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BAKER'S YEAST CATALYSED OXIDATIVE COUPLING OF THIOLS TO DISULFIDES+

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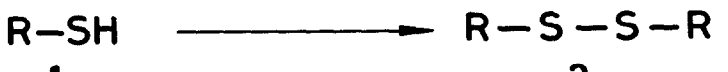
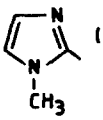
Abstract: Baker's yeast catalyses for the first time the formation of sulfur-sulfur bond by the oxidative coupling of thiols. The yields are in the range of 71-98%.

In recent years, enzymes and microorganisms are becoming increasingly important in organic synthesis due to their specificity, mild conditions, high yields and excellent stereoselectivities. Amongst these biocatalysts, Baker's yeast (Saccharomyces cerevisiae) occupies an unique position due to its versatility to catalyse an array of chemical reactions and is also inexpensive at the same time. However, various synthetically useful oxidative reactions involving Baker's yeast have been explored only to a limited extent[1], though it is well known for catalysing a variety of asymmetric reductions[2] and cycloadditions[3]. In this context, our continued interest on the use of enzymes as catalysts in organic synthesis[3] prompted us to investigate the utility of Baker's yeast in the formation of sulfur-sulfur bond as it is of considerable biological importance. It is present in the structure of a variety of natural products and contributes significantly to the tertiary structure of many proteins such as Insulin and Ribonuclease[4].

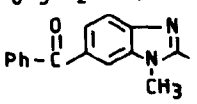
We report, herein, the first Baker's yeast catalysed oxidative coupling of thiols **1** to disulfides **2** in high yields. The thiol **1** (5 mmol) is taken in 20% ethanol (32 ml) and incubated at 37°C with Baker's yeast (1.6 g, Saccharomyces cerevisiae, Type I, purchased from Sigma Chemical Co., U.S.A) in pH 7.2 phosphate buffer (41.6 ml) for 24 h, extracted with dichloromethane and purified by flash chromatography. All the compounds are obtained in analytically pure form. ^{1}H NMR, mass spectra and other physical constants are in accordance with the earlier observations[5]. The general utility of this biocatalytic oxidative coupling is further shown by its successful application to thiols containing other functional groups.



2 R (% Yield) = C_6H_5 (97) ; 4-$CH_3C_6H_4$ (89) ; 4-ClC_6H_4 (88) ; O-$H_2NC_6H_4$ (98) ; $C_6H_5CH_2$ (71); $HOCH_2CH_2$ (85) ; $H_3C(CH_2)_{10}CH_2$ (94) ;



(76) ;



(82) .

However, in the control experiments in the absence of Baker's yeast, these oxidations under air proceed only to a minor extent (10-14%) as shown in Figure 1. These experiments clearly demonstrate the catalytic effect of Baker's yeast on S-S bond formation.

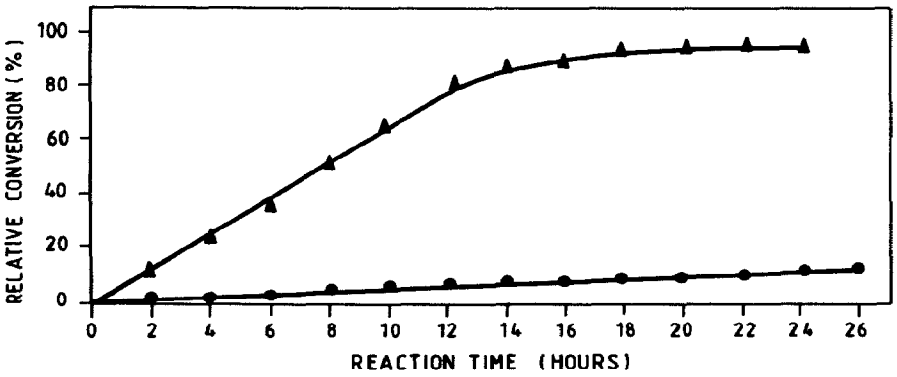


Figure 1. Time course of the incubation of thiophenol (C_6H_5SH) in the presence (▲) and in the absence (●) of Baker's yeast at 37°C at the indicated time intervals.

Thus, the utility of Baker's yeast as an oxidative catalyst for the bioconversion of thiols to disulfides may find wide applications in the fields of synthetic organic chemistry, protein engineering and biotechnology.

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