Synthetic Transformations using Iodotrimethylsilane: Regiospecific Deoxygenation of the Dihydroxyacetone Moiety at C-17 of Corticoid Steroids

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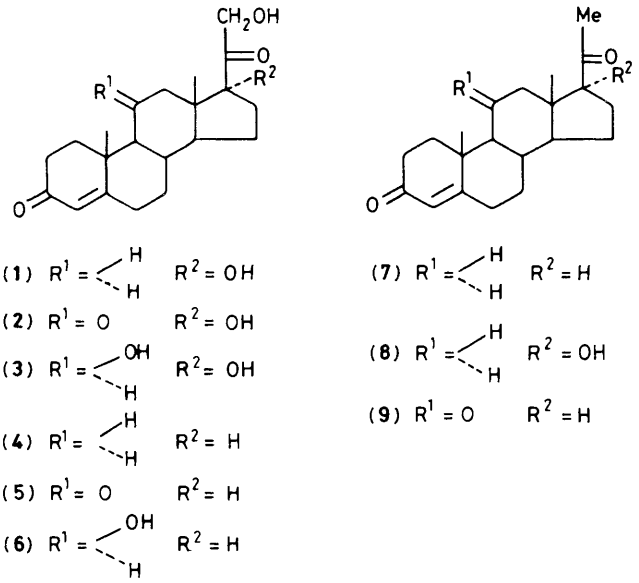
Corticoids having the dihydroxyacetone group >C(17)(OH)–C(20)(O)–C(21)H_2OH are regiospecifically converted into 21-hydroxy-20-ketones in high yields by treatment with iodotrimethylsilane.

Iodotrimethylsilane has recently been used in several important synthetic transformations,[1] namely, the cleavage of ethers, esters, and carbamates; the conversion of alcohols into halides; and the deoxygenation of sulphoxides to sulphides. Ho[2] has also reported the use of the iodosilane in the transformation of α-ketols to ketones. As part of our studies[3] on the construction of a corticoid side-chain, we were interested in exploring the reaction of the side-chain with the iodosilane. This communication reports the highly regiospecific and efficient deoxygenation occurring at the C-17 position of the dihydroxyacetone moiety with Me_3SiI.

When a series of corticoids (**1**)—(**3**) was treated with an excess of iodotrimethylsilane in MeCN (room temperature), regiospecific deoxygenation occurred at C-17 to give the corresponding 21-hydroxy-20-ketones (**4**)—(**6**) [(**4**), m.p. 139—140 °C (lit.[4] 141—142 °C); ^{1}H n.m.r. δ ($CDCl_3$) 0.70 (3H, s, 3 × 18-H), 1.20 (3H, s, 3 × 19-H), 4.18 (2H, s, 2 × 21-H), and 5.73 (1H, s, 4-H). (**5**), m.p. 176—177 °C (lit.[5] 179—181 °C); ^{1}H n.m.r. δ (CD_3OD) 0.67 (3H, s, 3 × 18-H), 1.40 (3H, s, 3 × 19-H), 4.18 (2H, s, 2 × 21-H), and 5.73 (1H, s, 4-H). (**6**), m.p. 179—181 °C (lit.[6] 179—182 °C); ^{1}H n.m.r. δ (CD_3OD) 0.90 (3H, s, 3 × 18-H), 1.47 (3H, s, 3 × 19-H), 4.15 (2H, s, 2 × 21-H), and 5.67 (1H, 4-H)] in high yields, where 20-ketones (**7**) and (**9**) were also isolated as minor products along with the ketols (**4**) and (**5**), respectively (Table 1). The ketols (**4**)—(**6**) were identical with the natural products in every respect.

On the other hand, employment of $CHCl_3$ as a solvent in the same reaction caused lower yields for the ketols (**4**) and (**5**)



(**1**) R^1 = 5α-H, R^2 = OH
(**2**) R^1 = O, R^2 = OH
(**3**) R^1 = 5α-OH, R^2 = OH
(**4**) R^1 = 5α-H, R^2 = H
(**5**) R^1 = O, R^2 = H
(**6**) R^1 = 5α-OH, R^2 = H
(**7**) R^1 = 5α-H, R^2 = H
(**8**) R^1 = 5α-H, R^2 = OH
(**9**) R^1 = O, R^2 = H

Table 1. Deoxygenation of corticoid side-chains with iodotrimethylsilane.[a]

	Conditions			Product (isolated yield/%)	
Substrate	Me_3SiI/ mol. equiv.	Solvent	Time/ h	21-Hydroxy-20-ketone	20-Ketone
(**1**)	10	MeCN	3	(**4**) (72)	(**7**) (5)
(**1**)	6	$CHCl_3$	3	(**4**) (48)	(**7**) (38)
(**2**)	8	MeCN	3	(**5**) (46)	(**9**) (27)
(**2**)	10	$CHCl_3$	2	(**5**) (10)	(**9**) (84)
(**3**)	6	MeCN	3	(**6**) (71)[c]	
(**4**)	20	MeCN	4		(**7**) (78)[b]
(**4**)	20	$CHCl_3$	2		(**7**) (90)[b]

[a] To a solution of substrate (1 mmol) in MeCN (50 ml) or $CHCl_3$ (100 ml) was added a 20% solution of Me_3SiI in the solvent and the mixture was allowed to stand at room temperature. The crude products obtained after the usual work-up were purified by column chromatography. [b] The crude product was crystallized to give a pure product. [c] The 20-ketone derivative could not be isolated.

than those just given, accompanied by markedly increased production of the 20-ketones (**7**) [m.p. 114—118 °C (lit.[7] 120 °C); ^{1}H n.m.r. δ ($CDCl_3$) 0.67 (3H, s, 3 × 18-H), 1.18 (3H, s, 3 × 19-H), 2.10 (3H, s, 3 × 21-H), and 5.73 (1H, s, 4-H)] and (**9**) [m.p. 169—173 °C (lit.[5] 172—173 °C); ^{1}H n.m.r. δ ($CDCl_3$) 0.65 (3H, s, 3 × 18-H), 1.42 (3H, s, 3 × 19-H), 2.12 (3H, s, 3 × 21-H), and 5.73 (1H, s, 4-H)]. The formation of the 21-deoxygenated derivatives, 17α-hydroxy-20-ketones, could not be detected in every experiment. When the 21-ketol (**4**) and its isomer, 17α-ketol (**8**), were treated with iodosilane as above, the ketol (**4**) was converted into the 20-ketone (**7**) in very high yield, while the reaction did not occur with the isomer (**8**). The results show that the 20-ketones (**7**) and (**9**) are formed from compounds (**1**) and (**2**) *via* the further 21-deoxygenation of the ketols (**4**) and (**5**) initially produced.

The 17α-hydroxy group of a 17α,21-dihydroxy-20-ketone and the 21-hydroxy group of a 21-hydroxy-20-ketone were regiospecifically and/or efficiently removed by treatment with iodotrimethylsilane. Treatment of the dihydroxyacetone moiety with acid (usually hydrochloric) can result in removal of the 17α-hydroxy group *via* the Mattox rearrangement to give the 21-acetal or -aldehyde.[8] If zinc–acetic acid is used, the 21-acetoxy-20-ketone is obtained directly in *ca.* 35% yield.[9] However, to our knowledge, this is the first direct and efficient deoxygenation of a corticoid side-chain giving a 21-hydroxy-20-ketone or a 20-ketone. Since the 17α-hydroxy group is selectively removed from the dihydroxyacetone side-chain by the iodosilane, while that of the 17α-hydroxy-20-ketone is not, the presence of a free 21-hydroxy group is evidently necessary for the hydrogenolysis of the C(17)–O bond.

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