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Efficient Enzymatic Hydrazone Hydrolysis by Baker's Yeast

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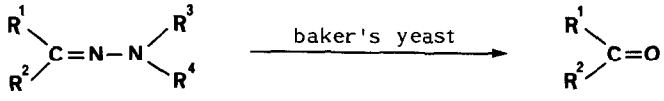
Abstract: The quantitative enzymatic conversion of N-phenyl and N,N-dimethyl hydrazones by baker's yeast to the corresponding aldehydes and ketones is described.

In the past few years, the protection of the carbon-oxygen double bonds as carbon-nitrogen double bonds has become a useful methodology in the synthesis of complex organic molecules[1]. This is mainly because of the number of advantages exhibited by the carbon-nitrogen double bonded derivatives over their parent carbonyl compounds, such as less susceptibility for self condensation and vast differences in reactivity. Stereospecific generation of hydrazones[2] and their subsequent reaction with electrophiles have produced, in good yields, and with high positional preference and unique stereoselectivity. This feature is well illustrated in the Corey's hydrazone alkylation[2,3]. As a result, the regeneration of aldehydes or ketones from their hydrazones has assumed added importance.

In the recent years, there has been a growing interest in biocatalysis and transformations mediated by baker's yeast[4]. Reduction of carbonyl compounds by baker's yeast has become a valuable strategy in organic synthesis[5]. The reduction or oxidation of other functional groups has not much been explored. In the course of our studies on the application of enzymes as biocatalysts[6,7,8], we herein report for the first time the hydrazone hydrolysis by baker's yeast in quantitative yields.



R^1, R^2, R^3, R^4 = H, alkyl, aryl

N-Phenyl and N,N-dimethyl hydrazones were obtained from the corresponding aldehydes or ketones, employing standard procedure[9]. The aldehydes and ketones were regenerated from their corresponding hydrazones on incubating with baker's yeast. In a typical procedure, to baker's yeast, Sigma type I (10 g) in 0.1 M phosphate buffer, pH 7.2 (100 ml) was added hydrazone **1a** (500 mg) taken in ethanol (5 ml) and incubated at 37°C. After the disappearance of hydrazone (12 h), the

suspension was filtered with celite. The filtrate extracted repetitively with ethyl acetate and the celite layer was also washed three times with ethyl acetate. The combined organic phase was dried over Na_2SO_4 and evaporated under vacuum to give the residue. This upon purification by column chromatography yields benzaldehyde **2a** in 98% yield.

Table 1. Baker's Yeast-Mediated Regeneration of Aldehydes and Ketones from hydrazones

Entry	R^3	R^4	Aldehydes and ketones (**2**)	Time (h)	Yield (%)
1a	H	Ph	Benzaldehyde	12	98
1b	Me	Me	Benzaldehyde	14	95
1c	H	Ph	Acetophenone	10	97
1d	Me	Me	Acetophenone	10	96
1e	H	Ph	Benzophenone	15	89
1f	Me	Me	Benzophenone	14	92
1g	H	Ph	Cyclohexanone	11	97
1h	Me	Me	Cyclohexanone	12	98
1i	H	Ph	Pinacolone	14	93
1j	H	Ph	2-Butanone	16	95
1k	H	Ph	2-Nonanone	12	97

This reaction offers a wide scope as various hydrazones (**1b-1k**) were hydrolyzed by baker's yeast to afford the corresponding aldehydes and ketones (Table 1). The reactions were monitored by HPLC[10]. The products were characterized by elemental analysis, spectroscopic data and by comparison with the standard samples.

It is noteworthy that the conventional procedures for the hydrolysis of hydrazones have several limitations: the use of expensive reagent like sodium periodate[2], large reaction volumes and very low reaction temperatures (-63°C) employing m-chloroperbenzoic acid[11]. However, the sodium perborate method[12] of oxidative hydrolysis is an exception.

In summary, the present biocatalytic method employing baker's yeast is a mild, convenient and commercially viable procedure for the oxidative cleavage of hydrazones to aldehydes or ketones.

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