contributes only at pH values near its pK). That H_2CrO_4 is not an effective oxidant is not surprising considering the previous conclusions[1,3] that OOH^- and $H_3O_2^+$ but not H_2O_2 readily oxidize boronic acids. That the reaction of $HCrO_4^-$ with boronic acids is much more sensitive to structure than is the reaction of HOO^- or $H_3O_2^+$ argues against its having the transition state II. We are therefore tentatively proposing the mechanisms shown.

$$HCrO_4^- + RB(OH)_2 \rightleftharpoons$$

$$\left[\begin{array}{l} H \\ O \\ | \\ R{-}B^-{-}OCrO_3H \\ | \\ O \\ H \end{array}\right]^* \longrightarrow III \longrightarrow ROH \quad (4)$$

$$H_3CrO_4^+ + RB(OH)_2 \longrightarrow [?] \longrightarrow ROH \quad (5)$$

The third application of this reaction in the acid-independent region is in the study of the large solvent and specific ion effects previously observed in chromic acid oxidations.[2a-d] Other chromic acid reactions involve high acidity dependencies.[2a-g] Consequently factors such as solvent and specific ion effects could not be quantitatively separated.[2b] With the discovery of an acid independent Cr^{VI} oxidation, this separation can now be made. Such studies are in progress.

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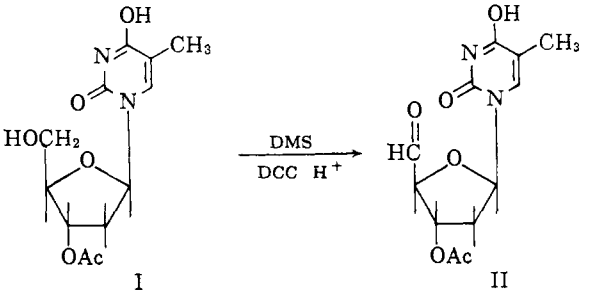
The Synthesis of Nucleoside-5′ Aldehydes

Sir:

We have recently observed that the addition of dicyclohexylcarbodiimide to an anhydrous solution of pyridinium thymidine-5′ phosphate in dimethyl sulfoxide results in rapid coloration of the reaction mixture and the release of a foul sulfide-like smell. Chromatographic examination of the products showed that within 1 hr. at room temperature the nucleotide had completely disappeared through degradation to thymine and inorganic phosphates, principally trimetaphosphate. Other ribo- and deoxyribonucleotides react in a similar way but at varying rates. A similar release of thymine resulted from P^1,P^2-dithymidine pyrophosphate or from thymidine or 5′-O-acetyl thymidine in the presence of anhydrous orthophosphate. 3′-O-Acetyl thymidine-5′ phosphate, 3′-deoxythymidine-5′ phosphate[1] (2′,3′-dideoxy-β-D-pentofuranosyl thymine 5′-phosphate), or the corresponding nucleosides in the presence of orthophosphate, gave, however, no release of thymine.

Treatment of 3′-O-acetyl thymidine (I) (1 mmole) in anhydrous dimethyl sulfoxide (3 ml.) in the presence of anhydrous orthophosphoric acid (0.5 mmole) and dicyclohexylcarbodiimide (3–5 mmoles) for several hours at room temperature gave no release of thymine. I was, however, converted in roughly 90% yield into a new compound clearly separated from the starting material by paper chromatography and giving a positive carbonyl test with dinitrophenylhydrazine spray. This material has now been shown to be 3′-O-acetyl thymidine-5′ aldehyde (II) which was isolated both as the noncrystalline free compound (λ_{max} 267 mμ in water) or as its crystalline 2,4-dinitrophenylhydrazone (m.p. 233–234°, λ_{max}^{MeOH} 261 and 350 mμ; ϵ_{max} 19,300 and 21,650. *Anal.* Calcd. for $C_{18}H_{18}N_6O_9$: C, 46.76; H, 3.92; N, 18.18; acetyl, 9.31. Found: C, 46.99; H, 4.16; N, 18.37; acetyl, 9.61). The structure of II was proved by reduction with sodium borohydride to thymidine (with concomitant hydrolysis of the acetyl group) and by oxidation with sodium hypoiodite to 3′-O-acetyl thymidine-5′ carboxylate, which upon alkaline hydrolysis gave thymidine-5′ carboxylate.[2] It is to be emphasized that no acidic nucleoside derivatives could be detected electrophoretically in the final reaction mixture, the method thus being completely selective for oxidation to the aldehyde level. This is to be contrasted with other oxidative techniques which have been applied to nucleosides and have led inevitably to carboxylic acids.[2-4]



The aforesaid release of thymine from thymidine-5′ phosphate, which first directed our attention to this oxidation procedure, is clearly the result of quantitative oxidation of the 3′-hydroxyl group to a ketone which spontaneously eliminates both the heterocyclic base and the phosphate moiety under the mildest of conditions. Further experiments designed to utilize this reaction for the stepwise degradation of deoxyoligonucleotides are in progress.

In a similar way, the reaction of 2′,3′-O-isopropylidene uridine with dicyclohexylcarbodiimide and 0.5 mole equiv. of pyridinium trifluoroacetate or pyridinium phosphate in anhydrous dimethyl sulfoxide, followed by treatment with 10% acetic acid at 100° for 1 hr., gave a high yield of uridine-5′ aldehyde, which has as yet resisted crystallization but which is readily separated from uridine on bisulfite-impregnated paper and gives a positive test for a carbonyl group. Also, a similar reaction on 2′,3′-O-isopropylidene adenosine gave, after acidic removal of the isopropylidene group, a major product chromatographically identical with a sample of the adenosine-5′ aldehyde isolated by Hogenkamp, *et al.*,[5] by ultraviolet irradiation of coenzyme B_{12}.

Further development of this highly selective and mild oxidation technique will be reported in detail shortly.[6]

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(6) For a preliminary account, see K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **85**, 3027 (1963).

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A New and Selective Oxidation of Alcohols

Sir:

We have recently observed that treatment of nucleoside derivatives, substituted such that only the primary

5′-hydroxyl group is free, with dicyclohexylcarbodiimide (or with related compounds such as diisopropylcarbodiimide) and phosphoric acid or pyridinium phosphate in anhydrous dimethyl sulfoxide leads to a rapid and selective oxidation to the aldehyde.[1] We have now applied this reaction to the oxidation of a considerable number of other primary and secondary alcohols. Thus, addition of dicyclohexylcarbodiimide (3 mmoles) to a solution of *p*-nitrobenzyl alcohol (1 mmole) and anhydrous phosphoric acid (0.5 mmole) in dry dimethyl sulfoxide leads to the quantitative (thin layer chromatography) formation of *p*-nitrobenzaldehyde, which was isolated in 92% yield as the dinitrophenylhydrazone (m.p. 316–317°). In a similar fashion oxidation of 1-octanol gave octylaldehyde isolated in 70% yield as its crystalline dinitrophenylhydrazone (m.p. 104–105°). Optimal reaction conditions have been determined using the oxidation of testosterone to Δ^4-androstene-3,17-dione as a model and following the course of the reaction by quantitative thin layer chromatography. It has thus been shown that acids such as phosphoric acid, phosphorous acid, cyanoacetic acid, or pyridinium phosphate promote a rapid oxidation within a few hours at room temperature. On the other hand, stronger acids such as trifluoroacetic acid serve only poorly and mineral acids such as hydrogen chloride or sulfuric acid lead to no oxidation. All three of these, however, function well as their pyridine salts. A considerable variation in the amounts of acid (0.1–2.0 mole equiv.) and of carbodiimide (2–5 mole equiv.) can be used and the sulfoxide (tetramethylene sulfoxide is entirely suitable) may be diluted to the extent of 90% with an inert solvent if required. Thus, overnight reaction at room temperature of testosterone (2 mmoles), pyridinium trifluoroacetate (1 mmole), and dicyclohexylcarbodiimide (6 mmoles) in anhydrous dimethyl sulfoxide (5 ml.) results in quantitative oxidation to Δ^4-androstene-3,17-dione (m.p. 169–170°), which was isolated by direct crystallization in 92% yield.

In similar fashions, the oxidation of various types of steroidal alcohols have been studied, the nature of the acid catalyst being given in parentheses. The products were usually isolated by chromatography on silicic acid or by direct crystallization.[2] Cholane-24-ol (H_3PO_4) gave cholane-24-al (hydrate, m.p. 95°) in 85% yield. Cholestanol (H_3PO_4) gave cholestanone (m.p. 129°) in 68% yield. 3β-Acetoxy-Δ^5-androstene-17-one-19-ol (pyridinium trifluoroacetate) gave the pure 19-aldehyde (m.p. 141–143°) in 53% yield. Δ^5-Androstene-3-β-ol-17-one (pyridinium trifluoroacetate) was converted to the extent of 90% into the unconjugated ketone Δ^5-androstene-3,17-dione as judged by thin layer chromatography and ultraviolet spectra before and after mild acidic treatment, but partial migration of the double bond into conjugation occurred on attempted column chromatography. The pure Δ^5-3-one, λ_{max} 240 and 290 mμ; Σ_{max} 47 and 40 in methanol (m.p. 167–169° with migration of the double bond on heating[3]), was isolated in 55% yield by direct crystallization from acetone. The equatorial hydroxyl group of 11α-hydroxyprogesterone (pyridinium trifluoroacetate) was smoothly oxidized giving 11-keto-progesterone[4] (m.p. 175–177°) in 68% yield. On the other hand, the axial 11β-hydroxyl of corticosterone-21-acetate was completely inert using pyridinium trifluoroacetate and was only partially dehydrated (22%) to 21-acetoxy pregna-4:9(11)-diene-3,20-dione[5] (22%) (m.p. 157–159°) using phosphoric acid. A similar pattern obtains with 11β-hydroxyprogesterone. The much less hindered pair of epimeric 3α- and β-hydroxy-5β-pregn-16-ene-20-ones, however, were oxidized at remarkably similar rates using either phosphoric acid or pyridinium trifluoroacetate to the 3-ketone and an anhydro compound (presumably Δ^2) in a ratio of 6:1 as determined by quantitative thin layer chromatography. The oxidation of hydroxy compounds containing strongly basic functions requires the addition of a molar excess of acid relative to the base for satisfactory oxidation. Thus, spegazzinidine dimethyl ether[6] is smoothly oxidized in the presence of 1.5 mole equiv. of phosphoric acid to give 3-dehydrospegazzinidine dimethyl ether[6] in 83% yield.

This method of oxidation thus appears to be of rather general utility and is particularly suited for use with otherwise labile compounds. The completely selective oxidation of primary alcohols to aldehydes with no trace of the corresponding acid is to be particularly noted. Further studies on this reaction, which somewhat resembles the Kornblum oxidation of alkyl halides or tosylates,[7] and a discussion of its probable mechanism will be presented shortly.

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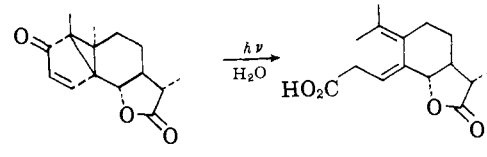
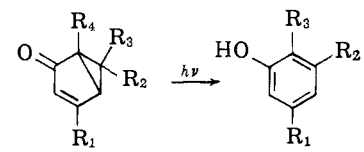
A Mechanistically Significant Intermediate in the Lumisantonin to Photosantonic Acid Conversion[1]

Sir:

We wish to report the isolation and identification of a mechanistically significant intermediate in the lumisantonin (I) to photosantonic acid (II) conversion.[2,3] This intermediate points to a clear relationship between the conversion of I to II and the photoisomerization of



I II



III IV

a, R_1 = CH_3; R_2 = R_3 = H; R_4 = $CH(CH_3)_2$
b, R_1 = R_4 = H; R_2 = R_3 = C_6H_5

a, R_1 = CH_3; R_2 = H; R_3 = $CH(CH_3)_2$
b, R_1 = H; R_2 = R_3 = C_6H_5

(1) Part VIII of the Photochemical Transformations Series. For Part VII see O. L. Chapman, H. G. Smith, R. W. King, D. J. Pasto, and M. R. Stoner, *J. Am. Chem. Soc.*, **85**, 2031 (1963).

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