HETEROCYCLES, Vol. 31, No. 12, 1990

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

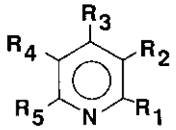
Mitsuhiro Takeshita and Sachiko Yoshida
Tohoku College of Pharmacy, 4-4-1 Komatsushima, Aobaku,
Sendai 981, Japan

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 groups[2] 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, NH_2, 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(1<u>H</u>)- pyridones (**2a and 2b**) were treated with baker's yeast at 33 °C for 77-95 h, the corresponding aminpyridones (**2c and 2d**) were obtained in 52 and 26 % yields, respectively (Table II).

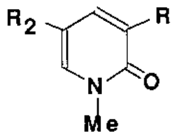
Table I. Reduction of Nitropyridine Derivatives with Baker's Yeast


(1)

Substrate						Time[a)]	Product						Yield
	R_1	R_2	R_3	R_4	R_5	h		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

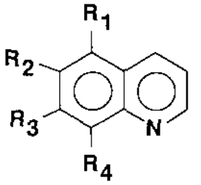

(2)

Substrate			Time[a)]	Product			Yield
	R_1	R_2	h		R_1	R_2	%
2a	NO_2	H	77	2c[b)]	NH_2	H	52
2b	H	NO_2	95	2d[b)]	H	NH_2	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



(3)

Substrate					Temp.	Time	Product					Yield
	R_1	R_2	R_3	R_4	°C	h		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 $CHCl_3$ using a Soxlet 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 (24 g) column chromatography using CH_2Cl_2 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 $CHCl_3$ using a Soxlet 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 (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 Soxlet 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

1. Cf. reviews: T. Oishi and H. Akita, J. Syn. Org. Chem. Jpn., 1983, 41, 1031; T. Fujisawa, T. Sato, and T. Itoh, J. Syn. Org. Chem. Jpn., 1986, 44, 519 .
2 C. J. Sih and C.-S. Chen, Angew. Chem. Int. Ed. Engl., 1984, 23, 570 ; J. B. Jones, Tetrahedron, 1986, 42, 3351 and references cited therein.
3. C. Neuberg and E. Welde, Biochem. Z., 1914, 60, 472 ; C. Neuberg, Adv. Carbohydr. Chem., 1945, 4, 75 ; M. Takeshita and S. Yoshida, Heterocycles, 1990, 30, 871.
4. M. Takeshita, S. Yoshida, R. Kiya, N. Higuchi, and Y. Kobayashi, Chem. Pharm. Bull., 1989, 37, 615.
5. G. B. Barlin and W. Pfleiderer, J. Chem. Soc., B , 1972, 1425.
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.
7. D. Chapman and J. Hurst, J. Chem. Soc. Perkin Trans. I, 1980, 2398.
8. J. Buchingham (ed.), " Dictionary of Organic Compounds", Vol. I, Chapman and Hall, New York, 1982, p.197.
9. W. V. Farrar, J. Chem. Soc., 1954, 3252.

Received, 5th October, 1990