BAKERS' YEAST-MEDIATED REDUCTIONS OF SOME NITRO-DIBENZOFURANS

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Abstract: The reduction of 3 - nitro - 2 and 3,8 - dinitro-dibenzofurans 4 in biocatalytic conditions, with Bakers' Yeast is discussed. Selective reduction of the nitro groups was observed. The structures of the compounds obtained through reduction with Bakers' Yeast have been confirmed by spectral and elemental analysis.

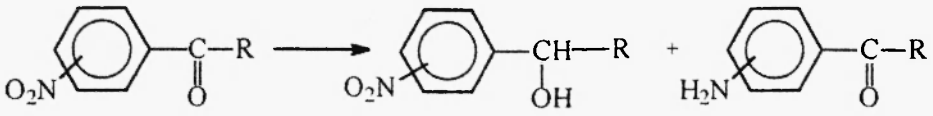
Introduction

The use of the common Bakers' Yeast (*Saccharomyces cerevisiae*), a microorganism which is an easily available "reagent" in every laboratory of organic chemistry for biocatalytic reduction, has been reviewed in two exhaustive reports (1,2). Bakers' Yeast is capable of reducing variously substituted carbonyl groups to the corresponding hydroxy compounds, activated double bonds and a few other functional groups. Little attention has been paid to the reduction of nitro compounds by Bakers'Yeast. Recently, Baik and Park (3) have reported the reduction of aromatic nitro compounds containing withdrawing groups in ortho, meta or para positions to the corresponding amino derivatives, in NaOH solution.

R=NO_2, CN,CF_3, COOEt

Scheme 1

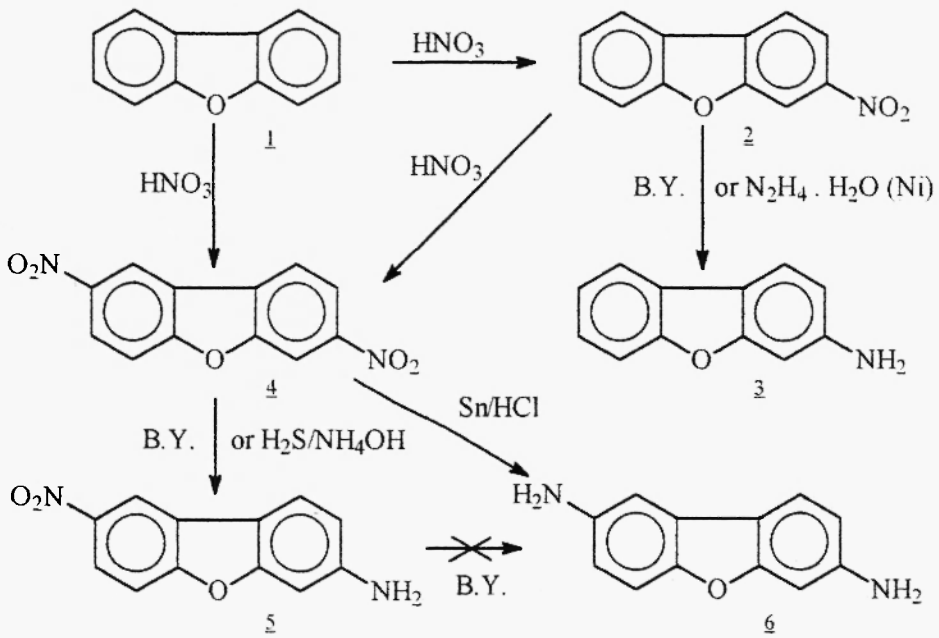
When the nitrobenzene is substituted by acyl groups, the reduction affords mixtures of the corresponding nitro-phenyl alcohols and amino-phenyl ketone (4).



R=Me, Ph

Scheme 2

As a part of our research in the reduction of organic compounds using Bakers' Yeast, we have examined the behaviour of 3-nitro-_2 and 3,8-dinitro-dibenzofuran 4 in biocatalytic conditions in comparison with the classic chemical reactions. The main paths of the transformation of these nitro compounds to the corresponding amino derivatives are presented in scheme 3.



Experimental

Melting points are given uncorrected. The purity of the compounds was checked by thin-layer chromatography on silicagel, using toluene : acetone (7 . 3 v/v) as eluent. The elemental analysis for C, H, N, O was within ± 0.4% in report with the theoretical values for compounds 2-5. For the recording of IR spectra, a Carl Zeiss Jena type UR-20 spectrophotometer, in KBr pellets, was used. The mass spectra were recorded on double focusing Varian MAT 311 spectrometer, with an electronic impact source at 70 eV and 300 μA.

3-Nitro-dibenzofuran 2 **and 3,8-dinitro-dibenzofuran** 4 were prepared by nitration of dibenzofuran 1 according to (5).

3-Amino-dibenzofuran

a) Biocatalytic reduction: The solution obtained from 0.5 g of 2 in 20 ml hot absolute ethanol was added to a fine suspension of 25 g Bakers' Yeast in 100 ml 5% NaOH aqueous solution. The mixture was stirred at room temperature for 48 hours and then extracted with 100 ml mixture of benzene-ethyl acetate (1:1 v/v).

The suspension was filtered and afterwards the organic layer was separated, dried with anhydrous Na_2SO_4 and subjected to concentration. After acidification of the residue with 100 ml HCl (16%) and filtration, the solution was neutralised with ammonium hydroxide (1:1). After the desired product precipitate, it was filtered. By recrystallization from ethanol results 0.2g (η=40%) of 3, white crystals, m.p. 94^{0}C (lit.94^{0}C (5a)). For $C_{12}H_9NO$ (183,27) calculated: 78.64%C, 4.95%H, 7.67%N, 8.73%O; found: 78.53%C, 4.82%H, 7.73%N, 8.92%O. IR Spectrum (KBr) ν_{max},cm^{-1} : 1660, 3200, 3400 (-NH_2). Mass spectrum m/z (rel.intensity, %): 184(38) M^++1, 183 (100)M^+, 182(21) M^+-1, 155(14) M^+-HCN, 154(17), 130(17), 128(20).

b) For comparison, 3-amino-dibenzofuran 3, was prepared from 2 by chemical reduction in ethanol with hydrazine hydrate and by using Ni from formiate as catalyst (η=32%) (6). The spectral data of this product 3 showed identical values with the one obtained through reduction with Bakers' Yeast.

3-Amino-8-nitro-dibenzofuran 5

a) Biocatalytic reduction: 0,35 g of 4 was dissolved in 50 ml hot absolute ethanol and added to a suspension of 80 g Bakers' Yeast in 800 ml of 5% NaOH aqueous solution. After 12 hours another portion of 20 g Bakers' Yeast was added and the mixture was stirred at room temperature another 12 hours. After extraction with 200 ml benzene and 200 ml ethyl acetate (30 min, with stirring), the suspension was filtered. The mixture was treated in the same way, as in the previous case. By recrystalization from acetic acid there results 0.13 g (η=28%)3-amino-8-nitro-dibenzofuran 5 m.p.=265^{0}C (lit.268^{0}C (7)). For $C_{12}H_8N_2O_3$ (228.21) calculated : 63.16%C, 3.53%H, 12.28%N, 21.03%O; found: 63.08%C, 3.62%H, 12.15%N, 21.15%O. IR Spectrum (KBr) ν_{max},cm^{-1} : 1360, 1540 (-NO_2), 1660, 3250, 3400 (-NH_2). Mass spectrum m/z, (rel.intensity,%): 229(11.3) M^++1, 228(60.8) M^+, 198(13.04) M^+-NO, 182(52.2), 170(13.04), 154(100), 127(59.13).

b) 5 was prepared for confirmation by reduction of 4 with H_2S/NH_4OH (7). This compound showed the same pattern of IR and MS spectra as the same bioproduct.

Results and discussion

Biocatalytic reduction of 2 and 4 with Bakers' Yeast is a convenient method for the preparation of aminoaromatic compounds in the series of nitro-dibenzofurans using aqueous NaOH medium. The yields are comparable with those of chemical reduction. 3-Amino-8-nitro-dibenzofuran 5 is obtained in two steps from dibenzofuran (dinitration, biocatalytic reduction), as in case of reduction with H_2S/ NH_4OH (7). In the crude product of Bakers'Yeast mediated reduction of dinitro-dibenzofuran 5 the presence of diamino compound 6 was not observed.The analytical data (MS, IR) were identical with those of the compounds obtained through the chemical ways.

The IR and MS spectra, the elemental analysis and m.p. of the product isolated from the biological reductions confirmed the structures of compounds 3 and 5. Some observations have to be mentioned:

a) The nitroderivatives 2 and 4 have very strong bands at 1350-1360 and 1550-1560 cm^{-1} characteristic for the nitro group which are not observed in the spectra of 3; in case of 3 and 5 at 3200 and 3400 cm^{-1} there appeared the typical bands of amino group.

b) Molecular peaks for 3 and 5 are clear with a relative abundance of 100% and 60.8% respectively. The characteristic peaks for fragmentation of amino (M-27) and nitro-aromatic compounds (M-30) were observed.

An explanation for the partial reduction of 3,8-dinitro-dibenzofuran 4 into 3-amino-8-nitro-dibenzofuran 5 may be found in the mild reduction capacity of Bakers' Yeast and the occurrence of the first amino group which increases the electronic density of the other nitro group. The nitro compounds can be easier biocatalytically reduced if withdrawing groups are contained in the aromatic rings(3).

The observed regiospecificity enables us to explore in the near future the Bakers' Yeast mediated reductions of the other possible dinitro-dibenzofurans of the type $C_{12}H_6O(NO_2)_2$.

Conclusion

The biocatalytic reduction of 3-nitro-dibenzofuran 2 and 3,8-dinitro-dibenzofuran 4 is an alternative and new synthetic procedure. The main advantages of biocatalytic reduction are the mild conditions and the selectivity. From 3,8 - dinitro - dibenzofuran 4 we obtained only 3-amino-8-nitro-dibenzofuran 5.

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