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Deprotection of ketone dimethylhydrazones using lipases

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Abstract

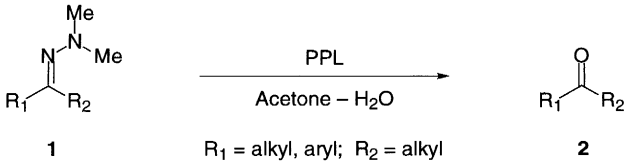
Deprotection of ketone dimethylhydrazone compounds with porcine pancreatic lipase (PPL) as a biocatalyst is described.

Keywords: hydrazones; hydrazines; ketones; enzymes; hydrolysis.

Hydrazones have been found to be one of the most useful synthetic precursors of aldehydes and ketones.[1] In this method, the key point is the deprotection of hydrazones[2] to their corresponding carbonyl compounds. Recently, the bi-catalyzed,[3] oxalic acid,[4] and TMSCl/NaI methods[5] have been reported. We have also previously reported the $CuCl_2$-catalyzed[6] and $Pd(OAc)_2$-catalyzed methods.[7] Kamal has reported hydrazone hydrolysis by using baker's yeast as a biocatalyst.[8] However, this method requires a large amount of baker's yeast compared to that of dimethylhydrazone.

On the other hand, lipases have been widely used over the past decade as a routine reagent for the preparation of chiral synthons and optically active natural products in organic synthesis.[9]

We describe here the lipase-catalyzed deprotection of ketone dimethylhydrazones to their corresponding ketones. This reaction is promoted by using lipases such as porcine pancreatic lipase, lipase from *Rhizopus arrhizus*, *Rhizopus niveus*, and *Mucor javanicus*. We used a catalytic amount of porcine pancreatic lipase (PPL) (Scheme 1) because PPL is the most economic of these lipases.



Scheme 1.

Table 1 shows representative results of the cleavage of ketone dimethylhydrazones. When the deprotection of aliphatic and alicyclic ketone dimethylhydrazones was carried out in the presence of PPL in

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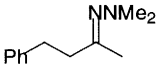
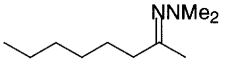
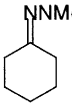
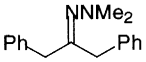
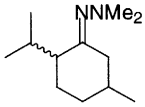
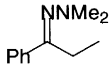
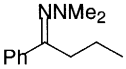
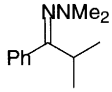
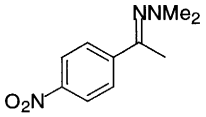
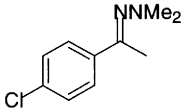
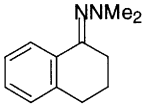
acetone/H_2O at room temperature, the corresponding deprotected compounds were obtained in good yields (Entries 1–4). However, menthone dimethylhydrazone (**1e**), which has bulky functional groups, such as *iso*-propyl at α-position, was used, and menthone was obtained in only an 11% yield (Entry 5). On the other hand, aromatic ketone dimethylhydrazones such as acetophenone dimethylhydrazone (**1f**) and others were hydrolyzed slowly (Entries 6–12).

Table 1
Deprotection of dimethylhydrazone **1**

Entry	Hydrazone **1**		Time (h)	Yield (%)[a]
1		**1a**	1	87
2		**1b**	3	96
3		**1c**	1	96
4		**1d**	96	94
5		**1e**	96	11
6		**1f**	72	82
7		**1g**	48	95
8		**1h**	72	95
9		**1i**	72	96
10		**1j**	96	89
11		**1k**	96	85
12		**1l**	96	81

[a] GLC yields.

In conclusion, the deprotection of hydrazone compounds was smoothly promoted using a porcine pancreatic lipase (PPL) in an acetone/H_2O system at room temperature and the reactivities depended on the substrate structures.

1. Typical procedure of deprotection

A solution of ketone dimethylhydrazone[10] (0.5 mmol) in acetone (3 mL) was added to a suspension of PPL (50 mg) in H_2O (5 mL). The reaction mixture was stirred at room temperature for 24 h, and then diluted with ether, washed with brine, and dried over $MgSO_4$. The evaporation of the solvent and the bulb-to-bulb distillation or silica gel column chromatography gave pure corresponding carbonyl compounds.[11] The yields were determined by GLC using biphenyl as an internal standard.

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11. The carbonyl compounds were identified by comparing the retention time of GLC with those of authentic samples or ^1H NMR (400 MHz) and GC–MS.