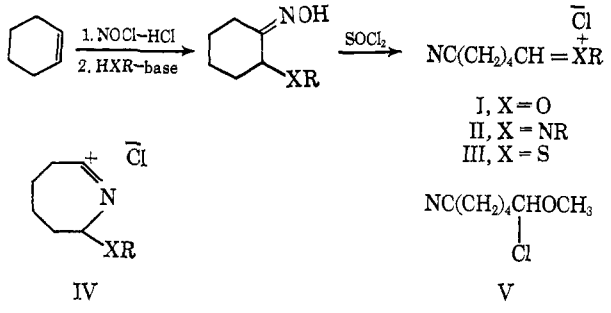
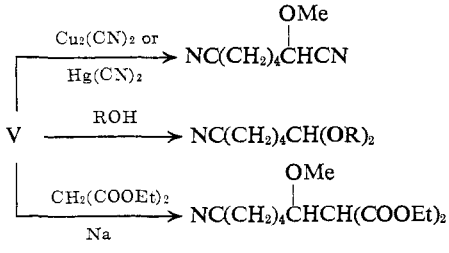
was considered to be formed *via* intermediates I, II, or III rather than cyclic nitrilium ion IV which might be sterically unfavorable. As a representative example, 2-methoxycyclohexanone oxime was chosen in this experiment.



A slight excess of thionyl chloride (3 g, 0.0252 mole) in dry carbon tetrachloride (10 ml) well cooled at 0° was added within a few minutes[5] to a carbon tetrachloride solution (10 ml) of 2-methoxycyclohexanone oxime (3 g, 0.0209 mole) also well cooled at 0°. Immediately after the addition, vigorous evolution of hydrogen chloride took place and an aliquot of the solution was quickly subjected to nmr measurement at 0°. The nmr spectrum of 2-methoxycyclohexanone oxime shows absorption peaks at δ 3.05 and 3.73 in a ratio of *ca.* 1:3 for the methine proton, which might be caused by a mixture of *syn* and *anti* configurations of the α-substituted oxime,[6] δ 3.20 for the methoxy group, and δ 10.33 for the hydroxy group. The nmr spectrum of the reaction mixture showed absorption peaks at δ 5.51 (1 H, triplet, J = 5 cps), which reasonably correspond to the α-hydrogen of chloro alkyl ether,[7] and no absorption of the methine proton of the starting material, δ 3.50 (3 H, singlet) for the methoxy group, which shifted to lower field by only 0.2 ppm, and δ 2.41 (2 H, triplet), which was assigned to the α-methylene of the nitrile group; these signals are all consistent with the structure of 1-chloro-5-cyanopentyl methyl ether.[8] This observation has demonstrated that the carbonium ion intermediate in the fragmentation of an α-methoxy oxime can be intercepted by chloride ion to yield α-chloro ethers. Simple addition of methanol and ethanol to the reaction



(5) When the same reaction was carried out at room temperature, the solution became brown in 10 min and a tarry material was obtained, which was difficult to identify.

(6) Various α-substituted oximes were prepared from displacement reactions of 2-chlorocycloalkanone oxime; see (a) M. Ohno, N. Naruse, S. Torimitsu, and M. Okamoto, *Bull. Chem. Soc. Japan*, 39, 1119 (1966); (b) M. Ohno and N. Naruse, *ibid.*, 39, 1125 (1966); (c) M. Ohno, S. Torimitsu, N. Naruse, M. Okamoto, and I. Sakai, *ibid.*, 39, 1129 (1966); a detailed investigation of the stereochemistry of them is in progress and the results will be published soon.

(7) For instance, see K. Nukada, O. Yamamoto, and T. Suzuki, *Anal. Chem.*, 35, 1892 (1963).

(8) If the trapped intermediate were (5-cyanopentylidene)methyloxonium chloride (I) expected from the electromerically assisted Beckmann fission, the nmr spectrum of the reaction mixture should contain signals for HC=⁺OCH₃ at much lower field. For instance see, B. G. Ramsey and R. W. Taft, *J. Am. Chem. Soc.*, 88, 3058 (1966).

mixture at 5–10° afforded the corresponding acetals[9] in 82 and 91% yields, respectively. This procedure is synthetically important in making a stable acetal of unstable 5-cyanopentanal.[10] The reaction mixture was treated with cuprous cyanide or mercuric cyanide, affording 2-methoxyheptanedinitrile[9] in 50% yield, bp 116° (1.5 mm), infrared at 2210 (CN) and 1118 cm^{-1} (OCH_3), nmr δ 4.08 (1 H, triplet, J = 6.01 cps) for tertiary hydrogen, 3.48 (3 H, singlet) for methoxy, 2.36 (2 H, triplet, J = 6.0 cps) for methylene α to nitrile, and 1.69 (6 H, broad) for other methylene. The treatment of the reaction mixture with the carbanion prepared from ethyl malonate and sodium gave ethyl (5-cyano-1-methoxypentyl)malonate[9] in 64% yield, bp 148° (7 × 10^{-3} mm), infrared 2220 (CN), 1732–1750 (ester), and 1030 cm^{-1} (OCH_3), nmr δ 4.15 and 1.25 for ester hydrogens, 3.70 and 3.50 for tertiary hydrogens, 3.32 for methoxy, 2.33 for methylene α to nitrile, and 1.58 for other methylene. These observations strongly confirm that the intermediate of the Beckmann fission of 2-methoxycyclohexanone oxime is acyclic 1-chloro-5-cyanopentyl methyl ether, and the chloro ether produced in this way undergoes the usual reactions[11] with cyanide and malonate ions to afford useful synthetic sequences, especially when coupled with our method of preparing the starting oximes.[2]

(9) Satisfactory elemental analyses have been obtained for all new compounds reported herein.

(10) The ethylene acetal was obtained only in 10–15% yields when 5-cyanopentanal was treated with ethylene glycol in the presence of *p*-toluenesulfonic acid in boiling benzene.

(11) L. Summers, *Chem. Rev.*, 55, 301 (1955).

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The Synthesis of a 4′,5′-Unsaturated Nucleoside

Sir:

The recent characterization of several nucleoside antibiotics containing unsaturated sugars[1,2] has stimulated considerable activity toward the synthesis of such compounds. Toward this end elegant methods for the synthesis of 2′,3′-unsaturated pyrimidine nucleosides have been developed by Horwitz, *et al.*,[3] and extended to the purine series by Robins[4] *via* a variety of elimination reactions. Some progress has also been made in the introduction of 2′,3′ unsaturation *via* desulfurization of 2′,3′-O-thionocarbonates.[5] In this paper we describe the first synthesis of a nucleoside containing a 4′,5′ double bond, a structural feature that is present in the nucleoside antibiotic angustmycin A (decoyinine, I).

The synthesis of 6-deoxy 5,6-unsaturated hexopyranosides through reaction of suitably protected 6-deoxy-6-iodopyranosides with silver fluoride in pyridine has

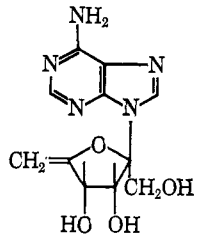
(1) H. Hoeksema, G. Slomp, and E. E. Van Tamelen, *Tetrahedron Letters*, 1787 (1964).

(2) N. Otake, S. Takeuchi, T. Endo, and H. Yonehara, *ibid.*, 1411 (1965).

(3) J. P. Horwitz, J. Chua, M. A. DaRooge, M. Noel, and I. L. Klundt, *J. Org. Chem.*, 31, 205 (1966).

(4) J. R. McCarthy, M. J. Robins, L. B. Townsend, and R. K. Robins, *J. Am. Chem. Soc.*, 88, 1549 (1966).

(5) W. V. Ruyle, T. Y. Shen, and A. A. Patchett, *J. Org. Chem.*, 30, 4353 (1965).



I

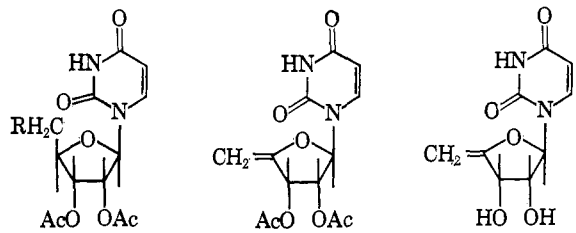
been known for many years.[6,7] Very recently Hough and Otter[8] have extended this reaction to the synthesis of protected 5-deoxy 4,5-unsaturated furanose derivatives.

Iodination of 2′,3′-di-O-acetyluridine[9] (IIa, 6.40 g, 19.5 mmoles) with methyltriphenoxyphosphonium iodide (13 g) in dimethylformamide (100 ml) for 2 hr at room temperature gave 7.2 g (84%) of 2′,3′-di-O-acetyl-5′-deoxy-5′-iodouridine (IIb), mp 163–164°, by direct crystallization of the extracted reaction mixture from chloroform–hexane,[10] λ_{max}^{MeOH} 258 mμ (ε 10,400). *Anal.* Calcd for $C_{13}H_{15}N_2O_7$: C, 35.64; H, 3.45; N, 6.39. Found: C, 35.89; H, 3.49; N, 6.29.

A solution of IIb (876 mg, 2 mmoles) in anhydrous pyridine (20 ml) was shaken in the dark at room temperature for 4 days with powdered silver fluoride (600 mg, 4.8 mmoles). The mixture was then filtered and the filtrate thoroughly shaken with water (50 ml) and ethyl acetate (50 ml). Evaporation of the ethyl acetate phase left 800 mg of a light-brown syrup that was purified by preparative thin layer chromatography on silicic acid using ethyl acetate as eluant, giving 525 mg (84%) of chromatographically homogeneous 1-(2,3-di-O-acetyl-5-deoxy-β-D-erythropent-4-enofuranosyl)uracil (III) as a dry froth which has not yet been obtained crystalline; λ_{max}^{MeOH} 258 mμ (ε 9250). *Anal.* Calcd for $C_{13}H_{14}N_2O_6$: C, 50.32; H, 4.55; N, 9.03. Found: C, 50.43; H, 4.86; N, 8.75. The structure was convincingly confirmed by the nmr spectrum in deuteriochloroform which showed the 5′-methylene group as a pair of doublets (J = 2.5 cps) centered at 4.45 and 4.69 ppm. Both the 4′ and 5′ protons of the starting material (IIb), which were present as a multiplet centered at 4.15 ppm and a doublet (J = 5 cps) centered at 3.52 ppm, respectively, were completely absent. Most of the other protons in III appeared at positions similar to those in IIb except that C_6–H was shifted upfield by 0.29 ppm and appeared as a doublet (J = 8 cps) at 7.32 ppm.

Treating III (450 mg) in a mixture of methanol (4.5 ml) and concentrated ammonium hydroxide (4.5 ml) for 1 hr at room temperature gave a single product upon examination by thin layer chromatography or paper chromatography. Evaporation of the solvent gave a crystalline residue (87%) of 1-(5-deoxy-β-D-erythropent-4-enofuranosyl)uracil (IV) which could be recrystallized from acetone and had mp 169–170°; λ_{max}^{MeOH} 261 mμ (ε 9600). *Anal.* Calcd for $C_9H_{10}N_2O_5$: C, 47.79; H, 4.96; N, 12.39. Found: C, 47.89; H, 4.62; N, 12.47. The nmr spectrum in deuteriodimethyl sulfoxide was less clear than that of III since the 5′-methylene protons and the C_2′ and C_3′ protons overlapped and appeared as a complex four-proton multiplet between 4.15 and 4.50 ppm. All other protons in IV were, however, clearly resolved.

Further work on the synthesis of other 4′,5′-unsaturated nucleosides is in progress and will be reported later.



IIa, R = OH
b, R = I

III

IV

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(6) B. Helferich and E. Himmen, *Ber.*, **61**, 1825 (1928).
(7) For a comprehensive review on unsaturated sugars see R. J. Ferrier, *Advan. Carbohydrate Chem.*, **20**, 67 (1965).
(8) L. Hough and B. Otter, *Chem. Commun.*, 173 (1966).
(9) A. M. Michelson and A. R. Todd, *J. Chem. Soc.*, 3459 (1956).
(10) See J. P. H. Verheyden and J. G. Moffatt, *J. Am. Chem. Soc.*, **86**, 2093 (1964), for other examples of iodination of nucleosides with this reagent.

A Method for the Determination of Nucleotide Sequences near the Terminals of Ribonucleic Acids of Large Molecular Weight

Sir:

We wish to report a method by which the terminal fragments produced by specific cleavage of ribonucleic acids can be oxidized by periodate, selectively absorbed on aminoethylcellulose, and subsequently recovered in a pure condition. The approach is especially suited to the study of the sequences of large ribonucleic acids, and some preliminary results are reported for the nucleic acid of the bacteriophage f2.

The absorption of periodate-oxidized ribonucleic acid to aminoethylcellulose has been used by Zubay[1] to purify sRNA specific for a particular amino acid. In this procedure the terminal *cis*-glycol groups of the bulk of the sRNA are not protected by the selected amino acid, and they are converted to dialdehydes by the periodate oxidation. When passed through an aminoethylcellulose column these ribonucleic acid chains are retained, presumably by chemical condensation of the aldehyde groups with the amino groups on the cellulose, while the unoxidized amino acyl sRNA passes through the column in an enriched condition. More recently, using similar columns, Habermann, *et al.*,[2] have also studied the absorption of periodate-oxidized oligonucleotides and their subsequent recovery with hydrochloric acid as the eluting agent.

In the present work the model compounds, uridylyl-(3′–5′)-adenosine and guanylyl-(3′–5′)-adenosine have been used to study the absorption and recovery of periodate-oxidized fragments on aminoethylcellulose, and, on the basis of these studies, a procedure for the isolation of such fragments from ribonucleic acids has been developed. In this approach the ribonuclease

(1) G. Zubay, *J. Mol. Biol.*, **4**, 347 (1962).
(2) V. Habermann, E. Maidlová, and R. Černy, *Collection Czech. Chem. Commun.*, **31**, 139 (1966).