Pergamon

Tetrahedron Letters, Vol. 36, No. 16, pp. 2793-2794, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)00398-3

Selective Reduction of Aromatic Nitroso Compounds with Baker's Yeast under Neutral Condition

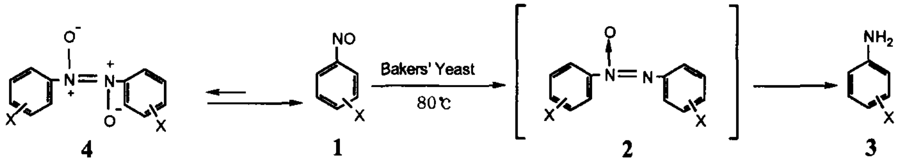
Woonphil Baik*, Jong Uk Rhee, Sang Hwi Lee, Nam Ho Lee[a], Byeong Hyo Kim[b] and Kyung Soon Kim

Department of Chemistry, Myong Ji University ,Yong In Kun, Kyung Ki Do,449-728, KOREA
[a] Cheju National University, [b]Kwangwoon University

Abstract: Aromatic nitroso compounds containing halogen and other labile substituents were selectively and rapidly reduced to their corresponding amino derivatives in good yields using Bakers' Yeast at 80 ℃.

Since the use of Bakers' Yeast has been developed in organic synthesis, it was published by many groups that carbonyl compounds, including β -keto ester, β -halo carbonyl and aryl methyl ketone, were enantioselectively reduced to give their hydroxy compounds.[1] However, little attention has been paid to the reduction of nitro compounds by Bakers' Yeast. Recently, we reported the selective reduction of nitroarenes to the corresponding amines by Bakers' Yeast.[2] The use of sodium hydroxide was crucial for this reaction. For the nitroarenes with electron-withdrawing groups, the reduction generally proceeded in excellent yields and showed high chemoselectivity over carbonyl and other labile substituents. Since we observed that the reduction of nitroarenes was strongly influenced by the chemical environments, we were forced to examine nitroso compounds under our reaction conditions. In this paper, we want to describe the result of selective reduction and its biotransformations of aromatic nitroso compounds to the corresponding anilines using Bakers' Yeast as a reductant.

Nitrosobenzene(0.5g), when treated with Bakers' Yeast(15g) in aqueous methanol at 80 ℃ for 8 h, gave exclusively aniline in high yield(as shown in the Table).



Surprisingly during the Bakers' Yeast reduction, the formation of intermediate, azoxybenzene, could be monitered by GC. After 30 min, nitrosobenzene was completely transformed to give azoxybenzene(76.8%) and aniline(11.7%) (entry 1), and then azoxybenzene was slowly further reduced to aniline(entry 2). Finally, the over-reduction was completed to aniline after 8 h(entry 3). As a control experiment, a suspension containing nitrosobenzene(0.5g) was stirred with varying amounts of Bakers' Yeast. As we decreased the amount of Bakers' Yeast, the over-reduction to aniline was not completed(entry 4). In contrary to the reduction of nitroarenes using Bakers' Yeast-NaOH, aromatic nitroso compounds can be efficiently reduced to their amino compounds in the absence of NaOH. In addition, halogen-substituted aromatic nitroso compounds were rapidly reduced to give their corresponding anilines within 2 h in 90~99% yields(entries 5~7). In these cases, an intermediate, azoxybenzene **2**, could not be detected. The common reducing agents were reported to provide dehalogenated products, especilly for the reduction of iodinated compounds. It is worth mentioning that dehalogenation did not occur in the Bakers' Yeast reduction of halonitrosobenzenes. In our previous paper[2], the reduction of nitroarenes with electron rich substituents, including methyl, alkoxy and hydroxyl groups, was shown to be inefficient under Bakers' Yeast-NaOH system. However, aromatic nitroso compounds containing electron-rich substituents were smoothly reduced to give anilines within 1 h in high yields(entries 8~10). Nitroso to amino reduction[3] is usually carried out under acidic[3c] or basic conditions.[3e] In protic solvents, *p*-hydroxynitrosobenzene is not inert to treatment of strong base(or acid). To the best of our knowledge, this is the first example of the selective reduction of *p*-hydroxynitrosobenzene to *p*-hydroxyaniline under neutral condition (entry 10). On the other hand, the reduction of *p*-nitrosoacetophenone gave a mixture of **2** and **3** (entries 11,12). In fact, this can be rationalized by the tendency of dimerization($1 \rightleftarrows 4$) in protic solvent.[4] Especially, electron-withdrawing groups enhance the stability of dimers which was perhaps reduced to give azoxy compound by Bakers' Yeast.

In summary, we can point out that Bakers' Yeast selectively reduces nitrosobenzenes containing halogen, hydroxy, and carbonyl groups to the corresponding anilines with high yields under neutral conditions. In addition, the major problems in the Bakers' Yeast reduction of carbonyl compounds are (1) use of excess amount of Bakers' Yeast and glucose (2) long reaction time and (3) tedious work-up process. On the basis of these considerations, Bakers' Yeast reduction of aromatic nitroso compounds carried out without sugar and NaOH show the following advantages: (1) a high yield within a short time with small amount of Bakers' Yeast, and (2) under these conditions, a less tedious work-up.

Table. Reduction of aromatic nitroso compounds by Bakers' Yeast[a]

entry	**1**(=X)	conditions	Yield[b] **3**	Yield[b] **2**
1	H	0.5h, BY(15g)	22	77
2	H	1h, BY(15g)	73	26
3	H	8h, BY(15g)	95	0
4	H	8h, BY(5g)	21	71
5	*o*-Cl	0.5h, BY(15g)	95	0
6	*m*-Br	1h, BY(15g)	99	0
7	*m*-I	1h, BY(15g)	94	0
8	*p*-CH_3	0.5h, BY(15g)	95	0
9	*p*-OMe	1h, BY(15g)	92	0
10	*p*- OH	8h,BY(15g)	90	10[c]
11	*p*-C(=O)CH_3	0.5h, BY(15g)	37	36(10.4)[d]
12	*p*-C(=O)CH_3	8h, BY(15g)	69	25

[a]The mixture of **1**(0.5g) and B.Y.(15g) in H_2O(50ml) and MeOH(20ml) was stirred at 80~85℃. After the reduction was completed, CH_2Cl_2 was poured into the flask. The organic layer was filtered through a celite pad, dried and concentrated. [b]GC Yield with internal standard. [c]The recovered starting material [d]azo compound.

Acknowledgments; The financial support from the Korea Science and Engineering Foundation is greatly acknowledged.

References

1. a)Tsuboi, S.; Sakamoto, J.; Kawano, T.; Utaka, M.; Takeda, A. *J. Org. Chem.*, **1991**, *56*, 7177. b) Nakamura, K.; Kondo, S.; Kawai, Y.; Ohno, A. *Tetrahedron Lett.*, **1991**, *32*, 7075. c)Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.*, **1985**, *26*, 771. d) Csuk, R.; Glanzer, B. *Chem. Rev.*, **1991**, *91*, 49. e)Servi, S. *Synthesis*, **1990**, 1. f) Mazur, P.; Nakanishi, K. *J. Org. Chem.*, **1992**, *57*, 1047. g)Utaka, M.; Konish, S.; Takeda, A. *Tetrahedron Lett.*, **1986**, *27*, 4737. h)Tsuboi, S.; Sakamoto, J.; Sakai, T.; Utaka, M. *Synlett.*, **1991**, 867.
2. Baik, W.; Han, J. L.; Lee, N. H.; Kim, B. H.; Hahn, J. T. *Tetrahedron Lett.*, **1994**, *35*, 3965.
3. a)Akita, Y.; Inaba, M.; Uchida, H.; Ohta, A. *Synthesis*, **1977**, 792. b)Sakaue, S.; Tsubakino, T.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.*, **1993**, *58*, 3633. c)Fieser, L. F. *Org. Syn. Coll. Vol.* **1943**, *2*, 42. d)Entwistle, I.D.; Johnstpne, R.A.W.; Wilby, A.H. *Tetrahedron*, **1982**, *38*, 419. e)Danis, F. B.; Keynon, W. O. *J. Am. Chem. Soc.*, **1931**, *53*, 2357.
4. Batt, I.. *The Chemistry of amino, nitroso and nitro compounds and their derivatives, part 1*, John Wiley and Sons, New York, **1982**, *pp*.441-442.

(*Received in Japan* 19 *December* 1994; *revised* 14 *February* 1995; *accepted* 24 *February* 1995)