *Proc. Soc. Exp. Biol. Med.*, 127, 432 (1968).
(12) Fellow in the Visiting Program of the U. S. Public Health Service, 1966–1969.

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Novel Pyrimidine Nucleoside Oxosulfonium Ylides and Their Photolysis to 2,2′-Methylenecyclonucleosides

Sir:

When 2,5′-, 2,2′-, or 2,3′-O-cyclopyrimidine nucleosides are treated with excess dimethyloxosulfonium methylide in THF, they are predominantly opened to stable sulfonium ylides and not converted to bicyclic 5,6-cyclopropylpyrimidines.[1]

In this way, 2′,3′-O-isopropylidene-2,5′-O-cyclouridine (I)[2] was quantitatively converted to dimethyloxosulfonium 1-(2,3-O-isopropylidene-β-D-ribofuranosyl)-4-oxo-1,4-dihydro-2-pyrimidinemethylide (II), mp 216°, $[\alpha]D$ −10.4° (MeOH), λ_{max}^{MeOH} 278, 236 nm (log ε 4.38, 4.30), whose structure was established by spectral data and elemental analysis (Chart I). The nmr spectrum (DMSO-d_6) showed a singlet peak at τ 6.30 ($(CH_3)_2S$–) and a broad peak at τ 4.50 (–SCH) which disappeared on addition of D_2O.

2,2′-Anhydro-1-(5-O-trityl-β-D-arbinofuranosyl)-uracil,[3] in which the C-2 position is more stable to nucleophilic attack,[4] gave the arabinofuranosyl pyrimidinemethylide IX, mp 168°, $[\alpha]D$ +31.6° (MeOH), λ_{max}^{MeOH} 280, 231 nm (log ε 4.33, 4.34), in 46% yield. Likewise, 2,3′-anhydro-1-(5-O-trityl-2-deoxy-β-D-xylo- (or -lyxo-) furanosyl)thymine[5] and -uracil (mp 138°) afforded the pyrimidine methylides X, mp 206°, $[\alpha]D$ −9.8° (MeOH), λ_{max}^{MeOH} 280, 231 nm (log ε 4.33, 4.31), and XI ,mp 175°,

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