STUDIA UNIVERSITATIS BABEŞ-BOLYAI, CHEMIA, XLIII, 1-2, 1998

FURYL-BENZOTHIAZOLES. SYNTHESIS AND REACTIVITY

FL. D. IRIMIE, CS. PAIZS, C.CHENDER, FR. JOO, R. SILAGHI-DUMITRESCU[1], CORNELIA MAJDIK, MONICA TOŞA

ABSTRACT. Synthesis of some new furyl-benzothiazoles is presented. Formilation of these structures is possible when in position 6 of the benzothiazolic ring contained no vidrawing groups.

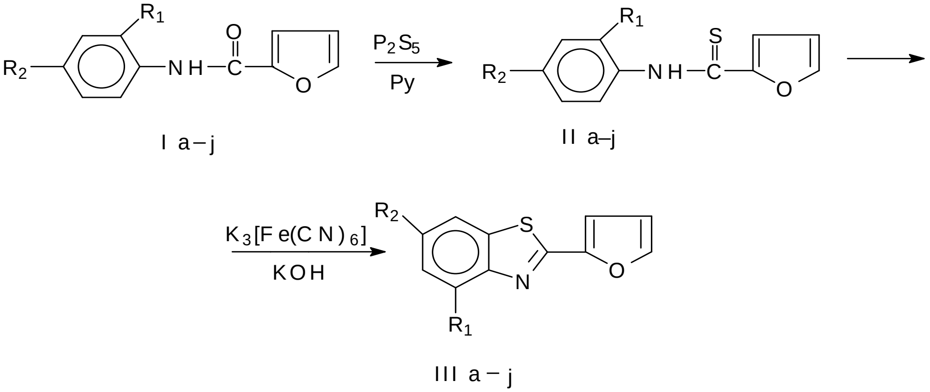
Reduction of these aldehydes with $NaBH_4$ is a convenient method for obtained corresponding hydroxymethyl derivatives.

INTRODUCTION

As a part of our research in the furan series the synthesis of some new 2-furyl-2-benzothyazoles its became necesarely for biological tests on bactericidal and bacteriostatic activity. It's well known that furyl-benzothiazolical structures have an antifungical activity [1] and its also known that the position of substituents at the benzenic ring have an influence on this biological activity [2].

In order to evaluate the biological behaviour of structures substituted in pozition 5 on the furan ring we formilated some of these structures and reduced them to the corresponding hydroxymethyl derivatives.

The 2-furyl-2-benzothiazoles were obtained from the corresponding tiofuranilides using the Jacobson method by oxidations with $K_3[Fe(CN)_6]$ in aqueous medium [3]. Tiofurananilides were obtained from furanilides using phosphorus pentasulphide (Scheme 1).



Scheme 1

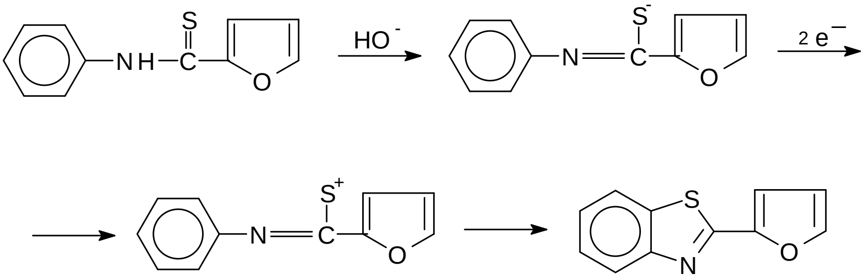
a: R_1 =H, R_2 = H f: R_1 =H, R_2 = CH_3

---

[1] *"Babeş-Bolyai" University, Faculty of Chemistry and Chemical Engineering, 11 Arany Janos St., 3400 Cluj-Napoca, Romania.*

b: R_1 =H, R_2 = F
c: R_1 =H, R_2 = Cl
d: R_1 = H, R_2 =Br
e: R_1 =H, R_2 = I
g: R_1 =H, R_2 = OCH_3
h: R_1 =CH_3, R_2 = H
i: R_1 =Br , R_2 = H
j: R_1 =I , R_2 = H

The mechanism of cyclisation presented in Scheme 2 was proposed by Metzger and Plank [4]. The anion appeared in basic medium, was oxidized to sulphurous cation.



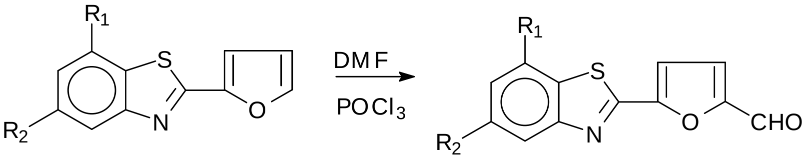
Scheme 2

The yield of cyclisation depends directly on the electron density in benzene ring (Tab.1):

Table 1

Structures	Yield %
I a	71
I b	22
I c	37
I d	61
I e	63
I f	74
I g	90
I h	72
I i	60
I j	63

The Vilsmeyer-Haack formilation of some of structures III is give in scheme 3:



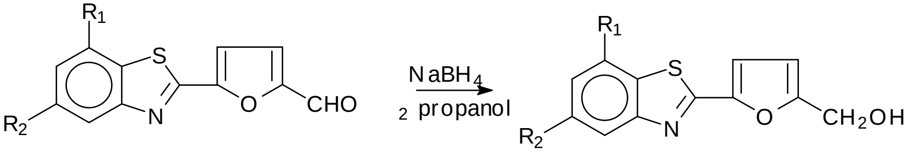
III IV

Scheme 3

a: R_1 = H, R_2 = H

d: R_1 = H, R_2 = Br
f: R_1 = H, R_2 = CH_3
g: R_1 = H, R_2 = OCH_3

The reducing of the formyl derivatives with $NaBH_4$ in 2- propanol is presented in scheme 4:



IV V

Scheme 4

a: R_1 = H, R_2 = H
d: R_1 = H, R_2 = Br
f: R_1 = H, R_2 = CH_3
g: R_1 = H, R_2 = OCH_3

EXPERIMENTAL

The elemental analysis for C, H, S, N and halogen were within +/- 0,4% of the theoretical values for III a-j, IV a, d, f, g, and V a, d, f, g. Melting points are given uncorrected. The reactions were monitored by TLC using benzene:ethylacetate 8:2 (v:v) as eluent, visualisation was made with an 260 nm wave light UV source.

The mass spectra were recorded on double focusing Varian Mat 311 spectrophotometer, 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.

Structures I a,d,f,i were prepared as in (5) and structures IV a,d,f as in [6].

General procedure for tionation: 0,003 mols of furanilide is dissolved in 50 ml boiling pyridine and its added 17,8 g (0,08 mols) fine pulvered small portions. Then the mass reaction is boiled 90 min. and after cooling its treated with 250 ml HCl (1:1). The precipitate is filtered, wash with cold water and treated with 250 ml 20% KOH solution and heated to 50 ^{0}C. The suspension is treated with active carbon, filtered, and after that solution is acidifiated with HCl (1:1) v:v. The precipitate is filtered, dryed and its recristalized from an ethanol: water mixture (3:1) v:v.

General procedure for cyclization: 0,005 mols of thioanilide is dizolved in 20 ml 40% KOH solution. To the solution is added 60 ml water and its warmed to 40-45^{0}C. To this solution is added 20 ml 20% $K_3[Fe(CN)_6]$ solution which is previously warmed to 40-45^{0}C. After 12 hrs. the precipitate is filtered, dryed and recrystalized from methanol.

General procedure for formilation: To a mixture of 3 ml ice-cooled dimethylformamide and 1 ml phosphorous oxychloride a solution of 0,5 g of furanilide is dropwire add. The mixture is warmed at 100^{0}C for 2 hrs. and then poured on 50 g ice. The pH is adjusted at 6 with a solution of sodium acetate (10 g in 15 ml water) is add allowed to stand at room temperature for a few hours. The precipitate is filtered, wash with water and recristalized from glacial acetic acid.

General procedure for reduction: 0,1 g $NaBH_4$ is add to seven ml isopropanol. The mixture is stirred for 1,5 hours, while adding the formyl-derivative (0,2 g) in small amounts. The solution is alowed to stand over night, then diluate HCl is add until no more gas evolution is observe. The organic compounds are extract with $CHCl_3$ (five times), then the solvent is evaporate affording the hydroxyl-derivative which is wash with isopropanol.

RESULTS AND DISCUSSION

2-furyl-2-(6-fluoro-benzothiazole) (III b) m.p.=113^{0}C; IR(cm^{-1}): 1610, 1580, 1450 (for benzothiazole ring); ^{1}H-NMR spectrum (DMSO d_6): 6.8 (q, 1H), 7.23 (d, 1H), 7.60(d,1H), 7.93 (d, 1H), 8.13(d,1H), 8.43(s, 1H); MS (m/e): 219(100)M, 220(13)M+1, 221(12) M+2, 218(9) M-1, 191(46)M-CO, 164(30), 126(26)

2-furyl-2-(6-chloro-benzothiazole) (III c) m.p.=119^{0}C; IR(cm^{-1}): 1605, 1575, 1450 (for benzothiazole ring); ^{1}H-NMR spectrum (DMSO d_6): 6.8 (q, 1H), 7.21 (d, 1H), 7.57(d,1H), 7.98 (d, 1H), 8.02(d,1H), 8.3(s, 1H); MS (m/e) 235(100)M, 237(37)M, 207(60), 209(20) M-CO, 172(20), 145(12)

2-furyl-2-(6-iodo-benzothiazole) (III e) m.p.=124^{0}C; IR(cm^{-1}): 1600, 1575, 1430; ^{1}H-NMR spectrum (DMSO d_6): 6.75 (q, 1H), 7.3 (d, 1H), 7.5(d,1H), 7.6 (d, 1H), 7.93(d,1H), 8.01(s,1H); MS (m/e): 313(30)M, 283(13) M-CO, 220(3), 95(100)

2-furyl-2-(4-methyl-benzothiazole) (III f) m.p.= 107^{0}C, IR(cm^{-1}): 1590, 1560, 1430 (for benzothiazole ring); ^{1}H-NMR spectrum (DMSO d_6): 2.63 (s, 3H), 6.77 (q, 1H), 7.34-7.99(m,5H) ; MS (m/e) 215(100)M, 287(29)M-CO, 154(30), 121(41)

2-furyl-2-(chloro-benzothiazole) (III i) m.p.=129^{0}C; IR(cm^{-1}): 1605, 1580, 1450 (for benzothiazole ring); ^{1}H-NMR spectrum (DMSO d_6): 6.8 (q, 1H), 7.43(m, 2H), 7.62(d,1H), 8.02(d,2H); MS (m/e) 235(100)M, 237(37)M, 207(60), 209(20) M-CO, 172(20), 145(12)

2-furyl-2-(4-iodo-benzothiazole) (III j) m.p.=131^{0}C, IR(cm^{-1}): 1600, 1570, 1440; ^{1}H-NMR spectrum (DMSO d_6): 6.8 (q, 1H), 7.16 - 8.15(m,5H); MS (m/e): 323(30)M, 283(13) M-CO, 220(3), 95(100).

5-[2](6-methoxi-benzothiazolil)]-furyl-2-carboxaldehyde (IV g) m.p.=137^{0}C, IR(cm^{-1}): 1680 (CHO); ^{1}H-NMR spectrum (DMSO d$_6$): 3.57(s.3H), 7.19(d,1H), 7.5(d,1H), 7.75(d,1H), 7.80(s,1H), 7.99(d,1H); MS (m/e): 259(100)M, 244(80), 216(43)M-CH_3-CO, 159(29), 95(34)

2-hydroxymethyl-5-(2-benzothiazole)-furan (V a): yield = 73%, white crystals, m.p.=178^{0}C; IR spectrum (KBr)ν_{max}cm^{-1}: 1050, 3400 (OH). MS: m/e (rel.intensity, %): 231 (100 M$^+$, 232(11) M$^+$+1, 233 (6) M$^+$+2, 230 (8) M$^+$-1, 214 (56) M$^+$-17, 202 (53), 168 (32); ^{1}H-NMR spectrum ($CDCl_3$): 4.62 2H (s), 6.60 1H (d), 7.29 1H (d), 7.3-8.2 4Har (m)

2-hydroxymethyl-5-[6-methyl-(2-benzothiazole)]-furan (V b): yield = 78%, white crystals, m.p.=181^{0}C; IR spectrum (KBr) n$_{max}$: 1050, 3400 (OH). MS: m/e (rel.intensity, %): 245 (100)M$^+$, 246 (10) M$^+$+1, 247 (8)M$^+$+2, 244 (9)M$^+$-1, 228 (54)M$^+$-17, 216 (32), 200 (19); ^{1}H-NMR spectrum ($CDCl_3$): 2.49 3H (s), 4.73 2H (s), 6.60 1H (d), 7.15 1H (d), 7.2-8.1 3Har (m)

2-hydroxymethyl-5-[6-methoxy-(2-benzothiazole)]-furan (V c): yield = 75%, collorlenes crystals, m.p.=184^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1050, 3400 (OH); MS: m/e (rel.intensity, %): 261 (100) M$^+$, 262 (26) M$^+$+1, 263 (11) M$^+$+2, 260 (11) M$^+$-1, 246 (20), 245 (9), 244 (46) M$^+$-17, 232 (15); ^{1}H-NMR spectrum ($CDCl_3$): 3.90 3H (s), 4.73 2H (s), 6.67 1H (d), 7.18 1H (d), 7.2-7.9 3Har (m)

2-hydroxymethyl-5-[6-bromo-(2-benzothiazole)]-furan (V d): yield = 81%, white crystals m.p.=211^{0}C; IR spectrum (KBr) ν_{max} cm^{-1}: 1050, 3300 (OH). MS: m/e (rel.intensity, %): 311(100) M, 309(20)M, 313(4) M+2, 308(93)M-1, 294(23)M-17, 293(8)M-17, 292(30), 214(17), 212(16), 185(10), 184(2);^{1}H-NMR spectrum ($CDCl_3$): 4.75 2H (s), 6.65 1H (d), 7.23 1H (d), 7.4-8.3 3Har (m).

The yield of oxidative cyclisation of tiofuranilides with $K_3[Fe(CN)_6]$ depends of the behaviour of the substituent at the phenylic ring. In case of vidrawing groups the yield decrease because the electrophylic substitution is concured by hydrolyse of thioanilide to anilide.

Molecular peaks for ***IV a-h*** and ***V a-d*** are clear, the characteristic peaks for fragmentation of the benzilic type alcoholic group (M-17) were observed in case of ***V a-h*** and the characteristic peaks of aldehydes (M-28) in case of ***IV a-h*** are observed too.

For the structures ***V a-d*** the presence of the singlet at δ = 4,6 corresponding for two protons, indicated the existence of the methylenic group. At the same time the signals for the aldehydical protons at δ = 9,60 which are characteristic the compounds ***IV a-h*** are not observed in case of ***V a-d***.

CONCLUSIONS

Oxidative cyclisation with $K_3[Fe(CN)_6]$ in KOH aq. medium is a convenient method for furyl-benzothiazole synthesis.

Formilation of these structures is possible when in position 6 of the benzothiazolic ring contained no vidrawing groups. Reduction of these aldehydes with $NaBH_4$ is a convenient method for obtained corresponding hydroxymethyl derivatives.

The advantage of reduction with $NaBH_4$ is the mild conditions, good yields and the symplicity of the method.

REFERENCES

1. V. Fărcăşan, F. Paiu, *Studia Universitatis Babeş-Bolyai. Chemia*, 1966, ***11***, 107.
2. Gh. Miron, Gh. Ripeanu, *Comunicările Acad. RPR*, 1961, ***11***, 241.
3. P. Jacobson, *Ber. dtsch. chem. Ges.,* 1886, ***19***, 1067.
4. J. Metzger, H. Plank, *Chemie et Industrie*, 1956, **75**, 929
5. V. Fărcăşan, I. Meşter, *Studia Universitatis Babeş-Bolyai. Chemia*, 1967, ***2***, 69.
6. V. Fărcăşan, F. Paiu, *Studia Universitatis Babeş-Bolyai. Chemia*, 1971, ***16***, 111.