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Baker's Yeast Reduction of Nitroarenes in NaOH Media 5. Reductive Cyclization of *o*-Nitrocinnamaldehydes.

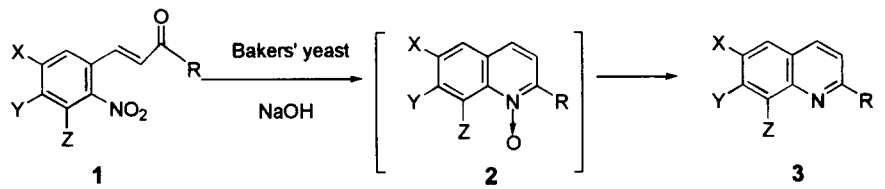
Woonphil Baik*, Dong Ik Kim, Hyun Joo Lee, Wook-Jin Chung, Byeong Hyo Kim[a], and Seok Woo Lee[b]

Department of Chemistry, Myong Ji University, Yong In, Kyung Ki Do, 449-728, **Korea.** [a] Department of Chemistry and RIBS, Kwangwoon University, [b]Organic Chemical Division, National Institute of Technology and Quality, **Korea**

Abstract: Reduction of 2-nitrocinnamaldehydes or 4-(2'-nitrophenyl)-3-buten-2-one by bakers' yeast has been found to be cyclized in NaOH media, resulting in the formation of quinolines *via* cyclized *N*-oxides. © 1997 Elsevier Science Ltd.

Bakers' yeast (*Saccharomyces cerevisiae*) has been known to reduce carbonyl compounds to their alcohols.[1] The ability of bakers' yeast to effect the reduction of nitroarenes to anilines was also reported, however, the reduction was prone to poor yields, low selectivity, and long reaction time.[2] On the other hand, in the reduction of nitroalkenes with bakers' yeast, carbon-carbon double bond was reduced to give the corresponding nitroalkanes[3] or nitro group was reductive cyclized to give isoxazoles in the case of (*Z*)-3-nitropropenenitriles.[4] We have recently found that the reduction of nitroarenes with bakers' yeast in NaOH solution proceeds to give the corresponding anilines with excellent yields and show high selectivity over carbonyl or other labile substituents.[5] Using this bakers' yeast-NaOH reduction system, deoxygenation of aromatic and heteroaromatic *N*-oxides is also achieved.[6] We have examined this reduction protocol on a series of *o*-nitrocinnamaldehydes, and we report our results which demonstrate that bakers' yeast-NaOH system is a selective procedure for the preparation of quinolines or their *N*-oxides.

2-Nitrocinnamaldehyde (0.5 g) with bakers' yeast (30 g)-NaOH (2 g) afforded quinoline *N*-oxide **2** in 91% yield (entry 1 in the Table). Neither reduction to *o*-aminocinnamaldehyde nor alcohol formation was observed.



1 **2** **3**

As a control experiment, a suspension containing *o*-nitrocinnamaldehyde (0.5 g) in aqueous ethanol was stirred with varying amounts of bakers' yeast-NaOH. Surprisingly, the reductive cyclization was greatly influenced by the amount of NaOH and reaction time. In the absence of NaOH, no product was formed and the unreacted nitroarene was recovered. When the reduction was performed using twice the amount of NaOH and a long reaction time, quinoline was obtained as the single product in 88% yield (entry 2). In this case, the reduction of **1** to **3** proceeded through an intermediate stage involving *N*-oxide **2**. Furthermore, isolated *N*-

oxide **2** was also smoothly reduced to give quinoline **3** with bakers' yeast-NaOH.[6] Therefore, reaction intermediate *N*-oxide **2** was converted to quinoline during the reduction. In addition, chloro substituted *o*-nitrocinnamaldehyde was efficiently reduced to give their corresponding quinoline or quinoline *N*-oxide without dehalogenation (entries 3 and 4). When an electron donating groups, such as methoxy, was substituted, the reduction proceeded very sluggishly (entry 5). In fact, this result which electron donating group impedes the reducing ability coincides with the case of nitroarenes.[2,5] It was found that electron withdrawing substituents greatly enhanced the rate of reduction (entries 3,4,and 6). In the case of 2,4-dinitrocinnamaldehyde, 4-nitro moiety was also reduced to give 7-aminoquinoline *N*-oxide in 51% yield (entry 6). Even though potassium tetracarbonylhydridoferrate, $KHFe(CO)_4$, reduces *o*-nitrocinnamaldehyde to quinoline in quantitative yield, bakers' yeast reduction is more selective than any other literature procedure for the preparation of *N*-oxides from their nitro compounds. Besides *o*-nitrocinnamaldehydes, the reductive cyclization of nitro to ketone moiety with bakers' yeast-NaOH was also performed to give 2-substituted quinoline *N*-oxides or quinolines (entries 7,8 and 9). In fact, the preparation of 2-phenylquinoline with ferrate gave a low yield (17%).[7] Thus, the bakers' yeast-NaOH protocol provides a selective and efficient method for the preparation of 2-substituted quinoline.

Table. Reductive cyclization of nitroarenes of by Baker's Yeast - NaOH[a]

entry	1				BY	NaOH	time	Yield,%	
	X	Y	Z	R	(g)	(g)	(h)	**2**	**3**
1	H	H	H	H	30	2	1	91	0
2	H	H	H	H	30	4	24	tr	88
3	Cl	H	H	H	30	1	1	88	tr
4	Cl	H	H	H	30	8	2	tr	61
5	H	H	OMe	H	40	2	1	10	0
6	H	NO_2	H	H	30	2	1	(51)[b]	0
7	H	H	H	CH_3	30	2	1	89	0
8	H	H	H	CH_3	30	8	24	tr	34
9	H	H	H	Ph	30	2	1	50	0

[a]To a suspension of bakers' yeast and NaOH in tap water (70 mL) and EtOH (30 mL) a substrate (0.5 g) was added. The resulting mixture was refluxed for the time period described in Table. [b]7-aminoquinoline *N*-oxide

In summary, we have found that bakers' yeast mediated reductive cyclization of *o*-nitrocinnamaldehydes was selectively achieved to give their quinoline *N*-oxides or quinolines with bakers' yeast and NaOH.

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