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NOVEL FURAN DERIVATIVES FROM 1-(4-CHLOROPHENYL)-3-(FURAN-2-YL)PROP-2-EN-1-ONE THROUGH ADDITION AND RING CLOSURE REACTIONS

BY

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Abstract. Starting from a furan-containing chalcone analogue, a series of furan derivatives have been prepared. Addition of 4-chlorothiophenol to this chalcone analogue afforded the corresponding β-arylmercapto ketone, which has been subsequently reduced to the β-arylmercapto alcohol. The Stetter reaction of chalcone analogue with benzaldehyde and thiophene-2-carboxaldehyde gave two hitherto unknown butane-1,4-diones. Hydrazine and phenylhydrazine converted the chalcone analogue into the expected pyrazolines.

Keywords: chalcone; thia-Michael addition; Stetter reaction; pyrazoline.

1. Introduction

Furan and its benzo- and heterocyle-fused derivatives, along with their partially or fully reduced analogues, are widespread structural motifs within the realm of natural compounds (Boto and Alvarez, 2011). In addition, furan is one of the privileged scaffolds in biologically active compounds, as shown by the significant number of drugs containing this heterocycle (Banerjee *et al*., 2012) and also by the large number of drug discovery-related papers reporting novel

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furan-containing compounds. Furthermore, owing to its relatively reduced aromaticity among monoaromatic five-membered heterocycles, the furan ring may easily undergo not only aromatic substitutions but also cycloadditions or ring opening reactions, which makes furan derivatives valuable synthons for the construction of complex, otherwise difficult to obtain polycyclic or acyclic structures, respectively (Lipshutz, 1986). In continuation of our previous work on the chemistry of heterocyclic chalcone analogues (Roman, 2015; Roman, 2016), the present study explores the derivatization of a furan-containing α,β-unsaturated ketone, employed as substrate in Michael additions and ring closure reactions for the synthesis of several hitherto unknown furan derivatives either useful as intermediates or having potential biological activities.

2. Experimental

Melting points were taken on a Mel-Temp II apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400-MHz spectrometer. The signals owing to residual protons in the deuterated solvents were used as internal standards for the ^{1}H NMR spectra. The chemical shifts for the carbon atoms are given relative to deuteriochloroform (δ = 77.16 ppm) and d_6-dimethyl sulfoxide (δ = 39.52 ppm). The chemical reagents and solvents were obtained from Sigma–Aldrich or Merck, and were used without prior purification.

1-(4-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3**. To a solution of 4-chloroacetophenone **1** (6.18 g, 40 mmol) and furan-2-carboxaldehyde **2** (3.84 g, 40 mmol) in 96% ethanol (16 mL) was added 10% NaOH (5 drops), and the mixture was stirred at room temperature for 5 h. The separated solid was filtered, washed with hexanes and air-dried. Recrystallization from a mixture of 2-propanol–*n*-hexane (1:1, v/v) afforded yellow needles (7.07 g, 76%), mp 77–78°C (lit. mp 77–78 °C (Zhao *et al*., 2013); 72–74°C (Zheng *et al*., 2011)); ^{1}H NMR ($CDCl_3$, 400 MHz): *ó* 6.52 (dd, *J* = 2.0 and 3.2 Hz, 1H), 6.73 (d, *J* = 3.2 Hz, 1H), 7.40 (d, *J* = 15.2 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 0.8 Hz, 1H), 7.59 (d, *J* = 15.2 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): *ó* 112.9, 116.7, 118.9, 129.1, 130.0, 131.2, 136.6, 139.3, 145.2, 151.7, 188.6.

(±)-3-(4-Chlorophenylthio)-1-(4-chlorophenyl)-3-(furan-2-yl)propan-1-one **4**. A mixture of 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3** (697.5 mg, 3 mmol), 4-chlorothiophenol (433.5 mg, 3 mmol) and triethylamine (5 drops) in 96% ethanol (10 mL) was heated at reflux temperature for 2 h. The mixture was refrigerated overnight, then the separated solid was filtered, air-dried and recrystallized from ethanol to give colorless crystals (815 mg, 72%), mp 79–80 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.49 (dd, *J* = 6.4 and 17.2 Hz, 1H), 3.63 (dd, *J* = 7.6 and 17.2 Hz, 1H), 4.91 (t, *J* = 7.0 Hz, 1H), 6.00 (d, *J* = 3.2 Hz, 1H), 6.23 (dd, *J* = 2.0 and 2.8 Hz, 1H), 7.23 (s, 4H), 7.32 (d, *J* = 1.2 Hz,

1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 41.9, 42.0, 107.8, 110.5, 129.1, 129.2, 129.7, 131.7, 134.6, 134.9, 135.5, 140.1, 142.2, 152.9, 195.2.

rac-3-(4-Chlorophenylthio)-1-(4-chlorophenyl)-3-(furan-2-yl)propan-1-ol **5**. A solution of 3-(4-chlorophenylthio)-1-(4-chlorophenyl)-3-(furan-2-yl)propan-1-one **4** (603 mg, 1.6 mmol) in abs. methanol (20 mL) was gradually treated with $NaBH_4$ (182.4 mg, 4.8 mmol). The mixture was stirred at room temperature overnight (17 h), and then solvent was removed under reduced pressure. The semi-solid residue was partitioned between ethyl acetate (20 mL) and water (20 mL). The organic phase was washed with water (10 mL) and brine (10 mL), and it was dried over anhyd. Na_2SO_4. The solvent was removed under reduced pressure to give a colorless oil (570 mg, 94%), R_f 0.27 (ethyl acetate–*n*-hexane 1:9, v/v); major diastereomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89 (br s, 1H, OH), 2.08–2.18 (m, 1H, -CH_2-), 2.31–2.42 (m, 1H, -CH_2-), 4.30 (dd, *J* = 6.4 Hz and 8.8 Hz, 1H, >CH-S-Ar), 4.98 (dd, *J* = 4.8 and 8.8 Hz, 1H, >CH-OH), 5.92 (d, *J* = 3.2 Hz, 1H, H-3 in furan), 6.24 (dd, *J* = 1.6 and 3.2 Hz, 1H, H-4 in furan), 7.11–7.40 (m, 9H); minor diastereomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89 (br s, 1H, OH), 2.25–2.32 (m, 2H, -CH_2-), 4.39 (dd, *J* = 6.4 and 8.8 Hz, 1H, >CH-S-Ar), 4.64 (dd, *J* = 5.2 and 8.4 Hz, 1H, >CH-OH), 6.00 (d, *J* = 3.2 Hz, 1H, H-3 in furan), 6.27 (dd, *J* = 2.0 and 3.2 Hz, 1H, H-4 in furan), 7.11–7.40 (m, 9H); both diastereomers: ^{13}C NMR ($CDCl_3$, 100 MHz): δ 42.1 (-$CH_{2\text{-major}}$), 42.7 (-$CH_{2\text{-minor}}$), 43.7 (>CH-S-Ar_{major}), 43.8 (>CH-S-Ar_{minor}), 71.1 (>CH-OH_{major}), 71.6 (>CH-OH_{minor}), 107.6 (furan C-3_{major}), 108.2 (furan C-3_{minor}), 110.4 (furan C-4_{major}), 110.5 (furan C-4_{minor}), 127.3, 127.4, 128.8, 128.9, 129.0, 129.1, 131.6, 131.8, 133.6, 133.7, 134.3, 134.4, 135.1, 135.3, 142.2 (furan C-5_{major}), 142.3 (furan C-5_{minor}), 142.4, 142.5, 153.1 (furan C-1_{minor}), 153.9 (furan C-1_{major}).

4-(4-Chlorophenyl)-2-(furan-2-yl)-1-phenylbutane-1,4-dione **6**. A mixture of 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3** (697.5 mg, 3 mmol), benzaldehyde (318 mg, 3 mmol), 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (171 mg, 0.6 mmol) and triethylamine (182 mg, 1.8 mmol) in 2-propanol (9 mL) was heated at reflux temperature overnight (17 h). The mixture was allowed to reach room temperature before it was refrigerated, the separated solid was filtered, air-dried and recrystallized from ethanol to give colorless crystals (477 mg, 47%), mp 118–119 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.39 (dd, *J* = 3.6 and 18.0 Hz, 1H), 4.16 (dd, *J* = 10.0 and 18.0 Hz, 1H), 5.45 (dd, *J* = 4.0 and 10.0 Hz, 1H), 6.15 (d, *J* = 3.2 Hz, 1H), 6.28 (dd, *J* = 2.0 and 3.2 Hz, 1H), 7.33 (d, *J* = 1.2 Hz, 1H) 7.41–7.50 (m, 4H), 7.51–7.58 (m, 1H), 7.94 (d, *J* = 8.8 Hz, 2H) 8.03–8.10 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 40.6, 42.3, 107.7, 110.9, 128.7, 129.0, 129.1, 129.7, 133.4, 134.8, 136.2, 140.0, 142.5, 151.4, 196.3, 196.6.

4-(4-Chlorophenyl)-2-(furan-2-yl)-1-(thiophen-2-yl)butane-1,4-dione **7**. This compound was obtained through the procedure described for the synthesis

of dione **6**, but replacing benzaldehyde with thiophene-2-carboxaldehyde (336 mg, 3 mmol). Colorless crystals (630 mg, 61%), mp 124–125 °C (ethanol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.37 (dd, J = 4.0 and 18.0 Hz, 1H), 4.14 (dd, J = 10.0 and 18.0 Hz, 1H), 5.27 (dd, J = 4.0 and 10.0 Hz, 1H), 6.23 (d, J = 3.2 Hz, 1H), 6.31 (dd, J = 2.0 and 3.2 Hz, 1H), 7.13 (dd, J = 4.0 and 4.8 Hz, 1H), 7.34 (d, J = 1.6 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.64 (dd, J = 0.8 and 4.8 Hz, 1H), 7.90 (dd, J = 0.8 and 4.0 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 40.1, 43.6, 107.7, 111.0, 128.3, 129.1, 129.7, 133.3, 134.3, 134.7, 140.0, 142.5, 143.1, 151.4, 189.0, 196.4.

3-(4-Chlorophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole **8**. A mixture of 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3** (465 mg, 2 mmol) and hydrazine hydrate (400 mg, 8 mmol) in 96% ethanol (4 mL) was heated at reflux temperature for 2 h. The solvent was removed under reduced pressure to give a colorless residue which was triturated with water (30 mL), filtered and air-dried. The solid was dissolved in warm 2-propanol (5 mL), the solution was cooled to room temperature and gradually diluted with hexanes (15 mL) under efficient stirring. The mixture was refrigerated to afford yellow crystals (266 mg, 54%), mp 76–78 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.24 (dd, J = 7.6 and 16.4 Hz, 1H), 3.35 (dd, J = 10.4 and 16.0 Hz, 1H), 5.00 (dd, J = 8.0 and 10.4 Hz, 1H), 5.02 (br s, 1H), 6.25 (d, J = 3.2 Hz, 1H), 6.32 (dd, J = 1.6 and 3.2 Hz, 1H), 7.32–7.39 (m, 3H), 7.61 (d, J = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 37.6, 57.4, 106.3, 110.5, 127.5, 128.9, 131.2, 134.9, 142.6, 151.2, 154.5.

3-(4-Chlorophenyl)-5-(furan-2-yl)-1-phenyl-4,5-dihydropyrazole **7**. A mixture of 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3** (465 mg, 2 mmol) and phenylhydrazine (238 mg, 2.2 mmol) in glacial acetic acid (5 mL) was heated at reflux temperature for 2 h. The mixture was allowed to cool to room temperature, and it was gradually diluted with water (40 mL) to give an emulsion which turned into a solid over the weekend. The solid was filtered, washed thoroughly with water and air-dried. Recrystallization from 2-propanol gave grey crystals (368 mg, 57%), mp 128–129 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.34 (dd, J = 7.2 and 17.2 Hz, 1H), 3.66 (dd, J = 12.4 and 17.6 Hz, 1H), 5.36 (dd, J = 6.8 and 12.4 Hz, 1H), 6.23 (d, J = 3.2 Hz, 1H), 6.30 (dd, J = 1.6 and 3.2 Hz, 1H), 6.82–6.90 (m, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.20–7.29 (m, 2H), 7.32–7.40 (m, 3H), 7.66 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 40.1, 58.4, 107.3, 110.6, 113.9, 119.9, 127.1, 128.9, 129.1, 131.3, 134.6, 142.4, 144.9, 146.3, 153.5.

3. Results and Discussions

Michael additions are the prominent feature of the chemistry of chalcones, their heteroaromatic analogues and other similar α,β-unsaturated systems (Dhar, 1981). Addition of carbon- and heteroatom-centered nucleophiles to the β-carbon in enones have been known to produce quite a few

structurally diverse classes of compounds, and recent developments of asymmetric variants have resulted in numerous efficient and highly enantioselective protocols for the preparation of chiral Michael adducts from these α,β-unsaturated systems (Almaşi *et al.*, 2007). Because furans are useful substrates in aminomethylations (Roman, 2013), a furan-containing chalcone analogue, namely 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3**, was synthesized through the Claisen-Schmidt condensation of 4-chloroacetophenone **1** with furan-2-carboxaldehyde **2**, with the view to serve as starting material in subsequent reactions leading to novel furan derivatives through Michael additions (Fig. 1). Chalcone analogue **3** has been previously reported in the literature, but only its ^{1}H NMR spectrum has been given so far (Zhao *et al.*, 2013; Zheng *et al.*, 2011); its ^{13}C NMR spectrum, which is reported for the first time in this paper, completes the NMR characterization of this heterochalcone.

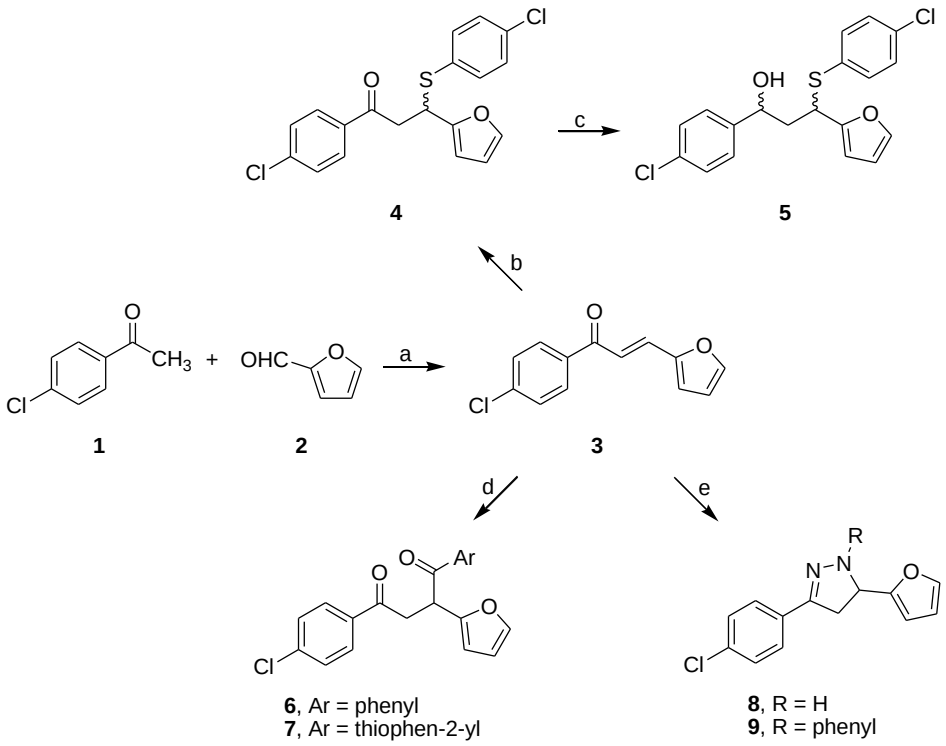

Fig. 1 – Synthesis and reactions of 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one **3**. a – ethanol, NaOH, rt, 5 h; b – 4-chlorothiophenol, TEA, ethanol, reflux, 2 h; c – $NaBH_4$, abs. methanol, rt, overnight; d – benzaldehyde (for **6**) or thiophene-2-carboxaldehyde (for **7**), 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride, 2-propanol, reflux, overnight; e – hydrazine hydrate, ethanol, reflux 2 h (for **8**), or phenylhydrazine, acetic acid, reflux, 2 h (for **9**).

Because the thia-Michael addition of thiophenols and mercaptoacetic acid to α,β-unsaturated ketones (including several furan-substituted analogues) has been recently used to synthesize a large number of β-thia-substituted ketones having good antimicrobial activity (Ceylan *et al.*, 2011; Karaman *et al.*, 2012; Gezegen *et al.*, 2012), the addition of 4-chlorothiophenol to chalcone analogue **3** was investigated first. Enone **3** was reacted with the aforementioned thiol in ethanol at reflux temperature in the presence of catalytic amounts of triethylamine (TEA), and adduct **4** separates upon refrigeration of the reaction mixture and is easily isolated through filtration (Fig. 1). The good yields recorded for this method are comparable to those reported for other synthetic approaches, while avoiding the use of catalysts such iodine (Karaman *et al.*, 2012), which is more expensive than TEA, or potassium *tert*-butoxide (Ceylan *et al.*, 2011), whose hygroscopic nature renders its handling more difficult than that of TEA. In the absence of a catalyst capable of inducing enantioselectivity, the thia-Michael addition of 4-chlorothiophenol to chalcone analogue **3** occurs with the formation of the racemate of **4**. Its proton spectrum presents the signals of the diastereotopic protons of the methylene group as a typical AB system consisting of two doublets of doublets, whereas the proton of the methine group appears as a triplet due to the superimposition of the two doublets. In addition, the ^{13}C NMR spectrum of compound **4** features two peaks at approximately 42 ppm; these signals correspond to the sp^3 carbon atoms formally derived from the sp^2 carbon atoms involved in the carbon-carbon double bond in starting chalcone analogue **3** following the thia-Michael addition.

In addition to the interesting biological activities, thia-adducts of type **4** could act as substrates in chemical transformations. For example, the reduction of the carbonyl function in β-arylmercapto ketones affords the corresponding β-arylmercapto alcohols, which are useful intermediates in the preparation of 2,4-diarylthiochromanes (Skarżewski *et al.*, 2003; Guha *et al.*, 2012). In one study, an optically pure (+)-(*R*)-thia-adduct underwent reduction of the carbonyl function with lithium aluminum hydride in anh. diethyl ether to give good yields of the corresponding (3*R*)-1,3-diphenyl-3-phenylsulfanylpropan-1-ol as a 1:1 mixture of diastereomers; the use of $NaBH_4$ as reducing agent has been reported to be ineffective (Skarżewski *et al.*, 2002). Nonetheless, a series of 1,3-diaryl-3-phenylsulfanylpropan-1-ols have been reported to arise from the hydrogenation of racemic β-arylmercapto ketones using $NaBH_4$ as reducing agent in abs. methanol, and the diastereomeric ratio for one of these compounds was evaluated by ^{1}H NMR and found to be 1:1 as well (Guha *et al.*, 2012). In our case, conversion of racemic thia-adduct **4** into the related β-arylmercapto alcohol **5** (Fig. 1) using a threefold molar excess of $NaBH_4$ as reducing agent in abs. methanol at room temperature overnight gave a mixture containing two diastereomers in an approximate relative ratio of 2:1 as the major contributors, and they were accompanied by traces (less than 3%) of at least another diastereomer, as shown by NMR. The presence of these two main diastereomers

is evidenced in the ^{1}H NMR spectra of compound **5** by the two distinct sets of signals in the aliphatic region corresponding to the protons in the propyl moiety, and also by the two sets of signals around 6 ppm attributed to two of the protons in the furan ring. On the other hand, the signals for the protons in the *para*-chlorophenyl and 4-chlorophenylthio moieties of both diastereomers of **5** are superimposed on a very short range (0.3 ppm), and can not be clearly distinguished from one another (see Experimental). In addition, two sets of adjacent (yet well-defined) peaks can be assigned in the ^{13}C NMR spectrum of **5** to the carbon atoms in the propyl bridge and to two of the carbon atoms in the furan ring. Adjacent but discernable sets of peaks are also present in the aromatic region of the spectrum for the other aromatic carbon atoms, thus confirming the presence of two diastereomers of **5**. The inseparable mixture was further examined using two-dimensional NMR spectroscopy with a view to assign more accurately the signals corresponding to the protons and carbon atoms in the propyl bridge and the furan ring in both these diastereomers. Although the signal corresponding to the protons of a particular diastereomer are usually distinguishable owing to their different integration values, the COSY experiment revealed that the signals for the protons of the methylene group in the major diastereomer are clearly separated, whereas in the case of the minor diastereomer, they coalesced. Also, the COSY experiment allowed the identification of the signals for H-5 in furan as doublets (J = 1.2 ppm) at 7.36 ppm and 7.38 ppm for the major and the minor diastereomer, respectively. The HMQC experiment showed that peaks at approximately 42 ppm correspond to the carbon atom of the methylene group in the diastereomers of **5**, a fact further substantiated by the DEPT experiment. Also, the peaks at approximately 43 ppm correlate with the signals in the 4.3–4.4 ppm range, whereas the peaks at approximately 71 ppm correlate with the signals centered at 4.64 ppm and 4.98 ppm (see Experimental). As for the furan ring, correlations in the COSY experiment have been observed between the signals of H-3 and peaks at approximately 107 and 108 ppm, and between the signals of H-4 and the peaks near 110 ppm. The HMBC experiment proved that the chemical shift values for C-5 are of approximately 142 ppm (tertiary carbon atoms according to the DEPT experiment), while those for C-1 are in the 153–154 ppm range (quaternary carbon atoms according to the DEPT experiment; see Experimental for details).

The Stetter reaction is an example of a Michael-type 1,4-addition of a carbon-centered nucleophile to an enone system. The Stetter reaction provides easy access in one step to 1,4-dicarbonyl compounds, which are valuable synthons for the preparation of monoheteroatomic five-membered heterocycles having significant and diverse biological activities (Kamal *et al*., 2013; Battilocchio *et al*., 2013; Diana *et al*., 2007; Hall *et al*., 2007; Mortensen *et al*., 2001). In addition, furan-substituted pyrrol-1-ylacetic acids have been recently reported compounds with significant activity against *Mycobacterium smegmatis*

and *M. tuberculosis* strain H37Rv while having low cytotoxicity against HEK-293T cell line, but their potency strongly depends with the position of the substituents on pyrrole ring (Pagadala *et al*., 2014). This study employed only a limited number of butane-1,4-diones substituted either with a single furan moiety at position 1 or with two furan moieties at position 1 and 2 as starting materials for the synthesis if the target compounds, but no butane-1,4-dione substituted with a single furan ring at position 2 was used for the generation of pyrrol-1-ylacetic acids. The synthesis of such butane-1,4-diones substituted with a furan ring at position 2 is reported herein, using the furan-containing chalcone analogue **3** and either benzaldehyde or thiophene-2-carboxaldehyde as reagents in the Stetter reaction (Fig. 1). Satisfactory yields of desired diones **6** and **7** were obtained when 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (0.2 equivalents) was employed as catalyst. The products separated from the reaction mixture upon cooling and were purified through recrystallization from ethanol. The proton spectra of diones **6** and **7** presented as their typical feature three doublets of doublets corresponding to the protons in the butane-1,4-dione moiety (Roman, 2015), whereas the carbon atoms in the aforementioned moiety have been assigned the two peaks in the aliphatic region of the ^{13}C NMR spectra and the two peaks at approximately 190 ppm. The spectra also allowed the identification of all the other signals for the aromatic protons and carbon atoms in the structure of diones **6** and **7**.

Treatment of chalcone and its analogues with hydrazine or its derivatives leads to 3,5-diarylpyrazolines (Dhar, 1981), which exhibit anti-inflammatory, analgesic, antimicrobial, anticancer or antidepressant activity (Alex and Kumar, 2014; Marella *et al*., 2013; Secci *et al*., 2012). Reaction of chalcone analogue **3** with excess of hydrazine in refluxing ethanol afforded the expected 1-unsubstituted pyrazoline **8** as a colorless solid after work-up. The solid is oxygen-sensitive, as it slowly turned yellow, and, over time, it became dark brown and agglomerated even after it was purified by recrystallization. The compound is also acid-sensitive, and its colour changed in solutions at low pH (*e.g.*, in $CDCl_3$) even faster than in solid state. The NMR analysis of the freshly recrystallized solid confirmed its structure and purity. The diastereotopic protons of the methylene group in **8** could be differentiated through their coupling constant (J_{trans} = 7.6 Hz; J_{cis} = 10.4 Hz) as well as their chemical shift (the resonance of the proton at C-4 occurs at higher field in *trans* pyrazolines than in *cis* pyrazolines (Hassmo and Michelson, 1962)). The proton at N-1 was assigned the broad singlet visible underneath the doublet of doublet associated with the proton at C-5. The presence of two peaks in the aliphatic region of ^{13}C NMR spectrum of **8** corroborated the formation of pyrazoline through ring closure of the initially formed α,β-unsaturated hydrazone. In order to obtain pyrazoline **9** substituted at N-1, chalcone analogue **3** was reacted with phenylhydrazine in glacial acetic acid. Previous studies have established that the reaction of furan-containing chalcone analogues often leads to resins when

conducted at low pH for long periods of time, and that the course of the reaction depends heavily on the nature of the aromatic substituents in the chalcone analogue (Lavrushin *et al*, 1965). In the case of chalcone analogue **3**, the corresponding pyrazoline **9** was isolated in moderate yield from the reaction mixture. Its structure was confirmed through the identification of the three doublets of doublets corresponding in the proton NMR spectrum to the protons at C-4 and C-5, and the presence of two peaks in the aliphatic region of the ^{13}C NMR spectrum corresponding to C-4 and C-5.

4. Conclusions

A small collection comprising several furans have been obtained from 1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one, a furan-containg chalcone analogue, through several selected chemical modifications. The aforementioned substrate easily undergoes a thia-Michael addition to give a β-arylmercapto ketone, which was subsequently reduced to the related β-arylmercapto alcohol – a well-known starting material in the preparation of 2,4-diarylthiochromans. The ratio of the two major diastereomers of the β-arylmercapto alcohol, as well as their structural assignments, has been established by the NMR analysis of their mixture. Addition of aromatic aldehydes to the furan-containg chalcone analogue under the conditions of the Stetter reaction afforded two novel butane-1,4-diones as potential intermediates in synthesis of monoheteroaromatic five-membered heterocycles. In addition, ring closure with hydrazine derivatives converted the starting chalcone analogue into furan-substituted pyrazolines.

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NOI DERIVAŢI DE FURAN DIN 1-(4-CLORFENIL)-3-(FURAN-2-IL)PROP-2-EN-1-ONĂ PRIN REACŢII DE ADIŢIE ŞI CICLIZARE

(Rezumat)

O serie de derivaţi de furan au fost preparaţi pornind de la un analog de calconă care conţine un nucleu furanic. Adiţia 4-clortiofenolului la acest analog de calconă a condus la β-arilmercapto cetona corespunzătoare, care a fost ulterior redusă la β-arilmercapto alcool. Reacţia Stetter a analogului de calconă cu benzaldehida şi tiofen-2-carboxaldehida a dat două noi 1,4-butandione. Hidrazina şi fenilhidrazina au transformat analogul de calconă în pirazolinele dorite.