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A Photoreductive Removal of the Toluene-*p*-sulfonyl Group[1]

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The steroidal toluene-*p*-sulfonyl esters have been cleaved rapidly to the corresponding alcohols by the photolysis in the presence of sodium borohydride. In this method, even cholesteryl toluene-*p*-sulfonate was converted into cholesterol without isosterol rearrangement.

Although the considerable utility of the toluene-*p*-sulfonyl group toward the protection of steroidal alcohols has been described,[3] it is scarcely used for the homoallylic steroidal alcohols such as cholesterol, because of a rearrangement on removal of the protective group by alkali.[4]

We now wish to report a convenient cleavage of the toluene-*p*-sulfonyl esters to corresponding alcohols by photoreduction in the presence of sodium borohydride.[5] Compared with the direct photolysis[6] the toluene-*p*-sulfonyl group was removed much rapidly under these conditions and even cholesteryl toluene-*p*-sulfonate (I) was converted into cholesterol (II) without isosterol rearrangement.

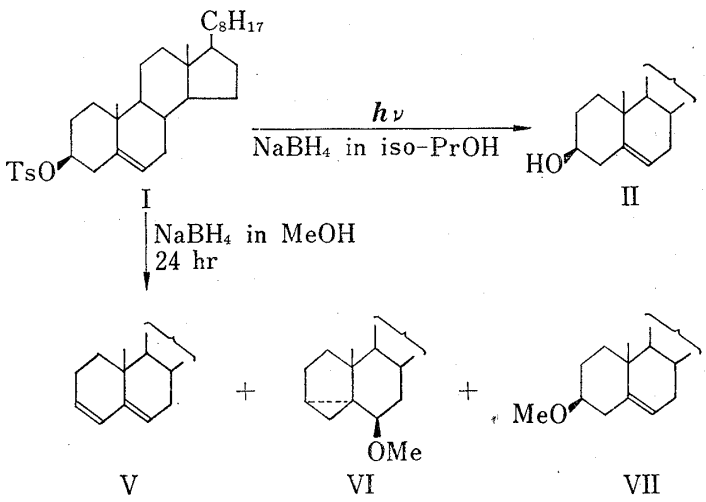

Chart 1.

A solution of I was irradiated in the presence of five molar equivalents of sodium borohydride at ambient temperature with a 450 W medium-pressure mercury lamp (Ushio UM 452) equipped with a Vycor filter. Aliquots of the solution were removed periodically from 0 to 30 min, and monitrored by silica gel thin-layer chromatography (TLC). Most of I disappeared within 20 min. The reaction mixture obtained showed single spot on TLC which was identical with that of II. Similarly, cholestanyl toluene-*p*-sulfonate (III) yielded cholestanol (IV) in quantitative yield when irradiated under the same conditions.

Steroidal toluene-*p*-sulfonates are usually resistant to reduction by sodium borohydride.[7] However, when I was allowed to react with excess of sodium borohydride for a sufficient length of time cholest-3,5-diene (V, 11.8%), 3α,5-cyclo-5α-cholestan-6β-ol methyl ether (VI, 4.1%), and cholesterol methyl ether (VII, 47.5%) were obtained.

1) On Photoreduction, Part VI. Part V: N. Shoji, Y. Kondo, and T. Takemoto, *Heterocycles*, 2, 51 (1974).
2) Location: *Aobayama, Sendai.*
3) J.F.W. McOmie, "Advance in Organic Chemistry, Methods and Results," ed. by R.A. Raphael, E.C. Taylor, and H. Wynberg, Vol. 3, Interscience Pub., New York, 1963, p. 222.
4) G.H. Whitham, *Proc. Chem. Soc.*, 422 (1961) and previous references cited therein.
5) Cf. Y. Kondo, *J. Synth. Org. Chem. Japan*, **29**, 1109 (1971).
6) D. Mellier, J.P. Pète, and C. Portella, *Tetrahedron Letters*, **1971**, 4559.
7) C.W. Shoppee and R.J. Stephenson, *J. Chem. Soc.*, **1954**, 2230.

Experimental[8]

Irradiation of Cholesteryl Toluene-*p*-sulfonate (I) in the Presence of Sodium Borohydride——To a solution of 1.5 g of I in 500 ml of iso-PrOH was added 0.5 g of $NaBH_4$ under mechanical stirring. The resulting solution was immediately irradiated for 20 min using an apparatus consisting of a 450 W medium-pressure mercury lamp (Ushio UM 452, intensity 6.1 W at 2537 A) in a water-cooled quartz immersion well equipped with a Vycor filter. At this time period an aliquot showed no starting material on TLC. The photolysate was quenched with a small amount of AcOH, concentrated *in vacuo*, and extracted with $CHCl_3$. The combined $CHCl_3$ extracts were washed with 5% $NaHCO_3$ aq, dried over Na_2SO_4, and removal of the solvent gave 1.202 g of a residue. The residue showed single spot on TLC (cyclohexane–acetone, 6: 4) which was identical with that of cholesterol (II). Crude cholesterol was further purified by alumina column chromatography (Woelm neutral, activity grade II, 80 g) using petr. benzine–ether (4: 1) as eluent. Recrystallization from acetone–MeOH afforded colorless plates, mp 144°. *Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 84.21; H, 11.84.

This material was identical with an authentic sample of cholesterol by direct comparison.

Irradiation of Cholestanyl Toluene-*p*-sulfonate (III) in the Presence of Sodium Borohydride——A solution of III in the presence of $NaBH_4$ was irradiated as described above. TLC analysis of the photoproduct (quantitative yield, mp 143—145°) showed one component identified as cholestanol (IV). *Anal.* Calcd. for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.87; H, 12.70.

Reduction of I with Sodium Borohydride——2.0 g of $NaBH_4$ was added portionwise to a solution of 2.0 g of I in MeOH under mechanical stirring. After stirring for 24 hr at ambient temperature, the solution was quenched with a small amount of AcOH and evaporated *in vacuo*. The residue was extracted with ether. The combined ethereal extracts were washed with 5% $NaHCO_3$ aq, dried and evaporated. The oily mixture (1.295 g) which showed three spots on TLC (petr. benzine–ether, 20: 1) was subjected to alumina column chromatography (Woelm neutral, activity grade II, 120 g). The column was eluted petr. benzine to give three crystalline fractions (V, VI and VII). V was recrystallized from acetone to afford colorless needles, mp 79°. 161 mg (11.8%). $[\alpha]_D^{30}$ −108.0° (c 1.2 in $CHCl_3$). UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 229 (4.32), 236.5 (4.36), 244 (4.16). Mass Spectrum *m/e*: 368 (M^+). *Anal.* Calcd. for $C_{27}H_{44}$: C, 87.97; H, 12.03. Found: C, 87.62; H, 11.82.

This material was identical with an authentic sample of cholest-3,5-diene[9] by direct comparison.

VI was recrystallized from acetone to afford colorless needles, mp 79—80°. 61 mg (4.1%). Mass Spectrum *m/e*: 400 (M^+). NMR ($CDCl_3$) ppm: 0.3—0.7 (2H, m, cyclopropane), 0.73 (3H, s, CH_3), 0.81 (3H, s, CH_3), 0.92 (3H, s, CH_3), 0.93 (3H, d, J=4.6 Hz, CH_3), 1.03 (3H, s, CH_3), 2.75 (1H, t, J=3 Hz, >C<u>H</u>–OCH_3), 3.30 (3H, s, OCH_3). *Anal.* Calcd. for $C_{28}H_{48}O$; C, 83.93; H, 12.07. Found: C, 84.03; H, 12.08.

This substance was identical with an authentic sample of 3α,5-cyclo-5α-cholestan-6β-ol methyl ether by direct comparison.

VII was recrystallized from acetone to give colorless needles, mp 75—76°. 704 mg (47.5%). Mass Spectrum *m/e*: 400 (M^+). NMR ($CDCl_3$) ppm: 0.68 (3H, s, CH_3), 0.80 (3H, s, CH_3), 0.90 (3H, d, J=5.0 Hz, CH_3), 0.91 (3H, s, CH_3), 1.00 (3H, s, CH_3), 2.92 (1H, br. s, >C<u>H</u>–OCH_3), 3.32 (3H, s, OCH_3), 5.31 (1H, br. s, olefinic proton). *Anal.* Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.07. Found: C, 83.71; H, 11.65.

This substance was identical with an authentic sample of cholesterol methyl ether by direct comparison.

8) All mps were taken on a Yamato MP-21 apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Shimazu Grating IR-27G spectrophotometer, and ultraviolet (UV) spectra in 95% EtOH solution were taken on a Hitachi EPS-3 spectrophotometer. Mass spectra were obtained on a Hitachi RMU-7 mass spectrometer. Nuclear magnetic resonance (NMR) spectra were determined on a Hitachi R-20 spectrometer using tetramethylsilane as internal standard.

9) Y. Kondo, J.A. Waters, B. Witkop, D. Guenard, and R. Beugelmans, *Tetrahedron*, **28**, 797 (1972).