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## A Simple and Efficient Heterogeneous Hydrolysis of *N,N*-Dimethylhydrazone Derivatives

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A simple and efficient method for the silica gel-promoted hydrolysis of *N,N*-dimethylhydrazone derivatives to ketones is described.

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*N,N*-Dimethylhydrazones are useful intermediates in organic synthesis and frequently employed for the ketone homologation through  $\alpha$ -alkylation followed by hydrolysis.<sup>1</sup> In the course of our programs directed towards natural product synthesis *via* stereoselective reduction of bicyclic ketals,<sup>2</sup> we needed a mild and efficient method for regeneration of the ketone function from dimethylhydrazone derivatives. Usually, such hydrolytic cleavage has been carried out by using several reagents including NaIO<sub>4</sub>, O<sub>3</sub>, and Cu(OAc)<sub>2</sub>.<sup>3</sup> However, these are not always satisfactory owing to the rather drastic conditions. Fortunately, we found that treatment of a dichloromethane solution (15 ml/mmol) of dimethylhydrazone derivatives (easily

prepared by the literature method<sup>1</sup>) with silica gel (3 g/mmol)<sup>4</sup> gave the parent ketones in good yields and the procedure has proven to be convenient and quite useful. The Table exhibits some successful results. From these results the following characteristics will be noted. (1) The acyclic dimethylhydrazones were hydrolysed more smoothly than the cyclic ones. (2) Entries 1-4 show that the acid sensitive protecting groups are sufficiently stable under these conditions.

Typical procedure for the preparation of (4a) is as follows. To a lithium salt of octan-2-one *N,N*-dimethylhydrazone (0.6 mmol), in tetrahydrofuran (THF) (1 ml) was introduced 4-iodo-1-(*t*-butyldimethylsilyloxy)butane (0.48 mmol)<sup>5</sup> in THF (1 ml)

**Table.** Silica gel-promoted hydrolysis of dimethylhydrazones<sup>a</sup>

Entry	Substrate (X = NNMe <sub>2</sub> )	Product	Yield (%) <sup>b</sup>
1 <sup>c</sup>			77
2 <sup>c</sup>			77
3 <sup>c</sup>			82
4 <sup>c</sup>	+SiO  (4)	+SiO  (4a)	81
5			100
6			90 <sup>d</sup>
7			91 <sup>d</sup>
8			90

<sup>a</sup> Conditions: see Text. <sup>b</sup> Isolated yields after flash chromatography or Kugelrohr distillation. <sup>c</sup> Overall yields for two-step reaction: alkylation on a lithium salt of octan-2-one *N,N*-dimethylhydrazone with appropriate halides followed by silica gel-promoted hydrolysis. Bold line indicates the C-C bond formed. Yields are based on the starting halides which reacted. <sup>d</sup> Incomplete reaction after 14 h.

at  $-78^{\circ}\text{C}$  and the mixture was allowed to warm to room temperature (2 h). Work-up gave the crude hydrazone (4), which was dissolved in dichloromethane (7.5 ml) and treated with silica gel (1.5 g) at room temperature overnight. Filtration followed by purification by flash chromatography afforded the ketone (4a) in 81% yield;  $\nu_{\text{max}}$ (neat) 1 715 (CO) and 1 255 (SiCH<sub>3</sub>) and 1 100 cm<sup>-1</sup> (SiO);  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 0.05 (6 H, s), 0.89 (12 H, s), 1.2–1.8 (14 H, m), 2.40 (4 H, t, *J* 7.3 Hz), and 3.60 (2 H, t, *J* 5.9 Hz).

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#### References

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