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Novel 1,3,4-thiadiazole compounds derived from 4-phenylbutyric acid: Synthesis, characterization and DFT studies

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Abstract

In this study; new 1,3,4-thiadiazole compounds were synthesized and their structural characterization were carried out by using FT-IR, ^{1}H-NMR, ^{13}C-NMR spectroscopic methods, and elemental analysis. Furthermore, the absorption properties of the synthesized compounds were also studied with UV-Vis. spectrophotometer. In addition, molecular conformation, electronic properties and UV-vis analysis of synthesized 1,3,4-thiadiazole compounds were theoretically investigated by using density functional theory (DFT), and how F, Cl and methoxy isomers affected the molecular configuration was analyzed.

Keywords: *1,3,4-thiadiazole, butyric acid, absorption, DFT.*

Yeni 4-fenilbütirik asit türevi 1,3,4-tiyadiazol bileşikleri: Sentezi, karakterizasyonu ve DFT çalışmaları

Özet

Bu çalışmada; literatürde daha önce sentezlenmemiş 1,3,4-tiyadiazol bileşikleri sentezlendi. Sentezlenen bu bileşiklerin FT-IR, ^{1}H-NMR, ^{13}C-NMR spektroskopik yöntemleri ve elementel analiz kullanılarak yapı tayini gerçekleştirildi. Daha sonra UV-vis. spektrofotometre cihazı kullanılarak elde edilen bileşiklerin absorpsiyon özellikleri de incelendi. Ayrıca, yoğunluk fonksiyonel teorisi (DFT) kullanılarak, sentezlenen 1,3,4-tiyadiazol bileşiklerinin moleküler konformasyonu, elektronik konfigürasyonu ve

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UV-vis analizleri teorik olarak yapılmış, F, Cl ve metoksi izomerlerinin moleküler konfigürasyonu nasıl etkilediği analiz edildi.

Anahtar Kelime: *1,3,4-tiyadiazol, butirik asit, absorpsiyon, DFT.*

1. Introduction

The importance of heterocyclic compounds is increasing day by day as it is related to many fields such as organic chemistry, biochemistry and pharmaceutical chemistry. While researches initially focused on their synthesis, after the finding of therapeutic properties of these compounds their synthesis and application studies have been carried out intensively. 1,3,4-thiadiazole compounds, one of the most important compound in this field, are five membered heterocyclic compounds containing two nitrogen and one sulfur atom. 1,3,4-thiadiazole was first synthesized by Fisher in 1882, but its real structure was first enlightened by Goerdeler et al. in 1956. [1]. 1,3,4-thiadiazole and their derivatives have been attracted scientist's more than the attention by the other isomers of thiadiazole. Their different derivatives are used for therapeutic purposes such as antimicrobials [2], antifungal [3], antibacterial [4], antileishmanial [5], analgesic, anti-inflammatory [6], antidepressant [7], antipsychotic [8] and anticonvulsant [8,9]. There are also studies about 1,3,4-thiadiazole derivatives exhibit interesting in vitro [10-12] and in vivo [13-16] antitumor activities.

In addition, substituted thiadiazoles can easily be metabolized by routine biochemical reactions and are increased lipid solubility due to their hydrophilic action. Moreover, some researchers have also shown that this substitute thiadiazole has other interesting activities such as antimicrobial, analgesic, anti-tuberculosis, anticonvulsant and anti-hepatitis B viral activities [17]. Density Functional Theory (DFT) is a quantum-mechanical method used to calculate the electronic structure of atoms, molecules, and solids in chemistry and physics. It is widely used to investigate the properties of materials ranging from molecular structures to ionization energies, from the calculation of electrical and magnetic properties to the analysis of reaction steps. It is especially preferred by researchers because of their accuracy and low computational costs. In the literature we see that DFT is successfully used for the analysis of various thiadiazoles and their derivatives [18-25].

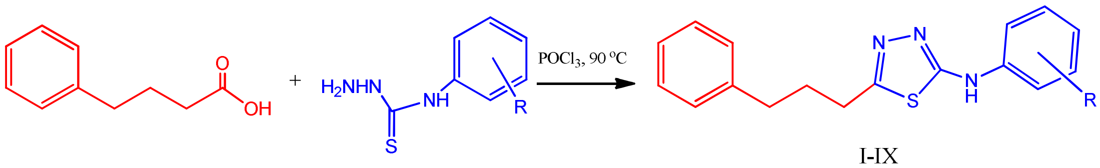
As a result of the mentioned features of this class, we synthesized some new 5-substituted-1,3,4-thiadiazole derivatives, and characterized their structures by using FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopic methods. Additionally, we also studied the absorption properties of the compounds by using UV-Vis spectrophotometer. In the last part of the study, the absorption properties of the compounds were analyzed by using the WB97XD and B3LYP methods and the 6-311++G (d, p) and 6-311++G (2d, 2p) basis sets, respectively. The results were compared with experimental data, and interpreted in detail.

2. Materials and methods

2.1. Synthesis of compound 5-(3-phenylpropyl)-N-(2-chlorophenyl)-1,3,4-thiadiazole-2-amine (I):

The general synthesis method for 1,3,4-thiadiazole compounds is as follows: 4-phenyl butyric acid (1 mol) and N-phenylthiosemicarbazide are taken into a 250 ml double necked flask. The $POCl_3$ (3 mol) is then slowly added to the mixture, and the resulting final mixture is heated up to 90 ^oC under reflux for 3 hours. The desired product is precipitated by adjusting to pH 8-9 with ammonia solution. The precipitate is filtered off and is washed with water and recrystallized from DMSO/water mixture (2:1). $C_{17}H_{16}ClN_3S$, MW: 329.85 g/mol yield: 72 %, mp: 113 ºC; FT-IR (cm^{-1}) υ_{max}: 3158.38- 1492.23 (-NH), 3058.04-2981.99 (aromatic C-H), 2949.92-2854.06 (aliphatic C-H), 1588.42 (C=N thiadiazole), 700.55 (C-S-C), ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^oC) δ (ppm): 2.62 (m, 2H –CH_2), 2.73 (t, 2H –CH_2), 2.95 (t, 2H –CH_2), 7.05-7.80 (9H, aromatic), 9,83 (b, -NH). Anal. Cald. for $C_{17}H_{16}ClN_3S$: C, 61.90 %; H, 4.89 %; N, 12.74 %; Found: C, 60.98 %; H, 4.21 %; N, 12.16 %.

General reaction route and molecular structures are shown **in Scheme 1**.



I-IX

R: I: 2-Cl IV: 2-F VII: 2-OCH_3
II: 3-Cl V: 3-F VIII: 3-OCH_3
III: 4-Cl VI: 4-F IX: 4-OCH_3

Scheme 1. Main reaction route.

2.2. Synthesis of compound 5-(3-phenylpropyl)-N-(3-chlorophenyl)-1,3,4-thiadiazole-2-amine (II):

$C_{17}H_{16}ClN_3S$, MW: 329.85 g/mol yield: 69 %, mp: 119 ºC FT-IR (cm^{-1}) υ_{max}: 3260.64-1493.62 (-NH), 3063.39-3021.26 (aromatic C-H), 2925.05-2818.56 (aliphatic C-H), 1598.14 (C=N thiadiazole), 696.00 (C-S-C), ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^oC) δ (ppm): 2.13 (m, 2H –CH_2), 2.78 (t, 2H –CH_2), 3.10 (t, 2H –CH_2), 7.04-7.50 (9H, aromatic), 10.13 (g, -NH). Anal. Cald. for $C_{17}H_{16}ClN_3S$: C, 61.90 %; H, 4.89 %; N, 12.74 %; Found: C, 61.25 %; H, 5.02 %; N, 12.58 %.

2.3. Synthesis of compound 5-(3-phenylpropyl)-N-(4-chlorophenyl)-1,3,4-thiadiazole-2-amine (III):

$C_{17}H_{16}ClN_3S$, MW: 329.85 g/mol yield: 74 %, mp: 147 ºC FT-IR (cm^{-1}) υ_{max}: 3248.28-1493.20 (-NH), 3026.92 (aromatic C-H), 2980.95-2936.04 (aliphatic C-H), 1595.87 (C=N thiadiazole), 696.47 (C-S-C), ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^oC) δ (ppm): 2.15 (m, 2H –CH_2), 2.78 (t, 2H –CH_2), 3.04 (t, 2H –CH_2), 7.04-7.42 (9H, aromatic). Anal. Cald. for $C_{17}H_{16}ClN_3S$: C, 61.90 %; H, 4.89 %; N, 12.74 %; Found: C, 61.57 %; H, 4.80 %; N, 12.42 %.

2.4. Synthesis of compound 5-(3-phenylpropyl)-N-(2-fluorophenyl)-1,3,4-thiadiazole-2-amine (IV):

$C_{17}H_{16}FN_3S$, MW: 313.39 g/mol yield: 65 %, MP: 114 ºC; FT-IR (cm^{-1}) υ_{max}: 3197.94-1495.22 (-NH), 3052.78 (aromatic C-H), 2981.73-2953.46 (aliphatic C-H), 1562.55 (C=N thiadiazole), 697.58 (C-S-C),^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^{o}C) δ (ppm): 2.14 (m, 2H –CH_2), 2.76 (t, 2H –CH_2), 3.03 (t, 2H –CH_2), 7.01-8.02 (9H, aromatic). Anal. Cald. for $C_{17}H_{16}FN_3S$: C, 65.15 %; H, 5.15 %; N, 13.41 %; Found: C, 64.35 %; H, 4.80 %; N, 12.85 %.

2.5. Synthesis of compound 5(3-phenylpropyl)-N-(3-fluorophenyl)-1,3,4-thiadiazole-2-amine (V):

$C_{17}H_{16}FN_3S$, MW: 313.39 g/mol yield: 68 %, mp: 134 ºC; FT-IR (cm^{-1}) υ_{max}: 3264.77-1493.05 (-NH), 3062.08 (aromatic C-H), 2981.56-2855.76 (aliphatic C-H), 1567.48 (C=N thiadiazole), 696.14 (C-S-C), ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^{o}C) δ (ppm): 2.16 (m, 2H –CH_2), 2.77 (t, 2H –CH_2), 3.05 (t, 2H –CH_2), 6.72-7.36 (9H, aromatic). Anal. Cald. for $C_{17}H_{16}FN_3S$: C, 65.15 %; H, 5.15 %; N, 13.41 %; Found: C, 64.95 %; H, 4.84 %; N, 12.83 %.

2.6. Synthesis of compound 5-(3-phenylpropyl)-N-(4-fluorophenyl)-1,3,4-thiadiazole-2-amine (VI):

$C_{17}H_{16}FN_3S$, MW: 313.39 g/mol yield: 73 %, mp: 101 ºC; FT-IR (cm^{-1}) υ_{max}: 3186.96-1504.28 (-NH), 3023.93 (aromatic C-H), 2981.89-2889.37 (aliphatic C-H), 1569.42 (C=N thiadiazole), 693.42 (C-S-C), ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^{o}C) δ (ppm): 2.05 (m, 2H –CH_2), 2.71 (t, 2H –CH_2), 2.90 (t, 2H –CH_2), 7.03-7.44 (9H, aromatic), 10.82 (g, -NH). Anal. Cald. for $C_{17}H_{16}FN_3S$: C, 65.15 %; H, 5.15 %; N, 13.41 %; Found: C, 65.00 %; H, 5.00 %; N, 12.95 %.

2.7. Synthesis of compound 5-(3-phenylpropyl)-N-(2-methoxyphenyl)-1,3,4-thiadiazole-2-amine (VII):

$C_{18}H_{19}N_3OS$, MW: 325.43 g/mol yield: 71 %, mp: 93 ºC; FT-IR (cm^{-1}) υ_{max}: 3164.58-1495.01 (-NH), 3007.19 (aromatic C-H), 2937.11-2872.61 (aliphatic C-H), 1598.79 (C=N thiadiazole), 693.42 (C-S-C), 1098.86 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^{o}C) δ (ppm): 2.04 (m, 2H –CH_2), 2.30 (t, 2H –CH_2), 3.20 (t, 2H –CH_2), 3.91 (s, 3H *o*-OCH_3), 6.89-7.87 (9H, aromatic). Anal. Cald. for $C_{18}H_{19}N_3OS$: C, 66.43 %; H, 5.88 %; N, 12.91 %; Found: C, 65.58 %; H, 5.70 %; N, 12.58 %.

2.8. Synthesis of compound 5-(3-phenylpropyl)-N-(3-methoxyphenyl)-1,3,4-thiadiazole-2-amine (VIII):

$C_{18}H_{19}N_3OS$, MW: 325.43 g/mol yield: 75 %, mp: 130 ºC FT-IR (cm^{-1}) υ_{max}: 3255.59-1494.22 (-NH), 3057.96 (aromatic C-H), 2901.57-2867.38 (aliphatic C-H), 1573.26 (C=N thiadiazole), 699.96 (C-S-C), 1095.37 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^{o}C) δ (ppm): 2.16 (m, 2H –CH_2), 2.77 (t, 2H –CH_2), 3.03 (t, 2H –CH_2), 3.87 (s, 3H *m*-OCH_3), 6.59-7.36 (9H, aromatic). Anal. Cald. for $C_{18}H_{19}N_3OS$: C, 66.43 %; H, 5.88 %; N, 12.91 %; Found: C, 66.96 %; H, 6.07 %; N, 12.64 %.

2.9. Synthesis of compound 5-(3-phenylpropyl)-N-(4-methoxyphenyl)-1,3,4-thiadiazole-2-amine (IX):

$C_{18}H_{19}N_3OS$, MA: 325.43 g/mol yield: 68 %, mp: 106 ºC; FT-IR (cm^{-1}) υ_{max}: 3246.43-1490.11 (-NH), 3046.09 (aromatic C-H), 2936.39-2936.41 (aliphatic C-H), 1555.85 (C=N thiadiazole), 695.37 (C-S-C), 1077.05 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6, 25 ^oC) δ (ppm): 2.10 (m, 2H –CH_2), 2.76 (t, 2H –CH_2), 2.98 (t, 2H –CH_2), 3.82 (s, 3H *p*-OCH_3), 6.90-7.38 (9H, aromatic). Anal. Cald. 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 %.

3. Results and discussion

3.1. FT-IR, ^{1}H-NMR and ^{13}C-NMR Studies

The FT-IR absorptions of the compounds are summarized in **Table 1.** The absorptions in the IR regions were interpreted for clarifying structures of the obtained compounds. In the IR spectra of the compounds, the N-H stretching vibrations, N-H bending vibrations, the aromatic C-H stretching vibrations, -C=N stretching vibrations, C-S-C vibrations and the aliphatic C-H stretching vibrations were determined at the range of 3264.77-3158.38 cm^{-1}, 1504.28-1490.11 cm^{-1}, 3063.39-3007.19 $cm^{-1,}$ 1598.79-1555.85 cm^{-1}, 700.55-690.86 cm^{-1} and 2981.89-2818.56 cm^{-1}, respectively. Additionally, in the compounds VII-IX, the C-O vibration was determined at 1098.86-1077.05. In addition to these observations, the disappearance of the characteristic carbonyl peak of the starting materials has been demonstrated to occur 1,3,4-thiadiazole derivatives via the cyclization reaction

Table 1. FT-IR absorptions of the synthesized compounds.

COMPOUND	ν N-H	ν C-H_{Ar}	ν C-H_{Aliph}	ν C=$N_{thiadiazole}$	ν C-S-C	ν C-O
I	3158.38 1492.23	3063.39 3021.26	2980.95 2936.04	1588.42	700.55	-
II	3260.64 1493.62	3058.04	2949.92 2854.06	1598.14	696.00	-
III	3248.28 1493.20	3026.92	2925.05 2818.56	1595.87	696.47	-
IV	3197.94 1495.22	3052.78	2981.73 2953.46	1562.55	697.58	-
V	3264.77 1493.05	3062.08	2981.56 2855.76	1567.48	696.14	-
VI	3186.96 1504.28	3023.93	2981.89 2889.37	1569.42	693.42	-
VII	3164.58 1495.01	3007.19	2937.11 2872.61	1598.79	690.86	1098.86
VIII	3255.59 1494.22	3057.96	2901.57 2867.38	1573.26	699.96	1095.37
IX	3246.43 1490.11	3046.09	2936.39 2936.41	1555.85	695.37	1077.05

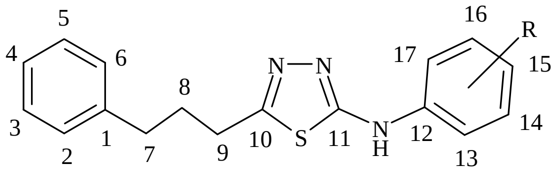
The ^{1}H-NMR data of the compounds (I-IX) are collected in Table 2a. The aromatic, aliphatic and secondary amine protons in the synthesized compounds were investigated for characterization of the structure. There are nine aromatic protons in all compounds. These aromatic protons were observed over the range of 6.59-8.02 ppm. The seconder amine proton was observed at the range of 9.83-10.82 ppm, but was not observed in the compounds III, IV, V, VII, VIII and IX. The three -CH_2 protons (between the 1,3,4-thiadiazole ring and the phenyl ring) were identified as two triplets and a multiplied due to adjacent proton splits. The triplet peaks were determined at the range of 2.30-3.20 ppm and the multiplied peaks were determined at the range of 2.04-2.62 ppm. And also, the protons of -OCH_3 group (compounds VII-IX) were observed at the range of 3.82-3.91 ppm as singlet.

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

COMPOUND	$\delta_{\text{Aliphatic-H}}$	$\delta_{\text{Aromatic-H}}$	$\delta_{\text{N-H}}$
I	2.95 (t, 2H –CH_2) 2.73 (t, 2H –CH_2) 2.62 (m, 2H –CH_2)	7.05-7.80 (9H, aromatic)	9.83 (g, -NH)
II	3.10 (t, 2H –CH_2) 2.78 (t, 2H –CH_2) 2.13 (m, 2H –CH_2)	7.04-7.50 (9H, aromatic)	10.13 (g, -NH)
III	3.04 (t, 2H –CH_2) 2.78 (t, 2H –CH_2) 2.15 (m, 2H –CH_2)	7.04-7.42 (9H, aromatic)	-
IV	3.03 (t, 2H –CH_2) 2.76 (t, 2H –CH_2) 2.14 (m, 2H –CH_2)	7.01-8.02 (9H, aromatic)	-
V	3.05 (t, 2H –CH_2) 2.77 (t, 2H –CH_2) 2.16 (m, 2H –CH_2)	6.72-7.36 (9H, aromatic)	-
VI	2.90 (t, 2H –CH_2) 2.71 (t, 2H –CH_2) 2.05 (m, 2H –CH_2)	7.03-7.44 (9H, aromatic)	10.82 (g, -NH)
VII	3.91 (s, 3H *o*-OCH_3) 3.20 (t, 2H –CH_2) 2.30 (t, 2H –CH_2) 2.04 (m, 2H –CH_2)	6.89-7.87 (9H, aromatic)	-
VIII	3.87 (s, 3H *m*-OCH_3) 3.03 (t, 2H –CH_2) 2.77 (t, 2H –CH_2) 2.16 (m, 2H –CH_2)	6.59-7.36 (9H, aromatic)	-
IX	3.82 (s, 3H *p*-OCH_3) 2.98 (t, 2H –CH_2) 2.76 (t, 2H –CH_2) 2.10 (m, 2H –CH_2)	6.90-7.38 (9H, aromatic)	-

^{13}C-NMR data of the compounds (I-IX) are given in Table 2b. There are two types of aromatic C atoms in the compounds: at the benzene ring (C1-C6 and C12-C17) and at the thiadiazole ring (C10 and C11). While the C10 and C11were determined at the range of 154.20-167.05 ppm and 143.20-160.34 ppm, the C12-C17 and C1-C6 carbons were determined over the range of 109.79-166.31 ppm and 119.05-141.78 ppm, respectively. Aliphatic C7, C8 and C9 carbon atoms were observed at the range of 29.21-40.40 ppm. The C atom of OCH_3 group (compounds VII-IX) was determined at the range of 55.39-56.15 ppm.

Table 2b. ^{13}C-NMR data of the synthesized compounds (δ, ppm, DMSO-d_6).



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

	I	II	III	IV	V	VI	VII	VIII	IX
C_1	140.63	141.78	141.78	141.08	131.08	141.75	144.26	141.15	141.22
C_2	128.43	128.50	128.80	128.48	128.80	126.36	121.03	128.48	128.45
C_3	128.50	128.54	128.86	128.51	128.86	128.80	122.76	128.52	128.51
C_4	128.32	126.13	126.36	123.57	126.36	125.45	119.05	126.11	126.06
C_5	128.50	128.54	128.86	128.51	128.86	128.80	122.76	128.52	128.51
C_6	128.43	128.50	128.80	128.48	128.80	126.36	121.03	128.48	128.45
C_7	34.83	34.99	34.73	34.97	34.72	34.70	39.57	34.99	35.01
C_8	29.60	29.63	29.26	29.64	29.24	29.21	40.40	29.65	29.70
C_9	30.59	31.07	31.30	31.10	31.25	31.20	39.35	31.11	31.20
C_{10}	167.05	163.20	164.12	161.05	154.52	160.24	160.05	160.75	163.39
C_{11}	159.81	160.05	160.34	154.46	143.20	158.45	158.78	159.09	156.39
C_{12}	136.03	141.09	140.15	126.11	141.78	128.84	129.96	141.89	134.32
C_{13}	126.41	117.64	119.17	162.05	113.52	116.16	159.52	109.05	121.30
C_{14}	130.27	135.26	129.31	115.41	160.57	119.71	111.36	166.31	114.82
C_{15}	121.35	123.07	123.43	124.85	164.08	164.70	113.63	103.79	158.70
C_{16}	128.56	130.56	129.31	123.50	130.98	119.71	114.90	130.32	114.82
C_{17}	125.66	115.94	119.17	124.81	119.65	116.16	112.05	109.79	121.30
C_{18} (-OCH_3)							56.15	55.39	55.57

3.2. Absorption study:

The UV-Visible absorption spectra of the compounds were recorded over the range of 200-700 nm, by using chloroform as solvent in concentration 10^{-4} M and results are summarized in Table 4. According to these results; all compounds apart from the compound VII were observed the single absorption peak at the range of 275.5-291.5 nm while the compound VII had two absorption peaks such as 275.5 and 302 nm.

In the compounds I, II and III, there is a decreasing effect of electron density in the structure due to the electron attracting property of the Cl group, which is bound to the -*o*, -*m* and -*p* corners of the phenyl group, respectively, while there is not much change in the maximum absorption points due to the mutual derivation of the structures. Decrease in electron density in the structure causes the hypochromic shift of the maximum absorption point. The maximum absorption point of the Cl atom in the -*para* position is observed bathochromic shift, when compared with the maximum absorption point of the Cl atom in the -*ortho* position. In addition, the maximum absorption point of compounds VII, VIII and IX to which electron-donating group -OCH_3 group is attached have bathochromic shift than others.

3.3. Theoretical study:

Structural optimization of the compounds was performed by using the DFT method with appropriate basis sets without any restriction on the geometry. The Kohn-Sham density functional theory (DFT) was used to calculate the ground state geometries and excitation energy levels of the compounds. The basic molecular structure optimizations of the compounds were performed using the WB97XD method and the Becke3-Lee-Yang-Parr hybrid functional B3LYP method with the 6-311 ++ G (d, p) and the 6-311 ++ G (2d, 2p) basis set, respectively.

Optimized geometries of the compounds were used for UV-Vis calculations. The calculations were performed in the chloroform phase (nstate=60) using the method and basis sets previously mentioned. In the UV calculations, the Self-Consistent Reaction Field (SCRF) method and the Conductor-Polarizable Continuum Model (CPCM) were used in which the solvent-soluble interactions were accounted. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energies, called frontier molecular orbitals (FMOs), were calculated using the same method and basis sets, and molecular electrostatic potential (MEP) surfaces were also obtained. FMO energy eigenvalues were used for calculations of the chemical hardness (η) and energy gab (ΔE). All calculations were performed by using the GAUSSIAN 09 software package program [25].

Table 3. Electronic data of the compounds calculated with B3lyp/6-311++g(2d,2p).

COMPOUND	***E* (au)**	**$E_{\mathbf{HOMO}}$ (eV)**	**$E_{\mathbf{ILUMO}}$ (eV)**	**ΔE**	**η (eV)**	***m (Debye)***
I	-1680.381	-6.133	-1.324	4.810	2.405	5.640
II	-1680.382	-6.148	-1.315	4.833	2.416	4.329
III	-1680.382	-6.037	-1.292	4.745	2.373	2.288
IV	-1320.027	-6.093	-1.277	4.816	2.408	5.555
V	-1320.029	-6.132	-1.287	4.844	2.422	4.250
VI	-1320.028	-6.028	-1.179	4.850	2.425	2.666
VII	-1335.320	-5.759	-1.111	4.648	2.324	4.896
VIII	-1335.320	-5.929	-1.159	4.770	2.385	3.223
IX	-1335.319	-5.757	-1.005	4.752	2.376	6.005

E: Energy; $\Delta \boldsymbol{E}$: $E_{LUMO} - E_{HOMO}$; $\boldsymbol{\eta}$: Chemical hardness ; $\boldsymbol{\chi}$: Electronagativity; $\boldsymbol{m}$: Dipole moment

As a result of the optimizations, the minimum molecular energies of the compounds were calculated to be around -1680 au for the Cl substitute group, -1320 au for the F substitute group and -1335 au for the methoxy substitute group. Also, as a result of calculations, it has been observed that the minimum molecular energy levels of the compounds are not too much affected by the *o*-, *m*- and *p*-positions of Cl, F or methoxy substituents. However, the positions of the substituents affected the HOMO-LUMO energies, which caused the change of ΔE energy range ($\Delta \boldsymbol{E}$: $E_{LUMO} - E_{HOMO}$) (Table 3). In the *o*-position of the F atom with the largest electronegativity among the substituents, while the HOMO-LUMO energy gab of F isomer structures had the lowest value, it had the highest value at the *p*-position. This situation was not observed in Cl and methoxy substituents. While the energy gab ΔE took the highest value at *m*-position of Cl and methoxy, it was the lowest value at *p*-position. Therefore, this change in electronic levels also affected the chemical hardness of the compounds. It was seen that, the electronegativity values of the Cl, F and methoxy directly affected the chemical hardness (or chemical softness) of the compounds. While the chemical hardness of isomer structures substituted with F having the highest electronegativity were highest, the chemical hardness of the isomeric group substituted with methoxy having the lowest electronegativity was calculated as the lowest. In addition, the dipole moments of the isomer compounds substituted with the Cl and F were calculated as the largest at *o*-position and the smallest at *p*-position. As a different case, the dipole moment in the methoxy isomer structures had the lowest value in the m- position and the largest value in the *p*-position.

Table 4. Experimental and theoretical UV-Vis data (nm).

		Theoretical	
COMPOUND	***Experimental***	**wB97XD**	**B3LYP**
I	284.5	266.73	297.18
II	285.0	265.22	294.04
III	291.5	266.63	299.86
IV	290.0	264.49	295.29
V	288.0	264.6	293.15
VI	277.0	258.34	289.97
VII	276/303	273.23	305.42
VIII	365.0	261.81	298.59
IX	288.5	250.2	393.41

The experimental data of UV absorption of the compounds and the results of the theoretical calculations are compatible with each other (Table 4). It is evident in both the experimental and theoretical calculations that, in the Cl and F isomeric compounds, the positions of the Cl and F substituents have little effect on UV absorption peaks. Besides, both in the theoretical and experimental results, the change of the F substituent from the *o*-position to the *p*-position in the F-isomeric structures caused an absorption that varied from long wavelength to short wavelength. Furthermore, the isomeric structures with F and Cl substituents are examined, it is seen that there is an inverse relationship between ΔE energy range and absorption wave length; That is, as ΔE decreases, the absorption shifts towards the longer wavelength.

4. Conclusions

The new nine substituted 1,3,4-thiadiazole compounds were synthesized and their structures were illuminated by using FT-IR, ^{1}H-NMR and ^{13}C-NMR. We also studied the absorption properties of the obtained compounds by using UV-Vis spectrophotometer. Furthermore, the electronic and chemical parameters were calculated to show how isomeric 1,3,4-thiadiazole compounds were affected by electronegativities of the F, Cl and methoxy substituents. Experimental UV-Vis data were supported by theoretical calculations and an attempt was made to establish a relationship between the HOMO-LUMO energy gab ΔE, chemical hardness and UV absorption wavelengths.

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