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SYNTHESIS AND CHARACTERIZATION OF SOME NEW 1,3,4-THIADIAZOLE COMPOUNDS DERIVED FROM α-METHYL CINNAMIC ACID AND THEIR ENERGETICS AND SPECTRAL ANALYSES BASED ON DENSITY FUNCTIONAL THEORY CALCULATIONS

Mahmut GÜR [1, *], Nesrin ŞENER [2]

[1] Department of Forest Industrial Engineering, Faculty of Forestry, Kastamonu University, Kastamonu, Turkey
[2] Department of Chemistry, Faculty of Art and Science, Kastamonu University, Kastamonu, Turkey

ABSTRACT

Some novel 1,3,4-thiadiazole compounds derived from α-methyl cinnamic acid was synthesized, in this study. The structures of these compounds were elucidated by using spectroscopic methods such as FT-IR spectroscopy, ^{1}H-NMR spectroscopy, ^{13}C-NMR spectroscopy. Then, the absorption characteristics of the compounds were also examined by using UV-Vis spectrophotometer. In addition, the geometrical and electronic properties as well as Ultraviolet Visible analyzes of the compounds were theoretically done by using the density functional theory. The electronic configurations of the compounds substituted fluoro, chloro and methoxy have been investigated and how to effect chemical reactivity parameters to this configuration have been analyzed by using frontier molecular orbital energies. The calculated values obtained by B3PW91 with 6-311++G basis set and B3LYP with cc-PVTZ basis set are in good agreement with the experimental data. The results show that the UV-Vis absorptions are noticeably influenced by the *o*-, *m*- or *p*- positions of Cl, F and methoxy substituents. The methoxy substituent has more effect on the LUMO energies when compared to the Cl and F substituents. Moreover, positions of the substituents in the isomeric compounds were found to influence the molecular electronegativity and absorption wavelength. The absorption wavelength has the greatest value as the electronegativity of the isomer structures in the *p*-position of the substituents is smaller.

Keywords: 1,3,4-thiadiazoles, α-methyl cinnamic acid, Computational chemistry, DFT

1. INTRODUCTION

The heterocyclic compounds have become increasingly attractive due to the fact that these compounds have many field applications. A wide variety of heterocyclic compounds such as pyrazole, tetrahydroquinoline, benzotriazole, 1,2,3,4-tetrazine, thiazole, 2-thiazoline, thiadiazoles, and so on have been extensively studied till now [1]. And also, 1,3,4-thiadiazole derivatives which applied in a wide variety of fields such as the pharmaceutical industry, materials science and organic synthesis, are important five-membered heterocyclic compounds (Figure 1) [2].

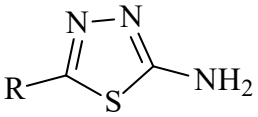


Figure 1. General structure of 2-amino-5-substituted-1,3,4-thiadiazole compounds

1,3,4-thiadiazoles have been studied more intensively than other isomers (1,2,4-thiadiazole, 1,2,5-thiadiazole and 1,2,3-thiadiazole). The 1,3,4-thiadiazole ring is a very weak base due to the inductive effect of the sulfur atom and has a relatively high aromaticity [1]. 1,3,4-thiadiazole compounds are relatively stable in acidic solutions, but may be exposed to ring cleaveage in basic media. In addition, they show electron deficiency due to the electron withdrawing effect of the nitrogen atoms on the ring. Although 1,3,4-thiadiazole ring is susceptible to nucleophilic attack, they are highly active due to the

*Corresponding Author: mahmutgur@kastamonu.edu.tr

groups at the 2 'or 5' position and readily react to form various derivatives. As a result of these mentioned chemical properties up to now, 1,3,4-thiadiazole derivatives are widely used in pharmaceutical and agricultural and chemical applications [1]. The acetazolamide compound, a renowned thiadiazole derivative (Figure 2), is used in the treatment of high altitude disease, epileptic seizures, idiopathic intracranial hypertension, hemiplegic migraine, cystinuria, obstructive sleep apnea, congenital myasthenic syndromes.

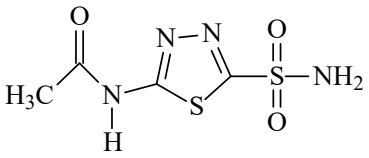


Figure 2. Structure of acetazolamide compound

In recent years, 1,3,4-thiadiazoles, to which variety aromatic moieties substituted different groups are attached, have been intensively investigated. In analytical, biological, and pharmaceutical fields, 1,3,4-thiadiazole derivatives are the most interesting isomeric form of the thiadiazole compounds [3,4]. =N-C-S part in the thiadiazole ring causes a variety of biological and pharmaceutical activities such as anti-glaucoma, anti-inflammatory, anti-tumor, antiulcer, antibacterial, antiviral, analgesic, antiepileptic, antifungal and radio-protective activities. Furthermore, the aromaticity of the thiadiazoles contributes to lower toxicity and durability in the living organism [5]. Many methods have been described for the synthesis of 1,3,4-thiadiazole compounds, in the literature. In these methods, the following substances appear as starting materials: thiosemicarbazites [6-8], thiocarbazides [9], dithiocarbazates [10,11], thioacylhydrazines [12], acylhydrazines [13], bitolyure derivatives [14]. Oruç et al. (2004), synthesized the 2,5-disubstitued-1,3,4-thiadiazole derivatives and evaluated for anti-tuberculosis activity against Mycobacterium tuberculosis H37Rv using the BACTEC 460 radiometric system and, they reported that 2-phenylamino-5-(4-fluorophenyl)-1,3,4-thiadiazole has a greater inhibitory potential than the other compounds tested [15].

As is known, Density Functional Theory (DFT) is a method that can result in a significant fraction of the electron correlation with a good accuracy, and with little calculation time. DFT has proven to be a valuable complement to experimental work as well as a powerful tool for deeper grasp of the reaction mechanisms and kinetics of quantum chemical calculations. Especially due to its accuracy and low computational costs is preferred by researchers. In the literature, we can see that different properties of various thiadiazoles and derivatives have been successfully studied by DFT analysis [16-21].

In this study, nine different N-phenyl-1,3,4-thiadiazole compounds derived from α-methyl cinnamic acid was synthesized and, their structures were elucidated by using FT-IR (Fourier Transform Infrared spectroscopy), ^{1}H-NMR (Proton nuclear magnetic resonance spectroscopy), ^{13}C-NMR (Carbon-13 nuclear magnetic resonance spectroscopy) and UV-Vis (Ultraviolet-Visible) spectroscopic methods. In addition, the molecular and electronic properties as well as UV-Vis absorptions of these compounds have been theoretically calculated and analyzed. In this context, the obtained compounds were analyzed using the B3PW91 (and 6-311 ++ G base set) and B3LYP (with the cc-PVTZ base set) methods which yielded very good results in DFT calculations. The results were compared and interpreted with experimental data.

2. METHOD

2.1. Synthesis of Compounds (I-IX)

The general method of synthesis of 1,3,4-thiadiazole derivatives: α-methyl cinnamic acid (n mol) and N-substittuted-phenylthiosemicarbazide derivatives (n mol) were placed into refrigerator, and then phosphorous oxychloride (3n mol) was added dropwise to the cold mixture with stirring and reflux

was continued for two hours. Once the reaction was completed, reaction flask was cooled to the room temperature and crude product was added to ice-cold water by stirring, and last mixture was neutralized with ammonia solution. The precipitated product was filtrated, washed with water, and crystallized by using solvent such as ethanol, tetrahydrofuran (THF). Spectral data of the compounds are summarized in Table 1, Table 2, Table 3 and Table 4. The synthetic route and general structure of the molecules are illustrated in Figure 3.

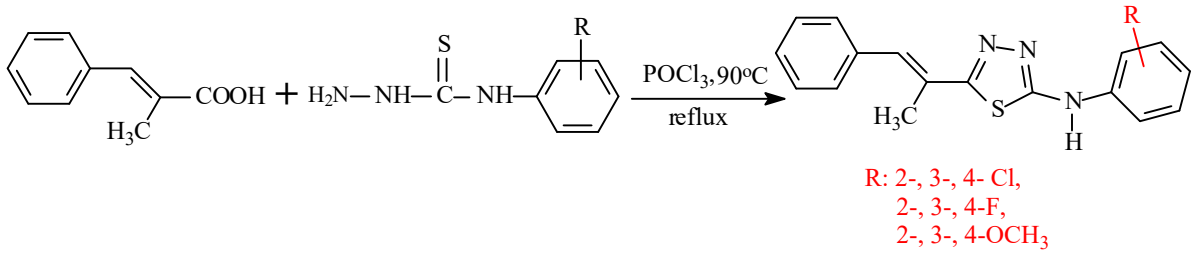


Figure 3. Main synthesis route for 1,3,4-thiadiazole compounds

5- (1-methyl-2-phenylethenyl)-N-[2′-chlorophenyl]-1, 3, 4-Thiadiazol-2-amine (**I**)

Yield%: (%78), M.P.: 120 ºC; **FT-IR (cm^{-1}) υ$_{maks}$**: 3296.91 (-NH stretching), 1493.65 (-NH bending), 3025.61 (aromatic C-H), 2961.91, 2918.67 (aliphatic C-H), 1594.51 (C=N thiadiazole), 1610 (C=C) 688.56 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d$_6$, 25 ºC) δ (ppm)**: 2.43 (s, 3H -CH$_3$), 7.11-7.97 (9H, aromatic), 8.47 (g, -NH), 7.06 (s, 1H, ethylenic); **^{13}C-NMR (DMSO-d$_6$, 25 ºC) δ (ppm)**: (in order of C1-C17), 135.64, 129.42, 129.07, 128.85, 129.07, 129.42, 128.19, 128.52, 15.77, 136.16, 165.17, 162.01, 125.61, 134.67, 120.49, 130.08, 124.66. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}ClN_3S$: C, 61.90; H, 4.89; N, 12.74 (%). Found: C, 60.78; H, 5.18; N, 12.16 (%).

5-(1-methyl-2-phenylethenyl)-N-[3′-chlorophenyl] -1, 3, 4-Thiadiazol-2-amine (**II**)

Yield%: (%67), M.P.: 193 ºC **FT-IR (cm^{-1}) υ$_{maks}$**: 3248.15 and 3185.08 (-NH, stretching), 1482.75 (-NH, bending), 3052.58 (aromatic C-H), 2981.48, 2917.99, 2811.16 (aliphatic C-H), 1595.57 (C=N thiadiazole), 1620.65 (C=C) 689.57 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d$_6$, 25 ºC) δ (ppm)**: 2.49 (s, 3H -CH$_3$), 6.94-7.63 (9H, aromatic), 10.80 (g, -NH), 7.15 (s, 1H, ethylenic): **^{13}C-NMR (DMSO-d$_6$, 25 ºC) δ (ppm)**: (in order of C1-C17), 133.97, 129.88, 129.45, 129.98, 129.45, 129.88, 128.27, 128.90, 16.06, 136.31, 163.37, 142.28, 117.42, 133.70, 121.98, 131.12, 116.44. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}ClN_3S$: C, 61.90; H, 4.89; N, 12.74 (%). Found: C, 61.25; H, 5.02; N, 12.58 (%).

5-(1-methyl-2-phenylethenyl)-N-[4′-chlorophenyl]-1,3,4-Thiadiazol-2-amine (**III**)

Yield%: (%68), M.P.: 216 ºC **FT-IR (cm^{-1}) υ$_{maks}$**: 3256.07 and 3185.65 (-NH stretching), 1495.15 (-NH, bending), 3052 (aromatic C-H), 2981.71, 2963.83 2869.78 (aliphatic C-H), 1598.01 (C=N thiadiazole), 1620.54 (C=C) 688.06 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d$_6$, 25 ºC) δ (ppm)**: 2.38 (s, 3H -CH$_3$), 7.15-7.59 (9H, aromatic), 10.65 (g, -NH), 7.09 (s, 1H, ethylenic); **^{13}C-NMR (DMSO-d$_6$, 25 ºC) δ (ppm)**: (in order of C1-C17), 129.86, 129.39, 128.55, 128.90, 128.55, 129.39, 128.25, 128.08, 16.07, 133.54, 163.52, 136.34, 119.54, 129.50, 125.92, 129.50, 119.54. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}ClN_3S$: C, 61.90; H, 4.89; N, 12.74 (%). Found: C, 61.57; H, 4.80; N, 12.42 (%).

5-(1-methyl-2-phenylethenyl)-N-[2′-fluorophenyl]-1,3,4-Thiadiazol-2-amine (**IV**)

Yield%: (%61), M.P.: 147 ºC; **FT-IR (cm^{-1}) υ_{maks}**: 3240.24 and 3137.01 (-NH stretching), 1502.49 (-NH, bending), 3022.47 (aromatic C-H), 2981, 2916 (aliphatic C-H), 1581.04 (C=N thiadiazole), 1615.38 (C=C) 696.73 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d_6, 25 ºC) δ (ppm):** 2.47 (s, 3H -CH_3), 7.31-7.43 (9H, aromatic), 8.05 (g, -NH), 7.10 (s, 1H, ethylenic); **^{13}C-NMR (DMSO-d_6, 25 ºC) δ (ppm)**: (in order of C1-C17), 133.67, 129.39, 127.84, 128.44, 127.84, 129.39, 124.90, 127.50, 15.92, 136.08, 154.22, 129.64, 163.20, 119.41, 124.87, 123.76, 123.83. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}FN_3S$: C, 65.15; H, 5.15; N, 13.41 (%). Found: C, 64.05; H, 4.70; N, 12.65 (%).

5- (1-methyl-2-phenylethenyl) -N-[3′-fluorophenyl]-1, 3, 4-Thiadiazol-2-amine (**V**)

Yield%: (%65), M.P.:189 ºC; **FT-IR (cm^{-1}) υ_{maks}**: 3257.12 and 3210.84 (-NH stretching), 1498.14 (-NH, bending), 3064.7 (aromatic C-H), 2981.76, 2904.08, 2853.42 (aliphatic C-H), 1574.38 (C=N thiadiazole), 1614.15 (C=C) 689.33 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d_6, 25 ºC) δ (ppm)**: 2.46 (s, 3H -CH_3), 7.28-7.46 (9H, aromatic), unobserved (NH), 7.12 (s, 1H, ethylenic); **^{13}C-NMR (DMSO-d_6, 25 ºC) δ (ppm):** (in order of C1-C17), 129.88, 128.91, 128.08, 128.29, 128.08, 128.91, 117.85, 119.58, 16.07, 133.69, 162.05, 136.31, 114.72, 164.45, 110.02, 129.45, 115.35. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}FN_3S$: C, 65.15; H, 5.15; N, 13.41 (%). Found: C, 64.95; H, 4.84; N, 12.83 (%).

5- (1-methyl-2-phenylethenyl) -N-[4′-fluorophenyl]-1, 3, 4-Thiadiazol-2-amine (**VI**)

Yield%: (%59), M.P.:187 ºC; **FT-IR (cm^{-1}) υ_{maks}**: 3261.46, 3213.76 and 3163.86 (-NH stretching), 1502.49 (-NH, bending), 3050.04 (aromatic C-H), 2887.26, 2820.26 (aliphatic C-H), 1582.17 (C=N thiadiazole), 1624.54 (C=C) 686.05 (C-S-C): **^{1}H-NMR (400 MHz, DMSO-d_6, 25 ºC) δ (ppm)**: 2.47 (s, 3H -CH_3), 7.25-7.50 (9H, aromatic), unobserved (NH), 7.07 (s, 1H, ethylenic); **^{13}C-NMR (DMSO-d_6, 25 ºC) δ (ppm)**: (in order of C1-C17), 129.85, 129.57, 128.21, 128.89, 128.21, 129.57, 128.04, 127.60, 16.06, 136.37, 161.42, 133.34, 119.72, 119.79, 163.97, 119.79, 119.72. **Elemental analysis:** Anal. Calcd. for $C_{17}H_{14}FN_3S$: C, 65.15; H, 5.15; N, 13.41 (%). Found: C, 65.95; H, 5.00; N, 12.84 (%).

5- (1-methyl-2-phenylethenyl) -N-[2′-methoxyphenyl]-1, 3, 4-Thiadiazol-2-amine (**VII**)

Yield%: (%71), M.P.:112 ºC; **FT-IR (cm^{-1}) υ_{maks}**: 3220.44 and 3230.54 (-NH, stretching), 1481.89 (-NH, bending), 3040 (aromatic C-H), 2981.83, 2963.90, 2870.43 (aliphatic C-H), 1583.31 (C=N t thiadiazole), 1602.36 (C=C) 711.00 (C-S-C): **^{1}H-NMR (DMSO-d_6, 25 ºC) δ (ppm)**: 2.48 (s, 3H -CH_3), 3.94 (s, 3H *o*-OCH_3), 9.0-7.99 (9H, aromatic), unobserved (NH), 7.06 (s, 1H, ethylenic); **^{13}C-NMR (400 MHz, DMSO-d_6, 25 ºC) δ (ppm)**: (in order of C1-C18), 136.25, 129.85, 129.20, 129.42, 129.20, 129.85, 128.41, 129.38, 15.94, 147.89, 162.50, 133.14, 163.84, 116.83, 121.18, 127.70, 123.04, 55.80. **Elemental analysis:** Anal. Calcd. for $C_{18}H_{17}N_3OS$: C, 66.43; H, 5.88; N, 12.91 (%). Found: C, 65.58; H, 5.70; N, 12.58 (%).

5- (1-methyl-2-phenylethenyl) -N-[3′-methoxyphenyl]-1, 3, 4-Thiadiazol-2-amine (**VIII**)

Yield%: (%68), M.P.: 188 ºC, **FT-IR (cm^{-1}) υ_{maks}**: 3263.1 and 3204.8 (-NH, stretching), 1499.8 (-NH, bending), 3055.22 (aromatic C-H), 2981.0, 2966.7, 2933.4, 2866.8 (aliphatic C-H), 1599.9 (C=N thiadiazole), 1622.00 (C=C) 699.00 (C-S-C): **^{1}H-NMR (DMSO-d_6, 25 ºC) δ (ppm)**: 2.47 (s, 3H -CH_3), 3.91 (s, 3H *m*-OCH_3), 6.66-7.45 (9H, aromatic), unobserved(NH), 7.08 (s, 1H, ethylenic); **^{13}C-NMR (400 MHz, DMSO-d_6, 25 ºC) δ (ppm)**: (in order of C1-C18), 133.35, 129.86, 128.90, 128.95, 128.90, 129.86, 128.04, 128.58, 16.07, 136.62, 160.22, 142.36, 104.01, 162.52, 103.85, 130.37,

110.44, 55.51. **Elemental analysis:** Anal. Calcd. for $C_{18}H_{17}N_3OS$: C, 66.43; H, 5.88; N, 12.91 (%). Found: C, 66.96; H, 6.07; N, 12.64 (%).

5- (1-methyl-2-phenylethenyl) -N-[4'-methoxyphenyl]- 1,3,4-Thiadiazol-2-amine (**IX**)

Yield%: (%69), M.P.: 158 ºC; **FT-IR (cm^{-1}) υ_{maks}**: 3248.33 and 3198.95 (-NH, stretching), 1511.32 (-NH, bending), 3047.45 (aromatic C-H), 2902.95, 2830.27 (aliphatic C-H), 1572.56 (C=N thiadiazole), 1618.74 (C=C) 711.85 (C-S-C): **^{1}H-NMR (DMSO-d$_6$, 25 ºC) δ (ppm)**: 2.46 (s, 3H -CH_3), 3.84 (s, 3H *p*-OCH_3), 6.93-7.44 (9H, aromatic), unobserved (NH), 7.03(s, 1H, ethylenic); **^{13}C-NMR (400 MHz, DMSO-d$_6$, 25 ºC) δ (ppm)**: (in order of C1-C18), 134.05, 129.91, 128.38, 129.34, 128.38, 129.91, 127.43, 127.60, 15.89, 136.34, 156.55, 132.61, 121.46, 114.84, 160.81, 114.84, 121.46, 55.58. **Elemental analysis:** Anal. Calcd. for $C_{18}H_{19}N_3OS$: C, 66.43; H, 5.88; N, 12.91 (%). Found: C, 65.70; H, 5.33; N, 12.61 (%).

2.2. Theoretical Section

In this work, density functional theory was used for quantum-chemical modeling of compounds. During the molecular optimization performed at the first step of the theoretical calculations, no restrictions were placed on the geometry of the compounds. The Kohn-Sham density functional theory (DFT) [22, 23] was used to calculate the ground state geometries and TD-DFT was used to calculate excitation energies. For the molecular optimizations of the compounds, the B3PW91 method with 6-311 ++ G basis set and commonly used Becke3-Lee-Yang-Parr hybrid functional B3LYP method with the cc-pvtz basis set were used, and the results compared with the experimental data.

3. RESULTS and DISCUSSION

3.1. FT-IR Spectroscopy

The IR absorption data of the obtained compounds (I-IX) are written in Table 1. Structural characterization for compounds (I-IX) was carried out by tracking the IR absorptions of the -NH, -C-H (aromatic and aliphatic), -C=N (for the thiadiazole ring), -C=C- and C-S-C functional groups. It has been reported in the literature that the seconder amine group (-NH-) have a stretching vibration and a bending vibration at the range of 3350-3310 cm^{-1} and 1580-1490 cm^{-1}, respectively. In addition, it has been also reported that the stretching vibrations of C=N, aromatic C-H, aliphatic C-H and aromatic C=C are observed at the range of 1689-1471 cm^{-1}, 3100-3000 cm^{-1}, 3000-2840 cm^{-1} and 1650-1450 cm^{-1}, respectively. Moreover, the peaks belonging to the conjugated C=C and C-S-C are found at around 1645 cm^{-1} and 700 cm^{-1}, respectively [24,25].

In the compounds obtained in this work: the vibrations of N-H stretching, N-H bending, aromatic C-H stretching, aliphatic C-H stretching, -C=N stretching (in the thiadiazole ring) and C-S-C were determined at the range of 3291.91-3137.08 cm^{-1}, 1511.32-1481.89 cm^{-1}, 3064.7-3022.47 cm^{-1}, 2981.83-2811.16 cm^{-1}, 1599.9-1572.56 cm^{-1}, 711.85-686.05 cm^{-1}, respectively. Moreover, as a further proof of the conversion of α-methylcinnamic acid to the thiadiazole, there was no peak belonging to the group >C=O characterized with a strong peak over the range of 1750-1700 cm^{-1}. Consequently, the observation of secondary amine, the C=N and C-S-C peaks, and the absence of absorption of the carbonyl group proved that desired final products were synthesized successfully.

Table 1. The absorption data of the molecules in the FT-IR region

Compounds	νN-H	νC-H_{Ar}	νC-H_{Aliph}	νC=$N_{thiadiazole}$	νC-S-C	νC=C
I	3296.91 (stretching) 1493.65 (bending)	3025.61	2961.91 2918.67	1594.51	688.56	1610
II	3248.15 and 3185.08 (stretching) 1482.75 (bending)	3052.58	2981.48 2917.99 2811.16	1595.57	689,57	1620.65
III	3256.07 and 3185.65 (stretching) 1495.15 (bending)	3052	2981.71 2963.83 2869.78	1598.01	688.06	1620.54
IV	3240.24 and 3137.01 (stretching) 1502.49 (bending)	3022.47	2981 2916	1581.04	696.73	1615.38
V	3257,12 and 3210,84 (stretching) 1498,14 (bending)	3064.7	2981.76 2904.08 2853.42	1574.38	689.33	1614.15
VI	3261.46, 3213.76 and 3163.86 (stretching) 1502.49 (bending)	3050.04	2887.26 2820.26	1582.17	686.05	1624.54
VII	3220.44 and 3230.54 (stretching) 1481.89 (bending)	3040	2981.83 2963.90 2870.43	1583.31	711.00	1602.36
VIII	3263.1 and 3204.8 (stretching) 1499.8 (bending)	3055.22	2981.00 2966.7 2933.4 2866.8	1599.9	699.00	1622,.00
IX	3248.33 and 3198.95 (stretching) 1511.32 (bending)	3047.45	2902.95 2830.27	1572.56	711.85	1618.74

3.2. ^{1}H-NMR Spectroscopy

Table 2. ^{1}H-NMR data of the compounds (δ, ppm, DMSO-d_6)

Compounds	δ Aliphatic-H	δ Aromatic-H	δ N-H	$\delta_{ethylenic\ C-H}$
I	2.43 (s, 3H -CH_3)	7.11-7.97 (9H, aromatic)	8.47 (g, -NH)	7,06 (s, 1H)
II	2.49 (s, 3H -CH_3)	6.94-7.63 (9H, aromatic)	10.80 (g, -NH)	7.15 (s, 1H)
III	2.38 (s, 3H -CH_3)	7.15-7.59 (9H, aromatic)	10.65 (g, -NH)	7.09 (s, 1H)
IV	2.47 (s, 3H -CH_3)	7.31-7.43 (9H, aromatic)	8.05 (g, -NH)	7.10 (s, 1H)
V	2.46 (s, 3H -CH_3)	7.28-7.46 (9H, aromatic)	Unobserved	7.12 (s, 1H)
VI	2.47 (s, 3H -CH_3)	7.25-7.50 (9H, aromatic)	Unobserved)	7.07 (s, 1H)
VII	2.48 (s, 3H -CH_3) 3.94 (s, 3H *o*-OCH_3)	6.90-7.,99 (9H, aromatic)	Unobserved	7.06 (s, 1H)
VIII	2.47 (s, 3H -CH_3) 3.91 (s, 3H *m*-OCH_3)	6.66-7.45 (9H, aromatic)	Unobserved	7.08 (s, 1H)
IX	2.46 (s, 3H -CH_3) 3.84 (s, 3H *p*-OCH_3)	6.93-7.44 (9H, aromatic)	Unobserved	7.03(s, 1H)

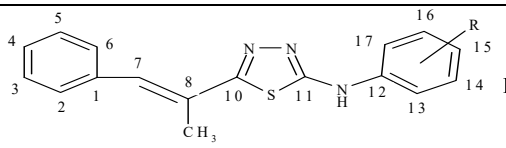
^{1}H-NMR data of the compounds (I-IX) were collected in Table 2. The synthesized compounds include aromatic, aliphatic, alkenic and secondary amine protons. Determination of the ^{1}H-NMR signals of these protons is important for the determination of the structures of the synthesized compounds.

Aromatic protons were observed between 6.66-7.99 ppm. The protons of the -CH_3 group bound to the alkenic structure and -OCH_3 protons (compounds IV-IX) were determined at the range of 2.38-2.49 ppm (as singlet) and 3.84-3.94 ppm (as singlet), respectively. As compared compounds VII, VIII and IX substituted a methoxy group at *orto*-, *meta*- and *para*- positions, it was observed that they had a signal such as 3.94, 3.91 and 3.84 ppm, respectively. The other words, it was seen that the signal of the C atom of methoxy group shifted to more upfield at *para*-position than *meta*- and *orto*-positions. Seconder amine protons were determined between 8.05 and 10.80 but amine peaks were not observed in the V-IX compounds. The ethylenic proton shifted to the aromatic region due to the conjugation with two aromatic rings and it was determined at the range of 7.03 to 7.15 ppm.

3.3. ^{13}C-NMR Spectroscopy

^{13}C-NMR data of the compounds (I-IX) are given in Table 3. There are two types of aromatic C atoms in the compounds: at the benzene ring and the thiadiazole ring. The C11 atom (adjacent to the seconder amine) was affected by the electronegative N atom. Thus, it gave a signal at the range of 154.22-165.17 ppm by shifting at the down-field in accordance with C10. Likewise, C10 was observed at 133.54-147.89 ppm in the down-field. While the phenyl carbons (C12-C17) adjacent to the seconder amine resonated at the range of 110.02-162.01 ppm the C atoms (C1-C6) of the phenyl rings adjacent to the alkene double bond gave signals at the range of 127.84-136.25 ppm. There are two reasons why the signals of the C12-C17 atoms are wider than the signals of the other phenyl ring C atoms: to substitution of F, Cl, and OCH_3 groups to the ring and changes at -*ortho*, -*meta* and -*para* positions. The C atom (CH_3) bound to the alkenic structure was observed in the range of 15.77-16.07 ppm. Alkenic C7 and C8 atoms resonated in the range of 117.85-129.38 ppm. In other words, the resonance of C8 atom close to the thiadiazole ring was shifted to upper-field by 0.17-2.60 ppm due to the inductive effect of the electron-donor methyl group. While the C9 atom of CH_3 group was detected in the aliphatic region (at the range of 15.77-16.07 ppm) the C18 atom of the OCH_3 group in the VII-IX compounds was determined at the range of 55.51-55.85.

Table 3. ^{13}C-NMR data of the compounds (δ, ppm, DMSO-d6)



R: I: 2-Cl, II: 3-Cl, III: 4-Cl, IV: 2-F, V: 3-F, VI: 4-F, IV: 2-OCH_3, V: 3-OCH_3, VI: 4-OCH_3

	I	II	III	IV	V	VI	VII	VIII	IX
C_1	135.64	133.97	129.86	133.67	129.88	129.85	136.25	133.35	134.05
C_2	129.42	129.88	129.39	129.39	128.91	129.57	129.85	129.86	129.91
C_3	129.07	129.45	128.55	127.84	128.08	128.21	129.20	128.90	128.38
C_4	128.85	129.98	128.90	128.44	128.29	128.89	129.42	128.95	129.34
C_5	129.07	129.45	128.55	127.84	128.08	128.21	129.20	128.90	128.38
C_6	129.42	129.88	129.39	129.39	128.91	129.57	129.85	129.86	129.91
C_7	128.19	128.27	128.08	124.90	117.85	128.04	128.41	128.04	127.43
C_8	128.52	128.90	128.25	127.50	119.58	127.60	129.38	128.58	127.60
C_9	15.77	16.06	16.07	15.92	16.07	16.06	15.94	16.07	15.89
C_{10}	136.16	136.31	133.54	136.08	133.69	136.37	147.89	136.62	136.34
C_{11}	165.17	163.37	163.52	154.22	162.05	161.42	162.50	160.22	156.55
C_{12}	162.01	142.28	136.34	129.64	136.31	133.34	133.14	142.36	132.61
C_{13}	125.61	117.42	119.54	163.20	114.72	119.72	163.84	104.01	121.46
C_{14}	134.67	133.70	129.50	119.41	164.45	119.79	116.83	162.52	114.84
C_{15}	120.49	121.98	125.92	124.87	110.02	163.97	121.18	103.85	160.81
C_{16}	130.08	131.12	129.50	123.76	129.45	119.79	127.70	130.37	114.84
C_{17}	124.66	116.44	119.54	123.83	115.35	119.72	123.04	110.44	121.46
C_{18}(-OCH_3)							55.80	55.51	55.58

3.4. UV-Vis Absorption Studies

The UV-Visible absorption spectra of the compounds I-IX were recorded over the range of 200-700 nm, by using chloroform as solvent in concentration 10^{-5} M. According to the UV-Vis spectrum results shown in Table 4, in the spectra of all compounds apart from the compounds VII and IX have been observed to exhibit two maximum peaks. It has been clearly observed that there is not much variation between the absorption of molecules. In compounds (I, II, III, IV, V and VI) including the -Cl and -F atoms at the -*ortho*, -*meta* and -*para* positions are decreased electron density in the structure due to the electron withdrawing properties of these atoms. In compounds (VII, VIII and IX), -OCH_3 group is bonded at the -*ortho*, -*meta* and -*para* positions, and thus, the electron density are increased due to the electron donating effect of this group. Therefore, the increase of electron density in these molecules caused that the first maximum absorbance peaks monitored for the compounds expose a bit more bathochromic shift than the other compounds. While the second maximum absorption point for compound VIII also exhibits bathochromic shift in the same way, the second maximum absorption for compound VII and IX was not observed. This situation were explained that the electron pair of the O atom of OCH_3 group use in the intramolecular H bond. As a result, the second absorption underwent the hypsochromic shift. Also, for Compound VIII, we think that the same situation is not observed due to the substitution at the *meta* position.

Table 4. UV-Vis absorptions of compounds (I-IX) (nm)

Compounds	Experimental UV-Vis Absorptions	
I	265	330
II	267	333
III	268	339
IV	262	333
V	264	336
VI	267	335
VII	281	-
VIII	266	340
IX	294	-

3.5. Theoretical Process

The UV-Vis absorption properties and vertical excitation energies of the compounds were calculated using the B3PW91 method with 6-311++G basis set and B3LYP method with the cc-pvtz basis set in the chloroform phase over the optimized ground state geometries. Vibrational frequency calculations were used to characterize a stationary point, and no imaginary frequencies were obtained for vibrational frequencies computations at the optimization. For the geometry optimizations of the molecules in solvent media, and for UV calculations, Conductor-Polarizable Continuum Model (CPCM) and Self-Consistent Reaction Field (SCRF) method, in which solvent and soluble interactions participate in the calculation, were used. In addition, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energies, called frontier molecule orbitals (FMO), were calculated with the same method and base set. Molecular electrostatic potential (MEP) surfaces were also obtained. FMO energy eigenvalues were used to calculate the chemical hardness (η) and electronegativity (χ) of the compounds (Table 5 and Table 6). All calculations were performed using the GAUSSIAN 09 software package program [26].

Table 5. Electronic data of the compounds calculated with B3PW91/6-311++g

Molecule	*E* (au)	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE	η (eV)	χ (eV)	*m (Debye)*
I	-1678.40396904	-6.211	-2.118	4.093	2.046	4.165	6.246
II	-1678.40564950	-6.210	-2.117	4.092	2.046	4.164	4.504
III	-1678.40577577	-6.159	-2.100	4.059	2.030	4.129	2.159
IV	-1318.06370148	-6.169	-2.105	4.064	2.032	4.137	6.365
V	-1318.06573567	-6.209	-2.114	4.095	2.048	4.161	4.489
VI	-1318.06517849	-6.150	-2.067	4.083	2.042	4.109	2.246
VII	-1333.32869415	-5.875	-1.978	3.897	1.948	3.926	5.656
VIII	-1333.32703250	-6.070	-2.028	4.042	2.021	4.049	6.643
IX	-1333.32603067	-5.935	-1.930	4.005	2.002	3.932	5.982

E: Energy; **ΔE**: $E_{LUMO} - E_{HOMO}$; **η**: Chemical Hardness ; **χ**: elektronegatiflik; ***m***: Dipole moment

Table 6. Electronic data of the compounds calculated with B3LYP/cc-pvtz

Molecule	*E* (au)	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE	η (eV)	χ (eV)	*m (Debye)*
I	-1679.20857945	-5.904	-1.869	4.036	2.018	3.886	5.377
II	-1679.21020193	-5.920	-1.868	4.052	2.026	3.894	4.017
III	-1679.21005759	-5.849	-1.848	4.000	2.000	3.849	2.007
IV	-1318.85170407	-5.871	-1.848	4.023	2.012	3.860	5.169
V	-1318.85390767	-5.903	-1.854	4.049	2.025	3.879	3.900
VI	-1318.85253542	-5.804	-1.807	3.997	1.999	3.806	2.459
VII	-1334.14602160	-5.618	-1.761	3.856	1.928	3.689	4.810
VIII	-1334.14652439	-5.784	-1.792	3.992	1.996	3.788	5.732
IX	-1334.14458686	-5.582	-1.734	3.848	1.924	3.658	5.380

E: Energy; **ΔE**: $E_{LUMO} - E_{HOMO}$; **η**: Chemical Hardness ; **χ**: elektronegatiflik; ***m***: Dipole moment

As a result of the calculations, the ground state minimum molecular energies of the compounds were found to be about -1679 au for the Cl isomer structures (I, II, III), -1318 au for F isomer structures (IV, V, VI) and -1334 au for methoxy isomers isomer structures. The minimum molecular energy values of the Cl isomers were calculated to be the smallest, while the F isomer structures were the highest. Besides, if each isomer structure is evaluated in itself, it is seen that the presence of Cl, F, and methoxy substituents at *o*-, *m*- or *p*- positions does not significantly affect the molecular energy. However, for the dipole moments of the compounds, a change due to the electronegativity differences of the substituents was observed. In the *o*-position of the F and Cl subtitles having high electronegativity, the dipole moments of the isomers have the greatest value while they has the smallest value in the *p*- position. It can be directly seen that the different electronegativity values of the Cl, F and methoxy substituents, where F has the greatest electronegativity while methoxy is the smallest, affect the molecular electronegativity of the isomer groups. The electronegativity of the Cl isomeric molecules was calculated to be the highest and the methoxy isomers to be the lowest. Naturally, these results are influenced directly by the HOMO-LUMO energies of the compounds and by the energy gap (ΔE). The calculations showed that the positions of the Cl, F and methoxy substituents did not significantly affect the FMO energy eigen values of the compounds. Moreover, in the *m*-position of the substituents, the HOMO energies of the all compounds were found to be partially highest. In addition, the chemical hardness of the compounds in the *p*-position of the substituents were also calculated to the highest (Table 5 and Table 6).

The UV-Vis calculations and the experimental results of the compounds are compared, it is seen that the theoretical and experimental results are compatible with each other (Table 7). When the results of excited state calculations are examined, the correlations of both wB97XD and B3LYP methods with

the experimental results are quite good. Pearson's correlation coefficient between the experimental results and the theoretical data of wB97XD was calculated as R = 0.8528 while R = 0.9297 for B3LYP. The correlation between the results obtained from the B3LYP method and the experimental data is higher than the correlation with the wB97XD. Although both correlations are high, it were used the results of the B3LYP method for UV-Vis interpretations. Both correlations are quite good, but the results of B3LYP were used in this section for UV-Vis interpretations. When experimental data and theoretical results are examined, it was observed that the UV-Vis absorptions are hardly influenced by the *o*-, *m*- or *p*- positions of Cl, F and methoxy substituents. It was sees that methoxy isomer structures exhibit longer wavelength absorption than Cl and F isomers. Also with very small differences, the UV absorptions have the greatest value in the *p*- position when they are the smallest in the *m*- position of the substituents. In addition, when each isomer structure is evaluated in itself, it is seen that there is an inverse relationship between the HOMO-LUMO energy gab and the UV absorption wavelength: the absorption wavelength grows up as ΔE decreases, which is a result consistent with the quantum mechanical relationship $\Delta E=hc/\lambda$ (E: energy, h: Planck constant, λ: wavelength, c: speed of light).

Table 7. Experimental and theoretical UV-Vis data

		Theoretical	
Molecule	***Experimental***	**wB97XD** 6-311++g	**B3LYP** cc-pvtz
I	331.0	350.15	355.86
II	332.5	350.22	354.34
III	338.0	352.68	358.46
IV	333.5	351.69	356.49
V	336.5	349.70	354.28
VI	335.0	350.04	357.78
VII	288.0	366.52	370.72
VIII	340.0	353.46	358.97
IX	295.0	356.28	371.76

4. CONCLUSION

In this work, 1,3,4-thiadiazole compounds derived from α-methyl cinnamic acid were obtained through the cyclisation reaction. Structural characterization of the obtained compounds was carried out by UV-Vis, IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy. Spectroscopic methods reveal that the desired compounds occurred in this study. In addition, electronic and chemical parameters were calculated to elucidate the effect of electronegativity of substituents on synthesized compounds. Experimental UV-Vis data were supported by theoretical calculations and the relationship between ΔE and UV absorption wavelengths was discussed. The positions of the substituents in the isomeric compounds affected the absorption wavelength and molecular electronegativity. The electronegativity of the isomer structures were the lowest at the *p*-position of the substituents, while the absorption wavelengths had the greatest value. Furthermore, the inverse correlation was noticed between the electronegativity of the substituents and the dipole moments of the isomeric groups. The other words, the electronegativity of the substituents increased, the dipole moments decreased. This is directly related to the electron distributions of the molecules to which the substituents are bonding.

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