

Deoxygenation of Steroidal Ring-D 16,17-Ketols with Trimethylsilyl Iodide

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Reaction of various steroidal 16,17-ketols, 16 α -hydroxy-17-ketones 1—3, and 15, 16 β -hydroxy-17-ketone 4, and 17 β -hydroxy-16-ketones 5—7, and 17, along with methyl ethers of 16 α - and 17 β -ketols 1 and 5, with an excess of trimethylsilyl iodide (TMSI) or with HI in CHCl₃, produced the deoxygenated products, a mixture of the corresponding 17- and 16-ketones, in low to quantitative yields, in which the 17-ketone was the major product in each case. When the 16 β -deuterated 16 α -ketol 3 and the 17 α -deuterated 17 β -ketol 7 were reacted with TMSI for a brief period (15 min), the deuterium content at C-16 β and C-17 α of the recovered steroids 3 and 7 was reduced by 17 and 35%, respectively. The present results indicate that the deoxygenation proceeds not only through a direct iodination pathway producing α -iodoketone but also through other reaction pathways.

Key words steroidal 16,17-ketol; trimethylsilyl iodide; deoxygenation; deuterium labeling

Trimethylsilyl iodide (TMSI) is one of the most important organosilicon reagents, offering a broad variety of useful functional group transformations under mild conditions.¹⁾ Its unique properties and high reactivity arise from a combination of the relatively high Lewis acidity of the silicon and the strong nucleophilicity of iodide ion. These properties of TMSI make it a versatile and selective reagent¹⁾ for cleaving oxygen-containing groups such as esters, lactones, ethers, ketals, and carbamates as well as for the conversion of alcohols and sulfoxides to iodide and sulfides, respectively. Ho²⁾ has reported the usefulness of this silyl reagent in the transformation of α -ketols to ketones. TMSI has also been used for the reductive removal of the *tert*-hydroxy group of α,β -unsaturated δ -*tert*-hydroxy ketones³⁾ and in the deoxygenation of *vic*-diols,⁴⁾ epoxides,⁵⁾ and carbonyl-conjugated allylic ethers.⁶⁾ We have previously reported regiospecific deoxygenation at C-17 of the dihydroxy acetone side-chain of corticoid steroids and the corresponding 17-methyl ethers with this silyl reagent.⁷⁾ Furthermore, 21-hydroxy-20-keto and 21-alkoxy-20-keto steroids are efficiently transformed to 20-keto steroids by this reagent in the presence of MeOH.⁸⁾

During the course of these studies, we became interested in the deoxygenation reaction of cyclic α -ketols such as steroidal D-ring 16,17-ketols with TMSI. Treatment of 16-hydroxy-17-ketones, 1—4 and 15, and 17 β -hydroxy-16-ketones, 5—7 and 17, along with methyl ethers of compounds, 1 and 5, with the silyl reagent in CHCl₃ gave essentially the corresponding 17-ketones, 9—11 and 16, as the major deoxygenated products, respectively.

Results and Discussion

Reaction of a series of 16 α -hydroxy-17-keto steroids, 1—3 and 15, and 17 β -hydroxy-16-keto steroids, 5—7 and 17, with excess TMSI (8 mol eq) in CHCl₃ at room temperature was initially explored under various conditions (Fig. 1 and Table 1). Treatment of the 16 α -ketol, 1, having a 5 α -3-keto structure with TMSI for 42 h produced a 94 : 6 mixture of 17- and 16-ketones, 9 and 12, in 24% yield (entry 3). On the other hand, similar reaction of its counterpart 17 β -ketol, 5, gave the deoxygenated product 17-ketone, 9, in 78% yield after an 8 h-reaction period, with no production of the 16-keto isomer, 12, by ¹H-NMR (400 MHz) analysis (<1% yield) (entry 5). In these reactions, each substrate was recov-

ered without rearrangement to the other 16,17-ketol. Similar treatment of other 16 α -ketols, 2 and 15, gave a mixture of 17-ketones, 10 and 16, and 16-ketones, 13 and 18, respectively (entries 6 and 8). In contrast to the experiment with the 5 α -3-keto steroid, 1, the 16 α -ketols, 2 and 15, rearranged to the corresponding 17 β -ketols, 6 and 17, during these reactions. Treatment of compounds 6 and 17 with TMSI also yielded a mixture of 17-ketones, 10 and 16, and 16-ketones, 13 and 18, respectively (entries 7 and 9), in which the ratio of the 17- to 16-ketone was essentially similar to that obtained

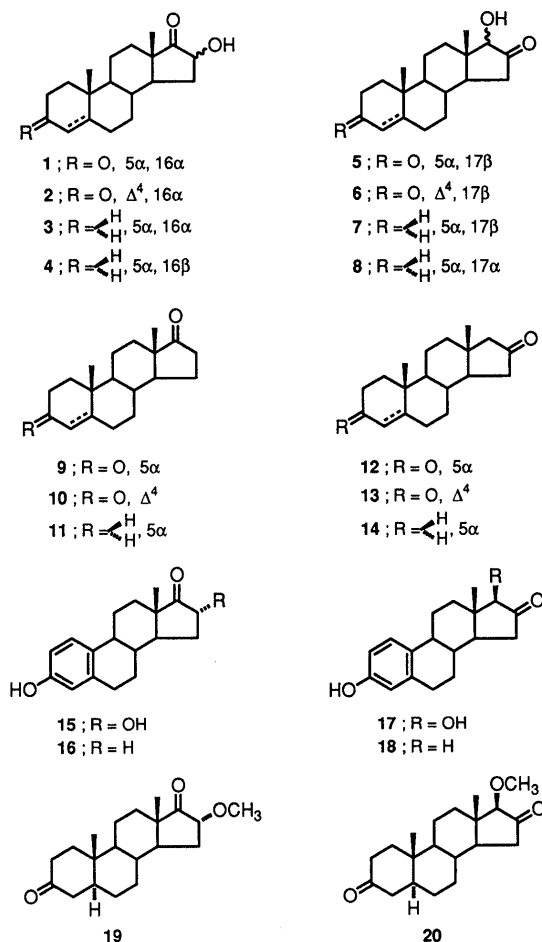


Fig. 1

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Table 1. Deoxygenation of 16-Hydroxy-17-oxo and 17-Hydroxy-16-oxo Steroids with TMSI^{a)}

Entry	Substrate	Conditions		Product (% yield)			
		TMSI (mol eq)	Time (h)	16-Ketol	17-Ketol	17- and 16-Ketones ^{b)}	Ketone ratio ^{c)} (17- to 16-Ketone)
1	1	8	2	1 (100)	— ^{d)}		
2	1	8	8	1 (84)	—	9 and 12 (16)	>99: 1
3	1	8	42	1 (35)	—	9 and 12 (24)	94: 6
4	5	8	2	—	5 (10)	9 and 12 (68)	97: 3
5	5	8	8	—	5 (9)	9 and 12 (78)	>99: 1
6	2	8	8	2 (16)	6 (37)	10 and 13 (31)	80:20
7	6	8	8	—	6 (22)	10 and 13 (57)	68:32
8	15	8	7	—	17 (21)	16 and 18 (56)	88:12
9	17	8	7	—	17 (19)	16 and 18 (68)	87:13
10	3	3	1			11 and 14 (98)	88:12
11	4	3	1			11 and 14 (90)	87:13
12	7	3	1			11 and 14 (95)	75:25
13	8	3	1		8 (14)		
14	19	8	8	1 (18)	—	9 and 12 (39)	>99: 1
15	20	8	8	—	5 (5)	9 and 12 (25)	>99: 1

a) Reactions were carried out in CHCl_3 at room temperature under N_2 . b) The product was obtained as a mixture of 17- and 16-ketones. c) The ratio of 17-ketone to 16-ketone was obtained by $^1\text{H-NMR}$ or GC analysis. d) No product detected.

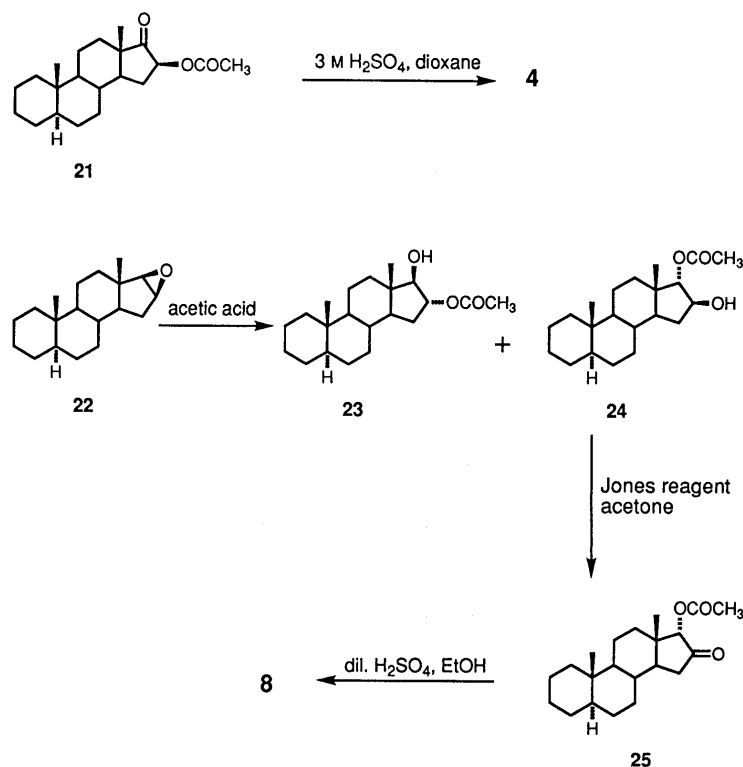


Chart 1

in the experiments with the corresponding 16 α -ketols, **2** and **15**. These results indicate that rearrangement of a 16 α -ketol to the 17 β -isomer is, at least in part, involved in the deoxygenation reaction. A conformational transmission of distortion through the B–C–D rings may be in operation during the rearrangement, although no detailed conformational analysis of these ketols is available. It is well known that the less stable 16 α -hydroxy-17-keto steroids isomerize to the most sta-

ble 17 β -hydroxy-16-ketone isomers under acidic and basic conditions through enolization of the 17-keto function.⁹⁾

Four possible 16,17-ketols, 16 α -ketol **3**, 16 β -ketol **4**, 17 β -ketol **7**, and 17 α -ketol **8**, having no functional group in the A-ring, were then subjected to the deoxygenation reaction. The ketols **4** and **8**, which had not been synthesized previously, were initially obtained as follows. The 16 β -hydroxy-17-ketone, **4**, was obtained on treatment of the known com-

pound, 16 β -acetoxyderivative **21**,¹⁰⁾ with 3 M H₂SO₄ in dioxane (Chart 1). Treatment of the 16 β ,17 β -epoxide, **22**,¹¹⁾ with acetic acid at 90 °C gave a 1:2.2 mixture of 16 α -acetoxy-17 β -ol, **23**, and 17 α -acetoxy-16 β -ol, **24**, in 61% yield. After separation by silica-gel column chromatography, the 16 β -ol, **24**, was treated with Jones reagent followed by hydrolysis with H₂SO₄ in EtOH to yield the 17 α -hydroxy-16-ketone, **8**, in 21% yield from the epoxide **22**. The ketols **3**, **4**, **7** and **8** were treated with a 3 mol eq of TMSI (Table 1, entries 10–13) and all the ketols, except for the 17 α -ketol **8**, were deoxygenated in good to excellent yields in a short period (1 h), producing about 75:25 to 88:12 mixtures of 17-ketone, **11**, and 16-ketone, **14**. In contrast, even if a longer reaction period (6 h) was employed in the reaction of compound **8**, no formation of the deoxygenated compounds, **11** and **14**, was detected by ¹H-NMR analysis, although a complex mixture of products was formed.

The time-course of the reaction of the 16 α -ketol, **1**, with TMSI (8 mol eq) over 2 h was monitored by IR spectroscopy. Upon adding TMSI to a solution of compound **1** in CHCl₃, the 16 α -hydroxy absorption (3550 cm⁻¹) completely disappeared within 3 min and the 17-carbonyl absorption (1750 cm⁻¹) was also reduced by one-half within 10 min. Similar spectroscopic behavior was also observed in the reaction of the 17 β -ketol, **5**, with the silyl reagent. The course of this reaction was further monitored by ¹H-NMR spectroscopy. Upon adding TMSI (2 mol eq) to a solution of compound **5** in CDCl₃, a resonance signal at δ 3.87 (17 α -H of compound **5** and its TMS derivative) immediately disappeared and a new peak was observed at δ 4.07 (within 5 min, probably the 17 α -H of TMSI adduct of compound **5** 17-TMS ether). In contrast, on similar treatment of the other ketol, **1**, a signal at δ 4.37 (the 16 β -H of compound **1** and its TMS derivative) did not change for 20 min and then gradually disappeared over the reaction period. The usual work-up of each reaction mixture obtained after a 20-min reaction period gave only the starting ketol. In addition, in the reaction of the 16 α -ketol, **1**, over a 1 h-reaction period, the only product obtained was the starting material. These results suggest that ketols **1** and **5** were initially converted into the 16 α - and 17 β -silyl ethers, respectively, followed by addition of TMSI to each carbonyl group of the silyl ethers. Jung *et al.*¹²⁾ reported that, in the absence of base, carbonyl-TMSI adducts which are stable in solution are readily formed from aldehydes by reaction with TMSI at room temperature and the usual work-up causes a reversible return to the aldehydes.

A direct iodination mechanism has been proposed for the deoxygenation of α -ketol with TMSI; silylation of the hydroxyl function of the ketol with TMSI followed by displacement of the siloxy group by I⁻ gave an α -iodoketone which is then transformed into the ketone product.^{5,7,8)} However, on the basis of the present deoxygenation results showing that a 17-ketone is the major deoxygenated product, irrespective of the substrates used, 16 α -ketols or 17 β -ketols, it seems that in addition to the direct iodination mechanism, other mechanisms currently unknown are also involved in the deoxygenation of steroidal 16,17-ketols.

To gain insight into what happens to the 16 β -proton of the 16 α -ketol, **3**, and the 17 α -proton of the 17 β -ketol, **7**, during the deoxygenation reaction, we synthesized [16 β -²H]-16 α -ketol **3** (*d*₀, 4 and *d*₁, 96 atom %) and [15,15,17 α -²H₃]-17 β -

Table 2. Reaction of 16 β -Deuterated 16 α -Ketol **3** and 17 α -Deuterated 17 β -Ketol **7** with 1 mol eq of TMSI^{a)}

Substrate ^{b)}	Reaction time (min)	Deuterium labeling at C-16 or C-17 ^{c)}	
		Recovered substrate (isolated yield, %)	Rearranged product
[16 β - ² H]- 3	15	79 at C-16 β (77)	64 at C-17 α (23)
[16 β - ² H]- 3	200	—	46 at C-17 α (94)
[17 α - ² H]- 7	15	65 at C-17 α (66)	—

a) The reaction was carried out in CHCl₃ at room temperature. b) [16 β -²H]-**3**: *d*₀ 4 and *d*₁ 96 atom %. [17 α -²H]-**7**: *d*₀ 2 *d*₁ 5, *d*₂ 15 and *d*₃ 78 atom % in which D-labeling at C-17 α was more than 95% by its ¹H-NMR spectrum and other deuterium atoms were incorporated at C-15. c) Deuterium content was determined by MS analysis in the experiments with [16 β -²H]-**3** or ¹H-NMR (400 MHz) analysis in the experiments with other substrates.

Table 3. Deoxygenation of 16 α -Hydroxy-17-oxo and 17 β -Hydroxy-16-oxo Steroids **3** and **7** with HI^{a)}

Substrate	Product (% yield ^{b)})			
	16 α -Ketol 3	17-Ketol 7	Ketones 11 and 14	Ratio of 11 to 14 ^{c)}
3	—	41	18	95:5
7	—	44	18	95:5

a) Compounds **3** and **7** were separately treated with 1 mol eq of HI in CHCl₃ for 5 h at room temperature. b) In addition to the ketol **7** and the ketones **11** and **14**, at least two products of undetermined structure were isolated in 1 to 22% yields in each reaction. c) Relative amount of the ketones, **11** and **14**, was determined by GC.

ketol **7** (more than 95 atom % of D-labeling at C-17 α) and subjected them to the reaction. Treatment of the deuterated ketols, **3** and **7**, with 1 mol eq of TMSI for 15 min reduced the deuterium content of the recovered compounds **3** and **7** by about 17 and 35%, respectively (Table 2). During treatment of the ketol, **3**, rearrangement product **7** was produced in 23% yield, and when a prolonged reaction time (200 min) was employed, almost all of substrate **3** was converted into the 17 β -ketol, **7**. Considering the relative stabilities of the 16,17-ketols,⁹⁾ the reduced D-content at the C-16 β position does not depend on enolization of the 17-carbonyl group of compound **3**, but an other unknown pathway is involved leading to a reduction in the D-content at the C-16 β position. On the other hand, the D-labeling at C-17 of the 17 β -ketol, **7**, produced from the 16 β -deuterated 16 α -isomer **3**, can be explained by enolization–ketonization of the 16-carbonyl function of the 17 β -ketol, **7**, through a 16-ene-16,17-diol. The D-labeling results also support the involvement of pathways other than direct iodination.

When methyl ethers of the 16 α - and 17 β -ketols **1** and **5**, compounds **19** and **20**, were treated with 8 mol eq of TMSI, in addition to the corresponding ketols, **1** and **5**, the 17-ketone **9** alone was obtained as the deoxygenated product in each experiment (Table 1, entries 14 and 15), similar to the reaction using the ketols **1** and **5** (entries 2 and 5). Considering these results, it is likely that demethylation of the methoxides **19** and **20** largely precedes deoxygenation, as previously reported in the 21-methoxy-20-ketone series.⁸⁾

Reaction of the 16 α - and 17 β -ketols, **3** and **7**, with 1 mol eq of HI in CHCl₃ for 5 h yielded a mixture of the 16- and 17-ketones, **11** and **14**, in 18% yield as well as the 17 β -ketol, **7** (41 and 44%, respectively) (Table 3). The relative amount of the 17- to 16-ketone corresponded largely to that

obtained in the reaction with TMSI. These results indicate that HI liberated by the reaction of the ketol with TMSI is involved, at least in part, in the deoxygenation reaction.

In conclusion, the steroidal 16 α - and 17 β -ketols were deoxygenated with TMSI or HI to produce the corresponding 17-ketone as the major product, probably through multi-reaction pathways, where the yield of the product depends on the A-ring structure.

Experimental

Melting points were measured on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were determined on a Shimadzu IR-430 or a Perkin Elmer FT-IR 1725X spectrophotometer. ¹H-NMR spectra were obtained with a JEOL PMX 60 (60 MHz) or a JEOL GX 400 (400 MHz) spectrometer and ¹³C-NMR were obtained on a JEOL GX 400 (100 MHz) instrument using tetramethylsilane as an internal standard. Mass spectra were measured on a JEOL JMS-DX 303 spectrometer. GC was carried out using a Shimadzu GC-7AG equipped with a hydrogen flame ionization detector.

Materials 17-Oxosteroids **9**, **10**, and **16** as well as 16-oxosteroids **12**, **13**, and **17** were purchased from commercial suppliers. TMSI and CHCl₃ were purified as described previously.⁸⁾ 16 α -Hydroxy-17-oxosteroids **1**,¹³⁾ **2**,¹⁴⁾ **3**,¹⁵⁾ and **15**,¹⁴⁾ as well as 17 β -hydroxy-16-oxosteroids **5**,¹⁶⁾ **6**,⁸⁾ and **7**,¹⁶⁾ were synthesized according to methods previously reported. 17-Oxosteroids **11**,¹⁷⁾ and 16-ketone **14**,¹⁶⁾ and **18**,¹⁸⁾ were also prepared according to a method previously reported.

[16 β -²H] 16 α -Hydroxy-5 α -androstan-17-one (3**)** To a solution of 16 α -bromo-5 α -androstan-17-one (300 mg, 0.85 mmol) in 18 ml pyridine^{14,19)} was added a mixture of 40 mg NaOH and 3 ml D₂O and the mixture was stirred at room temperature for 4.5 h. After this time, the reaction mixture was poured into 5% HCl solution (100 ml) with stirring and the precipitate was collected by filtration. The precipitate was dissolved in AcOEt (50 ml) and washed with 5% NaHCO₃ solution, then NaCl solution and dried (Na₂SO₄). After evaporation of the solvent, the residue was subjected to silica-gel column chromatography (hexane–AcOEt=3:1) to give crude product, which was recrystallized from ethyl ether to yield [16 β -²H] ketol **3** (160 mg, 65%), mp 164–166 °C (lit.¹⁵⁾ mp 151–154 °C for non-labeled **3**). MS *d*₀ 4 and *d*₁ 96 atom %.

16 β -Hydroxy-5 α -androstan-17-one (4**)** A mixture of 16 β -acetoxy-5 α -androstan-17-one (**21**)¹⁰⁾ (500 mg, 1.5 mmol), 1,4-dioxane (40 ml), water (10 ml), and 3 M H₂SO₄ (10 ml) was allowed to stand at room temperature for 7 d, and then diluted with AcOEt (500 ml). The reaction mixture was washed with water and dried over Na₂SO₄. After evaporation of the solvent, an oily product was purified by silica-gel column chromatography (hexane–AcOEt=5:1) followed by recrystallization from ethyl ether to afford **4** (152.1 mg, 35%) as colorless plates, mp 143–146 °C. IR (KBr) cm⁻¹: 3500 (OH), 1740 (C=O). ¹H-NMR (400 MHz, CDCl₃) δ : 0.81 (3H, s, 19-Me), 0.93 (3H, s, 18-Me), 3.93 (1H, dd, *J*=9.3, 8.3 Hz, 16 α -H). Anal. Calcd for C₁₉H₃₀O₂: C, 78.57; H, 10.41. Found: C, 78.51; H, 10.52.

[15,15,17 α -²H₃] 17 β -Hydroxy-5 α -androstan-16-one (7**)** To a solution of compound **7** (60 mg, 0.21 mmol) in 5.5 ml MeOD was added a mixture of 50 mg NaOH and 0.45 ml D₂O and the mixture was allowed to stand at room temperature for 19 h. After this time, the reaction mixture was diluted with AcOEt (50 ml) and washed with 5% HCl, 5% NaHCO₃ solution, saturated NaCl solution and dried (Na₂SO₄). After evaporation of the solvent, the residue was purified by silica-gel thin-layer chromatography (hexane–AcOEt=5:1, two developments) to give [15,15,17 α -²H₃] ketol **7** (11.8 mg), mp 134–137 °C (lit.²⁰⁾ mp 141–143 °C for non-labeled **7**). MS *d*₀ 2, *d*₁ 5, *d*₂ 15 and *d*₃ 78 atom %. D-content at C-17 α was almost 100% based on ¹H-NMR (400 MHz, δ 3.75 ppm for 17 α -H).

17 α -Hydroxy-5 α -androstan-16-one (8**)** 5 α -Androstan-16 β ,17 β -epoxide (**22**)¹¹⁾ (1000 mg, 3.67 mmol) was dissolved in 30 ml acetic acid and the solution was heated at 90 °C for 3 h. The reaction mixture was poured into NaHCO₃ solution, extracted with AcOEt, washed with NaCl solution and dried over Na₂SO₄. After evaporation of the solvent, the residue was chromatographed on a silica-gel column. The first eluate with hexane–benzene (1:1) was recrystallized from ethyl ether to give 16 α -acetoxy-5 α -androstan-17 β -ol (**23**), (228 mg, 19%) as colorless plates, mp 153–154 °C. IR (KBr) cm⁻¹: 3550 and 3450 (OH), 1725 and 1700 (C=O). ¹H-NMR (60 MHz, CDCl₃) δ : 0.82 (6H, s, 18- and 19-Me), 2.10 (3H, s, 16 α -OCOMe), 3.55 (1H, d, *J*=5 Hz, 17 α -H), 4.80 (1H, m, 16 β -H). Anal. Calcd for C₂₁H₃₄O₃: C, 75.41; H, 10.24. Found: C, 75.70; H, 10.15. The second eluate with benzene was recrystallized from MeOH to yield 17 α -acetoxy-5 α -androstan-16 β -ol

(**24**), (510 mg, 42%) as colorless leaflets, mp 190–191 °C. IR (KBr) cm⁻¹: 3550 (OH), 1705 (C=O). ¹H-NMR (60 MHz, CDCl₃) δ : 0.78 (3H, s, 18-Me), 0.95 (3H, s, 19-Me), 2.07 (3H, s, 17 α -OCOMe), 3.97 (1H, m, 16 α -H), 4.37 (1H, s, 17 β -H). Anal. Calcd for C₂₁H₃₄O₃: C, 75.41; H, 10.24. Found: C, 75.13; H, 10.35.

The 16 β -ol (**24**), (372 mg, 1.11 mmol) was dissolved in 50 ml acetone. To this solution, Jones reagent (0.37 ml) was added under ice-cooling with continuous stirring. After 30 min, the reaction mixture was poured into ice-water and extracted with AcOEt. The organic layer was washed with saturated NaCl solution and dried over Na₂SO₄. After evaporation of the solvent, the residue (356 mg) was recrystallized from MeOH to give 17 α -acetoxy-5 α -androstan-16-one (**25**), (269 mg, 73%) as colorless plates, mp 131–132 °C. IR (KBr) cm⁻¹: 1752 and 1738 (C=O). ¹H-NMR (60 MHz, CDCl₃) δ : 0.83 (3H, s, 18-Me), 0.92 (3H, s, 19-Me), 2.12 (3H, s, 17 α -OCOMe), 4.65 (1H, s, 17 β -H). Anal. Calcd for C₂₁H₃₂O₃: C, 75.86; H, 9.70. Found: C, 75.58; H, 9.60.

Finally, the 16-one (**25**), (115 mg, 0.346 mmol) was dissolved in 10 ml 95% EtOH, then 10 ml 5% ethanolic sulfuric acid was added to this solution and the mixture was allowed to stand at room temperature for 4 d. The reaction mixture was diluted with AcOEt, washed with saturated NaCl solution, and dried over Na₂SO₄. After evaporation of the solvent, the residue was recrystallized from acetone to afford ketol **8** (67.4 mg, 67%) as colorless needles, mp 183–185 °C. IR (KBr) cm⁻¹: 3475 (OH), 1740 (C=O). ¹H-NMR (400 MHz, CDCl₃) δ : 0.83 (3H, s, 18-Me), 0.83 (3H, s, 19-Me), 3.40 (1H, s, 17 β -H). Anal. Calcd for C₁₉H₃₀O₂: C, 78.57; H, 10.41. Found: C, 78.52; H, 10.64.

16 α -Methoxy-5 α -androstan-3,17-dione (19**)** A mixture of compound **1** (200 mg, 0.66 mmol), Ag₂O (1000 mg, 4.31 mmol), and MeI (10 ml) was heated under reflux for 20 h. After the usual work up, the residue obtained was purified by silica-gel column chromatography (hexane–AcOEt=4:1) and recrystallized from MeOH to give **19** (136 mg, 65%) as colorless prisms, mp 142–144 °C. IR (KBr) cm⁻¹: 1744 and 1716 (C=O). ¹H-NMR (60 MHz, CDCl₃) δ : 0.93 (3H, s, 18-Me), 1.03 (3H, s, 19-Me), 3.49 (3H, s, 16 α -OMe), 3.93 (1H, m, 16 β -H). Anal. Calcd for C₂₀H₃₀O₃: C, 75.43; H, 9.50. Found: C, 75.70; H, 9.80.

17 β -Methoxy-5 α -androstan-3,16-dione (20**)** Compound **5** (270 mg, 0.88 mmol) was treated with Ag₂O (800 mg, 3.4 mmol) in MeI (10 ml) as above. The product was purified by silica-gel column chromatography (hexane–AcOEt=4:1) and recrystallized from acetone to give **20** (150 mg, 53%) as colorless prisms, mp 141–145 °C. IR (KBr) cm⁻¹: 1751 and 1711 (C=O). ¹H-NMR (60 MHz, CDCl₃) δ : 0.82 (3H, s, 18-Me), 1.05 (3H, s, 19-Me), 3.36 (1H, s, 17 α -H), 3.58 (3H, s, 17 β -OMe). Anal. Calcd for C₂₀H₃₀O₃: C, 75.43; H, 9.50. Found: C, 75.22; H, 9.51.

General Procedure for Reaction of 16,17-Ketols with TMSI A solution of the ketol substrate (0.3 mmol) and various amounts of TMSI in CHCl₃ (alcohol free, 1–10 ml) was stirred at room temperature for an appropriate time under N₂, and then the reaction mixture was poured into 5% Na₂S₂O₃ solution (10 ml) and extracted with AcOEt (50 ml). The organic layer was washed with 5% NaHCO₃ solution and saturated NaCl solution, then dried over Na₂SO₄. After evaporation of the solvent, the residue was purified by silica-gel thin-layer chromatography or column chromatography (hexane–AcOEt) to give a mixture of 16- and 17-ketones, and the recovered and/or rearranged ketols. The relative amounts of 16-hydroxy-17-ketone to 17 β -hydroxy-16-ketone and 17- to 16-ketone were determined by ¹H-NMR spectroscopy (using the 16- and 17-methine signals, the 18- and 19-angular methyl signals) or GC.

¹H-NMR data for the ketols: **1**: δ : 0.97 (3H, s), 1.04 (3H, s), 4.37 (1H, m). **2**: δ : 1.03 (3H, s), 1.23 (3H, s), 4.43 (1H, m), 5.77 (1H, s). **3**: δ : 0.76 (3H, s), 0.91 (3H, s), 4.32 (1H, m). **4**: δ : 0.81 (3H, s), 0.93 (3H, s), 3.93 (1H, m). **5**: δ : 0.77 (3H, s), 1.07 (3H, s), 3.80 (1H, s). **6**: δ : 0.80 (3H, s), 1.23 (3H, s), 3.82 (1H, s), 5.80 (1H, m). **7**: δ : 0.71 (3H, s), 0.82 (3H, s), 3.75 (1H, s). **8**: δ : 0.83 (6H, s), 3.40 (1H, s). **15**: δ : 0.97 (3H, s), 4.40 (1H, m). **17**: δ : 0.77 (3H, s), 3.85 (1H, s). ¹H-NMR data for the ketones: **9**: δ : 0.89 (3H, s), 1.04 (3H, s). **10**: δ : 0.92 (3H, s), 1.22 (3H, s), 5.75 (1H, s). **11**: δ : 0.81 (3H, s), 0.86 (3H, s). **12**: δ : 0.91 (3H, s), 1.05 (3H, s). **13**: δ : 0.94 (3H, s), 1.23 (3H, s), 5.76 (1H, s). **14**: δ : 0.81 (3H, s), 0.87 (3H, s). **16**: δ : 0.91 (3H, s). **18**: δ : 0.92 (3H, s).

GC Analysis of the Ketones The ketones were analyzed as their methoximes (**9**, **10**, **12**, and **13**), or methoxime-trimethylsilyl ethers (**16** and **18**) prepared as follows: i) Methoxime: the ketones (*ca.* 1 mg) were dissolved in 0.5 ml pyridine containing 3 mg *O*-methylhydroxylamine hydrochloride and the resulting solution was allowed to stand at room temperature for 12 h. After this time, the reaction mixture was evaporated to dryness and dried *in vacuo*. The residue was dissolved in 0.3 ml tetrahydrofuran

(THF), and then injected on to the GC column. ii) Methoxime-trimethylsilyl ether: methoxime initially prepared was dissolved in 0.2 ml of a mixture of pyridine, hexamethyldisilazane, and trimethylchlorosilane (3:2:1). The mixture was heated at 60 °C for 30 min, and then injected on to the GC column.

GC conditions and retention times. i) analysis of **9**, **10**, **12**, and **13**: 1% OV-1 on Chromosorb WAW DMCS 80/100, 4 m×3.5 mm i.d.; column oven temperature, 200–260 °C, 4 °C/min; injection port and detector temperature, 290 °C; N₂ 50 ml/min; retention time (*t_R*): **9** 24.1 min, **10** 24.8 min, **12** 25.3 min, **13** 25.8 min. Analysis of **16** and **18**: The same instrumental conditions as above were used except for the column temperature; column temperature 200 °C hold 16 min, then 200–260 °C, 4 °C/min. *t_R*: **16** 24.4 min, **18** 25.3 min. ii) Analysis of **11** and **14**: 3% SE-30 Chromosorb WAW DMCS 80/100, 3 m×3.5 mm i.d.; column temperature, 220 °C; injection port and detector temperature, 250 °C; N₂ 50 ml/min; *t_R*: **11** 17.2 min, **14** 18.4 min.

Reaction of 16 α -Ketol **3 and Its 17 β -Isomer **7** with Hydriodic Acid** To a solution of the ketols **3** and **7** (50 mg, 0.172 mmol) in 1.25 ml dry CHCl₃ was added 9% HI in CHCl₃⁸⁾ (0.25 ml, 0.172 mmol), and the mixture was stirred at room temperature for the appropriate time (5 h). After this, the reaction mixture was poured into 10% Na₂S₂O₃ solution, extracted with AcOEt, washed with saturated NaCl solution and dried over Na₂SO₄. After evaporation of the solvent, the residue was purified by silica-gel column chromatography and the ketone mixture was analysed by GC as above.

IR and ¹H-NMR Spectrometric Studies of the Reaction of the Ketols **1 and **5** with TMSI** IR Analysis: TMSI (38 μ l, 0.267 mmol) was added to a solution of **1** or **5** (10 mg, 0.033 mmol) in 0.2 ml CHCl₃, the mixture was immediately transferred to an IR cell (NaCl, 0.1 mm), and the spectrum between 4000 and 330 cm⁻¹ was first obtained after a 1-min reaction time (scan time, 4 min). The spectra were then measured repeatedly at 10-min intervals up to a reaction time of 1 h.

¹H-NMR (60 MHz) Analysis: TMSI (23 μ l, 0.164 mmol) was added to a solution of 25 mg **1** and **5** (0.082 mmol) in 0.4 ml CDCl₃ in an NMR tube, and the spectra between 0 and 10 ppm were obtained repeatedly at 10-min intervals for a reaction time of 1 h (scan time, 250 s).

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