

REDUCTION OF SOME MESYLOXY AND TOSYLOXY STEROIDS WITH SODIUM IODIDE AND ZINC DUST*

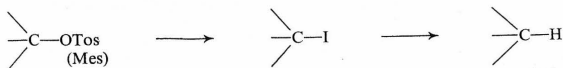
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Reduction of primary and secondary steroidal alcohols *via* their mesylates and tosylates with sodium iodide and zinc dust in 1,2-dimethoxyethane is shown to be a mild and simple preparative method for removing the hydroxyl from polyfunctional compounds. It may be successfully applied to substances with an isolated double bond, a keto group, a α -hydroxyketo, α,α' -dihydroxyketo, or α,β -unsaturated keto grouping, an isolated tertiary hydroxyl, an epoxide ring or a nitrile group. All these functions are not affected.

Some time ago, Fujimoto and Tatsuno¹ published a simple method of replacing a primary and secondary hydroxyl group by hydrogen. The general procedure is treatment of the corresponding *p*-toluenesulfonate or methanesulfonate with sodium iodide and zinc dust in boiling 1,2-dimethoxyethane (Scheme 1). The simplicity and good yields of this procedure make it a promising method² but more should be known about its limitations. Some experiments aimed at obtaining more information of this kind are reported in the present paper.



SCHEME 1

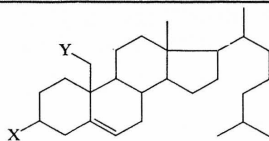
A group of polyfunctional steroids was investigated. Apart from the mesyloxy (or tosyloxy) grouping these compounds comprise the following functionalities: Double bond (*I, III, V, XVII, XXIII*), isolated keto group (*XI, XVII*), α -hydroxy keto grouping (*IX, XXI*), α,β -unsaturated keto grouping (*XIX, XXI*), isolated tertiary hydroxyl (*VII*), epoxide ring (*XIII, XV*), ester function (*III, XI*) and nitrile group (*XVII*). In all cases, TLC demonstrated homogeneity of the product. The figures listed in Table I are preparative yields obtained mostly from 300 mg of starting material; no attempts were made to obtain maximum yields.

* Part CCXIV in the series On Steroids. Part CCXIII: This Journal 44, 234 (1979).

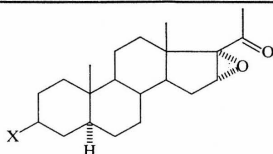
Several points may be commented on briefly. Formation of 5-cholestene (*II*) and B-nor-5-cholestene (*VI*) is particularly suitable for preparative purposes since the products are free of 3,5-cyclosteroids and simple crystallization provides pure specimens. This reduction constitutes a simpler alternative to the usual preparation of 5-cholestene from cholesterol *via* 3 β -chloro-5-cholestene^{3,4}. Similarly, we did not observe any participation of the homoallylic 5,6-double bond in the case of 19-mesyloxy derivative *III* where TLC demonstrated a negligible quantity of byproducts.

TABLE I
Yields, Analytical and Physical Data of the Products of Reduction

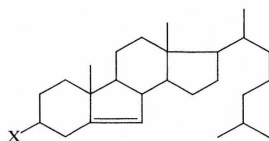
| Compound Yield, % | Formula (m.w.) | Calculated/Found | | M.p., °C [α] _D ²⁰ | Ref. |
|----------------------|---|------------------|----------------|---|------|
| | | % C | % H | | |
| <i>II</i> 84 | C ₂₇ H ₄₆ (370.7) | 84.49 84.32 | 12.51 12.44 | 91–93 –57° | 3, 4 |
| <i>IV</i> 48 | C ₂₉ H ₄₈ O ₂ (428.7) | 81.25 81.12 | 11.92 11.32 | 110–111 –43° | 5 |
| <i>VI</i> 34 | C ₂₆ H ₄₄ (356.6) | 87.56 87.42 | 12.44 12.31 | 68–69 –131° | 6 |
| <i>VIII</i> 54 | C ₂₇ H ₄₈ O (388.7) | 83.44 83.28 | 12.45 12.41 | 107–109 +14° | 7, 8 |
| <i>X</i> 47 | C ₂₇ H ₄₆ O ₂ (402.7) | 80.54 80.52 | 11.51 11.60 | 148–149 | 9 |
| <i>XII</i> 65 | C ₂₉ H ₄₈ O ₃ (444.7) | 78.33 78.18 | 10.88 10.93 | 139–140 –13° | — |
| <i>XIV</i> 63 | C ₂₇ H ₄₆ O (386.7) | 83.87 83.65 | 11.99 12.08 | 76–79 –53° | 10 |
| <i>XVI</i> 42 | C ₂₁ H ₃₂ O ₂ (316.5) | 79.70 79.62 | 10.19 10.21 | 130–132 +56° | — |
| <i>XVIII</i> 26 | C ₂₂ H ₃₁ NO (325.5) | 81.18 81.56 | 9.60 9.49 | 135–137° +18° | — |
| <i>XX</i> 39 | C ₂₁ H ₃₀ O ₂ (314.5) | 80.21 80.04 | 9.62 9.58 | 124–127 | 11 |
| <i>XXII</i> 67 | C ₂₁ H ₃₀ O ₄ (346.5) | 72.80 72.64 | 8.73 8.65 | 224–226 | 12 |
| <i>XXIV</i> 59 | C ₂₀ H ₃₂ O ₃ S (352.5) | 68.14 67.99 | 9.15 9.08 | 127–129 –88° | — |



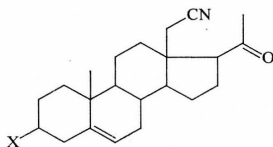
- I, X = TosO, Y = H
 II, X = H, Y = H
 III, X = AcO, Y = MesO
 IV, X = AcO, Y = H



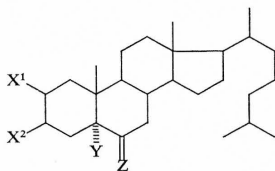
- XV, X = MesO
 XVI, X = H



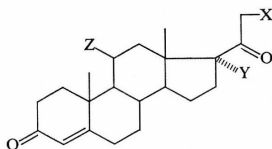
- V, X = MesO
 VI, X = H



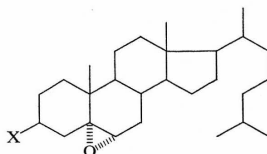
- XVII, X = TosO
 XVIII, X = H



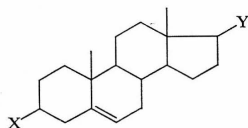
- VII, X¹ = H, X² = MesO, Y = OH, Z = H₂
 VIII, X¹ = H, X² = H, Y = OH, Z = H₂
 IX, X¹ = H, X² = TosO, Y = OH, Z = O
 X, X¹ = H, X² = H, Y = OH, Z = O
 XI, X¹ = AcO, X² = MesO, Y = H, Z = O
 XII, X¹ = AcO, X² = H, Y = H, Z = O



- XIX, X = MesO, Y = H, Z = H
 XX, X = H, Y = H, Z = H
 XXI, X = MesO, Y = OH, Z = OH
 XXII, X = H, Y = OH, Z = OH



- XIII, X = TosO
 XIV, X = H



- XXIII, X = MesO, Y = MesO
 XXIV, X = H, Y = MesO

Another observation of interest is the reduction of 3 β ,17 β -bis(methanesulphoxyloxy)-5-androstene (XXIII) where only the more accessible 3 β -mesyloxy group is removed. This behavior demonstrates the possibility of selective reductions of suitable substrates.

The reduction appears to be a simple, mild and selective method for replacing the primary or secondary hydroxyl by hydrogen in good yields.

TABLE II
Analytical and Physical Data of the New Mesylates and Tosylates

| Compound | Formula (m.w.) | Calculated/Found | | | M.p., °C |
|----------|--|------------------|-------|-------|----------|
| | | % C | % H | % S | |
| VI | C ₂₇ H ₄₆ O ₃ S (450.7) | 71.95 | 10.29 | 7.11 | 133—134 |
| | | 71.78 | 10.14 | 7.28 | |
| XI | C ₃₀ H ₅₀ O ₆ S (538.8) | 66.88 | 9.35 | 5.95 | 197—200 |
| | | 66.63 | 9.31 | 6.08 | |
| XV | C ₂₂ H ₃₄ O ₅ S (408.6) | 64.68 | 7.90 | 7.85 | 155—156 |
| | | 64.47 | 7.83 | 7.94 | |
| XVII | C ₂₉ H ₃₅ NO ₄ S (493.6) | 70.27 | 7.52 | 6.47 | 139—140 |
| | | 70.57 | 7.86 | 6.25 | |
| XIX | C ₂₂ H ₃₂ O ₅ S (408.6) | 64.68 | 7.90 | 7.85 | 127—129 |
| | | 64.32 | 7.74 | 7.49 | |
| XXI | C ₂₂ H ₃₂ O ₇ S (440.6) | 59.98 | 7.32 | 7.28 | 187—189 |
| | | 59.73 | 7.21 | 7.36 | |
| XXIII | C ₂₁ H ₃₄ O ₆ S ₂ (446.6) | 56.50 | 7.67 | 14.36 | 150—151 |
| | | 56.37 | 7.62 | 14.59 | |

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/0.2 Torr (26 Pa). Optical measurements were carried out in chloroform with an error of $\pm 3^\circ$. The IR spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane. The $^1\text{H-NMR}$ spectra were recorded on a Varian HA-100 instrument (100 MHz) in deuteriochloroform at 30°C with tetramethylsilane as internal reference. Chemical shifts are given in ppm. Apparent coupling constants were obtained from first order analysis. The identity of samples prepared by different routes was checked by mixture melting point determination, by thin-layer chromatography (TLC) and by infrared and $^1\text{H-NMR}$ spectra.

Mesylation

The alcohol (500 mg) was dissolved in pyridine (5–10 ml) and treated at 0°C with methane-sulfonyl chloride (1 ml) for 1 h. The mixture was decomposed with ice, the product was extracted with ether, the ethereal solution was washed with 5% aqueous hydrochloric acid, water, 5% aqueous potassium hydrogen carbonate solution, water, dried with anhydrous sodium sulfate and the solvent was evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield pure mesylates in all cases.

Reduction of Mesylates and Tosylates

The mesylate or tosylate (300 mg) was dissolved in 1,2-dimethoxyethane (3–6 ml), sodium iodide (300 mg), zinc powder (300 mg) and water (0.3 ml) were added and the mixture was refluxed while stirring for 4–6 h. The mixture was diluted with ether, the inorganic material was removed by filtration, the solution was washed with water, 5% aqueous hydrochloric acid, water, 5% aqueous potassium hydrogen carbonate solution, water, 5% aqueous sodium thio-sulfate solution, water, dried with anhydrous sodium sulfate and the solvent was evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield pure compounds, or in the cases of *XII*, *XIV*, *XVI* and *XVIII* chromatographed on a silica gel column (30 g) with a light petroleum–ether mixture and then crystallized from the mixture of acetone, methanol and water.

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