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OXIDATION WITH CHLORINE COMPLEXES. SPECIFIC OXIDATION OF SECONDARY HYDROXYL GROUPS IN THE PRESENCE OF PRIMARY HYDROXYL GROUPS IN POLYHYDRIC ALCOHOLS.

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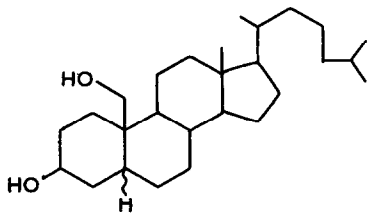
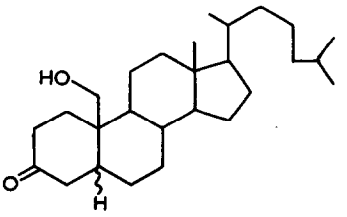
Recently oxidation of alcohols with complexes of chlorine and dimethyl sulphide[1], dimethyl sulphoxide[2], and iodobenzene[3] has been described. In the present communication we wish to report an oxidation of primary and secondary hydroxyl groups to aldehydes and ketones with chlorine and pyridine[4]. This simple reagent, although in both cases gives carbonyl compounds in high yield, allows for specific oxidation of secondary hydroxyl groups in presence of primary hydroxyl groups. Similarly, for convenient oxidation of secondary alcohols and for specific oxidation of secondary hydroxyl groups, 3-iodopyridine dichloride[5] might be used.

The oxidations are carried out in following experimental conditions:
To a stirred in ambient temperature solution of alcohol (1 equivalent) and py-





1 5 α 2 5 α

3 5 β 4 5 β

ridine (3-5 equivalents) in chloroform a solution of chlorine (1.2 - 2.0 equivalents) is added dropwise. During the addition temperature of reaction mixture is maintained below 30°. When the reaction is completed the excess of chlorine is blown out or reduced. The colorless solution is washed with diluted hydrochloric acid and the product is isolated in the usual manner. Examples of preparations of carbonyl compounds from corresponding alcohols are listed below.

Product	Yield (%)	Approximate reaction time at room temperature (min.)
hexanal	85[6a]	40
octanal	91[6a]	60
benzaldehyde	89[6a]	30
β-phenylpropionaldehyde	100[6a]	70
5-methylheptan-3-one	98[6a]	20
4-tert-butylcyclohexanone	87[6b]	20
5α-cholestan-3-one	77[6b]	15

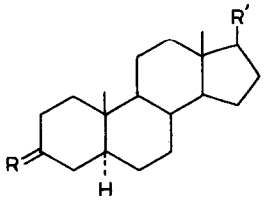
The selective oxidation with chlorine and pyridine was performed on steroid di- and triols:

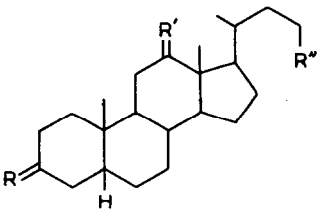
To a stirred solution of 5α-cholestane-3β,19-diol[7] 1 (200 mg, 0.49 mmole) in dry chloroform (8 ml) containing pyridine (0.2 ml, 2.5 mmole) a 0.73 M solution of chlorine in carbon tetrachloride (0.76 ml, 0.55 mmole) was added. After 15 min. to the clear solution one drop of propan-2-ol was added and after 5 min. the mixture was washed with 5% hydrochloric acid and then with water. The chloroform layer was dried and evaporated. The crystalline, chromatographically pure residue (197 mg) was recrystallized from acetone to give 5α-cholestane--19-ol-3-one[8] 2 (124 mg, 62%) m.p. 144-147°, $[\alpha]_D^{20}$ 45.95°.

The oxidation of 5β-cholestane-3β,19-diol[7] 3 with chlorine and pyridine gave 5β-cholestane-19-ol-3-one[9] 4 in nearly quantitative yield (sample recrystallized from acetone m.p. 155-157°, $[\alpha]_D^{20}$ 35.81°).

Oxidation of 21-nor-5α-pregnane-3,20-diol[10] 5 with 1.2 equivalent of chlorine and pyridine in 15 minutes at room temperature gave a mixture of two pro-

ducts. To the major component[11] (69%, m.p. 158-161°, $[\alpha]_D^{20}$ 33.4°) the structure of 21-nor-5α-pregnane-20-ol-3-one 6 was ascribed on the basis of its spectroscopic properties: i.r. (KBr) 3470, 1710 cm^{-1}; n.m.r. (100 MHz, $CDCl_3$) for C_{20} protons two overlapping quartets δ 3.72 and 3.55, J_{gem} = 13.0 Hz, J_{vic} = 8.7 and 8.0 Hz: m.s. m/e 304 (calc. 304). The minor reaction product (14%, m.p. 238-245°) containing no hydroxyl groups (i.r. 2715, 1710 cm^{-1}) and showing in its n.m.r. spectrum the signal of an aldehyde proton (δ 9.8) was regarded as 21-nor-5α-pregnane-3,20-dione 7.





5 R =  , R′ = CH_2OH

6 R = O , R′ = CH_2OH

7 R = O , R′ = CHO

8 R =  , R′ =  , R″ = CH_2OH

9 R =  , R′ = O , R″ = CH_2OH

10 R = R′ = O , R″ = CH_2OH

11 R = R′ = O , R″ = CH_2OAc

12 R = R′ = O , R″ = CHO

During the reaction of 5β-cholane-3α,12α,24-triol[12] 8 with one equivalent chlorine and pyridine a mixture of 12-monoketone 9 (59%) and 3,12-diketone (22%) was formed with some unchanged starting material. The structure of 5β-cholane-3α-24-diol-12-one 9 (m.p. 186-190°, $[\alpha]_D^{20}$ 111.3°) was derived from its spectral properties: i.r. (KBr) 1695 cm^{-1}; n.m.r. ($CDCl_3$) δ 1.03 (C_{18}-H overlapping with C_{19}-H) and δ 3.57 (multiplet C_{24}-H). The oily hydroxydiketone 10 was identified as acetate 11 (m.p. 93-94°, $[\alpha]_D^{20}$ 93.8°, n.m.r. 2 H triplet 4.01, J=6.0 Hz corresponding to C_{24}-H).

Oxidation of 8 with two equivalents of chlorine and pyridine gave hydroxydiketone 10 as major reaction product (68%), accompanied by monoketone 9 (6.4%)

and by less polar diketoaldehyde 12 (6.9%, colorless oil, $[\alpha]_D^{20}$ -0.5°). Finally, the oxidation of triol 8 with 3.5 equivalents of chlorine and pyridine and extension the reaction time to 2 hrs. gave a mixture of diketoaldehyde 12 (61%) and hydroxydiketone 10 (15%).

Oxidation of 5α-cholestane-3β,5,6β-triol 13 (210 mg, 0.5 mmole) with chlorine (0.55 mmole) and pyridine (0.3 ml, 3.7 mmole) in chloroform-methanol (20:1) for 15 minutes at room temperature gave 5α-cholestane-3β,5-diol-6-one 14 (155 mg, 73%), however oxidation of 5α-cholestane-3β,5,6α-triol 3-acetate 15 (m.p. 176-178°) proceeds slowly and, in similar conditions after 3 hrs. afforded corresponding 6-ketone only with 12% yield.

Essentially similar results were obtained on oxidations with 3-iodopyridine dichloride and pyridine. This reagent is transformed during reaction to easily removable products and presents a convenient alternative to iodobenzene dichloride.

References and footnotes

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