talline 3,5-di-O-*p*-chloro(or *p*-methyl)benzoyl-2-deoxy-D-ribosyl chlorides coupled readily with the relatively more reactive monomercurypyrimidines[9] to afford (after deacylation) *alpha* and *beta* anomers[11] of 2′-deoxynucleosides.

Methyl-2-deoxy-D-ribofuranoside[12] was converted to the 3,5-di-*O*-*p*-toluyl derivative (75%), m.p. 76.5°, $[\alpha]_D$ −6.2° ($CHCl_3$), found for $C_{22}H_{24}O_6$: C, 68.73; H, 6.21, which with HOAc–HCl gave (70%) 3,5-di-*O*-*p*-toluyl-2-deoxy-D-ribosyl chloride (I), m.p. 109°,[13] $[\alpha]_D$ +108° (dimethylformamide) found for $C_{21}H_{21}O_5Cl$: C, 64.94; H, 5.71; Cl, 9.03. Similarly, the 3,5-di-*O*-*p*-chloro analog (II) of I was prepared (65% over-all yield from 2-deoxy-D-ribose), m.p. 118–120°, found for $C_{19}H_{15}O_5Cl_3$: C, 52.56; H, 3.77; Cl, 25.01. Monomercurithymine (III, $C_5H_4O_2N_2Hg$, found: N, 8.48) was obtained by refluxing 1-acetylthymine[14] with mercuric acetate in methanol. Monomercuri-5-fluorouracil (IV, $C_4HO_2N_2FHg$, found: N, 8.02) was synthesized from 5-fluorouracil[15] and mercuric acetate in refluxing aqueous methanol. Crude monomercuri-5-fluorocytosine (V) was prepared similarly from 5-fluorocytosine[15] (found: N, 12.17). Condensation of halogenose (I) with III in hot toluene followed by the usual processing[7,10] afforded 3′,5′-di-*O*-*p*-toluylthymidine (VI, 50%), m.p. 197°, $[\alpha]_D$ −50° (pyridine), (found for $C_{26}H_{26}O_7N_2$: C, 65.57; H, 5.78; N, 5.94). Deacylation of VI gave thymidine. The α-isomer (VII) of VI obtained (4%) from the mother liquors, m.p. 138° (from MeOH), $[\alpha]_D$ −14.5° (pyridine), found: C, 65.20; H, 5.73; N, 5.92. Deacylation of VII afforded "α-thymidine," m.p. 187°, $[\alpha]_D$ +7.2° (water), found: C, 49.61; H, 5.60; N, 11.35. Similarly, reaction of I with IV yielded anomers of 1-(3′,5′-di-*O*-*p*-toluyl-2-deoxy-D-ribosyl)-5-fluorouracil (VIII); *beta* isomer (41% top fraction from pyridine), m.p. 229°, $[\alpha]_D$ −17° (pyridine), found for $C_{25}H_{23}O_2N_2F$: C, 62.77; H, 4.81; N, 5.80; *alpha* isomer (27% from mother liquors), m.p. 214–215°, $[\alpha]_D$ −72.5° (pyridine), found: C, 62.61; H, 4.68; N, 5.54. Deacylation of VIII yielded the corresponding nucleosides: β-FUDR,[5] m.p. 150–151°, $[\alpha]_D$ +37.5 (water); α-FUDR, m.p. 150–151°,[13] $[\alpha]_D$ −21° (water), found: C, 44.18; H, 4.30; N, 11.59; F, 8.11. Condensation of V with either halogenoses I or II and deacylation afforded a crystalline mixture of FCDR anomers: m.p. 167–170°, $[\alpha]_D$ −0.7°, found for $C_9H_{12}O_4N_3F$: C, 44.54; H, 5.15; N, 16.86, which exhibited about 50% of the antimicrobial activity[16] observed with authentic β-FCDR[6] ($[\alpha]_D$ +65.6°). Condensation of N-acetylcytosinemercury[10] with II in hot xylene gave anomers of 1-(3′,5′-di-*O*-*p*-chlorobenzoyl-2-deoxy-D-ribosyl)-4-acetamido-2(1H)-pyrimidinone: α-isomer (22% from ethyl acetate), m.p. 204.5–205°, $[\alpha]_D$ −66° ($CHCl_3$), found for $C_{25}H_{21}O_7N_3Cl_2$: C, 54.23; H, 4.10; N, 7.65: *beta* isomer (32% from ethanol), m.p. 128–130°, $[\alpha]_D$ −19°, found: C, 55.17; H, 4.09; N, 7.60. Deacylation of each anomer afforded high yields of *alpha* and *beta* cytosine-2′-deoxynucleosides: α-isomer (from ethanol), m.p. 192–193°, $[\alpha]_D$ −44° (1 *N* NaOH), found for $C_9H_{13}N_3O_4$: C, 47.76; H, 5.80; N, 18.53: β-anomer, m.p. 200–201°, $[\alpha]_D$ +78° (1 *N* NaOH), mixed m.p. with 2′-deoxycytidine undepressed.

We are indebted to Mr. T. Gabriel and Mr. V. Gruenman for technical assistance and to Dr. Al Steyermark for microanalyses.

(9) As in the case of N-acetylcytosinemercury,[10] the mercuripyrimidines employed in this report contain mercury and pyrimidine in a 1:1 ratio.

(10) J. J. Fox, N. Yung, I. Wempen and I. L. Doerr, THIS JOURNAL, **79**, 5060 (1957).

(11) The formation of both anomers is to be expected from this condensation reaction due to the absence of the 2-acyloxy function in the halogenose. See B. R. Baker in "The Chemistry and Biology of Purines," Ciba Foundation Symposium, Little, Brown and Co., Boston, Mass., 1957, p. 120.

(12) R. E. Deriaz, W. G. Overend, M. Stacey and L. F. Wiggens, *J. Chem. Soc.*, 2836 (1949).

(13) All melting points are uncorrected. Mixed-melting points of *alpha* and *beta* nucleoside anomers gave depressions.

(14) L. B. Spector and E. B. Keller, *J. Biol. Chem.*, **232**, 185 (1958).

(15) R. Duschinsky, E. Pleven and C. Heidelberger, THIS JOURNAL, **79**, 4559 (1957).

(16) Personal communication from Dr. J. Berger, Hoffman-LaRoche, Inc.

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A NEW AND SELECTIVE METHOD OF OXIDATION. THE CONVERSION OF ALKYL HALIDES AND ALKYL TOSYLATES TO ALDEHYDES

Sir:

Recently a procedure for oxidizing α-bromoketones to glyoxals, noteworthy for its exceptional simplicity and mildness, was described.[1] In our initial report it was emphasized that this procedure, which employs dimethyl sulfoxide as the oxidizing agent, is not satisfactory for benzyl bromides. Subsequent work has shown that with halides still less reactive than benzyl bromides aldehydes cannot be obtained by the original procedure.

TABLE I

THE OXIDATION OF HALIDES AND TOSYLATES TO ALDEHYDES

Starting compound	Product	Yield, %[a]
$CH_3(CH_2)_7$-Cl	$CH_3(CH_2)_6CHO$	71
$CH_3(CH_2)_7$-Br	$CH_3(CH_2)_6CHO$	74
$CH_3(CH_2)_6$-I	$CH_3(CH_2)_5CHO$	70
p-Br-C_6H_4-CH_2Br	*p*-Br-C_6H_4-CHO	76
p-CH_3-C_6H_4-CH_2Br	*p*-CH_3-C_6H_4-CHO	65
p-NO_2-C_6H_4-CH_2Br	*p*-NO_2-C_6H_4-CHO	76
$CH_3(CH_2)_7OTos$	$CH_3(CH_2)_6CHO$	78
$(CH_3)_3CCH_2OTos$	$(CH_3)_3CCHO$	0[b]
p-Br-C_6H_4-CH_2OTos	*p*-Br-C_6H_4-CHO	65
p-CH_3-C_6H_4-CH_2OTos	*p*-CH_3-C_6H_4-CHO	74
p-NO_2-C_6H_4-CH_2OTos	*p*-NO_2-C_6H_4-CHO	84

[a] The yields are those of the pure 2,4-dinitrophenylhydrazones. In a number of instances the pure aldehydes themselves were isolated in 5 to 10% lower yields. [b] Neopentyl tosylate quantitatively recovered.

We now describe a modification of the original method which enables one smoothly to oxidize, not only benzylic halides, but even strictly ali-

(1) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand and W. M. Weaver, THIS JOURNAL, **79**, 6562 (1957).

phatic halides to aldehydes; thus, 1-chlorooctane gives *n*-octaldehyde in 71% yield. Furthermore, by the new procedure the tosylates of primary alcohols readily are converted into aldehydes. Table I summarizes our results.

The oxidation of benzylic tosylates is accomplished by treatment with a mixture of sodium bicarbonate and dimethyl sulfoxide; the reaction is complete in less than five minutes at 100°. With a saturated tosylate, *e.g.*, *n*-octyl tosylate, the reaction is conducted at 150° for three minutes. Halides are oxidized to aldehydes by converting to the tosylate with silver tosylate and then treating the crude tosylate with the sodium bicarbonate–dimethyl sulfoxide mixture.

As a typical example: 1-iodoheptane (7.0 g.) is added to a solution of 11 g. of silver tosylate[2] in 100 ml. of acetonitrile at 0 to 5° (protected from light). The mixture is allowed to come to room temperature overnight and the product then is added to ice-water and extracted with ethyl ether. The ether solution is dried and concentrated *in vacuo;* the oil that results is added to a freshly prepared mixture made by adding 20 g. of sodium bicarbonate to *ca.* 150 ml. of dimethyl sulfoxide through which nitrogen is bubbling and which has been heated to 150° (some foaming occurs). After three minutes at 150° the reaction mixture is cooled rapidly to room temperature and the product is isolated as the 2,4-dinitrophenylhydrazone; m.p. 106–107°, a mixed m.p. with an authentic sample is undepressed; yield, 6.9 g. (70%). The procedure is identical when benzyl halides are used except that the dimethyl sulfoxide is heated to 100° and the reaction time is five minutes.

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(2) Prepared quantitatively by mixing equivalent amounts of silver oxide and *p*-toluenesulfonic acid monohydrate in acetonitrile (protect from light). After one-half hour the silver tosylate is isolated by filtering, evaporating the acetonitrile and drying *in vacuo* at 65°.

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THE IDENTIFICATION OF 4α-METHYL-Δ⁸-CHOLESTEN-3β-OL, A NEW STEROL FROM A PREPUTIAL GLAND TUMOR[1]

Sir:

A transplantable preputial gland tumor in C57BL/6 mice which is maintained in this laboratory has been found to contain relatively large amounts of a wide variety of sterols.[2,3] In addition to cholesterol, Δ⁷-cholestenol, 7-dehydrocholesterol, lanosterol, and 24,25-dihydrolanosterol, a sterol (referred to as B_2), which had not been reported previously, was isolated by chromatography on silicic acid–Celite.[3] This new sterol has now been identified as 4α-methyl-Δ⁸-cholesten-3β-ol (I).

The free sterol melted[4] at 136.5–137.5°, $[\alpha]_D$ +55° (*anal.*[5] calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 83.85; H, 12.27). The acetate (II) melted at 106.5–108.5°, $[\alpha]_D$ +64°. The benzoate softened at 119° and melted at 123–124°, $[\alpha]_D$ +82°. I gave positive selenium dioxide[6] and Tortelli–Jaffe tests. Identification of the sterol as a mono-saturated derivative of 4α-methylcholestan-3β-ol was made by several reactions. Hydrogenation of II in acetic acid over Adams catalyst (no hydrogen uptake) resulted in a steryl acetate m.p. 78–78.5°, $[\alpha]_D$ +37°. The free alcohol, m.p. 158–160.5°, $[\alpha]_D$ +19°, had an infrared spectrum identical with that of 4α-methyl-Δ⁸⁽¹⁴⁾-cholesten-3β-ol,[7] m.p. 160–163°, $[\alpha]_D$ +19°, and did not depress the melting point of the authentic sterol. Compounds obtained by migrating the double bond to the 14 position and by saturating the sterol had constants that agreed well with those reported by Djerassi.[8]

Since the selenium dioxide test is specific for allo- or Δ⁵-steroids with a double bond adjacent to the hydrogen in the 14 position,[6] and only Δ⁷ or Δ⁸ double bonds migrate to the 8(14) position when the sterol is hydrogenated with platinum oxide in glacial acetic acid,[9,10] the unsaturation is limited to one of these two positions. This further evidence indicated unsaturation in the 8 rather than in the 7 position. The physical constants for I and its ester derivatives were unlike those reported for 4α-methyl-Δ⁷-cholesten-3β-ol (lophenol)[8] or (methostenol)[11] (III), while the effect of the double bond on the optical rotation of the parent compound, $[M]_{D(I)} - [M]_{D(stanol)} = +120$, was strongly positive as is characteristic for a double bond in the 8 position and in contrast to the negative effect of unsaturation in the 7 position.[8,12,13] The infrared spectrum of I differed from that recorded for III and the reaction with the Liebermann–Burchard reagent differed from that for III and for Δ⁷-cholestenol.[11]

I appears to be of general significance in sterol metabolism. There is suggestive evidence for its presence in liver[3] and labeled acetate is incorpo-

(1) Supported by a research grant (C-2758) from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

(2) A. A. Kandutsch, E. D. Murphy and M. E. Dreisbach, *Arch. Biochem. and Biophys.* **61**, 450 (1956).

(3) A. A. Kandutsch and A. E. Russell, *J. Biol. Chem.*, in press.

(4) Melting points are corrected. Optical rotations in chloroform.

(5) Elementary analyses were performed by the Schwartzkopf Microanalytical Laboratory, Woodside 77, N. Y.

(6) L. F. Fieser, THIS JOURNAL, **75**, 4395 (1953).

(7) Kindly supplied by Dr. C. Djerassi, Wayne State University, Detroit, Michigan.

(8) C. Djerassi, G. W. Krakower, A. J. Lemin, L. H. Liu, J. S. Mills and R. Villotti, THIS JOURNAL, **80**, 6284 (1958).

(9) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, pp. 240–242.

(10) D. H. R. Barton and J. D. Cox, *J. Chem. Soc.*, 214 (1949), noted that the frequently made assumption that a 9(11) double bond resists hydrogenation and migrates to the 8(14) position under these conditions is without foundation.

(11) D. H. Neiderhiser and W. W. Wells, *Arch. Biochem. Biophys.*, **81**, 300 (1959).

(12) W. Klyne in E. A. Braude and F. C. Nachod "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, p. 111.

(13) The contribution of a 9(11) double bond was found to be +15° by L. F. Fieser and W. Huang, THIS JOURNAL, **75**, 5356 (1953), who noted that the value of +109° cited by D. H. R. Barton and W. Klyne, *Chemistry and Industry*, 755 (1948), was based on zymosterol which was at that time thought to have a 9(11) double bond.