Synthesis and Antioxidant Ability of New 5-amino-1,2,4-Triazole Derivatives Containing 2,6-dimethoxyphenol

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ABSTRACT

4-amino-3-(4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione was synthesized by to method the first one from melt reaction of 4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)benzoic acid with Thiocarbonyldihydrazide, the second method from convert the corresponded acid hydrazide to potassium 2-{4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)benzoyl}hydrazinecarbodiithioate salt then react with hydrazine hydrate. Newly Schiff base (7a-7f) were synthesized from reaction the 4-amino-1,2,4-triazoI with substituted hydroxybenzaldehyde. The resulting compounds were characterized by IR, 1H-NMR, 13C-NMR, and HRMS data. 2,2-Diphenyl-1-picrylhydrazide (DPPH) and ferric reducing antioxidant power (FRAP) assays were used to screened the antioxidant properties of the synthesized compounds. Compounds 7d , 7e and 7f exhibited significant free-radical scavenging ability in both assays.

Key words: 2,6-dimethoxyphenol, 4-amino-1,2,4-triazole, Schiff base, Antioxidant, DPPH, FRAP.

INTRODUCTION

The reactive oxygen species (ROS) and other related free radicals species are witty to react either directly or indirectly, to damage all biomolecules. This damage can cause many diseases 1, such as inflammatory 2, cancers 3, degenerative 4 and chronic diseases 5. The antioxidant compounds are the most important species which can inhibit the oxidative stress in biological system and prevent any free radicals damage. The phenolic compounds are one of the significant antioxidant type, as well reported it possess broad biological activity such as anti inflammatory 6, anticancer 7 and gastroprotective 8.

Generally, antioxidants compounds donate protons to become stable free radicals. This stability increases with the extent of delocalization and enhances the antioxidant ability 9, 10. As such, many synthesized compounds containing long chain resonance exhibited significant antioxidant
activity. Furthermore, the compounds which can be considered a strong antioxidant usually possess common structural features. They often own multiple phenolic hydroxyl groups like flavonoids\(^1\) or which have full conjugation $\delta$ system like carotenoids\(^2\). Moreover, exhibited substituted groups might influence on the scavenging ability. This indicates the existence of a close relationship between the chemical structure and the ability to scavenge free radicals.

Derivatives of 1,2,4-triazole exhibited various types of biological activities e.g. Antimicrobial\(^3\), antiviral\(^4\)\(^5\), inhibitors of Methionine Aminopeptidase-2\(^6\), Anhydrase inhibitors\(^7\), anti-cancer\(^8\), anti-inflammatory\(^9\), inhibitors of the HIV-1\(^10\), analgesic\(^11\), anti-inflammatory\(^12\) and antioxidant\(^13\). As well the compounds of Schiff base derivatives displayed broader properties and applications such as nonlinear optical devices\(^14\), liquid crystalline applications\(^15\) or which can be considered a strong antioxidant usually possess common structural features. They often own multiple phenolic hydroxyl groups like flavonoids\(^1\) or which have full conjugation $\delta$ system like carotenoids\(^2\). Moreover, exhibited substituted groups might influence on the scavenging ability. This indicates the existence of a close relationship between the chemical structure and the ability to scavenge free radicals.

The 2,6-dimethoxyphenol derivatives won wide attention in recent years as antioxidants\(^3\),\(^3\)\(^2\). In this work we presented the synthesis of new 4-((arylidine)amino)-3-(4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione (7a-7f) as new antioxidant material.

**MATERIAL AND METHOD**

**Chemistry**

The IR spectra were obtained with a Perkin Elmer 400 Fourier Transform Infrared (FTIR) Spectrometer. $^1$H and $^{13}$C-NMR spectra were recorded at Joel Lambda spectrometers at 400 MHz (UM, Malaysia). DMSO-$d_6$ were used as solvents with TMS as the internal standard. The mass spectra were recorded using an Agilent 5975 system for EI/MS and a Finnigan TSQ7000 for HREIMs (NUS, Singapore). For UV spectroscopy, a Power Wave X340 (BIOTEK Instruments, Inc., Winooski, VT, USA) was used to record the FRAP and DPPH. Melting points were measured on a Sturt-SMP10 melting point apparatus in open-end capillary tubes. Flash column chromatography on silica gel 60 (230–400 mesh, E. Merck) was employed. General grade solvents and reagents were purchased from commercial suppliers and used without further purification.

4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl) benzoic acid 4

This compound was synthesized according to the procedure described by K. F. Ali\(^3\). Recrystallized with ethanol to obtain white microcrystals. Yield 60 %, Mp 150-152 C \[^{[lit. ~152-154 ~C ~38]}\] . IR (KBr) $\nu_{\max}$ 3354 (OH), 3046 (CH$_2$), 2972, 2893 (CH$_{aliphatic}$), 1676 (C=O) 1585 (C=C), 1180 (Ar-O-C), cm$^{-1}$. $^1$H-NMR (400MHz, CDCl$_3$): 3.87 (6H, s, 2xOCH$_3$), 4.33 (2H, s, OCH$_3$), 4.38 (2H, s, OCH$_3$), 6.66 (s, 2H, H-3), 7.65 (2H, d, J 8.2, H-8) 8.12 (2H, d, J 8.0, H-9). 9.15 (1H, bs, OH), 13C-NMR (100 MHz, CDCl$_3$): 56.11(2C, OCH$_3$), 71.22(1C, CH$_{OCH_3}$), 72.77 (1C, CH$_2$OCH$_3$), 109.05(2C, CH), 129.84(2C,CH), 139.37(1C), 142.13(1C) 152.01 (2C), 169.58 (1C, C=O) HREIMs m/z = 318.1100 [M$^+$]$^2$ (calc. for C$_7$H$_9$O$_6$, 318.1103).

4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl) benzoxydihydrazide 5

This compound was synthesized according to the procedure described by K. F. Ali\(^3\).The crude was recrystallized from ethanol to give white solid. Yield 87%, Mp 150-152 C \[^{[lit. ~152-154 ~C ~38]}\] . The crude was recrystallized from ethanol to give white solid. Yield 60 %, Mp 150-152 C \[^{[lit. ~152-154 ~C ~38]}\] . IR (KBr) $\nu_{\max}$ 3354 (OH), 3046 (CH$_2$), 2972, 2893 (CH$_{aliphatic}$), 1676 (C=O) 1585 (C=C), 1180 (Ar-O-C), cm$^{-1}$. $^1$H-NMR (400MHz, DMSO-$d_6$): 3.71 (6H, s, 2xOCH$_3$), 3.93 (2H, s, OCH$_3$), 4.09 (2H, s, OCH$_3$), 4.63 (bs, 2H, NH$_2$), 6.52 (s, 2H, H-3), 7.65 (2H, d, J 8.1, H-8) 8.22 (2H, d, J 7.92, H-9), 8.863 (1H, bs, COOH), 9.21(1H, bs, OH), $^{13}$C-NMR (100 MHz, DMSO-$d_6$): 56.3 (2C, OCH$_3$), 71.14 (1C, CH$_{OCH_3}$), 72.60 (1C, CH$_2$OCH$_3$), 106.88(2C, CH), 129.11(2C,CH), 138.92(1C), 139.04(1C), 141.55(1C) 152.01 (2C), 169.58 (1C, C=O) HREIMs m/z = 332.1369 [M$^+$]$^2$ (calc. for C$_7$H$_9$O$_6$, 332.1372).

**General synthesis of 4-amino-3-(4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 6**

**Method A**

4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)benzoic acid (3.2gm 10.05mmol) and Thiocarbonyldihydrazide (1.17 gm , 11 mmol) was mixed then grinded after that the mixture was transferred to conical flask and heated until melt at 160-165 °C for three hour. The mixture left to cool...
to ambient temperature. The crude was boiled with (2×20 mL) dichloromethane then filtrated. The organic combined evaporated under reduced pressure. The crude precipitated was recrystallized from ethanol to afford white crystals. Yield 51% Mp 68-70 °C.

**Method B**

To a solution of 4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)benzohydrazide (0.51 mmol) was added to phenyl)-1,2,4-triazole-5-thione 7a-7f ((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl) -1,2,4-triazole-5-thione (0.2 gm, 0.51 mmol) in 5 mL glacial acetic acid and the mixture was refluxed for 9 h. After cooling the mixture was poured into 50 mL crushed ice. The precipitate collected, washed with cold distilled water and recrystallized from suitable solvent.

**General synthesis of 4-((arylidene)amino)-3-((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7a-7f**

An aryl aldehyde (0.51 mmol) was added to a stirred solution of 4-amino-3-((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl) -1,2,4-triazole-5-thione (0.2 gm, 0.51 mmol) in 5 mL glacial acetic acid.

**4-((4-hydroxybenzylidene)amino)-3-((4-(4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7a**

Recrystallized from methanol to give pale yellow precipitate. Yield 83%, Mp 115-117 °C IR (KBr) νₘₐₓ = 3498(OHphenol), 3152(NH), 3062(CHdimethoxy), 1623 (CH=N), 1607 (C=N₃), 1595, 1585 (C=O), 1247 (C=S), 1201 (C=O), cm⁻¹. ¹H NMR (DMSO-d₆, δ): 3.62 (6H, s, 2× OCH₃), 4.34 (2H, s, OCH₂), 4.52 (2H, s, OCH₂), 6.57 (2H, H-3), 6.84 (2H, d, J 8.2), 7.86 (4H, d, J 8.4), 7.93 (2H, d, J 8.2), 8.24 (2H, d, J 8.21), 8.46 (1H, s, CH=N), 9.22 (1H, bs, OH), 9.95 (bs, 2H, OCH₂), 14.21 (1H, bs, NH). ¹³C NMR (100 MHz, DMSO-d₆): 56.09 (2C, OCH₃), 70.88 (1C, CHOCH₃), 69.90 (1C, CH₂OCH₃), 107.85 (2C, CH), 116.11 (2C), 125.56 (1C), 129.07 (2C, CH), 129.25 (1C), 130.47 (2C), 131.23 (2C, CH), 133.09 (1C), 134.85 (1C), 142.17 (1C), 151.91 (2C), 157.17 (2C), 160.93 (1H, CH=O), 162.30 (1C, CH=O). HREIMs m/z = 492.1461 [M⁺] (calc. for C₂₅H₂₈N₄O₅S, 492.1467).

**4-((4-hydroxybenzylidene)amino)-3-((4-(4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7b**

Recrystallized from ethanol to afford yellow precipitate. Yield 78%, Mp 81-83 °C IR (KBr) νₘₐₓ = 3498(OHphenol), 3152(NH), 3062(CHdimethoxy), 1607 (CH=N), 1595, 1585 (C=O), 1247 (C=S), 1201 (C=O), cm⁻¹. ¹H NMR (DMSO-d₆, δ): 3.62 (6H, s, 2× OCH₃), 4.34 (2H, s, OCH₂), 4.52 (2H, s, OCH₂), 6.57 (2H, H-3), 6.84 (2H, d, J 8.2), 7.86 (4H, d, J 8.4), 7.93 (2H, d, J 8.2), 8.24 (2H, d, J 8.21), 8.46 (1H, s, CH=N), 9.22 (1H, bs, OH), 9.95 (bs, 2H, OCH₂), 14.21 (1H, bs, NH). ¹³C NMR (100 MHz, DMSO-d₆): 56.09 (2C, OCH₃), 70.88 (1C, CHOCH₃), 69.90 (1C, CH₂OCH₃), 107.85 (2C, CH), 116.11 (2C), 125.56 (1C), 129.07 (2C, CH), 129.25 (1C), 130.47 (2C), 131.23 (2C, CH), 133.09 (1C), 134.85 (1C), 142.17 (1C), 151.91 (2C), 157.17 (2C), 160.93 (1H, CH=O), 162.30 (1C, CH=O). HREIMs m/z = 492.1461 [M⁺] (calc. for C₂₅H₂₈N₄O₅S, 492.1467).
4-((4-hydroxy-3-ethoxybenzylidene)amino)-3-(4-((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7c

The crude product was recrystallized from acetonitrile to afford yellow crystals. Yield 71% Mp 104-106°C. IR (KBr) ν max 3584( OH, phenol), 3170(NH), 3037(CH), 2987, 2865(CH aliphatic), 1618(CH=N), 1607(C=N triazole), 1595, 1983(C=C), 1238(C=S). 1201(C-O), cm⁻¹. ¹H-NMR (400 MHz, DMSO-d₆) 1.43 (t, 3H, J=6.9, O-CH₃), 3.72(6H, s, 2x OCH₃), 3.92 (q, 2H, J=7.1, O-CH₂), 4.39 (2H, s, OCH₃), 4.74 (2H, s, OCH₃), 6.54 (s, 2H, H-3), 6.85 (d, 2H, J=8.0, 7.24 (1H, dd, J=8.1, 1.68) 7.71 (2H, d, J=8.22, H-8), 8.26 (2H, d, J=8.2), 8.59 (1H, s, CH=N), 9.16 (1H, bs, OH), 9.78 (1H, bs, OH), 14.14 (1H, bs, NH), ¹³C-NMR (100 MHz, DMSO-d₆): 14.94 (1C, O-CH₂ CH₃), 55.21(2C, OCH₃), 64.31 (1C, OCH₃), 70.96(1C, OCH₃), 69.87 (1C, CH₂OCH₃), 108.05(2C, CH), 111.32(1C), 117.13 (1C), 124.77 (1C), 127.51(1C), 129.39(2C, CH), 129.65(1C), 132.36(2C, CH), 134.16(1C), 138.82(1C), 142.72 (1C), 147.86 1C), 156.61 (1C), 151.89 (2C), 161.01(1C, CH=N), 163.12(C=N triazole), 181.34 (1C, C=S). HREIMs m/z = 553.1672 [M⁺] (calc. for C₃₇H₂₆N₅O₅S, 536.1730).

4-((4-hydroxy-3,5-dimethoxybenzylidene)amino)-3-(4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7d

Crude product recrystallized from chloroform-ethanol to afford yellow precipitate. Yield 73%. Mp 136-138°C. IR (KBr) ν max 3605(OH phenol), 3172(NH), 3062(CH), 2984, 2890 (CH aliphatic), 1614 (CH=N), 1565, 1595, 1980(C=C), 1221(C=S), 1198(C-O), cm⁻¹. ¹H-NMR (400 MHz, DMSO-d₆): 3.73(6H, s, 2x OCH₃), 3.85 (6H, 2xOCH₃) 4.42 (2H, s, OCH₃), 4.56 (2H, s, OCH₃), 6.59 (s, 2H, H-3), 7.24 (s, 2H), 7.71 (2H, d, J=8.2, H-8), 8.28 (2H, d, J=8.0), 8.51(1H, s, CH=N), 9.08(2H, s, OCH₃), 9.56(1H, bs, OH), 13.57(1H, bs, NH), ¹³C-NMR (100 MHz, DMSO-d₆): 56.28(2C, OCH₃), 56.31(2C, OCH₃), 70.17(1C, OCH₃), 68.99(1C, CH₂OCH₃), 106.07 (2C, CH), 107.92(2C, CH), 129.27(2C, CH), 124.78(1C) 129.28(1C), 131.25(2C, CH), 133.43(1C), 138.66(1C), 142.41 (2C) 151.85 (4C), 160.35(1C, CH=N), 162.13 (1C, C=N triazole), 181.22(1C, C=S). HREIMs m/z = 552.1673 [M⁺] (calc. for C₃₇H₂₆N₅O₅S, 552.1679).

4-((4-hydroxy-3,5-di-tert-butylbenzylidene)amino)-3-(4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7e

The crude product recrystallized from chloroform afforded off white precipitate. Yield 60%, mp 158-160, IR (KBr) ν max 3599.7 (OH phenol), 3177(NH), 3068 (CH), 2980-2885 (CH aliphatic), 1622(CH=N), 1608(C=N triazole), 1595-1589 (C=C) and 1262(C=S). ¹H NMR, 6.333334.65 (2H, s, OCH₃), 5.62 (1H, bs, OH), 6.64 (2H, s, H-3), 7.62 (2H, d, J=8.2, H-8), 7.91 (2H, J=8.2), 8.18 (2H, d, J=8.1), 8.60(1H, s, CH=N), 9.14(1H, bs, OH), 1H, bs, NH), ¹³C-NMR (100 MHz, DMSO-d₆): 30.37(6C, 4(C(CH₂)₃), 34.46(2C, O(CH₂)₃), 56.11(2C, OCH₃), 71.24(1C, CH₂OCH₃), 69.93(1C, CH₂OCH₃), 107.65(2C, CH), 116.86 (1C), 124.80 (1C), 129.07(2C, CH), 129.35(1C), 131.38(2C, CH), 133.14(1C), 138.85(1C), 142.17 (1C) 151.79 (2C), 157.15 (1C), 161.77 (1C, CH=N), 165.11 (C=N triazole), 182.71(1C, C=S). HREIMs m/z = 604.2715 [M⁺] (calc. for C₃₇H₂₄N₅O₅S, 604.2719).

4-((2-hydroxy-3,5-di-tert-butylbenzylidene)amino)-3-((4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl)phenyl)-1,2,4-triazole-5-thione 7f

The crude products recrystallized from chloroform-ethanol afforded pale yellow precipitate. Yield 73%, mp 122-124°C, IR (KBr) ν max 3603 (OH phenol), 3173(NH), 3068 (CH), 2980-2885 (CH aliphatic), 1621(CH=NH), 1604(C=N triazole), 1597-1589 (C=C) and 1262(C=S) ¹H NMR, 6.333334.65 (2H, s, OCH₃), 5.62 (1H, bs, OH), 6.64 (2H, s, H-3), 7.62 (2H, d, J=8.2, H-8), 7.91 (2H, d, J=8.2), 8.18 (2H, d, J=8.1), 8.60(1H, s, CH=N), 9.14(1H, bs, OH), 1H, bs, NH), ¹³C-NMR (100 MHz, DMSO-d₆): 30.37(6C, 4(C(CH₂)₃), 34.46(2C, O(CH₂)₃), 56.11(2C, OCH₃), 71.24(1C, CH₂OCH₃), 69.93(1C, CH₂OCH₃), 107.65(2C, CH), 116.86 (1C), 124.80 (1C), 129.07(2C, CH), 129.35(1C), 131.38(2C, CH), 133.14(1C), 138.85(1C), 142.17 (1C) 151.79 (2C), 157.15 (1C), 161.77 (1C, CH=N), 165.11 (C=N triazole), 182.71(1C, C=S). HREIMs m/z = 604.2715 [M⁺] (calc. for C₃₇H₂₄N₅O₅S, 604.2719).
Antioxidant DPPH assay

The assay was performed as reported by Gerhauser et al.5. Five microliters of the sample (dissolved in ethanol) was added into 195 μL of 100 mM DPPH reagent in ethanol (96%) and mixed in a 96-well plate. The intensity of the colour was measured for 3 h at an interval of 20 min at 515 nm. Ascorbic acid and BHT were used as reference.

FRAP assay

The FRAP assay was performed according to the Benzie and Strain method. The FRAP reagent was prepared by combining 300 mM acetate buffer and 10 mM 2,4,6-tripyridyl-s-triazine (TPTZ) solution in 40 mM HCl and 20 mM FeCl3·6H2O, in a ratio of 10:1:1. The FRAP reagent was incubated at 37 °C prior to use. Ten microliters of the sample was reconstituted in the carrier (solvent or ultrapure water) and mixed with 300 μL of FRAP reagent. The mixture was incubated at 37 °C for 4 min in a microplate reader. The absorbance of the complex was 593 nm. The FRAP value can be calculated using the following equation:

\[
\text{FRAP} = \left[ \frac{(0–4 \text{ min } \Delta A_{593 \text{ nm}} \text{ of test sample})}{(0–4 \text{ min } \Delta A_{593 \text{ nm}} \text{ of standard})} \right] \times \text{[standard] (µM)} \times Y \\
\times 1000
\]

Where; Y is absorbance of the spectrophotometer.

RESULTS AND DISCUSSION

Chemistry

The 4-(((4-hydroxy-3,5-dimethoxybenzyl)oxy)methyl) benzoic acid 4 and their corresponded acid hydrazide 5 were synthesized from according to the procedure described by K. F. Ali as depicted in Scheme 1.

The 4-amino-3-{4-(((4-hydroxy-3,5dimethoxybenzyl)oxy)methyl)phenyl}-1,2,4-triazole-5-thione. 6 were synthesized from two different methods. The first one, from melt reaction with Thiocarbonyldihiydrate for tree hour at 160-165 °C to obtained 51% yield. The second methods, was from converted the corresponded acid hydrazide 5 to their corresponded potassium hydrazinecarbodithioate salt as the first step. The next step was react this salt with hydrazine hydrate under reflux for 7h. this method exhibited yield higher than method one. The compound 7a-7f were synthesized from reaction compound 6 with hydroxyl substituted benzaldehyde in the presence of glacial acetic acid. As depicted in Scheme 2.

All synthesized compounds were characterized by IR, 1H-NMR, 13C-NMR spectrum beside the EIMS and HRMIS. The IR spectrum of compound 4 displayed rise a new band of C=O at 1676 cm⁻¹ and disappeared the band of Ca”N at 2243 cm⁻¹. compound 5 showed shifting at carbonyl group which is appeared at 1661 cm⁻¹ of acid to hydrazide as well new bands of NH and NH₂ were appeared at 3308-3218 cm⁻¹. The IR spectrum of compound 6 exhibited disappeared of carbonyl group and new interesting bands were appeared at 1628 cm⁻¹ corresponded the C=N group of the triazole ring as and at 1245 cm⁻¹ of C=S beside the value of NH and NH₂ bands were shifted to 3410,3330 and 3170 cm⁻¹ respectively. The spectra of 7a-7f.
displayed disappeared the band of NH2 and a new interesting band for the Schiff base was appeared at 1623-1614 cm\(^{-1}\) besides the C= N of the triazole ring which appeared at 1608-1604 cm\(^{-1}\). The \(^1\)H-NMR spectrum of compound 4 showed disappearing of trimethylsilyl group at 0.17 and appears of the broad singlet of OH for the converting the nitrile group to carboxylic acid. The \(^1\)H-NMR spectrum of compound 5 showed the disappearing hydroxyl group of the carboxylic as well a new two broad singlet of NH2 and NH were appeared at 4.63 \(\delta\) and 8.86 \(\delta\) respectively. The \(^1\)H-NMR of compound 6 displayed all expected peaks in triazole structure. The \(^1\)H-NMR spectra of compounds 7a-7f showed the appearance of new peaks represented the Schiff base (imin group) and the expected proton of the substituted hydroxybenzylidene (see the experimental suction) also appeared in their expected rang. The \(^13\)C-NMR spectrum of compound 4 exhibited two carbons of \(\text{CH}_2\text{OCH}_2\) at 3.87 & 433 \(\delta\), beside disappearing the carbon of \(\text{Ca"N}\) and raised a new carbon of \(\text{C=O}\). That enhances the evidence of successful convert

Scheme 2: Synthetic route of compound 6 and 7a-7f

Fig. 1: DPPH inhibitions % of 7a-7f
compound 3 to 4 besides the spectra of IR and $^1$H-NMR. The 13C-NMR showed change in value of carbonyl of compound 5 due to convert the acid to acid hydrazide. The spectrum of compound 6 showed two new carbons first on the C=N at 149.54 $\tilde{A}$ of triazole ring and the second one at 166.61 $\tilde{A}$ represented the C=S. The $^{13}$C spectra of compounds 7a-7f were showed an interested peak of CH=N beside the carbons of the hydroxybenzylidene. The substituent group for 7b-7f were appeared in the expected range. The EIMS spectra showed the molecular ion $M^+$ for all compounds and the base peak (100%) as well the HREIMS value was confirmed the accurate mass and the molecular formula as depicted in Table 1.

**Antioxidant activity**

The synthesized compound 6 and 7a-7f were showed high antioxidant ability in both assays (DPPH and FRAP). Compound 6 showed antioxidant ability higher than 7a-7b in both assays and that could attributed to exhibited a pro-oxidative effect \(^3\). Even though compounds 7a-7f exhibited significant antioxidant ability. The type of substituted at hydroxybenzylidene play an important role to enhance the antioxidant ability. Compound 7e exhibited higher antioxidant ability (slightly less than ascorbic acid) in both assays (DPPH and FRAP) as shown in Figure 1 and Figure 2.

Compound 7d showed free radical scavenging ability more than compound 7f and that could attributed to the t-Bu group at position para reduce the antioxidant ability \(^4\), the compound 7b and 7c exhibited nearly same antioxidant ability and that in agreement with most literatures. Finally compound 7a without any substituted group around the hydroxyl group of phenol show the less antioxidant ability.

**CONCLUSIONS**

A series of newly Schiff base compounds from 4-amino-1,3,4-triazole incorporating hindered phenol moieties were successfully synthesized and characterized. All of the newly compounds were tested for antioxidant activity by DPPH and FRAP assays. The antioxidant ability of these compound increases with increasing the hindered phenol.

**ACKNOWLEDGEMENTS**

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Table 1: The hydroxyl substituted and selected properties of synthesized compound 7a-7f

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<th>M.P.</th>
<th>C Molecular</th>
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<td>71</td>
<td>104-106</td>
<td>C_{27}H_{28}N_{4}O_{6}S</td>
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<td>604.2715</td>
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<td>C_{33}H_{40}N_{4}O_{5}S</td>
<td>604.2719</td>
<td>604.2716</td>
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REFERENCES

31. Huihui Ti, Qing Li, Rufen Zhang, Mingwei Zhang, Yuanyuan Deng, Zhencheng Wei, Jianwei Chi, Yan Zhang, *Food Chemistry* 2014, 159 166-174.