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Stereospecific Reductions of Isoilludin S and M on Alumina Chromatography

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Synopsis. Alumina column chromatography with ethanol as solvent converted planar α-ketols, illudin S and illudin M, to the dihydroxy compounds. The stereospecific reduction was discussed mechanistically as one of the Meerwein-Ponndorf-Verley reduction.

Though a number of reactions caused by alumina are known, very little has been recorded of the reduction of ketones on alumina chromatography.[1] This note describes the Meerwein-Ponndorf-Verley reduction of planar α-ketols, isoilludin S(**3**) and M(**4**), to dihydro compounds **6** and **7** on active alumina with alcohol as solvent.

In the course of structural investigations of illudin S(**1**), it was found that, when illudin S was adsorbed on alumina (Wako, 300 mesh) with ethyl acetate as solvent, only isomerised isoilludin S (**3**) was obtained.[2] However, on being adsorbed on alumina column for two days using ethanol instead of ethyl acetate, isomerized isoilludin S (**3**) was converted into a compound whose IR spectrum indicates the absence of the carbonyl group, the NMR spectrum showing a newly produced signal at τ 6.62 due to α proton to a hydroxyl group. From the results and correlation with the reduction product of isoilludin S with sodium borohydride, the compound was assigned to be dihydroisoilludin S (**6**). This suggests that isoilludin S is reduced to dihydroisoilludin S(**6**) on active alumina.

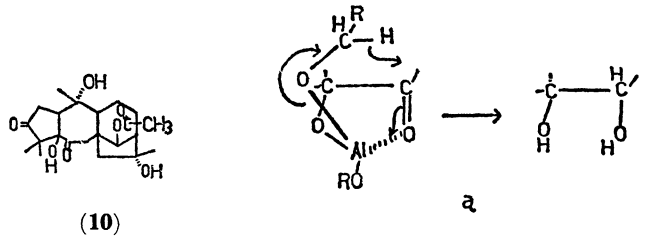
1 R=OH
2 R=H

3 R_1=OH, R_2=H
4 R_1=H, R_2=H
5 R_1=OAc, R_2=Ac

6 R_1=OH, R_2=H
7 R_1=H, R_2=H
8 R_1=H, R_2=Ac

The same kind of reduction on alumina column (Woelm, basic grade I) was observed with isoilludin M(**4**), which was obtained by isomerization of illudin M(**2**) on alumina column (Wako) using benzene, to give dihydroisoilludin M (**7**) in 64% yield. The stereochemistry of C-2 in compounds **6** and **7** was determined to be of *R* configuration since the proton signals due to equatorially oriented hydrogen in dihydro compounds **6** and **7** appear at τ 6.62 and 6.50 respectively, shielded effectively by neighboring cyclopropane ring.[3] This indicates that reduction of the ketols proceeded stereoselectively.

The same treatment on other ketols and ketones, *i.e.*, 3β-acetoxy-5α-hydroxycholestan-6-one (**9**), grayanotoxin derivative (**10**), cyclohexanone (**11**), tri-



(**10**) a

acetylisoilludin S (**5**), benzoin (**12**), was attempted but only the starting material was recovered. This might be due to the difficulty to form the intermediate (a) in the following surface process of the Meerwein-Ponndorf-Verley reduction. In compounds **9** and **10**, the carbonyl and vicinal hydroxyl groups are not planar, since the hydroxyl group is oriented axially in the plane containing the carbonyl group. Since compounds **3** and **4** have a moiety of planar ketols supported by the presence of a strong intramolecular hydrogen bond between the hydroxyl and carbonyl groups (see Experimental), the formation of planar intermediate (a) is possible. In compounds **11** and **5** which have no α hydroxyl group, it is unfavorable to combine with alumina surface. The intermediate arising from benzoin might have a fairly large steric repulsion between the two phenyl groups to cause recovery of the starting material.

Experimental

Reduction of Isoilludin S (3) with Aluminum Oxide. A solution of 50 mg of isoilludin S (**3**) in 1 ml of ethanol and 2 ml of chloroform was adsorbed on a 5 g of aluminum oxide (Wako, neutral 300 mesh) column and allowed to stand for 2 days at room temperature. The column was eluted with methanol and the eluate was evaporated *in vacuo* to give a crystalline material which was recrystallized from ethyl acetate to give 22 mg of dihydroisoilludin S (**6**), m.p. 198.5—199 °C. IR (cm^{-1}, Nujol) 3250, 1745 ($CH_3COOC_2H_5$), 1653, 1033: NMR (D_2O) after heating at 130 °C: τ 8.93 (3H, s, C-CH_3), 8.45 (3H, s, =C-CH_3), 6.62 (1H, s, H
C-OH), 4.27 (1H, s, =C-H).

Found: C, 66.08; H, 8.31%. Calcd for $C_{15}H_{22}O_4$ (1/2 $CH_3COOC_2H_5$); C, 65.78; H, 8.44%.

Reduction of Isoilludin S (3) with Sodium Borohydride. A solution of 100 mg of isoilludin S (**3**) in 3 ml of ethanol was treated with 50 mg of sodium borohydride and allowed to stand for 3 hr at room temperature. The reaction mixture was taken up into ethyl acetate and the extracts were filtered. The filtrate was dissolved in ethyl acetate and again filtered. The filtrate was concentrated *in vacuo* to give an amorphous solid. The solid was dissolved in ethanol and chromatographed on 2 g of aluminum oxide and eluted with ethanol. The eluate was concentrated and the residue was recrystallized from ethyl acetate to give a crystalline

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compound, mp 197—198 °C. The IR spectrum was identical with that of dihydroilludin S.

*Isomerization of Illudin M (**2**).* A solution of 50 mg of illudin M in benzene was adsorbed on 2.5 g of alumina (Wako) and allowed to stand for 2 days. The reaction product was eluted with methanol and the eluate was evaporated *in vacuo*. The residue was recrystallized from *n*-hexane-ether. mp 133—134.5 °C. IR (cm^{-1}, Nujol): 3450, 1705, 1605, 1608. NMR ($CDCl_3$) τ 8.97, 8.83, 8.52, 8.34 (each 3H, s, C–CH_3). 5.73 (1H, s, –C(H)–OH). 4.21 (1H, s, =C(H)–).

Found: C, 72.53; H, 8.11%. Calcd for $C_{15}H_{20}O_3$; C, 72.55; H, 8.12%.

*Reduction of Isoilludin M (**4**) with Aluminum Oxide.* A solution of 22 mg of isoilludin M in chloroform containing a small amount of ethanol as stabilizer was adsorbed on 2 g of aluminum oxide for 2 days. The column was eluted with chloroform and 6 mg of unchanged isoilludin M was recovered. Further elution with methanol gave 14 mg of dihydroisoilludin M (**7**). mp 193 °C. IR (cm^{-1}, Nujol) 3480, 1648, 1030. NMR ($CDCl_3$) τ 8.98, 8.87, 8.69, 8.41 (each 3H, s, C–CH_3), 6.50 (1H, s, –C(H)OH), 5.71 (1H, s, –C(H)OH), 4.34 (1H, s, =C(H)–).

*Acetylation of Dihydroisoilludin M (**7**).* A solution of 24 mg of dihydroisoilludin M with 0.5 ml of acetic anhydride 0.5 ml of dry pyridine was allowed to stand overnight at room temperature. The reaction mixture was poured into water, extracted with ether and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to give 28 mg of oily acetate. IR (cm^{-1}, film) 3480, 1740, 1648, 1235. NMR ($CDCl_3$) τ 9.00, 8.74, 8.68, 8.60 (each 3H, s, C–CH_3), 7.92 (6H, s, OAc), 5.12 (1H, s, –C(H)–OAc), 4.42 (1H, s, C(H)–OAc), 4.33 (1H, s, =C(H)–H).

*Treatment of Compounds **5**, **11**, **12**, **13** and **14** with Aluminum Oxide.* The compounds were treated under the conditions described above but none were reduced.

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References

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