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Synthesis, DPPH and ABTS Activity of Novel Furfuryl-Chalcone Derivatives

Fatih SÖNMEZ *[1], Enes AKGÜN[2], Zuhal ŞAHİN[1]

Abstract

In this study, novel furfuryl-chalcone derivatives substituted sulfonyl chloride or sulphonamide were synthesized. Their antioxidant properties were investigated via DPPH and ABTS assays. All furfuryl-chalcones had high antioxidant properties. Among them, (E)-5-(3-(4-(chlorosulfonyl)-3-hydroxyphenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4e) and (E)-5-(3-(3-(chlorosulfonyl)-4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4d) exhibited the highest DPPH activity with the IC_{50} values of 4.23 µM and 6.68 µM, respectively, which are almost 2- and 1.5-fold more than quercetin activity (IC_{50} = 8.69 µM), well-known as antioxidant agent and used as a standard. Also, 4e and 4d had the highest ABTS activity with the IC_{50} value of 5.55 µM and 7.84 µM, respectively, which are almost 2.8- and 2-fold higher than that of quercetin (IC_{50} = 15.49 µM). The structure-activity relationship results revealed that most of synthesized sulfonyl chloride derivatives (4a-e) have higher antioxidant activity than the sulphonamide derivatives (5a-c) and also 4d and 4e, including hydroxyl group, exhibited the strongest antioxidant activity as expected.

Keywords: Antioxidant activity, chalcone, furan

1. INTRODUCTION

Oxidative stress, which is one of the factors that cause many common diseases such as diabetes, cancer and aging, arises from the imbalance between the antioxidant defence system of the cell and reactive oxygen species (ROS) [1, 2]. While low levels of ROS show biological effects such as a defence mechanism against pathogenic microorganisms and intercellular communication, high concentrations of ROS cause damage to DNA, lipids and proteins, and even cell death [3, 4]. Therefore, the ROS level in the body should be kept at the right rate. To maintain this ratio, the antioxidant system is activated to reduce free radical toxicity [5].

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However, exceeding the antioxidant defence system capacity and excessive presence of superoxide radical result in the formation of ROS [6]. In these cases, the use of natural or synthetic antioxidants may be necessary. Antioxidants act an active role in the prevention of many diseases by catching free radicals in the living body [7, 8]. Therefore, the design and synthesis of effective new antioxidants continue to be the focus of interest for scientists.

It is known that chalcones (1,3-diphenyl-2-propen-1-one) have two aromatic rings linked by α,β unsaturated carbonyl system [9]. Natural and synthetic chalcones have widespread biological activity [10-12]. In particular, they have the potential to be developed as pioneer molecules for the discovery of antioxidant and anti-cancer agents [13]. In the researches, it has been determined that the α,β unsaturated carbonyl system acts a key role in the versatile biological activities of chalcones, and the elimination or deterioration of this structural feature causes loss of their bioactivities [14, 15]. Without disturbing this α,β unsaturated carbonyl system, new bioactive chalcone analogues can be synthesized by modifications to both phenyl rings [16]. Heteroaryl chalcones are obtained by modifications of phenyl rings [17]. Several studies have shown that heteroaryl chalcones have widespread biological potential such as anti-fungal, antibacterial, antimalarial, anticancer, anti-inflammatory, anti-angiogenic and anti-HIVactivities [18-20].

In this study, eight novel furfuryl-chalcones were synthesized as heteroarylchalcone derivatives and their heterocyclic and/or phenyl rings were modified by attaching of sulfonylchloride and sulfonamide moiety. Their DPPH and ABTS activities were evaluated as antioxidant property.

2. MATERIALS AND METHODS

The used solvents and chemicals were bought from Sigma-Aldrich. Varian Infinity Plus spectrometer were used for ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) analysis. Leco CHNS-932 instrument and BioTek Power Wave XS were used for the elemental analyses and antioxidant assay, respectively.

2.1. Synthetic Procedures and Spectral Data

Synthesis of furfuryl-chalcone derivatives (3a-e): 1.5 mmol of 2-furfuraldehyde (1) and 1 mmol of acetophenone derivatives (2a-e) were dissolved in 30 mL of ethanol. 5 mL of 10% aqueous NaOH was added. The mixture was stirred for 5 hours at 25 ^{o}C and the mixture was poured onto 100 mL of ice water acidified with 5 mL of 2 M HCl. The obtained precipitates were filtered and washed with cold water. The solids were dried in vacuum oven.

(E)-3-(furan-2-yl)-1-(p-tolyl)prop-2-en-1-one (3a): Yellow powder, 92% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 2.43 (3H, s), 6.50 (1H, s), 6.70 (1H, s), 7.28 (2H, d, J= 7.6 Hz), 7.41-7.61 (3H, m), 7.94 (2H, d, J= 7.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 21.9, 112.9, 116.3, 119.5, 128.8, 129.5, 130.6, 135.7, 143.9, 145.0, 151.9, 189.6.

(E)-3-(furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (3b): Cream powder, 96% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 3.87 (3H, s), 6.50 (1H, s), 6.68 (1H, s), 6.96 (2H, d, J= 8.2 Hz), 7.43-7.60 (3H, m), 8.04 (2H, d, J= 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 55.7, 112.9, 114.0, 116.2, 119.3, 130.2, 131.0, 131.2, 145.0, 152.0, 163.6, 188.3.

(E)-1-(4-chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one (3c): Yellow powder, 95% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 6.50-6.52 (1H, dd, J_1= 2.0 Hz, J_2= 3.2 Hz), 6.73 (1H, d, J= 3.2 Hz), 7.40 (1H, d, J= 15.2 Hz), 7.45 (2H, d,

J= 8.5 Hz), 7.53 (1H, s), 7.59 (1H, d, J= 15.2 Hz), 7.97 (2H, d, J= 8.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 113.0, 117.0, 118.8, 129.1, 130.0, 131.3, 136.6, 139.4, 145.4, 151.7, 188.7.

(E)-3-(furan-2-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one (3d): Cream powder, 88% yield. ^{1}H NMR ($CDCl_3$+DMSO-$_{d6}$, 300 MHz) δ/ppm: 6.28 (1H, t, J= 1.7 Hz), 6.47 (1H, d, J= 3.2 Hz), 6.67 (2H, d, J= 7.9 Hz), 7.20 (1H, d, J= 15.5 Hz), 7.25-7.31 (2H, m), 7.70 (2H, d, J= 8.2 Hz); ^{13}C NMR ($CDCl_3$+DMSO-$_{d6}$, 75 MHz) δ/ppm: 112.7, 115.6, 115.7, 119.3, 129.6, 129.7, 130.9, 144.8, 151.7, 162.3, 187.9.

(E)-3-(furan-2-yl)-1-(3-hydroxyphenyl)prop-2-en-1-one (3e): Cream powder, 90% yield. $_{1}$H NMR ($CDCl_3$, 300 MHz) δ/ppm: 6.50-6.52 (1H, dd, J_1= 2.6 Hz, J_2= 7.9 Hz), 7.36 (1H, t, J= 7.6 Hz), 7.46 (1H, d, J= 15.5 Hz), 7.50-7.60 (3H, m), 7.72 (1H, t, J= 2.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 113.0, 115.3, 117.1, 119.3, 120.7, 121.2, 130.1, 131.4, 139.6, 145.4, 151.8, 156.7, 190.4.

Synthesis of furfurylchalcone-sulfonylchloride derivatives (4a-e): 1 mmol of furfuryl-chalcone derivatives (3a-e) was placed in the reaction flask in an ice bath and 5 mL of chlorosulfonic acid was added and stirred at 25 ºC for 15 hours. Then, the mixture was poured dropwise onto 100 g of ice and stirred until the ice melted. The precipitates were filtered and washed with cold water. The solids were dried in vacuum oven.

(E)-5-(3-oxo-3-(p-tolyl)prop-1-en-1-yl)furan-2-sulfonyl chloride (4a): Brown powder, 77% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 2,39 (3H, s), 6.75 (1H, d, J= 3.5 Hz), 7.19-7.29 (3H, m), 7.50 (1H, d, J= 15.5 Hz), 7.68 (1H, d, J= 15.5 Hz), 7.91 (2H, d, J= 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 22.0, 115.3, 120.8, 125.6, 127.9, 129.1, 129.8, 134.8, 145.0, 150.1, 156.7, 188.3. Anal. Calcd. for $C_{14}H_{11}ClO_4S$: C, 54.11; H, 3.57; found: C, 54.18; H, 3.52.

(E)-5-(3-(3-(chlorosulfonyl)-4-methoxyphenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4b): Brown powder, 82% yield, ^{1}H NMR ($CDCl_3$+DMSO-d_6, 300 MHz) δ/ppm: 3.86 (3H, s), 6.75 (1H, d, J= 3.8 Hz), 7.05 (1H, d, J= 8.8 Hz), 7.14 (1H, d, J= 3.8 Hz), 7.33 (1H, d, J= 15.5 Hz), 7.42 (1H, d, J= 15.5 Hz), 8.14-8.17 (1H, dd, J_1= 2.4 Hz, J_2= 8.8 Hz), 8.29 (1H, d, J= 2.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 57.6, 113.6, 116.1, 120.6, 123.8, 129.4, 129.8, 131.0, 132.3, 137.7, 150.6, 156.0, 161.0, 185.4. Anal. Calcd. for $C_{14}H_{10}Cl_2O_7S_2$: C, 39.54; H, 2.37; found: C, 39.12; H, 2.22.

(E)-5-(3-(4-chlorophenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4c): Brown powder, 95% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 6.83 (1H, d, J= 3.2 Hz), 7.36 (1H, d, J= 3.0 Hz), 7.51 (2H, d, J= 7.6 Hz), 7.59 (1H, d, J= 15.6 Hz), 7.70 (1H, d, J= 7.6 Hz), 8.01 (2H, d, J= 7.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 115.7, 120.7, 124.8, 128.7, 129.5, 130.3, 135.6, 140.4, 150.4, 156.3, 187.6. Anal. Calcd. for $C_{13}H_8Cl_2O_4S$: C, 47.15; H, 2.44; found: C, 46.98; H, 2.47.

(E)-5-(3-(3-(chlorosulfonyl)-4-hydroxyphenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4d): Black powder, 62% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 6.90 (1H, d, J= 3.8 Hz), 7.29 (1H, d, J= 8.8 Hz), 7.37 (1H, d, J= 3.8 Hz), 7.66 (2H, s), 8.33-8.36 (1H, dd, J_1= 2.0 Hz, J_2= 7.0 Hz), 8.57 (1H, d, J= 2.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 116.3, 119.9, 120.7, 123.6, 128.9, 129.6, 129.7, 130.1, 138.0, 150.6, 155.9, 158.5, 185.3. Anal. Calcd. for $C_{13}H_8Cl_2O_7S_2$: C, 37.97; H, 1.96; found: C, 37.91; H, 2.02.

(E)-5-(3-(4-(chlorosulfonyl)-3-hydroxyphenyl)-3-oxoprop-1-en-1-yl)furan-2-sulfonyl chloride (4e): Black powder, 62% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 4.22 (1H, br, OH), 6.85 (1H, d, J= 3.8 Hz), 7.13-7.17 (1H, m), 7.36 (1H, d, J= 3.8 Hz), 7.42 (1H, t, J= 7.6 Hz), 7.54-7.68 (2H, m), 7.71 (1H, d, J= 15.5

Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 115.3, 115.7, 120.7, 121.5 (x2), 125.3, 128.6, 130.5, 138.6, 150.3, 156.3, 156.7, 189.1. Anal. Calcd. for $C_{13}H_8Cl_2O_7S_2$: C, 37.97; H, 1.96; found: C, 38.02; H, 1.92.

Synthesis of furfurylchalcone-sulfonamide derivatives (5a-e): 1 mmol of furfurylchalcone-sulfonylchloride derivatives (4a-e) were dissolved in 20 mL of ethanol and 15 mL ethanolic solution of methylamine was added dropwise to it in ice bath and was stirred at 25 ^{o}C for 2 hours. The mixture was evaporated under vacuum. The solid products were washed with chloroform (15 mL), filtered and dried in vacuum oven.

(E)-N-methyl-5-(3-oxo-3-(p-tolyl)prop-1-en-1-yl)furan-2-sulfonamide (5a): Brown powder, 90% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 2.38 (3H, s), 2.74 (3H, s), 6.71 (1H, d, J= 3.3 Hz), 7.07 (1H, d, J= 3.3 Hz), 7.26 (2H, d, J= 7.9 Hz), 7.50 (1H, d, J= 15.5 Hz), 7.56 (2H, d, J= 15.5 Hz), 7.90 (2H, d, J= 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 21.9, 29.5, 115.6, 118.6, 123.1, 129.0, 129.1, 129.7, 135.0, 144.6, 148.8, 154.8, 189.0. Anal. Calcd. for $C_{15}H_{15}NO_4S$: C, C, 59.00; H, 4.95; N, 4.59; found: C, 59.42; H, 4.75; N, 4.81.

(E)-5-(3-(4-methoxy-3-(N-methylsulfamoyl)phenyl)-3-oxoprop-1-en-1-yl)-N-methylfuran-2-sulfonamide (5b): Dark brown powder, 84% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 2.58 (3H, d, J= 5.2 Hz), 2.72 (3H, s), 4.00 (3H, s), 5.07 (1H, q, J= 5.2 Hz, NH), 5.35 (1H, br, NH), 6.72 (1H, d, J= 3.5 Hz), 7.07 (1H, d, J= 3.5 Hz), 7.10 (1H, d, J= 8.8 Hz), 7.53 (2H, s), 8.22-8.24 (1H, dd, J_1= 2.3 Hz, J_2= 8.8 Hz), 8.50 (1H, d, J= 2.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 29.5, 29.8, 57.2, 112.6, 116.3, 118.9, 122.0, 126.4, 129.9, 130.6, 131.7, 135.8, 149.0, 154.6, 160.0, 186.6. Anal. Calcd. for $C_{16}H_{18}N_2O_7S_2$: C, 46.37; H, 4.38; N, 6.76; found: C, 46.58; H, 4.14; N, 6.52.

(E)-5-(3-(4-chlorophenyl)-3-oxoprop-1-en-1-yl)-N-methylfuran-2-sulfonamide (5c): Brown powder, 73% yield, ^{1}H NMR ($CDCl_3$, 300 MHz) δ/ppm: 2.80 (3H, d, J= 5.0 Hz), 4.89 (1H, q, J= 5.2 Hz, NH), 6.77 (1H, d, J=3.5 Hz), 7.12 (1H, d, J= 3.5 Hz), 7.48 (2H, d, J= 8.5 Hz), 7.55 (2H, s), 7.98 (2H, d, J= 8.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ/ppm: 29.6, 116.0, 118.8, 122.5, 129.3, 129.7, 130.2, 135.9, 140.1, 148.9, 154.6, 188.0. Anal. Calcd. for $C_{14}H_{12}ClNO_4S$: C, 51.62; H, 3.71; N, 4.30; found: C, 51.12; H, 3.97; N, 4.72.

(E)-5-(3-(4-hydroxy-3-(N-methylsulfamoyl) phenyl)-3-oxoprop-1-en-1-yl)-N-methylfuran-2-sulfonamide (5d) and (E)-5-(3-(3-hydroxy-4-(N-methylsulfamoyl)phenyl)-3-oxoprop-1-en-1-yl)-N-methylfuran-2-sulfonamide (5e): Black crude products could not be purified.

2.2. Antioxidant Activity

1,1-diphenyl-2-picrylhydrazyl free radical was used for DPPH assay according to literature [21]. 2, 5, 10 and 20 μL from 1000 μM stock solutions of the compounds were taken. Their volumes were completed to 40 μL with ethanol and then 160 μL of 0.1 mM 1,1-diphenyl-2-picrylhydrazyl solution was added. The absorbance values of the prepared solutions were measured at 517 nm after 30 minutes of incubation in the dark at room temperature. Inhibition values (%) of the compounds were calculated from the obtained absorbance values.

2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid diammonium salt) solution was used for ABTS assay according to the literature [22]. This solution was kept in the dark for 24 hours at room temperature and used for the experiment after the absorbance of the solution was fixed to ~ 0.70 at 734 nm by dilution. The solutions of the compounds were prepared in 4 different concentrations (10, 50, 100 and 250 μM) of DMSO and added to a flat-bottomed 96-

well plate. The ABTS solution was added and incubated for 15 min at room temperature in the dark, and the absorbance was measured at 734 nm. Inhibition values (%) of the compounds were calculated from the obtained absorbance values.

3. RESULTS AND DISCUSSIONS

The synthesis route is shown in Figure 1. The furfuryl-chalcones were obtained by reacting 2-furfuraldehyde (1) with various acetophenones (2a-e) in alcoholic bases known as Claisen-Smith condensation. The furfuryl-chalcones (3a-e) were treated with excess chlorosulfonic acid to obtain sulfonyl chloride derivatives (4a and 4c, Figure 2). In this step for compounds 4b, 4d, and 4e (R_1 was methoxy or hydroxyl, which are strong electron donating groups), two sulfonyl chlorides were attached both heteroaryl ring and phenyl ring.

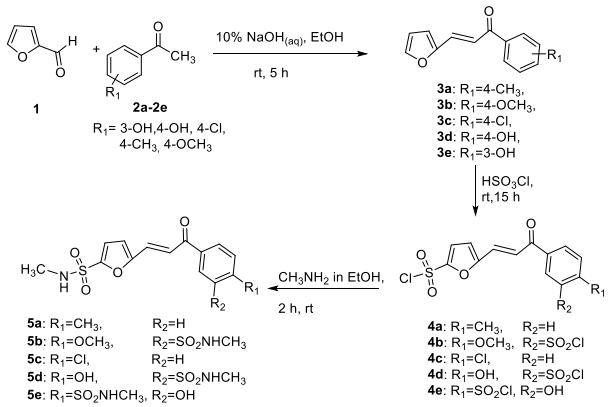

Figure 1 Synthesis of furfuryl-chalcone derivatives

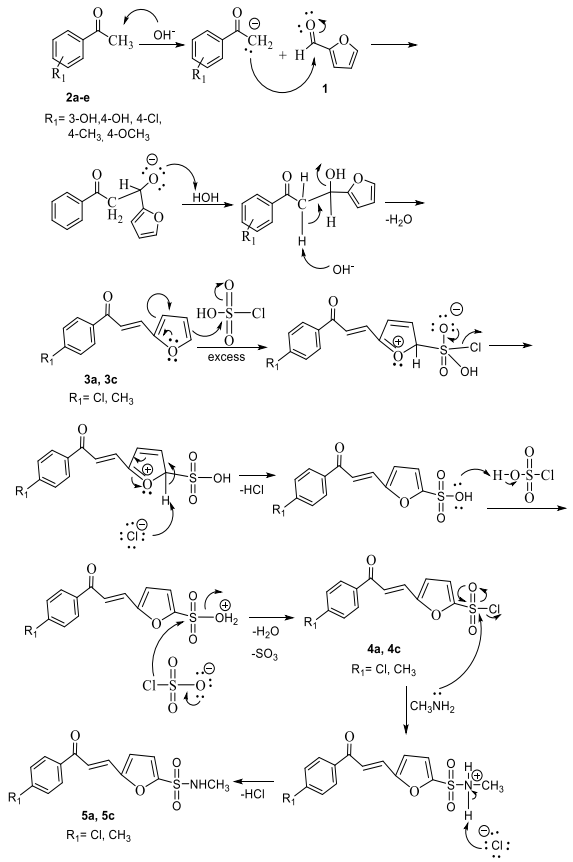

Figure 2 Mechanism of compounds 5a and 5c having one sulphonamide moiety

These compounds were treated with small amount of chlorosulfonic acid for binding sulfonyl chloride to only heteroaryl ring; however, compounds 4b, 4d, and 4e, (having two sulfonyl chloride groups) were obtained again. These results indicated that the reaction mechanism occurred through simultaneous sulfonation of both rings. The estimated mechanism is depicted in Figure 3. 4a-e was reacted with the methylamine in EtOH solution at 25 ^{o}C for 2h to give sulphonamide derivatives. In this step, compounds 5d and 5e were obtained as black sticky gel-like crude products in low yields and they could not be purified.

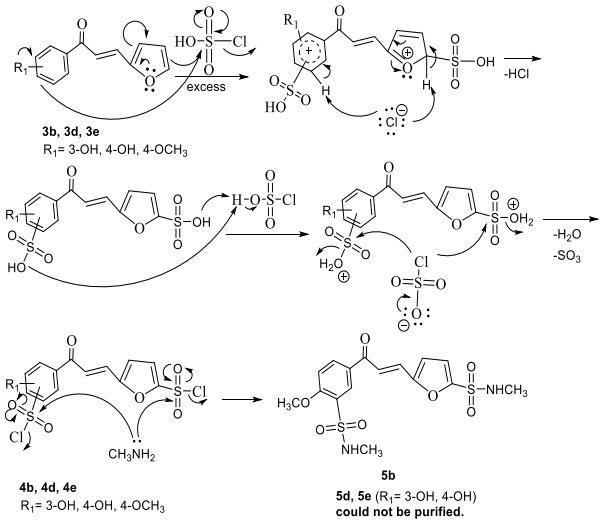

Figure 3 Mechanism of compounds 5b having two sulphonamide moieties

All synthesized compounds had the antioxidant futures. The IC_{50} values of them were between 4.23 μM and 106.51 μM in DPPH assay, while they were between 5.55 μM and 111.44 μM in ABTS assay.

Among them, 4e and 4d exhibited the strongest DPPH activity with the IC_{50} value of 4.23 μM and 6.68 μM, respectively, which are almost 2- and 1.5-fold stronger than quercetin activity (IC_{50} = 8.69 μM) used as a standard. Furthermore, 4e and 4d had the highest ABTS activity with the IC_{50} value of 5.55 μM and 7.84 μM, respectively, which are almost 2.8- and 2-fold higher than that of quercetin (IC_{50} = 15.49 μM).

It was reported that the many synthetic and natural antioxidants. Most of synthesized chalcones, in this study, exhibited stronger DPPH activity than bis-carbohydrazones (IC_{50} values of them ranging from 51.82 μM to not active) [23] and isatin derivatives (IC_{50} = 64.03-204.90 μM) [21], whereas they showed lower ABTS activity than bis-thiocarbohydrazones (IC_{50} = 2.69-5.32 μM) [23] and isatin derivatives (IC_{50} = 0.39-6.83 μM) [21]. On the other hand, the synthesized chalcones have higher ABTS activity than some reported natural extracts (IC_{50} = 40.22-106.01 μM) [24].

From Table 1, the structure–activity relationship (SAR) can be observed as follows:

Generally, most of synthesized sulfonyl chloride derivatives (4a-e) exhibited stronger both DPPH and ABTS activity than the sulphonamide derivatives (5a-c). Additionally, most of them showed better DPPH activity than ABTS. As expected, compounds 4d and 4e, containing hydroxyl group, have the highest antioxidant activity among the synthesized compounds. Changing the position of hydroxyl with sulfonyl chloride moiety did not significantly alter antioxidant activity.

Table 1 The results of DPPH and ABTS assays

Compound	**DPPH** (IC_{50}, μM)[a]	**ABTS**$^{\cdot+}$ (IC_{50}, μM)[a]
4a	48.27 ± 0.04	64.06 ± 0.53
4b	33.59 ± 0.12	52.20 ± 0.40
4c	56.42 ± 0.14	58.32 ± 0.51
4d	6.68 ± 0.06	7.84 ± 0.02
4e	4.23 ± 0.02	5.55 ± 0.04
5a	62.54 ± 0.24	70.78 ± 0.44
5b	50.31 ± 0.30	68.25 ± 0.77
5c	106.51 ± 1.18	111.44 ± 0.98
Quercetin	8.69 ± 0.04	15.49 ± 2.33

[a]IC_{50} values are given according to three parallel measurement results.

Compounds 4b and 5b, having $–OCH_3$ as R_1 substituent, showed the second most effective antioxidant activity after those containing hydroxyl group.

It is well-known that the DPPH and ABTS mechanisms involve an electron transfer process [25-28]. It is considered that 4e can oxidize to quinone product, known as one of the anticancer agents. Quinones act antitumor activity via reversible enzymatic reduction and oxidation [28, 29]. Therefore, the conversion of compound 4e to quinone may provide a distinct advantage in terms of its use in the treatment of some diseases.

4. CONCLUSION

The furfuryl-chalcone derivatives substituted sulfonyl chloride or sulphonamide were synthesized and their DPPH and ABTS activities were investigated as antioxidant features. All furfuryl-chalcones showed good antioxidant activities. Compound 4e and 4d exhibited the strongest antioxidant activities with the IC_{50} values of 4.23 μM and 6.68 μM for DPPH and 5.55 μM and 7.84 μM for ABTS activity, respectively. These values are better than that of quercetin (IC_{50} = 8.69 μM and 15.49 μM for DPPH and ABTS, respectively), used as a standard. Generally, all synthesized sulfonyl chloride derivatives (4a-e) have higher antioxidant activity than the sulphonamide derivatives (5a-c). As expected, among the synthesized compounds, 4d and 4e, including hydroxyl group, exhibited the strongest antioxidant activity. These results indicated that the hydroxyl groups linked to the phenyl ring can act a critical role for antioxidant agents.

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Authors' Contribution

The authors contributed equally to the study. F.S: Literature research, writing, editing, method, consultancy. E.A: Synthesis of compounds. Z.S: Antioxidant activity assay.

The Declaration of Conflict of Interest/ Common Interest

This study was produced from the MSc thesis entitled "Sülfonamit Grubu İçeren Furfurilşalkon Türevlerinin Sentezi" by Sakarya University, which was accepted in 2019.

The Declaration of Ethics Committee Approval

This study does not require ethics committee permission or any special permission.

The Declaration of Research and Publication Ethics

The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the paper and that they do not make any falsification on the data collected. In addition, they declare that Sakarya University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered, and that this study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.

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