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Selective Reduction of Aromatic Nitro Compounds to Aromatic Amines by Baker's Yeast in Basic Solution

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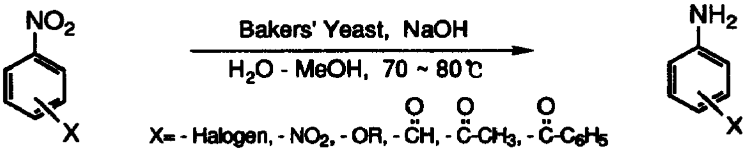
Abstract : Aromatic nitro compounds containing *o*-, *m*- or *p*-electron withdrawing groups, such as carbonyl, halogen and nitro, were selectively and rapidly reduced to their corresponding amino derivatives in good yields using Bakers' Yeast in basic solution.

Rapid and selective reduction of aromatic nitro compounds is of importance for the preparation of amine derivatives in organic synthesis, particularly when a molecule has other reducible substituents[1-5]. Therefore, numerous reagents have been developed for the reduction of aromatic nitro compounds[6]. While Bakers' Yeast has been used for the enantioselective reduction of carbonyl compounds[7], little attention has been paid to the reduction of aromatic nitro compounds[8]. Recently, one example reported the Bakers' Yeast in the reduction of aromatic nitro compounds[9]. However, excess use of Bakers' Yeast (250 g with 1 g of substrate) and long reaction time (around 100 hr) have impeded this reagent to employ as a good reducing agent in synthetic chemistry. Moreover, poor selectivity was reported in the reduction of aromatic nitro compounds which have carbonyl substituents. Therefore, we have examined several reaction conditions to improve the reduction process, and especially to obtain the selectivity over carbonyl or other labile substituents. In this paper we wish to report a selective, rapid and simple reduction of aromatic nitro compounds to the corresponding amino derivatives using Bakers' Yeast in basic solution.



In a typical procedure, a suspension of Bakers' Yeast(30 g) in water(80 mL) was heated for 5 min at 70 °C with vigorous stirring, and a mixture of an aromatic nitro compound(0.5 g) in methanol(40 mL) and NaOH(4 g) in H_2O(10 mL) was added. The resulting reaction mixture was vigorously stirred at 70~80 °C. After the reaction was completed by TLC analysis, CH_2Cl_2(50 mL) was poured into the reaction flask. After the phases were separated, the organic layer was filtered through a celite pad. The organic layer was washed, dried and concentrated under a reduced pressure. The residue was purified by flash column chromatography on silica gel to give the desired amino derivatives.

As shown in Table, Bakers' Yeast proved to be an efficient and selective reagent in the reduction of aromatic nitro compounds. In the case of carbonyl substituted aromatic nitro compound, the corresponding aniline was selectively obtained in high yield without any further reduction of carbonyl group(entries 1~4). Furthermore, aromatic halides showed remarkable selectivity to give the amine product without giving any dehalogenation (entries 5~8). Because trial of common reducing agents to iodinated aromatic nitro compound was reported to be troublesome to provide deiodinated side product or recovered starting mertrial[1,10], Bakers' Yeast will find useful in organic synthesis in the reduction of halogen substituted nitroarene compounds. In addition, it was worth commenting that dinitro compound was selectively converted to the mononitro product in high yield (entry 10). Table showed that the yields were generally high for the aromatic nitro compounds with electron deficient groups independent of the substitution position. And the reaction was completed within 5 hours under our reaction conditions. However, decreased reactivity was observed for the aromatic nitro compounds with electron rich substituents, giving reaction time more than 24 hours. The reduction of *o*- or *p*-nitrophenol was not successfully reduced with Bakers' Yeast in the variety of conditions(entries 15, 16). The observation suggest that phenoxide ion generated by NaOH may deactivate the Bakers' Yeast.

The obvious advantages over the previous method[9] are (1) selective reduction of aromatic nitro compounds in the presence of other reducible groups, (2) rapid reaction, (3) use of small amount of Bakers' Yeast, (4) excellent reduction of iodo-nitrobenzene without deiodination, and (5) high yields of substituted anilines. This procedure will therefore be of general use especially in cases where rapid, mild, and selective reduction is required.

Table. Reduction of aromatic nitro compounds

Entry	Nitro Compound	Hour	Product	Yield^a(%)
1	*o*-$NO_2C_6H_4COCH_3$	2	*o*-$NH_2C_6H_4COCH_3$	91
2	*p*-$NO_2C_6H_4COCH_3$	2	*p*-$NH_2C_6H_4COCH_3$	91
3	*p*-$NO_2C_6H_4COC_6H_5$	5	*p*-$NH_2C_6H_4COC_6H_5$	85^b
4	*p*-$NO_2C_6H_4CHO$	5	*p*-$NH_2C_6H_4CHO$	84
5	*m*-$NO_2C_6H_4I$	5	*m*-$NH_2C_6H_4I$	91^b
6	*m*-$NO_2C_6H_4Br$	4	*m*-$NH_2C_6H_4Br$	90
7	*o*-$NO_2C_6H_4Cl$	5	*o*-$NH_2C_6H_4Cl$	90
8	4-$ClC_6H_3(2\text{-}NO_2)NH_2$	3	4-$ClC_6H_3(2\text{-}NH_2)NH_2$	85^b
9	1-Nitronaphthalene	7	1-Aminonaphthalene	95
10	*m*-$NO_2C_6H_4NO_2$	2	*m*-$NH_2C_6H_4NO_2$	95
11	$C_6H_5NO_2$	20	$C_6H_5NH_2$	55^b
12	*o*-$NO_2C_6H_4OCH_2CH{=}CH_2$	24	*o*-$NH_2C_6H_4OCH_2CH{=}CH_2$	70
13	*p*-$NO_2C_6H_4OCH_2CH{=}CH_2$	24	*p*-$NH_2C_6H_4OCH_2CH{=}CH_2$	69^b
14	*p*-$NO_2C_6H_4OCH_3$	24	*p*-$NH_2C_6H_4OCH_3$	25
15	*o*-$NO_2C_6H_4OH$	24	*o*-$NH_2C_6H_4OH$	19(70)^c
16	*p*-$NO_2C_6H_4OH$	24	*p*-$NH_2C_6H_4OH$	18(73)^c

[a] GC yield with internal standard, typical percentage error ± 3% [b] Isolated yield

[c] Isolated yield based on the recovered starting material.

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