

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 $>\text{C}(17)(\text{OH})-\text{C}(20)(\text{O})-\text{C}(21)\text{H}_2\text{OH}$ 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 sulfoxides to sulphides. Ho² has also reported the use of the iodotrimethylsilane in the transformation of α -ketols to ketones. As part of our studies³ on the construction of a corticoid side-chain, we were interested in exploring the reaction of the side-chain with the iodotrimethylsilane. 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); ¹H n.m.r. δ (CDCl_3) 0.70 (3H, s, 3 \times 18-H), 1.20 (3H, s, 3 \times 19-H), 4.18 (2H, s, 2 \times 21-H), and 5.73 (1H, s, 4-H). (5), m.p. 176–177 °C (lit.⁵ 179–181 °C); ¹H n.m.r. δ (CD_3OD) 0.67 (3H, s, 3 \times 18-H), 1.40 (3H, s, 3 \times 19-H), 4.18 (2H, s, 2 \times 21-H), and 5.73 (1H, s, 4-H). (6), m.p. 179–181 °C (lit.⁶ 179–182 °C); ¹H n.m.r. δ (CD_3OD) 0.90 (3H, s, 3 \times 18-H), 1.47 (3H, s, 3 \times 19-H), 4.15 (2H, s, 2 \times 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)

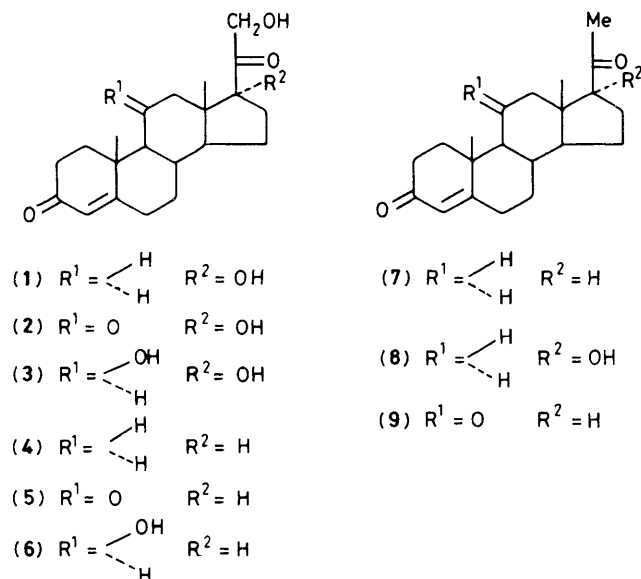


Table 1. Deoxygenation of corticoid side-chains with iodotrimethylsilane.^a

Substrate	Me ₃ SiI/ mol. equiv.	Conditions Solvent	Time/ h	Product (isolated yield/%)	
				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); ¹H n.m.r. δ (CDCl₃) 0.67 (3H, s, 3 \times 18-H), 1.18 (3H, s, 3 \times 19-H), 2.10 (3H, s, 3 \times 21-H), and 5.73 (1H, s, 4-H)] and (9) [m.p. 169–173°C (lit.⁵ 172–173°C); ¹H n.m.r. δ (CDCl₃) 0.65 (3H, s, 3 \times 18-H), 1.42 (3H, s, 3 \times 19-H), 2.12 (3H, s, 3 \times 21-H), and 5.73 (1H, s, 4-H)]. The formation of the 21-deoxygenated derivatives, 17 α -hydroxy-20-ketones, could not be detected in every experiment. When the 21-ketol (4) and its isomer, 17 α -ketol (8), were treated with iodotrimethylsilane 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 17 α -hydroxy group of a 17 α ,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 17 α -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 17 α -hydroxy group is selectively removed from the dihydroxyacetone side-chain by the iodotrimethylsilane, while that of the 17 α -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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