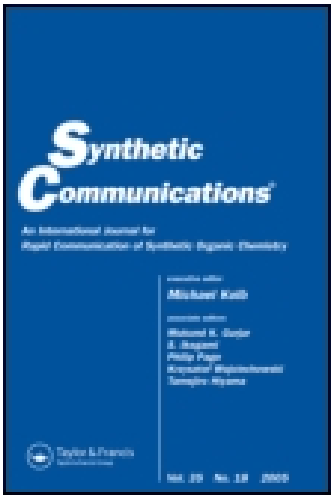

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Bakers' Yeast–Catalyzed Ring Opening of Benzofuroxans: An Efficient Green Synthesis of Aryl-1,2-diamines

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Abstract: A simple and inexpensive method for the reductive cleavage of N–O bond of benzofuroxans with bakers' yeast under nonfermenting condition in aqueous media was achieved. The procedure gives excellent yields of aryl-1, 2-diamines.

Keywords: Aryl-1,2-diamines, bakers' yeast, benzofuroxans, reductive cleavage

INTRODUCTION

The use of bakers' yeast (*Saccharomyces cerevisiae* BY) as a reagent in synthesis has been applied[1,2] since the beginning of the century, and still it continues to be of current interest.[3,4] A variety of new and novel applications of bakers' yeast have been reported.[5–7] Some examples include the biooxidative conversion of thio to an oxo functionality,[8] conversion of aromatic nitro compounds to hydroxylamines,[4] ester hydrolysis, bioreduction of PEG-acetoacetate,[7] reduction of aromatic nitro[9–12] compounds, reduction of aryl azides to aryl amines[13] and oximes to chiral amines,[14] and Hantsch pyridine synthesis,[6] but on the top had been enantioselective reduction of carbonyl function.[15,16] Bakers' yeast has been extensively used to carry out reductions of the aromatic nitro

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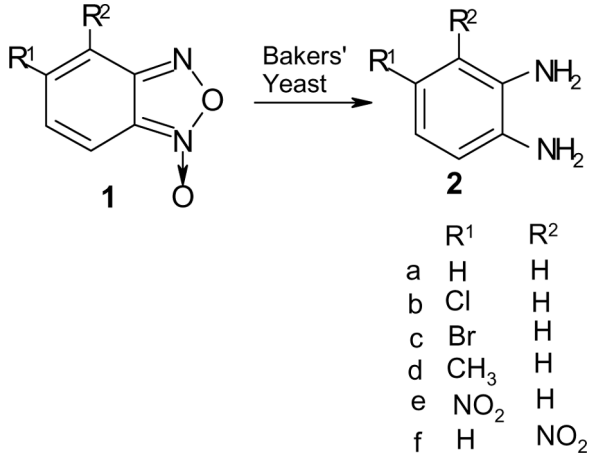

Scheme 1. Bakers' yeast–catalyzed synthesis of 1,3-diamines.

groups, but there has been little work on the application of this reagent to the reductive cleavage of heterocycles, although they have been employed for reductive cyclization.[5] Herein we have investigated bakers' yeast as a new catalyst for the reductive N–O bond cleavage of benzofuroxans **1**, leading to aryl-1,2-diamines **2** under aqueous and nonfermenting conditions in excellent yields (Scheme 1).

RESULTS AND DISCUSSION

Accordingly, treatment of 5(6)-chloro benzofuroxn **1a** with bakers' yeast at ambient temperature for 6 h, at pH 7.0 (monitored by thin-layer chromatography, TLC), followed by aqueous workup, yielded the corresponding 4-chloro-1,2-phenylenediamine predominantly in 90% yield without the formation of any side products. Similarly, other 5(6)-bromo and 5(6)-methyl benzofuroxans were reacted in presence of bakers' yeast at pH 7.0, and the corresponding 1,2-diamines were isolated in 92 and 80% yields respectively without the formation of any side products. The 4(7)-nitro and 5(6)-nitro benzofuroxans also gave the corresponding 3-nitro- and 4-nitro-1,2-phenylenediamines respectively in excellent yields without any further reduction of the nitro group. Further, in reaction with 4(7)-nitro and 5(6)-nitro benzofuroxans, when we doubled the amount of yeast, we did not observe the formation of any nitro group reduced products. Certainly, nitro groups remain intact in the final products, diamines. This finding is in contrast to an earlier report[17] where bakers' yeast reduced the nitro group to their corresponding amines. It

is also notable that the halogen-substituted benzofuroxans were rapidly reduced to give their corresponding 1,2-diamines without any dehalogenation. The common reducing agents were reported to provide dehalogenated side products or recovered starting material.[18–20] It is worth mentioning here that Easton et al. reported[21] a yeast-catalyzed cleavage of heterocyclic ring under fermenting conditions (cleavage of either an aromatic ring or a single bond), where they employed 75 g of sucrose in 400 ml of water for 0.5 g of the substrate in 24% yield after 24 h of reaction time. Our method is entirely different, and we did not employ any sucrose solution to get the corresponding 1,2-diamines during 6–6.5 h. The scope of this general procedure is shown in Table 1. Notably, when 1,4-dinitrosobenzene was reacted under similar conditions, the corresponding 1,4-diaminobenzene (Mp 143–145 °C) was obtained in 90% yield. Devey et al. have reported the reduction of only one nitro group in the case of a dinitro compound.[10] Also, the reduction of 2,2′-dinitrobiphenyl using bakers' yeast–NaOH system yields benzo[c]cinnoline N-oxide and benzo[c]cinnoline.[16] It must be emphasized here in the present investigation that we did not observe the formation of any azo or azoxy type of compounds or any other product, which is the problem with other chemical methods.[22] Convincingly, the yeast reduction of benzofuroxans is selective, mild, and most efficient over the existing chemical methods known.[23,24]

We have developed an efficient metal-free method for the reductive cleavage of N-O bond of benzofuroxans to afford medicinally important building blocks, employing a biocatalyst under nonfermenting and aqueous conditions that is inexpensive, nontoxic, environment friendly,

Table 1. Bakers' yeast–catalyzed synthesis of aryl-1,2-diamines **2**

Entry	Product No.	R^1	R^2	Mp (°C) Found	Mp (°C) Lit.	Yield[a] (%)	Reaction time[b] (h)
1	**2a**	H	H	103	103–105[25]	95	6.0
2	**2b**	Cl	H	75	75–76[25]	90	6.5
3	**2c**	Br	H	60	59–60[25]	92	6.5
4	**2d**	CH_3	H	89	89–90[25]	80	6.5
5	**2e**	NO_2	H	200	200–201[25]	80	6.0
6	**2f**	H	NO_2	158	157–159[25]	80	6.0

[a]Yield refer, to the yield of pure isolated products.

[b]Products were identified by the comparision of IR and NMR spectra and melting points with those of authentic samples.

and highly selective. It is beneficial that halogen and nitro groups were not suffered. Also yeast did not require sucrose or glucose in this reaction, resulting in appropriate regulation of the reducing ability of the yeast. This biotransformation technique will constitute a useful alternative to the commonly accepted chemical methods (when other sensitive groups or catalyst poisons are present in the molecule) for the synthesis of aryl-1,2-diamines.

EXPERIMENTAL

Melting points are determined by using a Buchi melting-point apparatus and are uncorrected. IR spectra are recorded for KBr discs on a Perkin-Elmer 240C analyzer. ^{1}H NMR spectra are recorded on 90-MHz spectrometers, and chemical shift values are recorded in δ units (ppm) relative to Me_4Si as internal standard. The 100-MHz NMR spectra are recorded with tetramethylsilane as internal standard (by RSIC, Shillong). Mass spectra are recorded in an AEIMS-30 spectrometer. Elemental analyses are performed on a Hitachi 026 CHN analyser.

Bakers' Yeast–Catalyzed Preparation of Aryl-1,2-diamines 2: General Procedure

To a well-stirred suspension of bakers' yeast (10 g) in buffer solution, pH 7.0 (30 ml), a solution of benzofuroxan (0.136 g) in methanol (15 ml) was added. The resulting mixture was kept at room temperature with occasional shaking for 6 h (monitored by TLC). After completion, ethylacetoacetate/dichloromethane (40 ml) was added, and the organic layer was filtered through a Celite pad. The organic layer was then dried over anhydrous sodium sulphate and concentrated under reduced pressure. The residue thus obtained 1,2-phenylenediamine in 95% yield, Mp 103–105 °C. The product gave a single spot on TLC (silica-gel plates with benzene as mobile phase). Similarly, other substituted benzofuroxans were reacted, and the corresponding 1-2-diamines were isolated in 80–92% yields (Table 1). The structure of the products **5** thus obtained were established by spectroscopic analysis and by comparison with authentic sample prepared by following the literature procedure.[25]

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