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# Enzymatic Oxidative Conversion of Thio to Oxo by Baker's Yeast in Thiocarbamates and Thioureas[1)]

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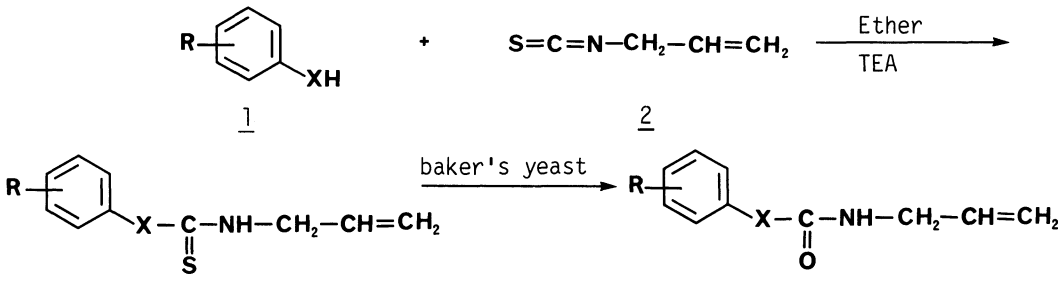
The enzymatic conversion of aryl allylthiocarbamates and 1-allyl-3-arylthioureas by baker's yeast to the corresponding carbamates and ureas in good yields is described.

The baker's yeast (Saccharomyces cerevisiae) mediated bioconversions by oxidoreductases found in this micro-organism have been recognized as a useful technique for synthetic organic chemists.[2-4)] Though it is well known that baker's yeast reduces carbonyl compounds to give chiral alcohols, the reduction or oxidation of other functional groups has not been much studied. However, the reductive conversion of aromatic nitro compounds to anilines by baker's yeast has been reported.[5)] Recently, microsomal metabolism studies of chlorpyrifos has been reported to give chlorpyrifos axon by the oxidation of the thiophosphate ester to the phosphate ester.[6)] In connection with our investigations on the application of enzymes as biocatalysts in organic synthesis,[7,8)] we herein report the bio-oxidative conversion of thiocarbamates and thioureas by baker's yeast to the corresponding carbamates and ureas.




1 2 3 4

X = O, NH, $NCH_3$; R = H, Cl

The starting materials 3a-3i were prepared by the reaction of substituted phenols and anilines with allylisothiocyanate in dry ether and 2-3 drops of triethylamine at room temperature. To compound 3a, 200 mg dissolved in ethanol (15 ml) and 0.1 M phosphate buffer (pH 7.4, 20 ml) was added baker's yeast (Sigma, Type I; 600 mg). The mixture was incubated at 37 °C for 8 h with shaking (200 rpm). The incubation mixture was then extracted thrice with chloroform (30 ml). The extract was dried over $Na_2SO_4$ and evaporated to dryness under

reduced pressure. The crude product obtained was recrystallized from ethanol to give 175 mg (96% yield, mp 118-120 °C, 98.8% purity by HPLC[9]) of phenyl allylcarbamate (4a). A Control incubation using boiled yeast preparation afforded 98% recovery of the starting compound.

In a similar manner, various substituted thiocarbamates and thioureas have been converted to the corresponding carbamates and ureas (4) in good yields, exhibiting the generality of this enzymatic reaction. The results are listed in Table 1.[10]

Table 1. Synthesis of aryl allylthio-carbamates/-ureas (3) and their conversion to aryl allyl-carbamates/-ureas (4) mediated by baker's yeast

| Entry | X | R | Yield of 3a-3i[a] % | Yield of 4a-4i[a] % |
|---|---|---|---|---|
| 1a | O | H | 78 | 96 |
| 1b | O | o-Cl | 72 | 82 |
| 1c | O | m-Cl | 75 | 79 |
| 1d | O | p-Cl | 81 | 78 |
| 1e | NH | H | 92 | 95 |
| 1f | $NCH_3$ | H | 94 | 88 |
| 1g | NH | o-Cl | 85 | 86 |
| 1h | NH | m-Cl | 87 | 81 |
| 1i | NH | p-Cl | 91 | 83 |

a) Isolated yield.

Though the non-enzymatic oxidation of cyclic thioureas to the corresponding urea compounds have been studied,[11] our attempts to oxidize thiocarbamates non-enzymatically resulted in the cleavage of -O-C(=S)- linkage of the thiocarbamoyloxy function.

Further, commercial allylisothiocyanate is far less expensive than allylisocyanate as such initial preparation of thiocarbamates and their bio-oxidative conversion by baker's yeast leads to the efficient preparation of carbamates. Thus, the present study develops a mild and convenient method for the formation of carbamates and ureas from their thio analogs and has a wide potential utility in the synthesis of biologically active compounds derived from isocyanates.

References

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9) TSK-ODS column (250 mmx4.6 mm), water-methanol (30:70) with 1% AcOH (v/v) at 254 nm and 0.5 ml/min flow rate.
10) The products were characterized by spectral analysis. 4a was also synthesized unambiguously by the reaction of 1a with allyl isocyanate. This sample was comparable to the product obtained by the enzymic method from the oxidative conversion of thio to oxo as their IR spectra were superimposable.
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