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

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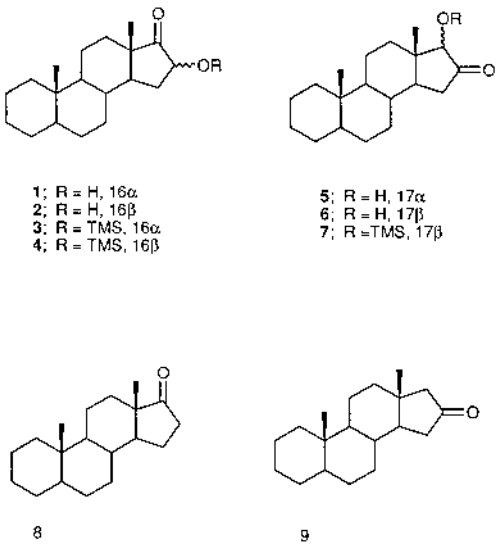
Deoxygenation reaction of steroidal 16,17-ketols 1, 2 and 6 as well as their silyl ethers 3 and 7 and 16- and 17-iodoketone analogs 11, 12, and 14 with trimethylsilyl iodide (TMSI) or HI under various conditions was examined. The results indicate that the deoxygenation producing 16- and 17-ketones 9 and 8 proceeds through multiple reaction pathways; a direct iodination of a siloxy group of the ketol silyl ethers by iodide ion to give the iodoketones (path b), addition of TMSI to a carbonyl group of the ketol silyl ethers to yield diiodo derivatives 22 and 23 through iodo-bis-TMS compounds 20 and 21 (path a), and cleavage of ether bond of dimers 15—18 initially produced are, at least, involved. In these sequences, rearrangement of the 16-ketols 1 and 2 to the 17β-ketol 6 also plays a significant role. The yields of the ketones 9 and 8 and their relative amounts would be dependent on the relative importance of each pathway in the reaction.

Key words trimethylsilyl iodide; deoxygenation; 16-hydroxy-17-keto steroid; 17β-hydroxy-16-keto steroid; steroid dimer

Trimethylsilyl iodide (TMSI) is one of the most important organosilicon reagents in organic synthesis, offering a broad variety of useful functional group transformations under mild conditions.[1] Ho[2] has reported the usefulness of this silyl reagent in the transformation of α-ketol to ketones. TMSI has also been used in reductive removal of *tert*-hydroxy group of α,β-unsaturated δ-*tert*-hydroxy ketones[3] and in the deoxygenations of *vic*-diols,[4] epoxides,[5] and carbonyl-conjugated allylic ethers.[6] We have previously reported the regiospecific deoxygenation at C-17 of the dihydroxy acetone side chain of corticoid steroids and the corresponding 17-methyl ether[7] and the reductive removal of an oxygen function at C-21 of 21-hydroxy-20-keto and 21-alkoxy-20-keto steroids[8] with this silyl reagent. Furthermore, treatment of cyclic steroidal α-ketols, 16α- and 16β-hydroxy-17-ketones as well as a 17β-hydroxy-16-ketone with TMSI in $CHCl_3$ gives a mixture of 16- and 17-ketones as the deoxygenated products in which the 17-ketone is a principal product irrespective of the substrate used, the 16-ketols or the 17β-ketol.[9] On the basis of this, we report that, in addition to a direct iodination mechanism which involves silylation of a hydroxyl function of the ketol with TMSI followed by displacement of the siloxy group by I^- and a subsequent reductive deiodination,[5,7,8] other mechanism(s) is(are) involved in the deoxygenation.

To gain insight into the mechanisms for the deoxygenation of the 16,17-ketols with TMSI, we used three possible 16,17-ketols, 16α-ketol **1**, 16β-ketol **2**, 17β-ketol **6** for the deoxygenation reaction (Fig. 1). It has previously been reported that on treatment with 3 mol eq of TMSI in $CHCl_3$ at room temperature for 1 h, all the ketols are deoxygenated in good to excellent yields, yielding about 75 : 25 to 88 : 12 mixtures of 17-ketone **8** and 16-ketone **9** (Table 1, entries 1, 5, and 8); in contrast, the formation of the deoxygenated compounds is not detected by ^{1}H-NMR analysis in the reaction of 17α-ketol **5** but a complex mixture of products is formed.[9] The course of these deoxygenation reactions was carefully monitored by TLC. This indicated that more than two intermediates were formed in the early stages and then disappeared from the reaction mixtures in proportion to the reaction time up to 1 h, being accompanied by the increased production of the deoxygenated products **8** and **9** in each experiment. In order to isolate the intermediates, the 16α-ketol **1** was treated with a decreased amount (1 mol eq) of TMSI for 15 min to 3.5 h (Table 1). Purification of the products with column chromatography afforded two (compounds **15** and **17**), three (compounds **15**, **17**, and **18**) or four steroids (compounds **15**—**18**) under the condition with a 15-min, 1-h, or 3.5-h reaction time, respectively, in 1—36% yields, as well as the starting material and/or its rearranged product **6** and the 17- and 16-ketones **8** and **9** (entries 2—4). Under similar conditions, the reaction of the 16β-ketol **2** and the 17β-ketol **6** yielded only compound **15** (21—31%) in addition to the ketones **8** and **9** (entries 6, 7, 9, and 10). However, compounds **15**—**18** principally did not correspond with the intermediates produced under the condition with 3 mol equivalent of TMSI, based on the TLC analysis.

IR spectra of the compounds **15**—**18** showed a carbonyl absorption at around 1750 cm^{-1}, respectively, and no hydroxy absorption was observed in any spectrum. Mass spec-



1; R = H, 16α
2; R = H, 16β
3; R = TMS, 16α
4; R = TMS, 16β

5; R = H, 17α
6; R = H, 17β
7; R = TMS, 17β

8 9

Fig. 1

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Table 1. Deoxygenation and Dimer Formation by the Treatment of Ketols **1**, **2**, and **6** with TMSI[a)]

Conditions				Product (% yield)			
Entry	Substrate	TMSI mol	Time h	Ketol	17-and 16-Ketones[b)]	Ketone ratio (17- to 16-ketone)[c)]	Dimers
1	**1**	3	1	—	**8** and **9** (28)	88 : 12[d)]	—
2	**1**	1	0.25	**1** (24), **6** (33)			**15** (11), **17** (4)
3	**1**	1	1	**6** (26)	**8** and **9** (28)	90 : 10	**15** (36), **17** (5), **18** (1)
4	**1**	1	3.5	**6** (12)	**8** and **9** (46)	93 : 7	**15** (27), **16** (7), **17** (2), **18** (1)
5	**2**	3	1	—	**8** and **9** (90)	87 : 13[d)]	—
6	**2**	1	0.25	**6** (46)			**15** (23)
7	**2**	1	1	**6** (30)	**8** and **9** (25)	95 : 5	**15** (23)
8	**6**	3	1	—	**8** and **9** (95)	75 : 25[d)]	—
9	**6**	1	0.25	**6** (65)			**15** (21)
10	**6**	1	1	**6** (40)	**8** and **9** (23)	96 : 4	**15** (31)

a) Reactions were carried out in $CHCl_3$ at room temperature under N_2 atmosphere. *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}H-NMR or GC analysis. *d*) Reference 9.

tra of all four compounds showed a molecular ion at *m/z* 562 in each one, suggesting that these compounds consisted of two molecules of various combinations of ketones **8** and **9** through an ether bond. X-Ray crystallographic analysis of product **18** indicated that this was a dimer produced by coupling of two molecules of the 16-ketone **9** through an ether bond at C-17β of each steroid (Fig. 2). The structures of other compounds **15**—**17** were established by ^{1}H–NMR spectroscopy using nuclear Overhauser effect (NOE) experiment; there was no significant NOE enhancement of the 18-methyl protons (δ 0.93 and 0.82, respectively) of the 16β-ketol **2** or the 17β-ketol **6** when the 16α-proton (δ 3.94) of compound **2** and the 17α-proton (δ 3.75) of the other were irradiated, whereas significant NOE enhancement (about 10%) of the 18-methyl protons (δ 0.91 and 0.83, respectively) of the 16α-ketol **1** and the 17α-ketol **5** was produced by irradiation of the 16β-proton (δ 4.32) of the former and the 17β-proton (δ 3.39) of the latter, respectively. Then, it was found that compounds **15** and **17** were the coupled products of the 17-ketone **8** with the 16-ketone **9** through an ether bond at C-16β-position of compound **8** and the C-17β position of the other and through an ether bond at C-16α of the former molecule and C-17β of the latter, respectively, whereas compound **16** consisted of two molecules of compound **8** through an ether bond at C-16β and C-16α of each molecule.

To further elucidate the role of these dimers in the deoxygenation reaction, the 16β,17β-dimer **15** was treated with TMSI or HI which is thought to be liberated in the reaction medium during the reaction (Table 2). Treatment of the dimer **15** with TMSI or HI under various conditions gave a 73 : 27 to 63 : 37 mixture of the 17- and 16-keto products **8** and **9**, respectively, in poor to moderate yields, along with the thermodynamically most stable 17β-ketol **6**[10] (entries 11—14); the reaction with 1 mol equivalent of TMSI for 0.5 h produced a mixture of the deoxygenated products (36%) (entry 11), whereas the reaction with 1 mol equivalent of HI for the same period did not give the deoxygenation product and only the ketol **6** was isolated. Employment of a large excess (6 mol eq) of TMSI or HI and a longer reaction time (16 h) in the reaction yielded the ketones **8** and **9** in 51 or 65% yield (entry 12 or 14), respectively. This yield is lower than those (90—98%) from the ketols **1**, **2**, and **6** under the condition with 3 mol eq of TMS and 1-h reaction period (Table 1, entries 5 and 8), indicating that not only the dimer **15** but also other dimers are not obligatory intermediates for the deoxygenation reaction of the 16,17-ketols.

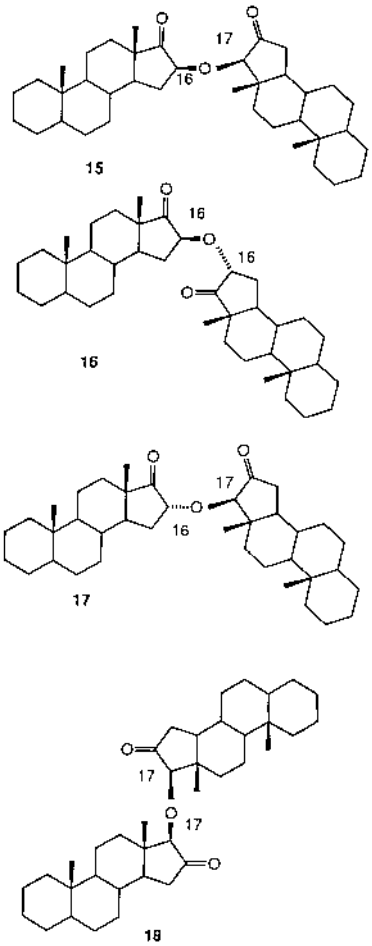

Fig. 2

Olah *et al.*[11] and we[7,8] have previously shown that a haloketone is quite easily transformed into the corresponding ketone by treatment with TMSI or HI. Thus, we prepared 16α- and 16β-iodo-17-ketones **11** and **12** on treatment of 16α-bromoketone **10** with NaI, whereas treatment of the 16-

Table 2. Reaction of Dimer **15** with TMSI or HI[a)]

Conditions			Product (% yield)			
Entry	Reagent mol	Time h	Ketol	17-and 16-Ketones[b)]	Ketone ratio (17- to 16-ketone)[c)]	Dimer
11	TMSI 1	0.5	**6** (13)	**8** and **9** (36)	63 : 37	**15** (33)
12	TMSI 6	16	**6** (10)	**8** and **9** (51)	73 : 27	
13	HI 1	0.5	**6** (38)			**15** (10)
14	HI 6	16	**6** (10)	**8** and **9** (65)	65 : 35	**15** (6)

a) Reactions were carried out in $CHCl_3$ at room temperature under N_2 atmosphere. *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}H-NMR or GC analysis.

Table 3. Reaction of Silyl Ethers **3** and **7** with TMSI or HI[a)]

Conditions				Product (% yield)			
Entry	Substrate	Reagent mol	Time h	Ketol	17-and 16-Ketones[b)]	Ketone ratio (17- to 16-ketone)[c)]	Dimers
15	**3**	TMSI 1	0.15	**1** (48), **6** (23)			**15** (12), **16** (4), **17** (6), **18** (3)
16	**3**	TMSI 1	1	**1** (4), **6** (13)	**8** and **9** (18)	75 : 25	**15** (2), **16** (2), **17** (4), **18** (1)
17	**3**	HI 1	1	**6** (36)	**8** and **9** (18)	91 : 9	**15** (21), **17** (2)
18	**7**	TMSI 1	0.15	**6** (84)	**8** and **9** (4)	87 : 13	**15** (5)
19	**7**	TMSI 1	1	**6** (40)	**8** and **9** (12)	73 : 27	**15** (2)
20	**7**	HI 1	1	**6** (33)	**8** and **9** (26)	85 : 15	**15** (17), **17** (2)

a) Reactions were carried out in $CHCl_3$ at room temperature under N_2 atmosphere. *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}H-NMR or GC analysis.

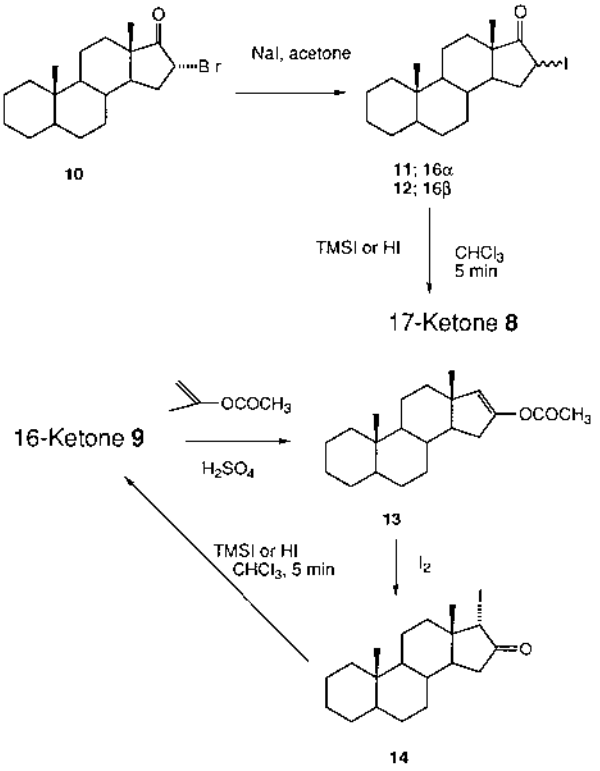

Chart 1

ketone **9** with isopropenyl acetate followed by reaction with I_2 gave 17α-iodo-16-ketone **14** (Chart 1). The structures of the iodoketones were determined principally by the ^{1}H-NMR experiments. Treatment of these iodoketones **11**, **12** and **14** with TMSI or HI in $CHCl_3$ for 5 min at room temperature produced quantitatively the corresponding reductively dehalogenated product, 17-ketone **8** or 16-ketone **9**, in each experiment. Based on these results, it seems likely that the iodoketones serve as precursors for the final step of the deoxygenation sequences as previously reported.[7)]

We next explored the reaction of 16α- and 17β-ketol silyl ethers **3** and **7** with TMSI or HI (Table 3). When these silyl ethers were briefly treated with 1 mol eq of TMSI for 10 min, four dimers **15**—**18** in the case of the 16α-silyl ether **3** (entry 15), and the dimer **15** in the case of the 17β-isomer **7** (entry 18) were produced, respectively. The production of the ketones **8** and **9** increased in a time-dependent manner. On the other hand, treatment of the silyl ethers with 1 mol eq of HI for 1 h resulted in the dimers **15** and **17** and the ketones being produced in each experiment (entries 17 and 20). It is noteworthy that compound **15** is produced as a principal dimer in the reaction of the 17β-silyl ether **7**, as seen in the reaction of the 17β-ketol **6**.

When a mixture of the 16-iodo-17-ketone **11** and the 17β-silyl ether **7** in $CHCl_3$ was allowed to stand at room temperature for 12 h, no dimers were observed in the reaction mixture but the steroids used were quantitatively recovered.

Doyle *et al.*[12)] reported the synthesis of an ether from a carbonyl compound and an alkoxy silane by silane reduction in acidic medium. Sassaman *et al.*[13)] also reported the synthesis of an ether from a carbonyl compound and an alcohol with TMSI as a catalyst. On the basis of these previous reports along with the present results, it was thought that 16β,17β-dimer **15** and the 16α,17β-dimer **17** would be formed from two molecules of the most stable 17β-ketol silyl ether **7** through a sequence shown in Chart 2. Other dimers **16** and **18** could be similarly formed by coupling of 16α-siloxy compound **3** to the 17β-siloxy isomer **7** through a sequence similar to that described above. However, in addition to these coupling reactions, the dimers could also be pro-

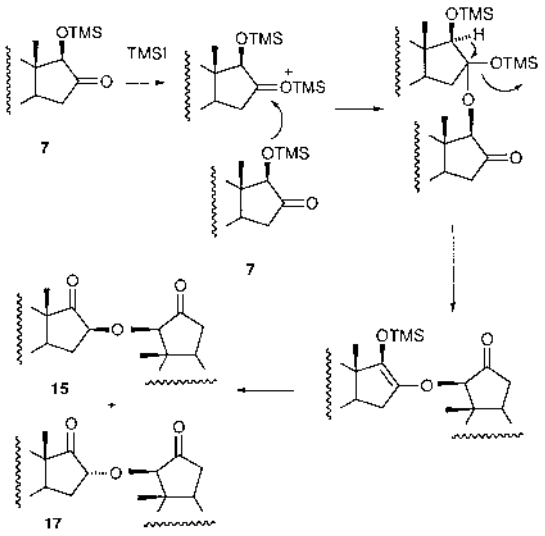

Chart 2

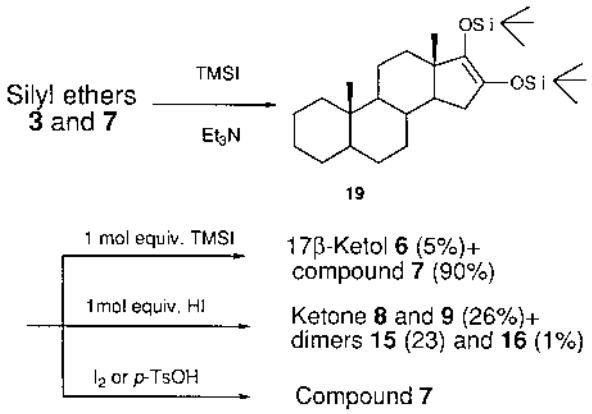

Chart 3

duced through other coupling combinations of the silyl ethers.

The results obtained by the reaction of the iodoketones and the silyl ethers with TMSI or HI indicate that the deoxygenation reaction of the dimers proceeds in a sequence which involves an initial dimer-cleavage to give the iodoketones and the silyl ethers or the ketols and a subsequent reaction of these products with another mole of the reagent.

In order to elucidate whether enediol bis-silyl ether **19** is involved in the deoxygenation reaction, this ether was prepared from the silyl ethers **3** or **7** on treatment with TMSI in Et_3N at room temperature for 5 d in almost quantitative yield (Chart 3). The spectral data of compound **19** obtained was consistent with the assigned structure. Reaction of compound **19** with TMSI (1 mol eq, 1 h) gave the 17β-ketol **6** in 90% yield, accompanied by a small amount of the 17β-silyl ether **7** (5%), whereas a mixture of the 16- and 17-ketones **8** and **9** (26%) and the dimer **15** (23%) and **16** (1%) were produced on treatment of this with HI (1 mol eq, 1 h). In contrast, brief treatment of compound **19** with I_2 (0.2 mol eq) or *p*-TsOH (0.25 mol eq) quantitatively afforded the silyl ether **7**; the 16-silyl ether bond of the bis-silyl ether **19** preferentially cleaved under a product development control, yielding the most stable 17β-ketol analog **7**. These results suggest that the bis-silyl ether **19** would be involved principally in a step of the

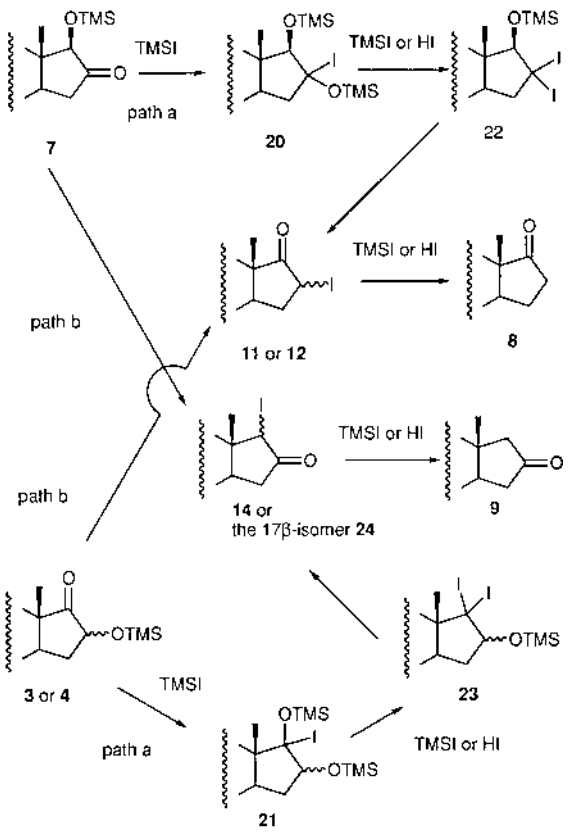

Chart 4

rearrangement of 16α- and 16β-ketols to a 17β-ketol in the deoxygenation reaction.

In conclusion, the deoxygenation reaction of the 16,17-ketols **1**, **2** and **6** with TMSI was found to proceed not solely through the direct iodination pathway (path b) but through multiple sequences (Chart 4). The addition of TMSI to the silyl ether **3** and **7** initially gives the adducts **21** and **20** (path a) of which further reaction with another mole of TMSI yields the diiodo derivative **23** and **22**, respectively, and dehydriodination of the diiodo compound followed by ketonization produces the 17-iodoketone **14** or its 17β-isomer **24** and the 16-iodoketone **11** or **12** which is efficiently converted into the corresponding deoxygenated product **9** or **8**, respectively. The cleavage of the ether bond of the dimers **15**—**18** principally produced through compounds **3** and **7** would also be involved in the reaction. The relative importance of each sequence in the deoxygenation should be one of the factors affecting not only the yield of deoxygenated products but also the relative amount of the 16- to 17-ketone.

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. ^{1}H-NMR spectra were obtained with a JEOL PMX 60 (60 MHz) or a JEOL GX 400 (400 MHz) spectrometer and ^{13}C-NMR were obtained on JEOL GX 400 (100 MHz) 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. TMSI and $CHCl_3$ were purified as described in the previous work.[8] The 16,17-ketols **1**,[14] **2**,[9] and **6**[15] and the 17- and 16-ketones **8**[16] and **9**[15] were synthesized according to the methods previously reported.

16α-Iodo-5α-androstan-17-one 11 and 16β-Iodo-5α-androstan-17-one (12) A mixture of 16α-bromo-5α-androstan-17-one[17] (800 mg, 2.27

mmol) and sodium iodide (1.3 g, 8.67 mmol) in acetone (20 ml) was heated under reflux for 4 h. The reaction mixture was then diluted with AcOEt, washed with water, and dried over Na_2SO_4. After evaporation of the solvent, the residue obtained was chromatographed on silica gel (hexane–AcOEt=100 : 1). The first eluate was recrystallized from ethyl ether to give compound **12** (189 mg, 21%) as colorless needles, mp 128—130 °C (lit.[18] mp 129—131.5 °C). ^{1}H-NMR ($CDCl_3$) δ: 0.80 (3H, s, 19-Me), 1.13 (3H, s, 18-Me), 4.37 (1H, t, J=9.0 Hz, 16-H). The second eluate was recrystallized from MeOH to give compound **11** (227 mg, 25%) as colorless needles, mp 171—174 °C (lit.[18] mp 163—165 °C). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (3H, s, 19-Me), 0.83 (3H, s, 18-Me), 4.83 (1H, s, 16-H).

17α-Iodo-5α-androstan-16-one (14) To a solution of **9** (458 mg, 1.67 mmol) in 10 ml of isopropenyl acetate was added 0.3 ml of a catalyst solution (10 ml of isopropenyl acetate containing 0.2 ml of concentrated sulfuric acid). After the slow distillation of about half the solvent over 5 h, an additional 5 ml of isopropenyl acetate and 0.3 ml of the catalyst solution were added and the slow distillation was continued for another 5 h. The solution was cooled, diluted with ethyl ether, and washed with 5% $NaHCO_3$ solution and then with water, and dried over Na_2SO_4. After evaporation of the solvent, the residue obtained was chromatographed on silica gel (hexane–ethyl ether=1 : 1) to give 5α-androst-16-en-16-yl acetate (**13**) (279 mg, 42%) as colorless prisms, mp 106—109 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.82 (3H, s, 18-Me), 0.85 (3H, s, 19-Me), 2.80 (1H, s, 16-OCOMe), 5.45 (1H, s, 17-H). IR (KBr) cm^{-1}: 1750 (C=O), 1640 (C=C). *Anal*. Calcd for $C_{21}H_{32}O_2$: C, 79.69; H, 10.20. Found: C, 79.52; H, 9.97.

A mixture of the enol acetate **13** (126 mg, 0.3987 mmol), iodine (111 mg, 0.44 mmol), and copper (II) acetate (87 mg, 0.44 mmol) in 5 ml of acetic acid was stirred at room temperature for 5 h.[19] The precipitate was removed by filtration, the filtrate was poured into water, and extracted with AcOEt. The extract was washed with 5% $NaHCO_3$ solution and water, and dried over Na_2SO_4. After evaporation of the solvent, the residue obtained was chromatographed on silica gel (hexane–AcOEt=100 : 1) and recrystallized from MeOH to give compound **14** (79 mg, 50%) as colorless needles, mp 107—110 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.82 (3H, s, 18-Me), 1.00 (3H, s, 19-Me), 4.30 (1H, s, 17β-H). ^{13}C-NMR ($CDCl_3$) δ: 11.96, 15.97, 20.50, 21.74, 26.39, 28.37, 28.57, 31.96, 34.71, 36.09, 36.76, 38.01, 38.23, 41.88, 45.66, 46.16, 46.50, 53.68, 211.42. IR (KBr) cm^{-1}: 1740 (C=O). *Anal*. Calcd for $C_{19}H_{29}IO$: C, 57.00; H, 7.30. Found: C, 57.20; H, 7.50.

16α-Trimethylsiloxy-5α-androstan-17-one (3) 16α-Ketol (**1**, 2 g, 6.89 mmol) was dissolved in 35 ml of dry tetrahydrofuran (THF). Trimethylchlorosilane (8.17 g, 75 mmol) and 22 ml of Et_3N was added to this solution and the mixture was stirred at room temperature for 1 d. The reaction mixture was then diluted with benzene, washed with water and dried over $MgSO_4$. After evaporation of the solvent, the residue was recrystallized from hexane to give compound **3** (2.41 g, 97%) as colorless needles, mp 128—129 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.15 (9H, s, $SiMe_3$), 0.79 (3H, s, 19-Me), 0.89 (3H, s, 18-Me), 4.30 (1H, m, 16β-H). ^{13}C-NMR ($CDCl_3$) δ: 0.13, 12.17, 14.67, 19.70, 22.08, 26.69, 28.69, 28.95, 30.66, 31.56, 32.53, 35.00, 36.38, 38.51, 46.95, 47.36, 48.39, 54.66, 71.92, 218.27. IR (KBr) cm^{-1}: 1742 (C=O). *Anal*. Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.77; H, 10.72.

17β-Trimethylsiloxy-5α-androstan-16-one (7) To a solution of 17β-ketol (**6**, 120 mg, 0.13 mmol) in 2 ml of THF, trimethylchlorosilane (0.86 g, 7.9 mmol) and 1 ml of Et_3N were added. The reaction mixture was stirred for 1 d. After the same workup as described for the silylation of compound **3**, the residue obtained was recrystallized from hexane to give compound **7** (143 mg, 96%) as colorless needles, mp 153—154 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.14 (9H, s, $SiMe_3$), 0.73 and 0.80 (3H each, s, Me), 3.65 (1H, s, 17-H). ^{13}C-NMR ($CDCl_3$) δ: 0.13, 11.81, 12.22, 20.09, 22.07, 26.73, 28.71, 28.92, 31.96, 34.59, 36.07,36.45, 36.78, 38.41, 42.43, 45.09, 47.03, 54.86, 87.02, 216.09. IR (KBr) cm^{-1}: 1742 (C=O). *Anal*. Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.77; H, 10.72.

16,17-Bis(trimethylsiloxy)5α-androst-16-ene (19) To a solution of compound **3** (880 mg, 2.43 mmol) in 10 ml of CCl_4, TMSI (2.43 g, 12.15 mmol) and 5 ml of Et_3N were added and the mixture was stirred at room temperature for 5 d. The mixture was then diluted with benzene, and the resulting solution was washed with water, and dried over $MgSO_4$. Evaporation of the solvent gave a solid which was recrystallized from hexane to give compound **19** (834 mg, 79%) as colorless needles, mp 97—99 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.17 (18H, s, $SiMe_3$), 0.83 (6H, s, Me). IR (KBr) cm^{-1}: 1675 (C=C). *Anal*. Calcd for $C_{25}H_{46}O_2Si_2$: C, 69.06; H, 10.66. Found: C, 68.83; H, 10.89. The similar treatment of compound **7** with TMSI and Et_3N gave the same product, compound **19** (85%), as described for the silylation of compound 3.

General Procedure for Reaction of 16,17-Ketols with TMSI A solution of the ketol substrate (0.3 mmol) and TMSI in $CHCl_3$ (alcohol free, 1 ml) was stirred at room temperature for an appropriate time under N_2, and then the reaction mixture was poured into 5% $Na_2S_2O_3$ solution (10 ml) and extracted with AcOEt (50 ml). The organic layer was washed with 5% $NaHCO_3$ solution and saturated NaCl solution, and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by silica gel thin layer chromatography or column chromatography (hexane–AcOEt) or recrystallization to give the deoxygenated 16- and 17-ketones, the dimer products, and the recovered and/or rearranged ketols. The ratios of 16-hydroxy-17-ketone to 17β-hydroxy-16-ketone were determined by ^{1}H-NMR (60 MHz) spectroscopy (methine signals at C-16 or C-17) without separation. The ratios of 17- to 16-ketone, the deoxygenated product, were determined by ^{1}H-NMR (400 MHz) spectroscopy (the 18- and 19-angular methyl signals) or GC.

^{1}H-NMR (60 MHz) data for the ketols. **1**: δ: 0.76 (3H, s, 19-Me), 0.91 (3H, s, 18-Me), 4.32 (1H, m, 16β-H). **2**: δ: 0.81 (3H, s, 18-Me), 0.93 (3H, s, 19-Me), 3.93 (1H, m, 16α-H). **5**: δ: 0.83 (6H, s, Me), 3.40 (1H, s, 17β-H). **6**: δ: 0.71 (3H, s, 18-Me), 0.82 (3H, s, 19-Me), 3.75 (1H, s, 17α-H). ^{1}H-NMR (400 MHz, $CDCl_3$) data for the ketones: **8**: δ: 0.81 (3H, s, 18-Me), 0.86 (3H, s, 19-Me). **9**: δ: 0.81 (3H, s, 18-Me), 0.87 (3H, s, 19-Me).

GC Analysis of Ketones The ketones were analyzed as their *O*-methoxime prepared as follows: *O*-methoxime; the ketones (*ca*. 1 mg) were dissolved in 0.5 ml of pyridine containing 3 mg of *O*-methyl-hydroxylamine 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 vacuum. The residue obtained was dissolved in 0.3 ml of THF, of which 1 μl was injected to GC.

GC conditions and retention times were as follows: 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, N_2 50 ml/min; t_R: **8**, 17.2 min; **9**, 18.4 min.

Isolation of 16β-(16-Oxo-5α-androstan-17β-yloxy)-5α-androstan-17-one (15), 16β-(17-Oxo-5α-androstan-16α-yloxy)-5α-androstan-17-one (16), 16α-(16-Oxo-5α-androstan-17β-yloxy)-5α-androstan-17-one (17), and 17β-(16-Oxo-5α-androstan-17β-yloxy)-5α-androstan-17-one (18) The solution of compound **1** (1.0 g, 3.44 mmol) in 15 ml of $CHCl_3$ was treated with TMSI (689 mg, 3.44 mmol) at room temperature for 3.5 h. The same workup as described above afforded an oily product which was chromatographed on silica gel. Elution with hexane–benzene (2 : 1) and recrystallized from AcOEt gave compound **18** (10 mg, 1%) as colorless plates, mp 288.5—290 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.80 (12H, s, 18-, 18′-, 19-, and 19′-Me), 3.92 (2H, s, 17α-, 17α′-H). ^{13}C-NMR ($CDCl_3$) δ: 11.90, 12.21, 20.02, 22.06, 26.74, 28.72, 28.95, 31.96, 34.41, 36.45, 36.65, 36.72, 38.39, 42.60, 45.08, 47.02, 54.76, 91.66, 216.64. IR (KBr) cm^{-1}: 1760 (C=O). MS *m/z* (rel. int. %): 562 (M^+, 40), 547 (22), 259 (100). *Anal*. Calcd for $C_{38}H_{58}O_3$: C, 81.09; H, 10.39. Found: C, 81.00; H, 10.58. Further elution with hexane–benzene (1 : 1) afforded a mixture of ketones, **1** and **6** as a solid (435 mg, 46%). Elution with benzene and recrystallization from ethyl acetate gave compound **17** (19 mg, 2%) as colorless needles, mp 204—206 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.76, 0.79, and 0.80 (3H, s, 3H each, 18′-, 19-, or 19′-Me), 0.86 (3H, s, 18-Me), 4.08 (1H, s, 17α-H), 4.38 (1H, d, J=7.3 Hz, 16β-H). ^{13}C-NMR ($CDCl_3$) δ: 11.90, 12.19, 12.21, 12.58, 19.78, 19.95, 22.07, 22.11, 26.72, 26.73, 28.71, 28.72, 28.95, 30.52, 30.74, 31.60, 31.92, 34.41, 34.92, 36.41, 36.44, 36.46, 36.57, 38.37, 38.37, 38.57, 42.23, 45.22, 47.01, 48.02, 48.46, 54.69, 54.73, 77.83, 92.03, 217.02, 218.27. IR (KBr) cm^{-1}: 1750 (C=O). MS *m/z* (rel. int. %): 562 (M^+, 12), 547 (5), 274 (95), 259 (100), 218 (35). *Anal*. Calcd for $C_{38}H_{58}O_3$: C, 81.09; H, 10.39. Found: C, 80.93; H, 10.64.

Elution with benzene : ethyl ether (50 : 1) and crystallization from acetone afforded compound **16** (68 mg, 7%) as colorless needles, mp 189—190 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.79, 0.80, and 0.95 (3H each, s, 18-, 19-, or 19′-Me), 0.88 (3H, s, 18′-Me), 4.08 (1H, m, 16α-H), 4.43 (1H, d, J=7.7 Hz, 16β-H). ^{13}C-NMR ($CDCl_3$) δ: 12.19, 12.23, 14.12, 14.25, 14.63, 19.75, 19.86, 22.10, 22.70, 26.72, 28.72, 28.97, 29.37, 29.58, 29.67, 29.71, 30.69, 31.16, 31.40, 31.91, 34.32, 35.02, 36.41, 36.49, 38.53, 38.56, 45.56, 46.97, 47.01, 47.27, 48.00, 48.58, 54.61, 55.05, 76.52, 79.51, 217.01, 217.12. IR (KBr) cm^{-1}: 1750 (C=O). MS *m/z* (rel. int. %): 562 (M^+, 6), 274 (100), 259 (35), 218 (95). *Anal*. Calcd for $C_{38}H_{58}O_3$: C, 81.09; H, 10.39. Found: C, 80.84; H, 10.58. Elution with benzene–ethyl ether (20 : 1) and recrystallization from MeOH gave compound **15** (262 mg, 27%) as colorless prisms, mp 171—174 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.78 (3H, s, 18- or 18′-Me), 0.80 (6H, s, 19-, 19′-Me), 0.99 (3H, s, 18′- or 18-Me), 3.98 (1H, s, 17α′-H), 3.99 (1H, m, 16α-H). ^{13}C-NMR ($CDCl_3$) δ: 12.08, 12.12, 12.21, 14.11, 19.82, 20.09,

22.05, 22.07, 26.70, 28.67, 28.69, 28.91, 28.94, 29.59, 31.12, 31.88, 34.32, 34.42, 36.34, 36.43, 36.46, 36.65, 37.25, 38.30, 38.38, 38.54, 42.49, 44.99, 45.31, 46.97, 46.99, 47.17, 54.63, 55.01, 80.32, 91.14, 214.73, 216.65. IR (KBr) cm^{-1}: 1750 (C=O). MS *m/z* (rel. int. %): 562 (M^+, 22), 547 (5), 274 (100), 259 (90), 218 (60). *Anal*. Calcd for $C_{38}H_{58}O_3$: C, 81.09; H, 10.39. Found: C, 81.12; H, 10.20. Elution with benzene–ethyl ether (4 : 1) and recrystallization from acetone afforded compound **7** (82.7 mg, 12%) as colorless needles, mp 141—144 °C (lit.[16] mp 144 °C).

Reaction of 16α- or 16β-Iodo-5α-androstan-17-ones (11, 12) and 17α-Iodo-5α-androstan-16-one (14) with Trimethylsilyl Iodide or Hydriodic Acid To a solution of the α-iodoketones (30 mg, 0.075 mmol) in 1 ml of dry $CHCl_3$ was added TMSI (15 mg, 0.075 mmol) or 9% HI in $CHCl_3$[8] (0.10 ml, 0.075 mmol), and the mixture was stirred at room temperature for an appropriate time (5 min). Thereafter the reaction mixture was poured into 10% $Na_2S_2O_3$ solution, extracted with AcOEt, washed with NaCl solution and dried over Na_2SO_4. After evaporation of the solvent, the residue obtained was subjected to GC as above.

Reaction of Silyl Ethers 3, 7, and 19 with TMSI or HI In a typical experiment, the silyl ethers **3**, **7**, **19** (100 mg, 0.23—0.28 mmol) in $CHCl_3$ (4 ml) were treated with TMSI or HI, respectively, as described above. The residue obtained was analyzed in a similar way to that of the reaction of ketols in each.

Reaction of the Dimer 15 with TMSI or Hydriodic Acid The dimer **15** (20 mg, 0.036 mmol) in 1 ml of $CHCl_3$ was treated with TMSI or 9% HI solution in $CHCl_3$, similar to the manner described above.

Reaction of Bistrimethylsilyl Ether 19 Treatment with Iodine: To a solution of compound **19** (100 mg, 0.23 mmol) in 4 ml of $CHCl_3$ was added 0.2 ml of the solution containing I_2 (58 mg, 0.23 mmol) in 5 ml of $CHCl_3$. After 3 min, the reaction mixture was diluted with AcOEt, washed with $Na_2S_2O_3$ solution and NaCl solution, and dried over Na_2SO_4. After evaporation of the solvent, the residue was crystallized from hexane to give compound **7** (79 mg, 95%).

Treatment with *p*-Toluenesulfonic Acid: To a solution of compound **19** (100 mg, 0.23 mmol) in 4 ml of $CHCl_3$ was added *p*-TsOH monohydrate (11 mg, 0.058 mmol) and the resulting reaction mixture was stirred at room temperature. After 30 min, the reaction mixture was diluted with AcOEt, washed with $NaHCO_3$ solution and NaCl solution, and dried over Na_2SO_4. After evaporation of the solvent, the residue was crystallized from hexane to give compound **7** (81 mg, 97%).

Crystal Structure Determination for Dimer 18 Data was collected on a Rigaku AFC-5R diffractometer, $C_{38}H_{58}O_3$, F. W.=562.9, a=7.098 (1), b=41.291 (9), c=6.188 (1) Å, β=115.49 (1)°, V=1637.1 $Å^3$, z=2, D=1.14 gcm^{-3}, μ(Cu-K)=0.5 mm^{-1}. The structure was solved using RASA system. R=7.7 (R_w=7.6%, w=1.0).

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