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SYNTHESIS AND REDUCTION OF SOME NITRO-BENZOFURANS

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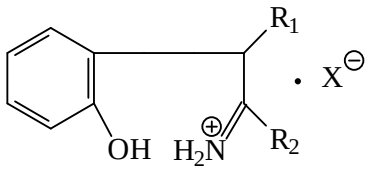
ABSTRACT. During the acid catalysis the o- and p-(nitrophenyl)-acetophenoxymes ***1a-e*** undergo a transposition-cyclisation to 2-phenyl-5-nitrobenzofurans and 2 phenyl-7-methyl-benzofurans ***2a-e***. The reduction of ***2a-k*** was made using the Bechamp method. The synthetised structures were characterized with the ^{1}H-NMR, IR and MS-Spectrometry.

INTRODUCTION

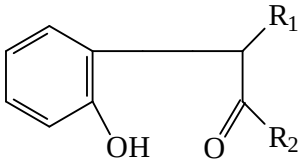
In a previous work [1] was related the synthesis of some o-(nitrophenyl)-acetofenoxymes from the corresponding ketooxymes and o-, p-nitro-clorbenzene.

In literature is presented the transpozition of these o-arylketooxymes followed by cyclisation which gives the corresponding nitro-benzofurans [2-5] like in the Fischer's indol synthesis. The reactions undergoes in acid catalysis in boiling anhydrous ethanol as medium in presence of gasous HCl or in glacial acetic acid at 100^0 in presence of etherated BF_3 [2].

Morandi and Dupont [5-6], proposed a cyclisation mechanism for aryl-oxymes analogue with the Fischer transposition. This mechanism was confirmed by isolation of the ammonium salts of ***4*** as hydrochlorides [5] or hydrobromides [7] or the ketoform ***5*** obtained from hydrolysis of ***4*** in mild conditions [7].



4 X= Cl, Br;



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Scheme 1

In this paper we present the synthesis of 2-phenyl-7-nitrobenzofuran and 2-phenyl-3-methyl-5-nitrobenzofuran.

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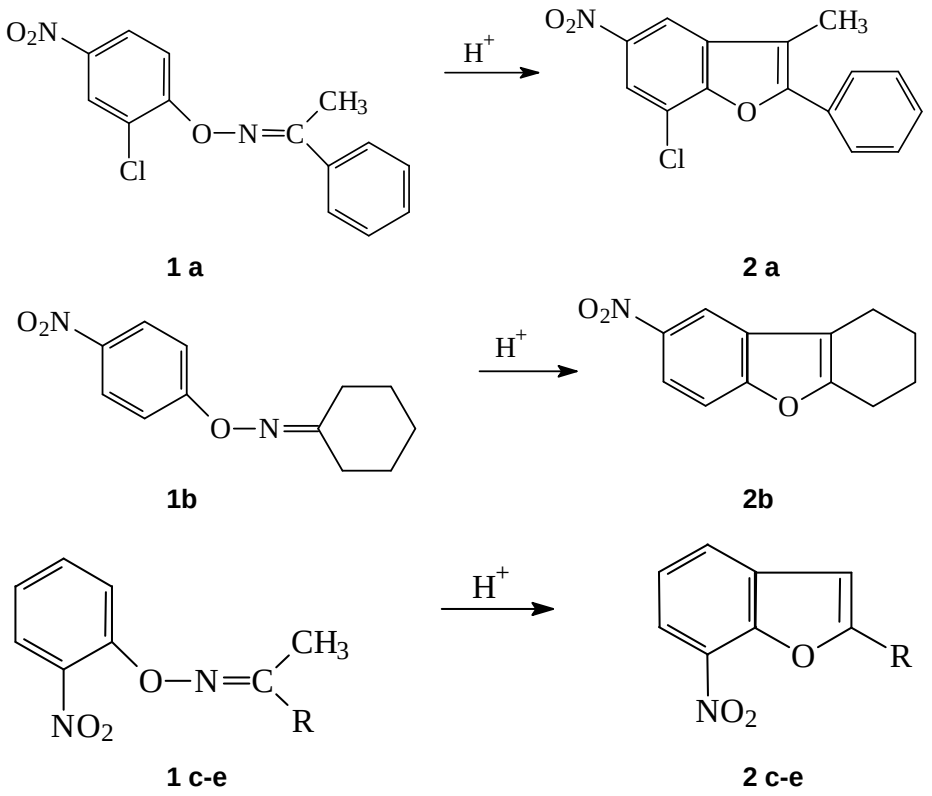


c) R = Ph ; d) R = 4-CH_3-O-Ph; e) R = 4-Cl-Ph

Scheme 2

EXPERIMENTAL

Reagents and solvents were standard grade comercial products and were used without further purification. The substances ***2f-k*** were prepared as in [8].

The elemental analysis for C, H,N and halogenes were within +/- 0,4% of the theoretical values for ***1 a-e*** and ***2 a-k***. Melting points are uncorrected and for ***2a-k*** are given for the chlorohydrates. The reactions were monitored by TLC using benzene:ethylacetate 8:2 (v:v) as eluent, visualisation was made with a 260 nm wave lenght UV source.

The mass spectra were recorded on double focusing Varian Mat 311 spectrometer, with an electronic impact source at 70 eV and 300 μA. ^{1}H-NMR spectra were recorded using $CDCl_3$ as solvent with a Varian Gemini 300 MHz Spectrometer. For the recording of IR spectra, a FT-IR Nicolet 205 spectrophotometer, in KBr pellets was used.

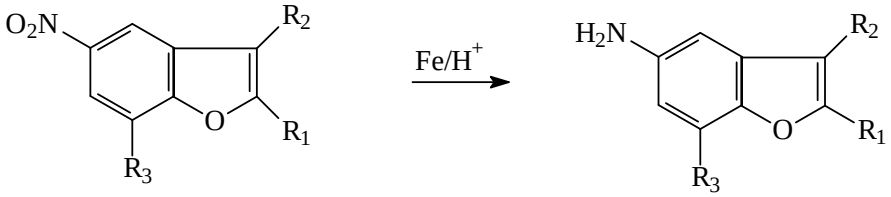
General method for synthesis of benzofurans from aryloxymes

0,1 Molls of ortho or para-nitro-aryloxyme was dissolved in 200 ml ethanol. The solution was refluxed and in this time dryed gasous HCl was barboted in the reaction mass. In case for a good solubilisation it was added 50-100 ml toluene. The heating was continued until the whole quantity of oxyme was transformed (the reaction was monitored by TLC). After that, the solvent was evaporated in vaquo, and the precipitate was washed with water and purified by recrystalization from glacial acetic acid.

General method for reduction

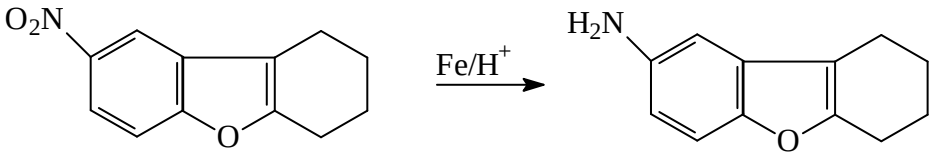
0,05 Molls nitro-benzofuran was suspended in 60 ml water and was added 15 g. $AlCl_3$ and 5 g NaCl. After that, to the suspension was added 50 ml toluene, 3 ml HCl 36% and 8 g powder iron. The mixture was stirred at 100^0C, 5 - 8 hours. The product was extracted with benzene, mass reaction was filtered, the organic layer was separated and concentrated in vaquo. The formed amino-benzofuran was recrystalised from ethanol.

For the reduction of nitrobenzofurans we used Bechamp method.

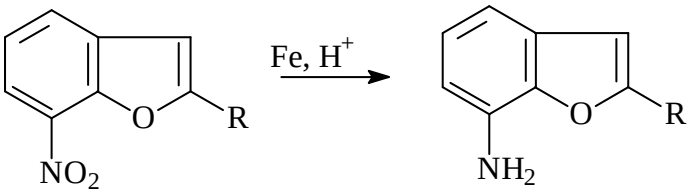


2 a-g **3 a-g**

a) $R_1 = CH_3$, $R_2 = H$, $R_3 = H$
f) $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = H$
g) R_1 = 4-SO_2Et-Ph, $R_2 = H$, R_3 =H
h) R_1 = 4-Br-Ph, $R_2 = H$, R_3 =H
i) R_1 = 4-Cl-Ph, $R_2 = H$, R_3 =H
j) R_1 = Ph, R_2 =CH_3, R_3 =Cl
k) R_1 = 4-F-Ph, $R_2 = H$, R_3 =H



2 b **3 b**



2 c-e **3 c-e**

c) R = Ph; d) R = 4-CH_3O-Ph; e) R = 4-Cl-Ph;

Scheme 3

RESULTS AND DISCUSSION

2-phenyl-3-methyl-7-chloro-5-nitro-benzofuran ***2a***: yield = 73% yellow crystals, m. p.= 173^{0}C. IR spectrum (KBr) ν_{max} cm^{-1}: 1570(C=C), 1380, 1490(NO_2), Mass spectrum: m/e (rel.intensity, %): 273(33) M, 275(10) M, 229(5), 227(16), 199(90), 163(100). ^{1}H-NMR spectrum ($CDCl_3$): 2.50(s, 3H), 7.52- 7.87(m, 5H), 8.33(s, 1H), 8.64(s, 1H).

8-nitro-1, 2, 3, 4- tetrahidro-dibenzofuran ***2b***: yield = 68% yellow crystals, m.p.= 157^{0}C. IR spectrum (KBr) ν_{max} cm^{-1}: 1600(c=c), 1370, 1480(NO_2), Mass spectrum: m/e (rel.intensity, %): 217(70) M, 202(5), 189(100), 171(15). ^{1}H-NMR spectrum ($CDCl_3$): 1.88-1.97(d.d.,4H), 2.73(d,4H), 7.45(d,1H), 8.14(d,1H), 8.33(s,1H).

2-phenyl-7-nitro-benzofuran ***2c***: yield = 65%, yellow crystals, m.p.= 133^{0}C, IR spectrum (KBr) ν_{max} cm^{-1}: 1580(C=C), 1380, 1470(NO_2); Mass spectrum: m/e (rel.intensity, %): 239(43) M, 223(2), 209(3), 193(18), 165(100); ^{1}H-NMR spectrum ($CDCl_3$): 7.13(s,1H), 7.33-7.98(m,7H), 8.12(d, 1H).

2-(4-methoxy-phenyl)-7-nitro-benzofuran ***2d***: yield = 69%, yellow crystals, m.p.= 113^{0}C, IR spectrum (KBr) ν_{max} cm^{-1}:1580(C=C), 1350, 1470(NO_2); Mass spectrum: m/e (rel.intensity, %): 269(38) M, 254(8), 223(35), 208(10),195(40), 152(100); ^{1}H-NMR spectrum (DMSO d_6): 3.82(s,3H), 7.12(d,2H), 7.46(s,1H), 7.49(m,1H), 7.92(d,2H), 8.06(d,1H), 8.12(s,1H).

2-(4-chloro-phenyl)-7-nitro-benzofuran ***2e***: yield = 57%, yellow crystals, m.p.= 133^{0}C, IR spectrum (KBr) ν_{max} cm^{-1}:1600(C=C), 1370, 1480(NO_2); Mass spectrum: m/e (rel.intensity, %): 273(33) M, 275(10)M, 216(3), 21490),180(100); ^{1}H-NMR spectrum ($CDCl_3$): 7.12(s,1H), 7.34-7.48(m,4H), 7.88(d,2H), 8.13(d,1H).

2-(4-chloro-phenyl)-5-amino-benzofuran ***3a***: yield = 56%, white crystals, m.p.= 183^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1650, 3240, 3420(NH_2); Mass spectrum: m/e (rel.intensity, %): 243(100)M, 245(33)M, 216(2), 214(6), 180(20); ^{1}H-NMR spectrum (DMSO d_6):4.73(NH_2), 6.61(d,1H), 6.72(s,1H), 7.25(s,1H), 7.29(d,1H), 7.85(d,1H)

8- *amino-1,2,3,4-tetrahydro-dibenzofuran* ***3b***: yield = 59%, white crystals, m.p.= 225^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1650, 3280, 3430(NH_2); Mass spectrum: m/e (rel.intensity, %): 180(100)M, 153(23), 125(50); ^{1}H-NMR spectrum (DMSO d_6): 188-197(d.d.,4H), 2.73(d,4H), 7.45(d,1H), 8.14(d,1H), 8.33(s,1H)

2-phenyl-7-amino-benzofuran ***3c***: yield = 60%, white crystals, m.p.= 182^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1640, 3190, 3300(NH_2); Mass spectrum: m/e (rel. intensity, %): 209(100)M, 182(7), 180(29), 152(8); ^{1}H-NMR spectrum (DMSO d_6): 5.40(NH_2), 6.57(d,1H), 6.80-7.98(m,9H)

2-(4-methoxy-phenyl)-7-amino-benzofuran ***3d***: yield = 55%, white crystals, m.p.= 263^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1650, 3380, 3450(NH_2); ^{1}H-NMR spectrum (DMSO d_6): 3.82(s,3H), 5.30(NH_2), 6.77-6.94(m,3H), 7.06(d,2H), 7.13(s,1H), 7.89(d,2H)

2-(4-chloro-phenyl)-7-amino-benzofuran ***3e***: yield = 55%, white crystals, m.p.= 193^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1630, 3360, 3430(NH_2); Mass spectrum: m/e (rel.intensity, %): 243(100)M, 245(33)M, 216(3), 214(9), 180(20); ^{1}H-NMR spectrum (DMSO d_6): 3.94(NH_2), 7.13-7.44(m,3H), 7.56(s,1H), 7.62(d,2H), 8.00(d,2H)

2,3-dimethyl-5-amino-benzofuran ***3f***: yield = 60%, white crystals, m.p.= 220^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1620, 3200, 3400(NH_2); ^{1}H-NMR spectrum (DMSO d_6): 2.38(s,3H), 2.52(s,3H), 3.98(NH_2), 7.18(d,1H), 7.41(s,1H), 7.53(d,1H)

2-(4-sulpho-ethyl-phenyl)-5-amino-benzofuran ***3g***: yield = 55%, white crystals, m.p.= 193^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1630, 3350, 3450(NH_2); Mass spectrum: m/e (rel.intensity, %): 239(100)M, 224(46), 212(8), 197(3), 196(13)

2-(4-bromo-phenyl)-5-amino-benzofuran ***3h***: yield = 58%, white crystals, m.p.= 192^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1640, 3350, 3420(NH_2); Mass spectrum: m/e (rel. intensity, %):285(100)M, 287(100)M, 260(8), 258(8), 209(11), 180(30); ^{1}H-NMR spectrum (DMSO d_6): 4.93(NH_2), 6.63(d,1H), 6.75(s,1H), 7.21(d,2H), 7.63(d, 1H), 7.84(d,2H)

2-methyl-5- amino-benzofuran ***3i***: yield = 52%, white crystals, m.p.= 220^{0}C, IR spectrum (KBr) ν_{max} cm^{-1}: 1620, 3400, 3550(NH_2); ^{1}H-NMR spectrum ($CDCl_3$): 2.48(s,3H), 4.21(NH_2), 6.73(s,1H), 7.19(d,1H), 7.40(s,1H), 7.53(d,1H)

2-phenyl-3-methyl-7-chloro-5-amino-benzofuran ***3j***: yield = 60%, white crystals, m.p.= 274^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1630, 3210, 3330, 3440(NH_2); ^{1}H-NMR spectrum (DMSO d_6): 2.50(s,3H), 5.14(NH_2), 6.66-7.77(m,7H)

2-(4-fluoro-phenyl)-5-amino-benzofuran ***3k***: yield = 51%, white crystals, m.p.= 243^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1650, 3300, 3460(NH_2); Mass spectrum: m/e (rel.intensity, %): 227(100)M, 210(2), 209(2), 200(15),170(8); ^{1}H-NMR spectrum (DMSO d_6): 4.89(NH_2), 6.59(d,1H), 6.72(s,1H), 7.17(s,1H), 7.26(d,1H), 7.32(d.1H), 7.87(d,2H), 7.89(d,2H).

The IR, MS and ^{1}H-NMR spectra and the elementhal analysis confirmed the structures of compounds ***2a-e*** and ***3a-k***.

The nitroderivatives ***2a-e*** have very strong bands at 1350 - 1380 and 1540-1560 cm^{-1}, characteristic for the nitro group which are not observed in the spectra of ***3a-k***; in that case at 1640-1680 and 3200-3400 cm^{-1} there appeared the tipical bands of amino-group. Molecular peaks for ***2a-e*** and ***3a-k*** are clear, the characteristic peaks for nitro (M-46) and amino-aromatic compounds (M-27) were observed. In case of ^{1}H-NMR spectra for ***3a-k*** which appeared in domenium δ= 6.4 - 7.8 ppm confirmed the presence of the amino-group at the phenylic ring and the disparition of the nitro group (in this case signals are appeared between δ=7-8.6).

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