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MAGNESIUM-METHANOL AS A SIMPLE CONVENIENT REDUCING AGENT FOR α,β -UNSATURATED ESTERS

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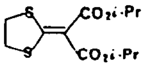
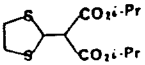
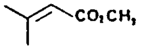
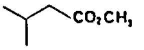
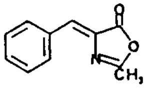
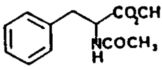
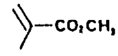
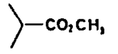
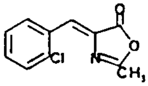
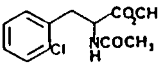
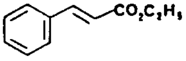
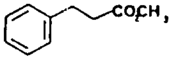
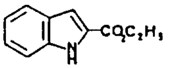
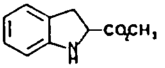
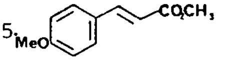
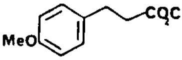
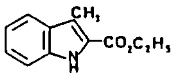
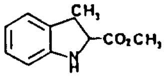
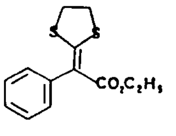
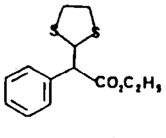
Abstract : Various α,β-unsaturated esters undergo double bond reduction by magnesium in methanol to give the corresponding saturated ones in almost quantitative yields.

Although reduction of olefinic double bond of α,β -unsaturated esters can be executed with catalytic hydrogenation or with hydride reagents, these reduction methods often either lack of selectivity toward isolated double bond and susceptible functionality or suffer from low yields, especially, in case of heteroatom substituted system.[1] In connection to our current interest to reduce indole-2-carboxylate to its corresponding indolines[2], we found that magnesium in methanol is a reagent of choice and is generally applicable to various α,β-unsaturated esters, in particular, heteroatom substituted ones as summarized in Table 1.

Table 1. Reduction of α,β -unsaturated esters with magnesium in methanol

No.	Substrate	Product	≠ Yield(%)	No.	Substrate	Product	≠ Yield(%)
1.			76(98)	7.			93
2.			78(100)	8.			94
3.			80(94)	9.			92
4.			93	10.			96
5.			96	11.			98
6.			90				

≠. Yields in parenthesis were determined by g.l.c., otherwise isolated yields.

Although isolated yields are relatively low due to its volatility, simple α,β-unsaturated aliphatic esters(1-3) were reduced in almost quantitative yields as determined by g.l.c.. Cinnamate(4,5) were also reduced easily with simultaneous ester exchange, which is normally observed for all ester except 6,7.

Magnesium in methanol reductions is even applicable to the ketene thioacetal derivatives(6,7) where the conjugation was extented with thiolane group, and reduction underwent in high yields to give the corresponding half protected 1,3-dicarbonyl compounds. This type of compound might have been encountered difficulty for its susceptible nature of sulfur atom to catalytic hydrogenation or hydride reagent.[4] Usefulness of this reagent was further examplified by one pot synthesis of ring substituted N-acetyl phenyl alanine methyl esters from azlactones(8.9). To reduce azlactone (8), Roper at al.[5] used high pressure catalytic hydrogenation (200 psi, 50°C), under this harsh condition dehalogenation of 9 might be expected.

The most striking feature of this reagent is reduction of aromatic double bond which is conjugated with ester group. Thus indole-2-carboxylates(10,11) were reduced smoothly into the corresponding indolines almost quantitatively. Even though a number of methods to reduce substituted indoles to its indolines are known, reduction of electron withdrawing group substituted indoles such as indole-2-carboxylate is not straightforward and no other method is comparable to magnesium in methanol reagent in its simplicity and yields.[2,6] Thus to a stirred solution 18.9g (0.1 mole) of ethyl indole-2-carboxylate(10) in 500 ml of dry methanol was added 4.86g (0.2 mole) of magnesium turning under nitrogen. After 1/2 hr induction period mild exothermic reaction started with evolving hydrogen gas. Stirring was continued another 2 hrs to dissolve magnesium completely with maintaing the pot temperature at 10°C in an ice bath. The reaction mixture was poured into 300 ml of ice-cooled 3 N hydrochloric acid and stirred vigorously to make clear solution. The acidic solution was treated with 3 N ammonium hydroxide to adjust its pH to 8.5-9.0. After usual work up 17 g. of pure methyl indoline-2-carboxylate was obtained as an oil(96% yield).

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