

## Tin(II) Chloride Dihydrate—a Mild Reagent for the Transformation of 6-Nitro- $\Delta^5$ -steroids to 5 $\alpha$ -Hydroxy-6-ketosteroids

Gireesh M. Singhal, Nalin B. Das, and Ram P. Sharma\*

Natural Products Chemistry Division, Regional Research Laboratory, Jorhat—6, Assam, India

Reaction of excess hydrated tin(II) chloride with 6-nitro- $\Delta^5$ -steroids (**1a—g**) and (**5**) in tetrahydrofuran furnishes 5 $\alpha$ -hydroxy-6-ketosteroids (**2a—g**) and (**6**) respectively, in good yields.

In connection with some other problem we were interested in the preparation of 5 $\alpha$ -chloro-6-hydroxyiminosteroids. Since the reaction of  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  with epoxides has been reported<sup>1</sup> to give chlorohydrins and the same reagent effects the reduction of aromatic nitro compounds to amines,<sup>2</sup> it was expected that the reaction of 6-nitro- $\Delta^5$ -steroids with  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  would give the corresponding 5 $\alpha$ -chloro-6-hydroxyiminosteroids. However, the reaction of excess hydrated tin(II) chloride with 6-nitro- $\Delta^5$ -steroids (**1a—g**) furnished the corresponding 5 $\alpha$ -hydroxy-6-ketosteroids (**2a—g**) in 60—80% yields (see Table 1).<sup>†</sup> In each case 8—12% of the corresponding 5 $\alpha$ -hydroxy-6-hydroxyiminosteroids (**3a—g**) were also isolated.<sup>‡</sup> Reaction of 3 $\beta$ -acetoxy-5 $\alpha$ -hydroxy-6-

hydroxyiminocholestane (**3b**) with excess  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  in tetrahydrofuran (THF) gave the ketonitrile (**4**) in 90% yield; no 3 $\beta$ -acetoxy-5 $\alpha$ -hydroxycholestan-6-one (**2b**) could be detected in this reaction, thus eliminating the possibility of the oximes being formed as intermediates.<sup>§</sup> In order to assess the scope of this reaction compound (**5**), prepared from a natural product,<sup>3</sup> was treated with  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  (10 mol equiv.) giving compound (**6**) in 40% yield, together with unreacted starting material.

In all the reactions given in Table 1, addition of extra water to the reaction medium did not increase either the rate or the yield of the reaction, indicating that only the water of crystallisation present in  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  participates in the reaction.

Kabalka *et al.*<sup>4</sup> have reported that the reaction of nitrostyrene (**7a**) and  $\beta$ -methyl- $\beta$ -nitrostyrene (**7b**) with 1.50 equiv. of  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  in alcoholic media furnishes the corresponding

<sup>†</sup> Several solvents were used but the best yields were obtained in THF. Reaction of (**1b**) with a stoichiometric amount of  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  was very slow and only 15% of (**2b**) was formed after 8 h.

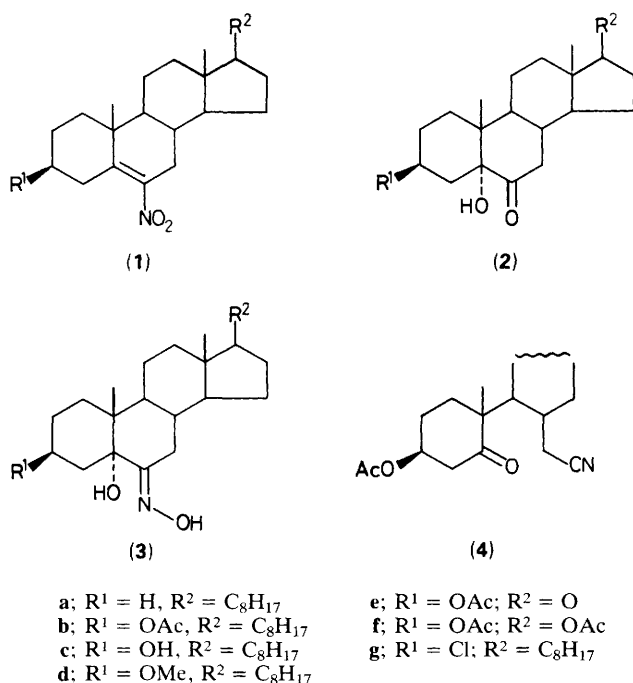
<sup>‡</sup> The stereochemistry of the oximes was established as *E* by NMR analysis.

<sup>§</sup> This is the first report of the conversion of hydroxyoximes to ketonitriles with  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ .

**Table 1.** Reduction of 6-nitro- $\Delta^5$ -steroids with  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ .<sup>a</sup>

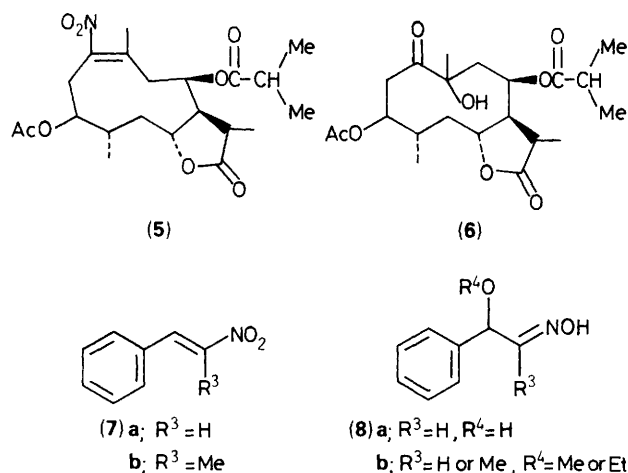
Substrate	Reaction time/h	Product <sup>b</sup> (% yield)
(1a)	4	(2a) (65), (3a) (10)
(1b)	3	(2b) (80), (3b) (8)
(1c)	8	(2c) (60), (3c) (12)
(1d)	4	(2d) (75), (3d) (8)
(1e)	2	(2e) (70), (3e) (8)
(1f)	3	(2f) (75), (3f) (10)
(1g)	6	(2g) (70), (3g) (8)

<sup>a</sup> In a typical experiment a solution of compound (1b) (1 mmol) in 4 ml of THF was treated with  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  (10 mmol) with stirring at room temperature and the reaction was monitored by TLC. Aqueous work-up of the reaction mixture followed by purification by  $\text{SiO}_2$  TLC furnished compounds (2b) and (3b) in the yields given. <sup>b</sup> All compounds were characterized by spectral analysis and by direct comparison with their authentic samples.



$\alpha$ -alkoxy oximes (8b) in high yield.<sup>5</sup> However, when we studied the reaction of nitrostyrene (7a) with excess  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  in THF,  $\alpha$ -hydroxy oxime (8a) was obtained quantitatively.¶

¶ The NMR spectrum of compound (8a) indicated it to be a mixture of *E* and *Z* isomers (70:30).



Reaction of 3 $\beta$ -acetoxy-6-nitrocholest-5-ene (1b) with excess  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  in MeOH as the solvent also furnished compound (2b) in 70% yield.

Compound (1b) showed no reaction with  $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$  after 4 h and the unchanged starting material was recovered quantitatively.

This simple and mild procedure for converting vinyl nitrosteroids|| to  $\alpha$ -hydroxyketosteroids is a useful addition to the existing methods.

We thank Dr. J. N. Baruah (Director, Regional Research Laboratory) for providing the necessary facilities.

Received, 29th November 1989; Com. 9/05116C

## References

- 1 C. Einhorn and J. L. Luche, *J. Chem. Soc., Chem. Commun.*, 1986, 1368.
- 2 F. D. Bellamy and K. Ou, *Tetrahedron Lett.*, 1984, **25**, 839.
- 3 J. C. Sarma, N. C. Barua, R. P. Sharma, and J. N. Baruah, *Tetrahedron*, 1983, **39**, 2843.
- 4 R. S. Varma and G. W. Kabalka, *Chem. Lett.*, 1985, 243.
- 5 Recently Shafiullah *et al.* have reported similar results for vinyl nitrosteroids using  $\text{BF}_3$  instead of tin(II) chloride, see *e.g.*, Shafiullah, Shamsuzzaman, and R. K. Singh, *Indian J. Chem.*, 1989, **28B**, 191. When we attempted the reaction of compound (1b) with excess  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  in the presence of ethanethiol or ethane-1,2-dithiol, compound (2b) was formed as the major product but the reaction was very slow and a few other products were also formed.

|| 6-Nitro- $\Delta^5$ -steroids can be prepared from the corresponding alkenes under mild reaction conditions using chlorotrimethylsilane and sodium nitrite followed by mild base treatment. These results will be published separately.