

REDUCTION OF HETERO-AROMATIC NITRO COMPOUNDS WITH BAKER'S YEAST

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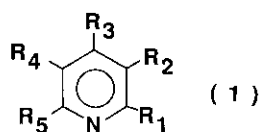
Abstract— Reduction of nitro group on hetero-aromatics with
baker's yeast has been examined.

Baker's yeast (*Saccharomyces cerevisiae*) has been used widely for the syntheses of chiral building blocks in organic synthesis due to the low cost and easiness to handle.¹

However, very few reports other than chiral reduction of carbonyl groups² have been disclosed to date.³ In the previous paper,⁴ we showed the conversion of nitrobenzene derivatives into the corresponding amino compounds with baker's yeast. For the further extensive study of this reduction, we examined the reduction of nitro group substituted on hetero-aromatics.

At first, as shown in Table I, when nitropyridine derivatives (**1a-1e**), having an electron-donating group (MeO, NH₂, OH) on the ring were treated with baker's yeast at 33 °C for 72-115 h, the reduction proceeded in low yields (**1j**, **1m**)⁶ (26 and 40 %, respectively) or did not proceed at all (**1k**, **1l**, **1n**) (0 %). However, by substitution of an electron-withdrawing group (Cl) on the pyridine ring (**1f-1i**), the reduction proceeded smoothly to give amines (**1o-1r**) (41-88 %). When 1-methyl-3-nitro- and 1-methyl-5-nitro-2(1H)-pyridones (**2a** and **2b**) were treated with baker's yeast at 33 °C for 77-95 h, the corresponding aminopyridones (**2c** and **2d**) were obtained in 52 and 26 % yields, respectively (Table II).

Table I. Reduction of Nitropyridine Derivatives with Baker's Yeast

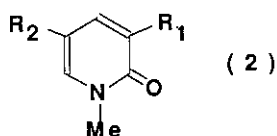


Substrate						a) Time h	Product						Yield %
	R ₁	R ₂	R ₃	R ₄	R ₅			R ₁	R ₂	R ₃	R ₄	R ₅	
1a	OMe	H	H	NO ₂	H	115	1j ^{b)}	OMe	H	H	NH ₂	H	26
1b	NH ₂	H	H	NO ₂	H	110	1k	NH ₂	H	H	NH ₂	H	0
1c	OH	H	H	NO ₂	H	94	1l	OH	H	H	NH ₂	H	0
1d	OH	NO ₂	H	H	H	72	1m ^{c)}	OH	NH ₂	H	H	H	40
1e	NO ₂	OH	H	H	H	84	1n	NH ₂	OH	H	H	H	0
1f	Cl	H	H	NO ₂	H	41	1o ^{b)}	Cl	H	H	NH ₂	H	88
1g	Cl	H	Me	NO ₂	H	73	1p ^{d)}	Cl	H	Me	NH ₂	H	77
1h	Cl	NO ₂	H	H	H	90	1q ^{b)}	Cl	NH ₂	H	H	H	78
1i	Cl	NO ₂	H	H	Cl	66	1r ^{e)}	Cl	NH ₂	H	H	Cl	41

a) Temperature : 33 °C. b) Commercially available. c) see ref. 5.

d) see ref. 7. e) see ref. 8.

Table II. Reduction of 1-Methyl-2(1H)-nitropyridones with Baker's Yeast



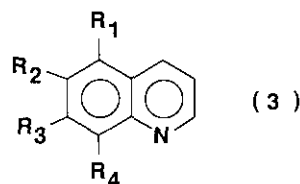
Substrate			a) Time h	Product		Yield
	R ₁	R ₂				%
2a	NO ₂	H	77	2c ^{b)}	NH ₂	52
2b	H	NO ₂	95	2d ^{b)}	H	26

a) Temperature : 33 °C. b) see ref. 5 .

Secondly, we applied this microbial transformation for the reduction of nitroquinoline derivatives (3a- 3e). In those reactions, 5-nitro- and 6-nitroquinolines (3a and 3c) and 6-methoxy-8-nitroquinoline (3e) were reduced to give the amines (3f, 3h, and 3j ⁹)

in good yields (74, 87, and 95 %, respectively). However, 8-hydroxy-6-nitro- and 5-amino-6-nitroquinolines (**3b** and **3d**) were inert under the same conditions (Table III).

Table III. Reduction of Nitroquinoline Derivatives with Baker's Yeast



Substrate					Temp. ° C	Time h	Product					Yield %
	R ₁	R ₂	R ₃	R ₄				R ₁	R ₂	R ₃	R ₄	
3 a	NO ₂	H	H	H	32	45	3 f ^{a)}	NH ₂	H	H	H	74
3 b	NO ₂	H	H	OH	33	45	3 g	NH ₂	H	H	OH	0
3 c	H	NO ₂	H	H	33	87	3 h ^{a)}	H	NH ₂	H	H	87
3 d	NH ₂	NO ₂	H	H	33	87	3 i	NH ₂	NH ₂	H	H	0
3 e	H	MeO	H	NO ₂	33	89	3 j ^{b)}	H	MeO	H	NH ₂	95

a) Commercially available. b) see ref. 9

EXPERIMENTAL

Reduction of 2-Methoxy-4-nitropyridine (**1a**) with Baker's Yeast.

A mixture of 2-methoxy-4-nitropyridine (**1a**) (1 g) and baker's yeast (250 g) (purchased from Oriental Yeast Co.) in water (125 ml) was incubated at 33 °C for 114 h. The mixture was extracted with CHCl₃ using a Soxhlet apparatus, and the extract was dried over Na₂SO₄. The solvent was removed under reduced pressure to give the residue which was purified by silica gel (24 g) column chromatography using CH₂Cl₂ as an eluting solvent to yield **1j** (0.21 g, 26 %). bp 100° C/ 1.5 mmHg. Obtained **1j** was completely identical with the authentic sample purchased from Aldrich Chemical Company, Inc.

Reduction of 1-Methyl-3-nitro-2(1H)-pyridone (**2a**) with Baker's Yeast.

A mixture of 1-methyl-3-nitro-2(1H)-pyridone (**2a**) (1 g) and baker's yeast (250 g) in water (125 ml) was incubated at 33 °C for 77 h. The mixture was extracted with CHCl₃ using a Soxhlet apparatus, and the extract was dried over Na₂SO₄. The solvent was removed

under reduced pressure to give the residue which was purified by silica gel (24 g) column chromatography using CH_2Cl_2 as an eluting solvent to yield **2c** (0.42 g, 52 %). bp 135 °C / 1 mmHg.⁵

Reduction of 6-Methoxy-8-nitroquinoline (**3e**) with Baker's Yeast

A mixture of 6-methoxy-8-nitroquinoline (**3e**) (1 g) and baker's yeast (250 g) in water (125 ml) was incubated at 33 °C for 89 h. The mixture was extracted with CHCl_3 using a Soxhlet apparatus, and the extract was dried over Na_2SO_4 . The solvent was removed under reduced pressure to give the residue which was purified by silica gel (20 g) column chromatography using CH_2Cl_2 as an eluting solvent to yield **3j** (0.65 g, 95 %). bp 105 °C / 1.5 mmHg (lit.,⁹ bp 169 °C/ 3 mmHg).

REFERENCES AND NOTES

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6. In the reduction of 2-hydroxy-5-nitro- and 3-hydroxy-2-nitropyridines (**1c** and **1e**) with baker's yeast, extracted reaction mixtures were dark brown and no starting material was recovered. Thus, it seemed that the reductions occur to give unstable products in those reactions.
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