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# Kinetic Resolution of 1-Aryl- and 1-Heteroaryl Ethanols by Oxidation with Baker's Yeast

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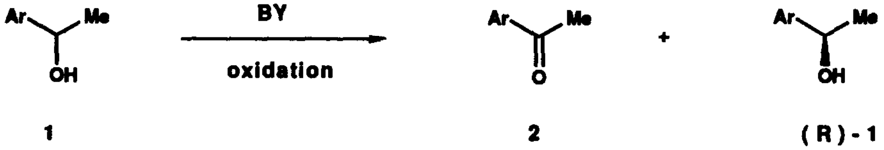
*Key Words:* Kinetic resolution, Oxidation, Baker's yeast, 1-Aryl ethanol, 1-Heteroaryl ethanol

*Abstract:* The kinetic resolution of racemic 1-aryl and 1-heteroaryl ethanols **1a-e** via oxidation by Baker's yeast to give the R-enantiomer is reported.

Enantiomerically pure secondary alcohols are useful chiral auxiliaries in organic chemistry both for analytical and synthetic applications.[1] Chiral aryl secondary alcohols were mainly obtained by the enantioselective reductions of the corresponding ketones with chiral hydride donors,[2] micro-organisms,[3] and oxidoreductases,[4] using the classical resolution techniques *via* diastereoisomers[5] or the enantioselective hydrolysis of the corresponding esters with hydrolases or microorganisms.[6] On the other hand lipase-catalyzed kinetic resolution of secondary alcohols via hydrolysis, esterification and transesterfication was widely used to have homochiral compound.[7] In comparison with the reductions of ketones, furthermore, there are few reports of microbial oxidations of alcohols[8] and this mild oxidation conditions were scarsely used for a kinetic resolution of a mixture of racemic alcohols.[9] In this field, although Baker's yeast was extensively employed for the reduction of ketones,[10] only one example is reported on its use in oxidation to give *via* kinetic resolution an enantiomerically pure alcohol.[11] In this work we describe the oxidation of 1-aryl- and 1-heteroaryl ethanols **1a-e** with the whole Baker's yeast cells in resting state as a new method for the kinetic resolution of this compounds (Scheme).



To a suspension of BY (2.5 g) in 20 mL of the appropriate phosphate buffer the selected racemic alcohol **1** (0.2 mmol) in DME or DMF (0.1 mL) was added (see Table). The flask was shaken on a reciprocatory shaker at 32 °C for the appropriate time. The suspension was removed by centrifugation, a saturated solution of NaCl was added and the mixture extracted with diethyl ether and dried over anhydrous $Na_2SO_4$. Chromatography on a short column (silica gel, petroleum ether:diethyl ether 1:1) gave almost quantitative yields (90-95%) of the mixture of **1** and **2** that were analyzed by GLC on a chiral column.[12] The results are summarized in the Table.

**Table.** Kinetic resolution of compounds **1a-e** *via* oxidation.

| alcohol | Ar | Ox. Time (days) | **2** : **1** (ratio %)[a] | ee(%) (conf.)[b] of **1** |
|---|---|---|---|---|
| **1a** | 2-Furyl | 8[c] | **2a** : **1a** (79 : 21) | 100 (R) |
| "" | " | 7[c] | **2a** : **1a** (68 : 32) | 90 (R) |
| "" | " | 9[d] | **2a** : **1a** (73 : 27) | 95 (R) |
| **1b** | 2-Thienyl | 9[e] | **2b** : **1b** (90 : 10) | 95 (R) |
| **1c** | Phenyl | 9[e] | **2c** : **1c** (84 : 16) | 95 (R) |
| "" | " | 13[f] | **2c** : **1c** (64 : 36) | 86 (R) |
| **1d** | 2-Pyridyl | 8[e] | **2d** : **1d** (46 : 54) | 40 (R) |
| **1e** | 2-Thiazolyl | 10[g] | **2e** : **1e** (10 : 90) | 0 |

[a] Obtained by GLC. [b] Absolute configuratin is determined by comparison of the sign of the specific rotation with the reported value.[13] [c] Reaction carried out at pH 5 in DME. [d] Reaction carried out at pH 6 in DMF. [e] Reaction carried out at pH 5 in DMF. [f] Reaction carried out at pH 7.2 in DME. [g] Reaction carried out at pH 6 in DME.

The oxidation of the alcohols **1a-c** afforded the corresponding ketones **2a-c** leaving unreacted the R-enantiomers **1a-c** (ee 95-100%). Worse results were obtained with **1d** (54%, ee = 40%) while for the 2-thiazolyl derivative **1e** the oxidation was very low (10% after 10 days). It is worth mentioning that the reduction occurs in about 2 days while the oxidation is significant at longer time (8-9 days). Moreover in comparison with the reduction of the ketones that gives the prevalence of the S-enantiomer, the oxidation with BY represents a new method of kinetic resolution and affords the corresponding R-enantiomer in good enantiomeric excess. On the other hand this a mild oxidative methodology to obtain the ketones **2a-d**.

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12. Enantiomer separation on Megadex 1 column (25m X 0.32 mm) containing permethylated β-cyclodextrine in OV 1701 from Mega s.n.c.: carrier gas: helium (0.5 atm); temp: 150-200 °C ( 2 °C:min) for **1b** and **1e**; 150 °C for **1c**; 110-200 °C (1.5 °C/min) for **1a**; helium (1 atm) 100-200 °C (2.5 °C/min) for **1d**.
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