

REGIOSELECTIVE REDUCTION OF POLYKETONES ON SILICA GEL SURFACE
WITH BORANE-TRIMETHYLAMINE COMPLEX

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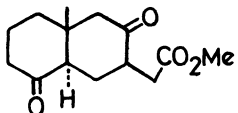
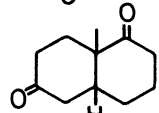
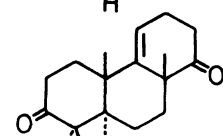
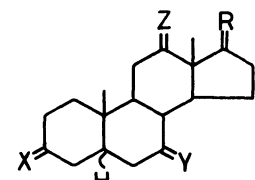




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Steroidal diones and trione, bicyclic diones (7 and 8) and a tricyclic dione were adsorbed on silica gel and reduced with $\text{BH}_3\cdot\text{NMe}_3$. The carbonyl groups at C-3 of the steroids, at C-4 of 7 and at C-3 of 8 were reduced regioselectively. The FT-IR spectra of 5α - and 5β -androstand-3,17-dione adsorbed on silica gel were measured.

Liquid chromatography on silica gel is a quite effective method for separation and purification of polyfunctionalized organic compounds. The efficiency of the separation should be dependent on the regio- and stereoselectivity of the adsorption of the functional groups on silica gel due to the steric and electronic factors. The complex compounds which have several carbonyl groups in the molecule may be adsorbed on the silica gel regioselectively. The reaction of polyfunctionalized organic compounds on adsorbent surface thus could be expected to proceed regio- and stereoselectively.¹⁻⁴) We report here the reduction of adsorbed polyketones (bi-, tri-, and tetracyclic compounds) on silica gel surface by $\text{BH}_3\cdot\text{NMe}_3$ without any protection of carbonyl groups and FT-IR (defused reflection) study about the regioselectivity of adsorption of polyketones on silica gel.

Steroidal ketones (1 - 6), bicyclic compounds (7 and 8) and a tricyclic compounds (9) were used for the reduction as model compounds. The reduction of carbonyl groups with $\text{BH}_3\cdot\text{NMe}_3$ proceeds in presence of Lewis acid for the amine acceptor.⁵) The reducing agent ($\text{BH}_3\cdot\text{NMe}_3$) is stable in presence of water. Thus the reagent $\text{BH}_3\cdot\text{NMe}_3$ was desirable for our reduction on silica gel surface. The typical procedure was as follows Silica gel (10 g) which was pregelated with $\text{FeCl}_3\cdot 6\text{H}_2\text{O}$ or ZnCl_2 (1 mol equiv.) as catalyst was added to a benzene

Table 1. Reduction of Ketones

Ketones	Time /h	Conditions	Products ^{d)} (yield/%)		Unreacted starting materials/%
			3 α -OH	3 β -OH	
<u>1</u> 5 β -Androstane- 3,17-dione	2	SiO ₂ -FeCl ₃ -PhH	58.2(69.2)	16.5	15.1
	18	SiO ₂ -ZnCl ₂ -PhH	48.5	5.0	16.0
	18	ZnCl ₂ -PhH	20.5	4.5	71.5
<u>2</u> 5 α -Androstane- 3,17-dione	2	SiO ₂ -FeCl ₃ -PhH	20.9	60.2(67.1)	10.3
	20	SiO ₂ -ZnCl ₂ -PhH	19.8	45.2	12.0
	20	ZnCl ₂ -PhH	9.8	22.5	54.0
<u>3</u> 5 α -Pregnane- 3,20-dione	2	SiO ₂ -FeCl ₃ -PhH	32.5	66.4	-
	20	SiO ₂ -ZnCl ₂ -PhH	29.8	56.5	12.2
	20	ZnCl ₂ -PhH	7.4	18.7	68.3
<u>4</u> Methyl 3,7,12-tri- oxo-5 β -cholanate	2	SiO ₂ -FeCl ₃ -PhH	3-OH ^{a)} 63.2		20.3
<u>5</u> Methyl 3,12-dioxo- 5 β -cholanate	2	SiO ₂ -FeCl ₃ -PhH ^{b)}	3 α -OH	3 β -OH	5.1
	2	SiO ₂ -FeCl ₃ -PhH	73.5(77.4)	14.5	20.3
<u>6</u> Methyl 3,7-dioxo- 5 β -cholanate	2	SiO ₂ -FeCl ₃ -PhH ^{b)}	73.7(77.0)	14.1	4.3
<u>7</u> 	2	SiO ₂ -FeCl ₃ -PhH ^{b)}	4 α -OH	4 β -OH	3.5
	2	SiO ₂ -FeCl ₃ -PhH	14.1	74.8(77.5)	3.9
<u>8</u> 	2	SiO ₂ -FeCl ₃ -PhH	3 α -OH ⁷⁾	diol	13.0
	2	FeCl ₃ -PhH	66.5(76.4)	8.4	49.3 ^{c)}
<u>9</u> 	2	SiO ₂ -FeCl ₃ -PhH	3 α -OH	diols	13.5
	<u>1</u>	X = R = O, Z = Y = H ₂	<u>4</u>	X = Y = O, R = H,	
	<u>2</u>	X = R = O, Z = Y = H ₂	<u>5</u>	X = Z = O, R = H,	
	<u>3</u>	X = O, Z = Y = H ₂ , R = 	<u>6</u>	X = Y = O, R = H,	
				Z = H ₂ ,	

a) The produced 3 α - and 3 β -alcohols could not be separated by HPLC.b) Water (5% to SiO₂) was added before addition of ketone.

c) Formation of other products was detected by TLC.

d) The yields which are calculated from the reacted starting materials are given in parenthesis.

solution (25 ml) of a ketone (100 mg) with vigorous stirring. The catalytic strength of FeCl_3 was superior to that of ZnCl_2 . Inclusion of water (about 5%) on silica gel accelerated the reaction rate, which is probably due to the increase of amine acceptability. After 30 min, no keto-compound was detected in the benzene solution by TLC. The whole keto-compound was adsorbed on the silica gel. The reducing agent, $\text{BH}_3\cdot\text{NMe}_3$ (3 mol equiv.) was added to the mixture with stirring at ambient temperature. The stirring was continued for 2 h and the reaction was stopped by addition of excess acetone. The products were extracted with ethyl acetate and separated by HPLC. The results are summarized in Table 1.

The C-3 carbonyl groups of the steroidal compounds (1 - 6) were reduced preferentially to the C-7, C-12, C-17, or C-20 carbonyl group in all cases. The reduction reaction of ketones (1 - 8) in benzene solution with $\text{BH}_3\cdot\text{NMe}_3$ in presence of $\text{FeCl}_3\cdot 6\text{H}_2\text{O}$ or ZnCl_2 was slow and complex mixtures.

The FT-IR spectra (differential spectra of defused reflection) of 5α - and 5β -androsterane-3,17-dione were measured. The two stretching vibrations of the carbonyl groups of 5α - and 5β -androsterane-3,17-dione adsorbed on silica gel were observed relatively sharp in lower wave number (Table 2). The shift value of C-17 carbonyl group is larger than that of C-3 carbonyl group. This suggests that the adsorption mode of each molecule is almost uniform rather than random and the C-17 carbonyl groups adsorbed on silica gel more tightly than the C-3 carbonyl groups by hydrogen bonding. The regioselectivity of the reduction of polyketones on silica gel surface should be rationalized by the protection of carbonyl groups due to the adsorption on silica gel. The tightly adsorbed carbonyl group is surrounded closely by the silica gel and is inhibited to react with the reducing agent. The C-3 carbonyl groups of steroidal ketones therefore could be reduced regioselectively. Our FT-IR experiments represent the more hindered carbonyl group sometimes adsorbed more tightly than the other less hindered carbonyl group on silica gel.

The similar reduction of bicyclo[4.4.0]decanedione compounds (7 and 8) were examined. The C-4 carbonyl group of the compound (7) and the C-3 carbonyl group of the compound (8) were reduced easier than the C-8 carbonyl group of the compound (7)⁶ and the C-9 carbonyl group of the compound (8)⁷ respectively.

The reduction of tricyclic dione (9) showed low regioselectivity. This

can be attributed to the small difference of adsorption potential of the two carbonyl groups.

In summary, we showed here an effective method of regioselective reduction of polyketones adsorbed on silica gel.

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Table 2. IR data of carbonyl groups

Compounds	Conditions	C-17 (ν/cm^{-1})	C-3 (ν/cm^{-1})
5 β -Androstane- 3,17-dione	on SiO ₂ (2%) ^{a)}	1708.6	1691.3
	in CCl ₄ (1%)	1742.0	1717.0
Shift value		33.4	25.7
5 α -Androstane- 3,17-dione	on SiO ₂ (2%) ^{a)}	1726.0	1712.0
	in CCl ₄ (1%)	1743.0	1717.0
Shift value		17.0	5.0

a) differential spectra of defused reflection (FT-IR)

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- 7) The conformation of the produced cis-decalin keto-alcohol (equatorial alcohol-steroidal conformation) [¹H-NMR (δ , in CDCl₃) 3.61 (dddd, J=11.2, 11.2, 4.2, and 4.2 Hz, C-3 β -H)] was changed to axial alcohol (non-steroidal conformation) [¹H-NMR (δ , in CDCl₃) 4.0 (s, $W_{1/2}$ =7.6 Hz, C-3 β -H)] by ketalization with HOCH₂CH₂OH-TsOH-PhH. The structure of the product is thus obviously 3 α -alcohol.

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