

Cadmium Chloride–Magnesium–Water: a New System for Regioselective Transformation of Conjugated Nitroalkenes to Ketocompounds; Conversion of 6-Nitro- Δ^5 -steroids to 6-Ketosteroids

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Reaction of 6-nitro- Δ^5 -steroids and nitroalkenes in tetrahydrofuran with CdCl_2 –Mg– H_2O furnished 6-ketosteroids and ketocompounds, respectively, in good yield.

Nitro compounds are important precursors in organic synthesis,^{1–3} the reduction of conjugated nitroalkenes to ketones being one important transformation, and various reagents have been used.^{4–9} Expensive reagents and stringent reaction conditions are the major drawbacks of most of these reported procedures.

The reaction of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ with 6-nitro- Δ^5 -steroids has been reported to give 5 α -hydroxy-6-keto steroids¹⁰ and the Nernst potential difference of Cd/Cd^{2+} , Mg/Mg^{2+} is higher than that of Sn/Sn^{4+} ,¹¹ it was therefore expected that the combination of CdCl_2 –Mg in a protic solvent would be a useful reducing system for the transformation of conjugated nitroalkenes to other functionalities. Our surmise indeed proved to be correct when we treated 3 β -acetoxy-6-nitro-cholest-5-ene in tetrahydrofuran (THF) with CdCl_2 –Mg– H_2O system at room temp., within 15 min 3 β -acetoxy-5 α -cholestan-6-one was obtained in 85% yield. In this reaction 15% of 3 β -acetoxy-5 β -cholestan-6-one was also obtained.

To illustrate the potentiality of the present method a number of reactions of various conjugated α,β -unsaturated nitrosteroids were examined, and the corresponding reduced

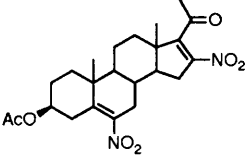
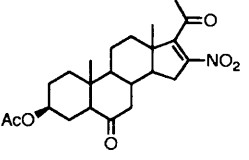
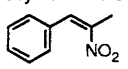
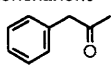
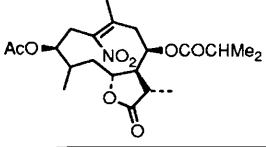
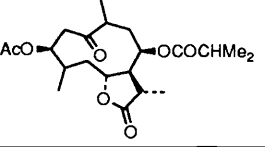
ketosteroids were obtained in high yield (Table 1). The reaction of entry 5, hence the regioselectivity of the reducing system, is noteworthy as the 16-nitro group remained intact during the reaction time.

In order to assess the scope of the reaction, 1-nitro-1-cyclohexene, β -methyl- β -nitro-styrene and the compound obtained from natural products¹² (entry 9) were treated with the CdCl_2 –Mg– H_2O system and in each case corresponding ketocompounds were obtained in 60–85% yield (Table 1).

Although the mechanism of this reduction process is not clearly defined at this stage, the following observations were noted. Anhydrous CdCl_2 and Mg in anhydrous THF does not react even after long exposure. But addition of a few drops of water to this mixture initiates vigorous exothermic reaction with evolution of hydrogen (deuterium when D_2O is added) and the formation of metallic cadmium particles. Since CdCl_2 is not hydrolysed readily and the pH of the system is *ca.* 7, hydrogen is released from the water present and is possibly replaced by magnesium.

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Table 1 Reduction of nitroalkenes to ketocompounds^a

Entry	Substrate	Product ^b	Yield ^c (%)	t/min
1	3 β -Acetoxy-6-nitrocholest-5-ene	3 β -Acetoxystigmasteran-6-one	100	15
2	3 β -Acetoxy-6-nitrostigmast-5-ene	3 β -Acetoxystigmastan-6-one	90	15
3	6-Nitrocholest-5-ene	Cholestan-6-one	95	15
4	3 β -Chloro-6-nitrocholest-5-ene	3 β -Chlorocholestan-6-one	90	15
5			90	15
6	3-Nitrocholest-2-ene	Cholestan-3-one	95	15
7	1-Nitrocyclohex-1-ene	Cyclohexanone	85	15
8			80	15
9			60 ^d	15

^a In a typical reaction, 1 mmol of the nitroalkenes in dry THF (3 cm³) was added with stirring to a mixture of anhydrous CdCl₂ (8 mmol), Mg powder (15 mmol). Then water (100 mmol) was added dropwise to this mixture over a period of 5 min. The exothermic reaction took place instantly with the liberation of hydrogen. After 15 min, the reaction mixture was thoroughly washed with CH₂Cl₂ (200 cm³). The CH₂Cl₂ solution was dried (Na₂SO₄), evaporated under reduced pressure to give a residue which on purification by TLC gave the product as a gum or solid. All products were characterized by spectral analysis and direct comparison with authentic compounds. ^b For entries 1–5, both 5 α -ketosteroid and 5 β -ketosteroids are formed in a ratio of 85:15, respectively. ^c The reaction was conducted with other protic solvents such as MeOH, EtOH, glycols, diglyme and in each case the yield was found to be same. ^d In this reaction 37% of the unreacted starting material was also recovered from the reaction mixture.

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References

- 1 A. G. M. Barrett and G. G. Grabski, *Chem. Rev.*, 1986, **86**, 751.
- 2 R. S. Verma and G. W. Kabalka, *Heterocycles*, 1986, **24**, 2645.
- 3 G. Rosini, R. Ballini, M. Petrini, M. Marotta and P. Righi, *Org. Prep. Proc. Int.*, 1990, **22(6)**, 707.
- 4 L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis*, vol. 1, New York, 1967, p. 1276; J. Mauthner and W. Suida, *Monatsh. Chem.*, 1894, **15**, 85; 1903, **24**, 648; A. Windaus, *Berichte*, 1903, **36**, 3752.
- 5 J. M. Aizpurua, M. Oiarbide and C. Palomo, *Tetrahedron Lett.*, 1987, **28**, 5365.
- 6 M. S. Mourad, R. S. Verma and G. W. Kabalka, *Synthesis*, 1985, 654.
- 7 R. S. Verma, M. Verma and G. W. Kabalka, *Tetrahedron Lett.*, 1985, **26(32)**, 3777.
- 8 S. Toru, H. Tanaka and T. Katoh, *Chem. Lett.*, 1983, 607.
- 9 G. M. Singhal, N. B. Das and R. P. Sharma, *J. Chem. Soc., Chem. Commun.*, 1989, 1470.
- 10 G. M. Singhal, N. B. Das and R. P. Sharma, *J. Chem. Soc., Chem. Commun.*, 1989, 498.
- 11 S. Glasstone, *Introduction to Electrochemistry*, Van Nostrand, NY, 1962, p. 243, 267; J. D. Lee, *A New Concise Inorganic Chemistry*, ELBS and Van Nostrand and Reinhold Company Ltd., London, 1979, p. 104–109.
- 12 J. C. Sarma, N. C. Baruah, R. P. Sharma and J. N. Baruah, *Tetrahedron*, 1983, **39**, 2843.

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