Turk J Chem
36 (2012) , 457 – 466.

doi:10.3906/kim-1110-43

Synthesis, characterization, and antioxidant activities of new trisubstituted triazoles

Kemal SANCAK*, Yasemin ÜNVER, Dilek ÜNLÜER, Esra DÜĞDÜ, Gülcan KÖR, Fatih ÇELİK, Emrah BİRİNCİ

Department of Chemistry, Karadeniz Technical University, 61080 Trabzon-TURKEY

e-mail: unver.yasemin@hotmail.com

Received: 25.10.2011

A series of new 4-(3,4dimethoxyphenethyl)-3,5-akyl/aryl-4H-1,2,4-triazoles **(3a-g)** were obtained by reaction of ethyl N'-(alkylidene/arylidene)hydrazonate **(1)** and 2-(3,4-dimethoxy phenyl)ethanamine **(2).** Compounds **4d**, **e**, and **g** were synthesized from the reaction of corresponding compounds **3d**, **e**, and **g** with BBr_3, respectively. The 10 new compounds synthesized were characterized by elemental analyses, IR, ^{1}H-NMR, and ^{13}C-NMR spectral data. The structure of compound **3g** was inferred through IR, ^{1}H-, ^{13}C-NMR, elemental analyses, and X-ray spectral techniques. In addition, the newly synthesized chemicals were screened for their antioxidant properties. Among the chemicals tested, **4d**, **e**, and **g** exhibited the highest degree of antioxidant activity.

Key Words: Synthesis, 1,2,4-triazole, antioxidant activity, boron tribromide, X-ray

Introduction

Triazole and its derivatives represent an important class of heterocycles. They are of biological importance and are used in the synthesis of drugs[12] Triazole derivatives are also used in the synthesis of antibiotics, fungicides, herbicides, and plant growth hormone insulators and are potentially good corrosion inhibitions[3–5] The incorporation of various substituents into the 1,2,4-triazole ring and its fusion with various heterocyclic systems yield compounds with enhanced biological activities. The arrangement of 3 basic nitrogen atoms in the triazole ring induces the antiviral activities in the compounds containing this ring.[6] The 1,2,4-triazole nucleus has been incorporated into a wide variety of therapeutically interesting drug candidates including H1/H2 histamine receptor blockers, cholinesterase active agents, CNS stimulants, antianxiety and sedatives,[7] and those

*Corresponding author

with antimycotic activity such as fluconazole, itraconazole, and voriconazole.[8,9] Moreover, there are some known drugs containing 1,2,4-triazole moiety, e.g., triazolam, alprazalam, etizolam, furacylin, and ribavirin.[10–14] In the present study, prompted by these observations, the synthesis and antioxidant screening of new trisubstituted 1,2,4-triazole derivatives and as hybrid molecules including different pharmacophores were examined.

Experimental

Materials and measurements

Ethyl N'-(alkylidene/arylidene)hydrazonate **(1)** was prepared according to procedures reported in the literature.[15] All other chemicals were obtained from Merck or Sigma-Aldrich and used as supplied. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian XL-200 NMR spectrophotometer in DMSO-d_6. IR spectra were recorded on a Perkin-Elmer Spectrum one FT-IR spectrometer in KBr pellets. The MS spectra were measured with an Micromass Quattro LC/ULTIMA LC-MS/MS spectrometer with EtOH as solvent. The experiment was performed in the positive ion mode. Elemental analyses were performed on a Hewlett-Packard 185 CHN analyzer. Melting points were measured on an electrothermal apparatus and are uncorrected.

General procedure for the preparation of compounds (3a-g)

4-(3,4-dimethoxyphenethyl)-3,5-alkyl/aryl-4*H*-1,2,4-triazole (3a-g): Ethyl N'-(alkylidene/arylidene) hydrazonate **(1)** (10 mmol) together with 2-(3,4-dimethoxy phenyl)ethanamine **(2)** (10 mmol) was heated without solvent in a sealed tube for 2 h at 130-140 °C. Then the mixture was cooled to r.t. and a solid formed. The crude product was recrystallized using ethyl acetate/petroleum ether (1:2) to afford the desired compound.

4-(3,4-dimethoxyphenethyl)-3,5-dimethyl-4*H*-1,2,4-triazole (3a)

Yield: 1.6 g (69%); colorless crystals, mp 154-157 °C. IR (KBr, ν, cm^{-1}): 1649 (C=N), 1591 (C=C), 1260 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.08 (s, 6H, CH_3), 2.81 (t, 2H, Ar–CH_2), 3.67 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 4.02 (t, 2H, N-CH_2), 6.54-6.61 (m, 2H, arom. H), 6.81-6.85 (m, 1H, arom. H); ^{13}C-NMR (DMSOd_6, δ, ppm): 10.01 (2CH_3), 34.55 (Ar-CH_2), 44.27 (N-CH_2), 55.23 and 55.33 (2OCH_3), arom. C [111.56 (CH), 112.62 (CH), 120.80 (CH), 129.91 (C), 147.48 (C), 148.45 (C)], 150.50 (C=N). Anal. Calc. For $C_{14}H_{19}N_3O_2$ MS: m/z 261.32 (M^+) C, 64.35; H, 7.33; N, 16.08. Found: C, 64.34; H, 7.44; N, 16.14%.

4-(3,4-dimethoxyphenethyl)-3-ethyl-5-methyl-4*H*-1,2,4-triazole (3b)

Yield: 2.8 g (80%); colorless crystals, mp 69-70 °C. IR (KBr, ν, cm^{-1}): 1677 (C=N), 1591 (C=C), 1259 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 1.15 (t, 3H, C$\underline{H}_3$-CH_2) 2.10 (s, 3H, CH_3), 2.44 (q, 2H, CH_3-C$\underline{H}_2$), 2.80 (t, 2H, Ar–CH_2), 3.66 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 4.01 (t, 2H, N-CH_2), 6.55-6.62 (m, 2H, arom. H), 6.81-6.85 (m, 1H, arom. H); ^{13}C-NMR (DMSOd_6, δ, ppm): 10.03 ($\underline{C}H_3$-CH_2), 11.15 (CH_3), 17.38 ($CH_3\underline{C}H_2$), 34.55 (Ar-CH_2), 44.27 (N-CH_2), 55.23 and 55.33 (2OCH_3), arom. C [111.64 (CH), 112.60 (CH), 120.85 (CH), 129.89 (C), 147.52 (C), 148.50 (C)], 150.52 and 154.63 (2C=N). Anal. Calc. For $C_{15}H_{21}N_3O_2$ MS: m/z 275.35 (M^+) C, 65.43; H, 7.69; N, 15.26. Found: C, 65.40; H, 7.60; N, 16.56%.

4-(3,4-dimethoxyphenethyl)-3-methyl-5-(thiophene-2-yl-methyl)-4*H*-1,2,4-triazole (3c)

Yield: 2.9 g (82%); colorless crystals, mp 63-64 °C. IR (KBr, ν, cm^{-1}): 1607 (C=N), 1516 (C=C), 1262 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.10 (s, 3H, CH_3), 2.58 (t, 2H, Ar–CH_2), 3.67 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.99 (t, 2H, N-CH_2), 4.17 (t, 2H, thiophene-CH_2), 6.52-6.55 (m, 2H, thiophene H), 6.82-6.86 (m, 1H, thiophene H), 6.97-7.02 (m, 2H, arom. H), 7.40-7.44 (m, 1H, arom. H); ^{13}C-NMR (DMSOd_6, δ, ppm): 9.97 (CH_3), 24.97 (thiophene-CH_2), 34.53 (Ar-CH_2), 44.36 (N-CH_2), 55.25 and 55.32 (2OCH_3), arom. C [111.60 (CH), 112.44 (CH), 120.75 (CH), 129.65 (C), 138.98 (C)], thiophene C [125.34 (CH) 126.12 (CH), 126.88 (CH), 104.18 (C)] 152.08 and 153.05 (2C=N). Anal. Calc. For $C_{18}H_{21}N_3O_2S$ MS: m/z 343.44 (M^+) C, 62.95; H, 6.16; N, 12.23. Found: C, 62.90; H, 6.16; N, 12.28%.

4-(3,4-dimethoxyphenethyl)-3,5-diphenyl-4*H*-1,2,4-triazole (3d)

Yield: 3.4 g (80%); colorless crystals, mp 209-211 °C. IR (KBr, ν, cm^{-1}): 1648 (C=N), 1591 (C=C), 1235 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.39 (t, 2H, Ar-CH_2), 3.46 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 4.36 (t, 2H, N-CH_2), 6.07-6.10 (m, 2H, arom. H), 6.62-6.66 (m, 1H, arom.H), 7.55 (s, 10H, arom. H); ^{13}C-NMR (DMSOd_6, δ ppm): 34.86 (Ar-CH_2), 46.78 (N-CH_2), 55.59 and 56.19 (2OCH_3), arom. C [112.10 (CH), 112.30 (CH), 120.80 (CH), 129.20 (CH), 129.50 (CH), 130.4 (CH), 128.50 (C), 148.20 (C), 148.40 (C), 149.20 (C)], 156.25 (C=N). Anal. Calc. For $C_{24}H_{23}N_3O_2$ MS: m/z 385.18 (M^+) C, 74.78; H, 6.01; N, 10.90. Found: C, 74.79; H, 6.00; N, 10.90%.

4-(4-(3,4-dimethoxyphenethyl)-5-(thiophene-2-yl-methyl)-4*H*-1,2,4-triazole-3-yl)phenol (3e)

Yield: 4.7 g (75%); colorless crystals, mp 127-130 °C. IR (KBr, ν, cm^{-1}): 3401 (OH), 1611 (C=N), 1590 (C=C), 1281 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.44 (t, 2H, Ar-CH_2), 3.61 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 4.11 (t, 2H, N-CH_2), 4.28 (t, 2H, thiophene-CH_2), thiophene + arom. H [6.31-6.38 (m, 1H), 7.02 (s, 1H), 6.73-6.77 (m 1H), 7.30-7.34 (m, 2H), 6.83-6.88 (m, 3H), 7.46 (m, 2H)], 9.85 (s, 1H, OH); ^{13}C-NMR (DMSOd_6, δ, ppm): 25.09 (thiophene-CH_2), 38.84 (Ar-CH_2), 40.94 (N-CH_2), 55.85 and 56.13 (2OCH_3), thiophene + arom. C [116.13 (CH), 118.96 (C), 119.56 (CH), 121.12 (CH), 123.89 (CH), 124.67 (C), 126.21 (CH), 127.73 (CH), 127.98 (CH), 129.95 (C), 130.69 (CH) 131.67 (CH), 137.45(C), 139.49 (C)], 148.20 and 151.38 (2C=N). Anal. Calc. For $C_{23}H_{23}N_3O_3S$ MS: m/z 421.51 (M^+) C, 65.54; H, 5.50; N, 9.97. Found: C, 65.64; H, 5.42; N, 9.82%.

3-(4-chlorophenyl)-4-(3,4-dimethoxyphenethyl)-5-(thiophene-2-yl-methyl)-4*H*-1,2,4-triazole (3f)

Yield: 2.2 g (81%); colorless crystals, mp 121-122 °C. IR (KBr, ν, cm^{-1}): 1604 (C=N), 1513 (C=C), 1266 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.46 (t, 2H, Ar-CH_2), 3.56 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 4.22 (t, 2H, N-CH_2), 4.36 (t, 2H, thiophene-CH_2), thiophene + arom. H [6.21-6.25 (m, 2H), 6.67-6.71 (m, 1H), 7.01-7.05 (m, 2H), 7.42-7.54 (m, 5H)]; ^{13}C-NMR (DMSOd_6 δ, ppm): 25.09 (thiophene-CH_2), 34.65 (Ar-CH_2), 40.60 (N-CH_2), 54.90 and 55.30 (2OCH_3), thiophene + arom. C [111.40 (CH), 111.70 (CH), 118.47 (CH), 120.30 (CH), 126.30 (C), 130.5 (CH), 134.20 (C), 138.50 (C), 147.50 (C), 148.40 (C), 125.49 (CH), 126.42 (CH),

126.94 (CH), 128.83 (C)] 153.86 and 153.50 (2C=N). Anal. Calc. For $C_{23}H_{22}ClN_3O_2S$ MS: m/z 439.96 (M^+) C, 62.79; H, 5.04; Cl, 8.06; N, 9.55. Found: C, 62.75; H, 7.60; Cl, 8.06; N, 9.59%.

4-(5-benzyl-4-(3,4-dimethoxyphenethyl)-4*H*-1,2,4-triazole-3-yl)phenol (3g)

Yield: 6.5 g (79%); colorless crystals, mp 120-121 °C. IR (KBr, ν, cm^{-1}): 3402 (OH), 1614 (C=N), 1588 (C=C), 1241 (C-O-C); ^{1}H-NMR (DMSO-d_6, δ, ppm): 2.37 (t, 2H, Ar–CH_2), 3.61 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 4.05 (t, 2H, N-CH_2), 4.27 (s, 2H, triazole-CH_2-Ar), 6.26 (s, 2H, arom. H), 6.83-6.87 (m, 4H, arom. H), 7.26-7.36 (m, 6H, arom. H), 9.85 (s, 1H, OH); ^{13}C-NMR (DMSOd_6, δ, ppm): 30.31 (triazole-CH_2-Ar), 34.47 (Ar-CH_2), 45.85 (N-CH_2), 55.04 and 55.32 (2OCH_3), arom. C [111.50 (CH), 111.80 (CH), 115.30 (CH), 118.3 (C), 120.20 (CH), 126.60 (CH), 128.50 (CH), 129.10 (C), 129.80 (CH), 130.26 (C), 136.40 (CH), 147.40 (CH), 148.40 (C), 158.40 (C)], 153.25 and 153.99 (2C=N). Anal. Calc. For $C_{25}H_{25}N_3O_3$ MS: m/z 415.19 (M^+) C, 72.27; H, 6.06; N, 10.11. Found: C, 72.27; H, 6.00; N, 11.17%.

General procedure for the preparation of compounds 4-(2,3-diaryl-4*H*-1,2,4-triazole-4-yl) ethyl)benzen-1,2-diol (4d, e, g): A solution of the 4-(3,4dimethoxyphenethyl)-3,5-alkyl/aryl-4H-1,2,4-triazole (**3d**, **3e**, **3g**) (10 mmol) in chloroform (100 mL) was added to a solution of boron tribromide (10 mmol) in chloroform (200 mL) at 0 °C. The reaction mixture was then stirred under nitrogen atmosphere, at ambient temperature, for 1 h, and was poured into ice containing sufficient 50% sodium hydroxide to attain pH 10. Addition of concentrated sulfuric acid provided a precipitate, which was extracted into ether. The combined organic extract was washed with water and brine, and then dried and concentrated in vacuo to obtain compounds (**4d**, **e**, **g**). The crude product was recrystallized using ethyl acetate/petroleum ether (1:4) to afford the desired compound (Scheme 1).

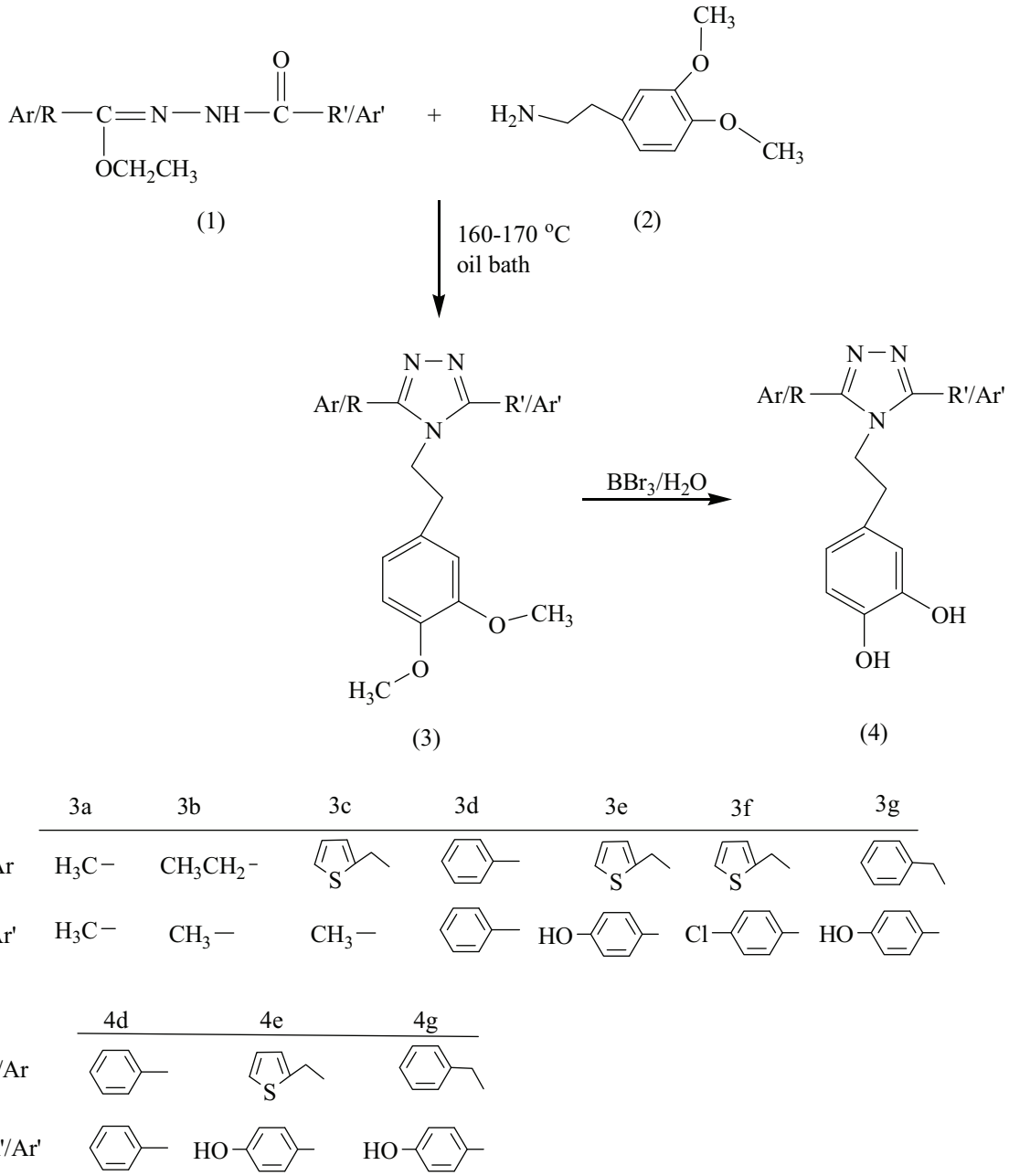
4-(2-(3,5-diphenyl-4*H*-1,2,4-triazole-4-yl)ethyl)benzen-1,2-diol (4d)

Yield: 2.4 g (79%); colorless crystals, mp 230-232 °C IR (KBr, ν, cm^{-1}): 3296 (OH), 1606 (C=N), 1584 (C=C); ^{1}H-NMR (DMSOd_6, δ, ppm): 2.29 (t, 2H, Ar-CH_2), 4.20 (t, 2H, N-CH_2), 5.85-5.89 (m, 1H, arom. H), 6.03 (s, 1H, arom. H), 6.42-6.46 (m, 1H, arom. H), 7.55 (t, 10H, arom. H), 8.71 (s, 2H, OH); ^{13}C-NMR (DMSO-d_6, δ, ppm): 33.71 (Ar-CH_2), 34.03 (CH_2-Ph), 45.99 (N-CH_2), arom CH [115.34, 115.56, 118.75, 128.60, 128.72] arom. C [127.19, 127.72, 129.76, 143.88, 145.02], 154.55 (C=N). Anal. Calc. For $C_{22}H_{19}N_3O_2$ MS: m/z 357.41 (M^+) C, 73.93; H, 5.36; N, 11.76. Found: C, 73.90; H, 5.37; N, 11.78%.

4-[2-[3-(4-hydroxyphenyl)-5-(thiophene-2-yl-methyl)-4*H*-1,2,4-triazole-4yl]ethyl]benzen-1,2-diol (4e)

Yield: 2.2 g (59%); colorless crystals, mp 281-284 °C IR (KBr, ν, cm^{-1}): 3412 (OH), 1613 (C=N), 1547 (C=C); ^{1}H-NMR (DMSOd_6, δ, ppm): 2.71 (t, 2H, Ar-CH_2), 4.22 (t, 2H, N-CH_2), 4.25 (s, 2H, thiophene-CH_2), thiophene + arom. H [6.17 (d, 1H), 6.32-6.55 (m, 2H), 6.82-7.05 (m, 4H), 7.36-7.44 (m, 3H)], 9.85 (s, 1H, OH), 10.36 (s, 2H, OH); ^{13}C-NMR (DMSO-d_6, δ, ppm): 25.80 (thiophene-CH_2), 38.88 (Ar-CH_2), 41.34 (N-CH_2), thiophene + arom. CH [105.00, 116.70, 119.68, 120.04, 123.95, 127.01, 128.78, 131.43], thiophene + arom. C [118.96, 124.80, 136.90, 139.50, 144.97, 146.02], 153.67 and 154.38 (2C=N). Anal. Calc. For

$C_{21}H_{19}N_3O_3S$ MS: m/z 393.46 (M^+) C, 64.10; H, 4.87; N, 10.68; S, 8.15. Found: C, 63.10; H, 5.87; N, 10.00; S, 8.87%.



Scheme 1. Synthetic pathway for the preparation of compounds **3** and **4**.

4-(2-(3-benzyl-5-(4-hydroxyphenyl)-4*H*-1,2,4-triazole-4-yl)ethyl)benzen-1,2-diol (4g)

Yield: 2.8 g (63%); colorless crystals, mp 243-246 °C IR (KBr, ν, cm^{-1}): 3335 (OH), 1611 (C=N), 1520 (C=C); ^{1}H-NMR (DMSOd_6, δ, ppm): 2.29 (t, 2H, Ar-CH_2), 3.97 (t, 2H, N-CH_2), 4.02 (s, 2H, triazole-CH_2-

Ar), arom. H [6.08 (d, 1H), 6.29 (s, 1H), 6.55-6.59 (m 3H), 7.23-7.43 (m, 7H)] 8.78 (s, 1H, OH), 8.80 (s, 1H, OH), 9.93 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6, δ, ppm): 31.16 (triazole-CH_2-Ar), 35.27 (Ar-CH_2), 43.16 (N-CH_2), arom CH [104.9, 116.25, 116.64, 119.88, 121.13, 127.46, 129.35, 130.69], arom. C [119.13, 128.45, 137.20, 144.74, 145.89, 159.34], 154.07 and 154.70 (2C=N). Anal. Calc. For $C_{23}H_{21}N_3O_3$ MS: m/z 393.46 (M^+) C, 71.30; H, 5.46; N, 10.85. Found: C, 71.20; H, 5.54; N, 10.76%.

Results and discussion

This paper has presented the synthesis of new trisubstituted triazole derivatives incorporating different pharmacophores as hybrid molecules possessing antioxidant activities (Scheme 1).

In the first part of this study, compounds **3a-g** were synthesized via the reaction of compounds **1** with compound **2** (Scheme 1). Analytical and spectroscopic data of compounds **3** confirmed the success of the cyclization reaction. The IR data indicated the formation of compounds **3** by the disappearance of C=O band and NH stretching frequency of compounds **1** about at 1700-1750 cm^{-1} and 3300 cm^{-1}, respectively, and the appearance of a new band at 1604-1649 cm^{-1} belonging to C=N of the 1,2,4-triazole ring. In the ^{1}H-NMR spectrum of compounds **3**, the existence of **3** was revealed by the disappearance of the chemical shifts belonging to O-C_2H_5 and NH protons (δ=9.15-11.59 ppm) in the precursor **1** after the cyclization and the appearance of a new peak at δ=3.66-3.69 ppm belonging to O-CH_3 protons. ^{13}C-NMR, elemental analyses, and mass spectral data were also in agreement with the proposed structure.

The synthesis of 4-(2,3-diaryl-4*H*-1,2,4-triazole-4-yl)ethyl)benzen-1,2-diol (**4d**, **e**, **g**) was performed by the reaction of compounds **3** with BBr_3 at the reflux temperature in the presence of chloroform (Scheme 1).

Antioxidant activity

DPPH assay: T Radical scavenging activity of synthesized compounds against stable free radical 2,2-diphenyl-2-picrylhydrazyl hydrate (DPPH, Sigma-Aldrich Chemie, Steinheim, Germany) was determined spectrophotometrically. When DPPH reacts with an antioxidant compound, which can donate hydrogen, it is reduced. Following the reduction, its deep violet color in methanol bleaches to yellow, showing a significant absorption decrease at 517 nm. Fifty milliliters of various concentrations of the compounds dissolved in methanol was added to 5 mL of a 0.004% methanol solution of DPPH. After a 30 min incubation period at room temperature, the absorbance was read against a blank at 517 nm (ATI-Unicam UV-2 UV–Vis spectrophotometer, Cambridge, UK). Free radical DPPH inhibition as a percentage (I%) was calculated as follows:

I% = $(A_{blank} - A_{sample}/A_{blank}) \times 100$, where A_{blank} is the absorbance of the control reaction (containing all reagents except the test compound), and A_{sample} is the absorbance of the test compound. Compounds' concentration providing 50% inhibition (IC50) was calculated from the graph plotted as inhibition percentage against compound concentration (Figures 1 and 2). Tests were carried out in triplicate, and butylated hydroxytoluene (BHT) was used as a positive control.[16]

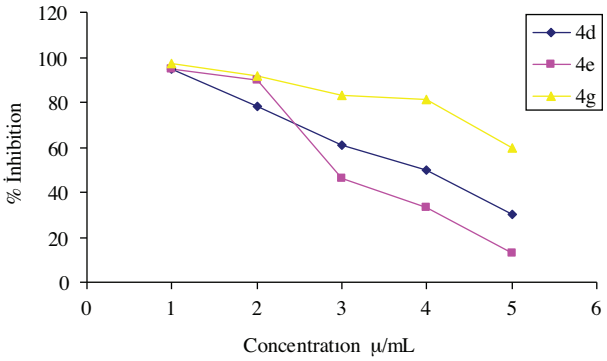


Figure 1. %I values of compounds **4d**, **e**, **g.**

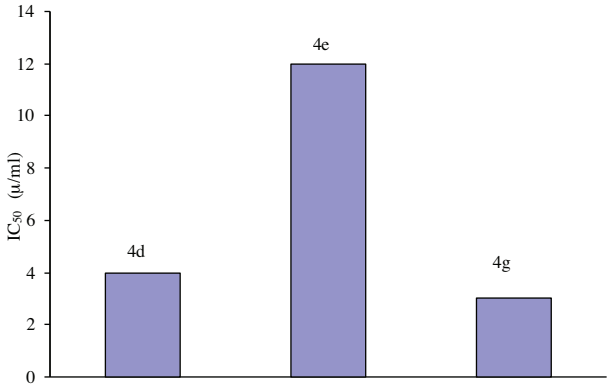


Figure 2. IC_{50} values of compounds **4d**, **e**, **g.**

Crystal structure determination of 3g

Data collection

A block single crystal with dimensions 0.570 × 0.357 × 0.110 mm was mounted on a goniometer and data collection was performed on a STOE IPDS II[17] diffractometer by the ω scan technique using graphite-monochromatic MoK_α radiation ($\lambda = 0.71073$ Å) at 296 K. The intensity symmetries indicate the triclinic $C2/c$ space group. A total of 20,262 reflections (5759 unique) were performed within 2θ range 1.45° and 28.50°.

Correction for absorption ($\mu = 0.086$), by comparison of the intensities of equivalent reflections, was applied using X-RED software and cell parameters were determined by using X-AREA software.[17] The initial partial solution obtained by direct methods as implemented in the program SHELXS-97 was expanded and refined by means of the program SHELXL-97.[18] The program ORTEP-3 for Windows was used in the preparation of the figure.[19] All non-hydrogen atoms were refined anisotropically. The refinement carried out by full matrix least squares method on the positional and anisotropic temperature parameters of non-hydrogen atoms corresponding to 297 crystallographic parameters. All H atoms were included in calculated positions and refined using a riding model. The structure was refined to $R_{int} = 0.0591$ with 2856 observed reflections by the condition of $I > 2\sigma(I)$ threshold. The absorption correction was applied with integration type ($T_{\min} = 0.9573$ and $T_{\max} = 0.9889$).

Results and riscussion

The crystallized structure of compound **3g** ($C_{25}H_{27}N_3O_4$) is in the monoclinic space group C 2/c with Z = 8 in the unit cell (Table 1, Figure 3). In the molecule of compound **3g**, $C_{25}H_{27}N_3O_4$, contains the 1,2,4-triazole ring and the aromatic ring groups are bridged by triazole moiety. The whole molecule is not planar but each ring system is planar individually. The triazole ring is oriented with respect to the 5-benzyl and 3,4-dimethoxyphenethyl rings at dihedral angles of 86.74(1)° and 7.44(1)°, respectively, which shows that triazole and benzyl rings are almost perpendicular to each other. The triazole ring system is almost planar with the maximum deviation of -0.003(2)Å for atom C8. In the molecule of compound **3g**, the bond lengths

and angles are within normal ranges and they are comparable with those of the related structure.[20] Compound **3g**, $C_{25}H_{27}N_3O_4$, containing the triazole ring, displays the characteristic features of 1,2,4-triazole derivatives. From analysis of the values therein, it can be concluded that for the structure N1=C8 and N2=C9 are well defined double bonds, and are the shortest bonds in the heterocycle ring. The torsion angle {(N3-C16-C17-C18) is 161.65(16)°} shows that for compound **3g** the side chain conformation is induced by the anti-conformation.

Structurally, compound **3g** forms C-H...O and O-H...N type intermolecular hydrogen bonds and an O-H...O type intramolecular hydrogen bond. The intermolecular contacts are C24-H24A...O3^{i}, O4-H33...N1^{ii} and O4-H22...N2^{iii} where the H atoms of the water molecule are engaged in hydrogen bonding with N1 and N2 atoms of the triazole system [symmetry codes: (i) –x + 3/2, –y + 1/2, –z + 1; (ii) x + 1/2, –y + 1/2, z + 1/2; (iii) –x + 2, y, –z + 1/2]. There is also an intramolecular contact, namely O1-H1...O4. C-H... π interaction is present in compound **3g**, between the benzene ring and the C17 atom [C17-H17A...Cg (2), Cg (2) is C1/C2/C3/C4/C5/C6 with symmetry code: x, y, z]; the details of the bonds are given in hydrogen bonding Table 2.

Table 1. Crystal data and structure refinement parameters for compound **3g**.

Formula: $C_{25}H_{27}N_3O_4$	$\theta_{min} = 1.45°\theta_{max} = 28.50°$
Formula weight: 433.50	$R_1 =$ 0.054
Crystal system: monoclinic	$(\Delta/\sigma)_{max} =$ 0.000
Space group: $C2/c$	$(\Delta\rho)_{max} =$ 0.147 eÅ^{-3}
Z = 8	$(\Delta\rho)_{min} =$ −0.210 eÅ^{-3}
a = 23.8517(17) Å	F(000) = 1840
b = 17.7443(7) Å	$\mu = 0.086mm^{-1}$
c = 11.2917(7) Å	Measurement: STOE IPDS II
$\beta = 106.130(5)$	Program system: STOE X-RED
V = 4590.9(5) Å^3	Structure determination: Direct methods
No. of reflections used = 20,262	Refinement: Full matrix

Table 2. Hydrogen-bond geometry (Å, °).

D-H...A	D-H	H...A	D...A D-	H...A
C24-H24A...O3^{i}	0.96	2.46	3.413(2)	170.7
O4-H33...N1^{ii}	0.86(3)	2.03(3)	2.890(2)	176(2)
O4-H22...N2^{iii}0.89(3)	1.90(3)	2.768(2)	164(3)	
O1-H1...O4	0.82	1.86	2.684(2)	178.8
C17-H17A...Cg (2)^{iv}	0.97	2.770	3.670	154.0

Symmetry codes: (i) –x + 3/2, –y + 1/2, –z + 1; (ii) x + 1/2, –y + 1/2, z + 1/2; (iii) –x + 2, y, –z + 1/2; (iv) x, y, z

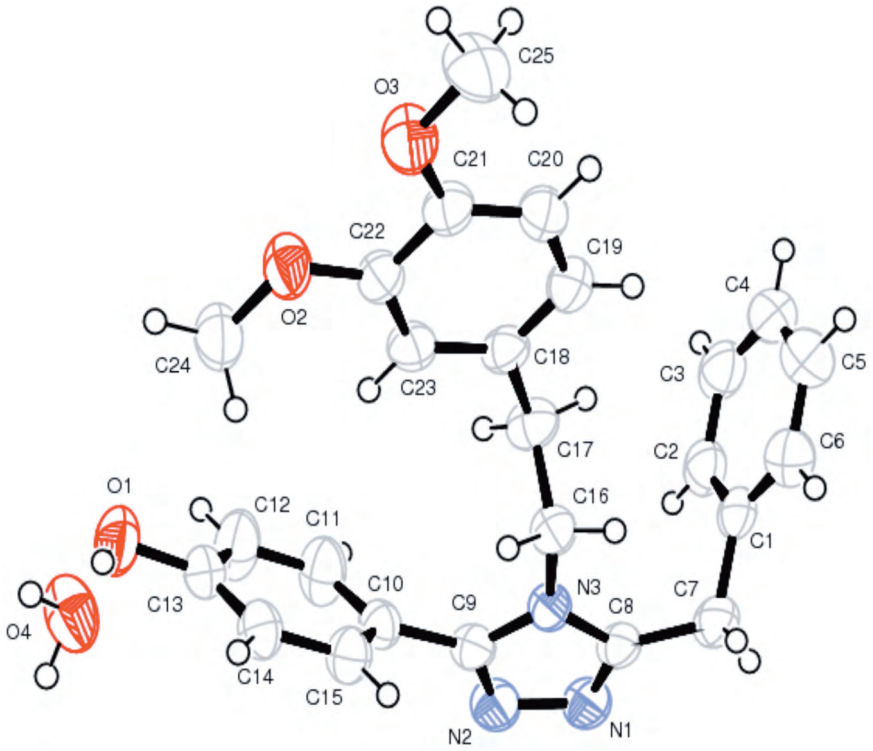


Figure 3. Ortep III diagram of compound **3g**. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

Conclusions

New trisubstituted 1,2,4-triazole derivatives were synthesized and characterized based on elemental analysis, ^{1}H- and ^{13}C-NMR spectra, mass spectra, and IR. In addition, compound **3g** was characterized by combination of X-ray crystallography and theoretical methods. The crystal structure of the compound **3g** is stabilized by C-H. . . O and O-H. . . N type intermolecular hydrogen bonds and O-H. . . O type intramolecular hydrogen bond.

To support the solid state structure, the geometric parameters and single crystal X-ray diffraction technique were used. Good correlation was found between the experimental and computed values. Furthermore, the antioxidant activities of compounds **4d**, **e**, and **g** were evaluated. Strong scavenging effects of compounds **4d**, **4e**, and **4g** were noted on the level of DPPH radical. These results show that in vitro the newly synthesized 4-(2,3-diaryl-4*H*-1,2,4-triazole-4-yl)ethyl)benzen-1,2-diols (**4d**, **e**, **g**) possess highly potent antioxidant properties.

Acknowledgments

This work was supported by the Research Fund of Karadeniz Technical University (Turkey). We are grateful to Dr. Yavuz Köysal (for X-ray data).

References

1. Ünver Y.; Düğdü E.; Sancak K.; Er M.; Karaoğlu Ş. A. *Turk J Chem* **2009** *33* 135147
2. Sancak K.; Ünver Y.; Kazak, C.; Düğdü E.; Arslan, B. *Turk J Chem* **2010** *34* 771- 780.
3. Li, W.; Wu, Q.; Ye, Y.; Luo, M.; Hu, L.; Gu, Y.; Niu, F.; Hu, J. *Spectrochim Acta A* **2004** *60* 2343-2354.
4. Kritsanida, M.; Mouroutsou, A.; Marakos, P.; Pouli, N.; Papakonstantinou-Garoufalias C, M. *Il Farmaco* **2002**, *57*, 253-257.
5. Holla, B. S.; Poorjary, K. N.; Rao, B. S.; Shivananda, M. K. *Eur. J. Med. Chem.* **2002**, *37*, 511-517.
6. Masuda, K.; Toga, T.; Hayashi, N.; *Labelled Compd.* **1975**, *11*, 301-304.
7. Schreier, E. *Helv. Chim. Acta* **1976**, *59*, 585-606.
8. The Merck Index, *12th ed. Merck Co. Inc*, Whitehouse Station, NJ, USA, **1996**.
9. Haber, J. *Cas, Lek. Cek* **2001**, *140*, 596.
10. Brucato, A.; Copoola, A.; Gianguzza, S.; Provenzano, P. M. *Bull. Soc. Ital. Biol. Sper.* **1978**, *54*, 1051.
11. Coffen, D. L.; Fryer, R. I. *U.S. Patent* **1974**, *3*, 849, 434; *Chem. Abstr.* **1975**, *82*, 730044v.
12. Shiroki, M.; Tahara, T.; Araki, K. *Jap Patent* **1975**, 75100096, *Chem. Abstr.* **1976**, *84*, 59588k.
13. Povelista, F. D.; Gural, A. G. *Antibiotiki Moscow* **1973**, *18*, 71; *Chem. Abstr.* **1973**, *78*, 93044.
14. Sidwell, R.W.; Allen, L. B.; Hoffman, J. H.; Witkowsti, J. T.; Simon, L. N.; *Proc. Soc. Exp. Biol. Med.* **1975**, *148*, 854-858.
15. İkizler A. A., Sancak, K. *Collect. Czech. Commun.* **1995**, *60*, 903-909.
16. Yüksek, H.; Alkan, M.; Çakmak, I.; Ocak, Z.; Bahçeci, Ş.; Çalapoğlu, M.; Elmastaş, M.; Kolomuç, A.; Aksu, H. *J. Mol. Sci.* **2008**, *9*, 12-32.
17. Stoe & Cie; X-AREA (Version 1.18) and X-RED32 (Version 1.04). Stoe & Cie, Darmstadt, Germany, **2002**.
18. Sheldrick G. M; SHELXS-97 and SHELXL-97, Programs for the Solution and Refinement of Crystal Structures, University of Göttingen, Germany, **1997**.
19. Burnett, M. N.; Johnson, C. K.; ORTEPIII. Report ORNL-6895, Oak Ridge National Laboratory, Tennessee, USA, **1996**.
20. Hanif, M.; Qadeer, G.; Rama, N. H.; Wong, W. *Acta Cryst. E* **2008**, *64*, 2180.