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Synthesis and antioxidant evaluation of some new sulphadimidine incorporating thiophene moiety

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ABSTRACT

A few new sulphadimidine incorporating thiophene moiety are synthesized. These compounds were assessed by analytical and spectral data. Antioxidant evaluation for the investigated compounds was evaluated by ABTS assay and bleomycin-dependent DNA-damage; the compounds exhibited weak activities.

1. Introduction

Sulphadrugs have attracted special attention from their therapeutic importance as they were used against a wide spectrum of bacterial aliments [1]. Some sulphadrugs have been used in the treatment of cancer, malaria, leprosy and tuberculosis [2,3]. Moreover, many thiophene derivatives were reported to exhibit different biological properties, such as A1 adenosine receptor, allosteric enhancers [4,5], inhibitors of Human Leukocyte Elastase [6,7], antitumor [8], virucides, virostatic agent, [9], antitumor and anti-HIV activities [4]. Different methods were reported for the syntheses of azo sulphadrugs [10-15].

Considering the facts that nearly all of the classes of heterocyclic compounds are biologically active and as a part of our continuous efforts towards the development of more potent antioxidant agents [16-20]. It was thought of interest to combine the above mentioned boilable rings together in a molecular framework to investigate the additive effect of these rings towards antioxidant activity.

2. Experimental

2.1. Instrumentations

All melting points are determined on Gallenkamp electric melting point apparatus (uncorrected). Thin layer chromatography (TLC) analysis was carried out on silica gel $60F_{254}$ precoated aluminum sheets. The IR spectra were recorded (KBr) on a Mattson 5000 FTIR Spectrophotometer at the Microanalytical Unit, Faculty of Science, Mansoura University. The ^{1}H NMR spectra were determined on a Varian XL 200 MHz at the Microanalytical Center, Faculty of Science, Cairo University, Egypt using DMSO-d_6 as solvents and tetramethylsilane as internal standard. The mass spectra (EI) were recorded on 70 eV with Kratos MS equipment at the Microanalytical Center, Cairo University, Egypt. Elemental analyses (C, H and N) were carried out at the Microanalytical Center of Cairo University, Egypt. Biological activities were carried out at Pharmacognosy Department, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt.

2.2. Synthesis

2.2.1. Synthesis of 2-cyano-N-(3-cyano-4-phenylthiophen-2-yl)acetamide (4)

A mixture of compound **2** (2.8 g, 14 mmol) and 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-oxopropanenitrile (**3**) (2.39 g, 14

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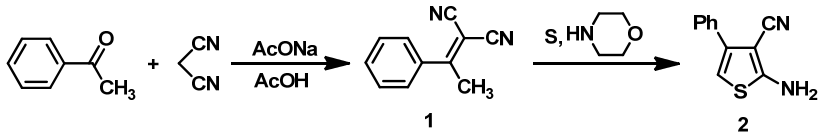
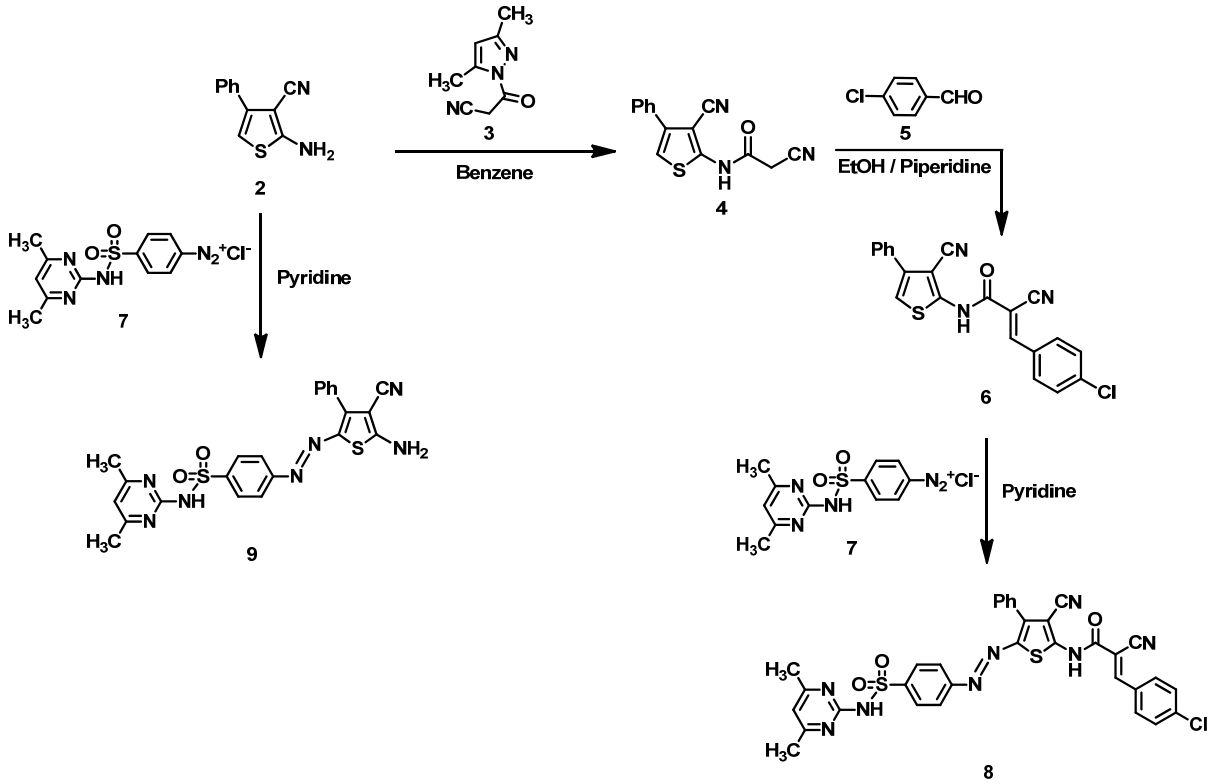


Scheme 1



Scheme 2

mmol) in benzene (20 mL) was refluxed for 8 h. The solvent was evaporated under vacuum and the residue was crystallized form ethanol to give carboxamide **4** (Scheme 1 and 2). Color: White powder. Yield: 44%. M.p.: 230-232 °C. FT-IR (KBr, ν, cm^{-1}): 3212 (NH), 2242, 2217 (2CN), 1693 (CO). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 4.24 (s, 2H, CH_2), 7.60-8.42 (m, 6H, Ar-H, C_5-H of thiophene), 11.12 (brs., 1H, NHCO). MS (EI, *m/z* (%)): 269 (M^++2, 1.3), 268 (M^++1, 3.6), 267 (M^+, 18.7), 225 (0.3), 201 (14.2), 200 (100.0), 172 (10.4), 168 (1.7), 155 (12.6), 146 (1.2), 128 (3.9), 93 (1.8), 74 (0.5). Anal. calcd. for $C_{14}H_9N_3OS$ (267.05): C, 62.91; H, 3.39; N, 15.72%. Found: C, 62.88; H, 3.45; N, 3.34%.

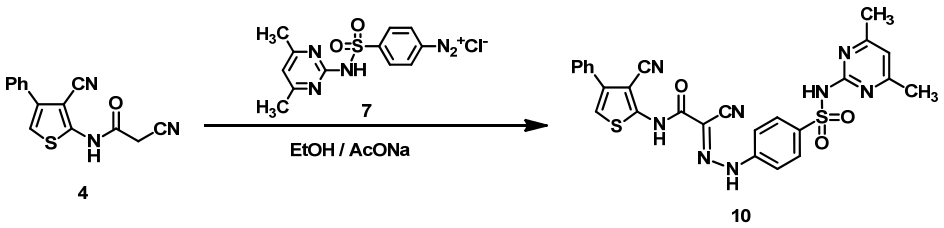
2.2.2. Synthesis of (E)-3-(4-chlorophenyl)-2-cyano-N-(3-cyano-4-phenylthiophen-2-yl) acrylamide (6)

A mixture of compound **4** (1.3 g, 5 mmol), piperidine (0.2 mL) and *p*-chlorobenzaldehyde (0.7 g, 5 mmol); in ethanol (15 mL) was stirred at 80 °C for 1 h. The separated crystals was filtered, dried and recrystallized from ethanol to give compound **6** (Scheme 2). Color: Orange powder. Yield: 97%. M.p.: 198-200 °C. FT-IR (KBr, ν, cm^{-1}): 3316 (NH), 2200, 2182 (2CN), 1670 (CO), 700 (C-Cl). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 7.20- 7.85 (m, 11H, ArH + C_5-H of thiophene + CH=), 11.44 (s, br, 1H, NH). MS (EI, *m/z* (%)): 389 (M^+, 1.2), 366 (4.3), 359 (38.7), 355 (9.1), 308 (4), 267 (3.6), 256 (15.0), 224 (5.9), 200 (100.0), 174 (13.0), 163 (45.8), 135 (7.9), 128 (7.5), 99 (16.6), 89 (7.9), 67 (1.2), 60 (25.7). Anal. calcd. for $C_{21}H_{12}ClN_3OS$ (389.04): C, 64.70; H, 3.10; N, 10.78. Found: C, 64.67; H, 3.18; N, 10.81%.

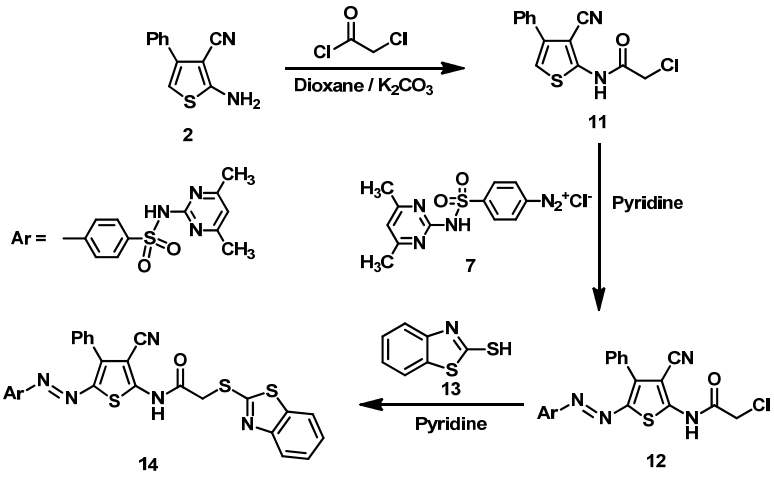
2.2.3. General procedure for the synthesis of aryl azothiophene and aryl hydrazone derivatives 8, 9, 10 and 12

To a well-stirred cooled solution of sulphadimidine (1.5 g, 5 mmol) in concentrated HCl (4 mL), a solution of $NaNO_2$ (0.4 g, 5 mmol in 5 mL H_2O) was added drop wise. The above cooled diazonium solution was added slowly to a well-stirred solution of compound **6** (1.94 g, 5 mmol), **2** (1 g, 5 mmol) or **11** (1.38 g, 5 mmol) in pyridine (15 mL) or **4** (1.34 g, 5 mmol) in ethanol (30 mL) containing sodium acetate (3.28 g, 40 mmol). The reaction mixture was stirred for 2 h. The crude product was filtered off, dried well and recrystallized from the appropriate solvent to afford compounds **8**, **9**, **10** and **12**, respectively (Scheme 2-4).

(E)-3-(4-Chlorophenyl)-2-cyano-N-(3-cyano-5-((E)-(4-(N-(4,6-dimethylpyrimidin-2-yl)sulfamoyl)phenyl)diazenyl)-4-phenylthiophen-2-yl)acrylamide (**8**): Color: Brown powder. Yield: 67%. M.p.: 252-254 °C. FT-IR (KBr, ν, cm^{-1}): 3361, 3226 (2NH), 2228, 2206 (2CN), 1697 (CO), 1488 (N=N), 700 (C-Cl). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 2.24 (brs., 6H, $2CH_3$), 6.74 (s, 1H, C_5-H of pyrimidine), 7.50-8.37 (m, 14H, Ar-H+CH=),



Scheme 3



Scheme 4

11.35 (brs., 1H, NHCO), 12.28 (brs., 1H, $NHSO_2$). MS (EI, *m/z* (%)): 677 (M^+-1, 0.7), 610 (1.5), 570 (100.0), 556 (96.3), 551 (20.0), 497 (2.2), 430 (3.0), 357 (2.2), 322 (15.6), 279 (40.7), 214 (39.3), 200 (30.4), 167 (45.9), 148 (94.8), 140 (14.1), 110 (17), 88 (5.8), 69 (16.3). Anal. calcd. for $C_{33}H_{23}ClN_8O_3S_2$ (678.1): C, 58.36; H, 3.41; N, 16.50%. Found: C, 58.40; H, 3.49; N, 16.45%.

(E)-4-((5-Amino-4-cyano-3-phenylthiophen-2-yl)diazenyl)-N-(4,6-dimethylpyrimidin-2-yl)benzenesulfonamide (**9**): Color: White. Yield: 90%. M.p.: 192-194 °C. FT-IR (KBr, ν, cm^{-1}): 3328, 3286, 3235 (NH_2, NH), 2197 (CN), 1452 (N=N). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 2.23 (brs., 6H, $2CH_3$), 6.74 (s, 1H, C_5-H of pyrimidine), 7.43-8.0 (m, 9H, Ar-H), 8.90 (brs., 2H, NH_2), 11.95 (brs., 1H, $NHSO_2$). MS (EI, *m/z* (%)): 492 (M^++3, 0.3), 491 (M^++2, 0.7), 490 (M^++1, 1.6), 489 (M^+, 4.3), 459 (0.3), 425 (53.3), 407 (0.8), 382 (1.5), 350 (0.4), 318 (8.2), 303 (10.2), 289 (3.4), 246 (3.7), 227 (6.5), 213 (80.6), 198 (33.9), 155 (16.5), 123 (100.0), 108 (22.1), 96 (33.8), 64 (59.6). Anal. calcd. for $C_{23}H_{19}N_7O_2S_2$ (489.1): C, 56.43; H, 3.91; N, 20.03%. Found: C, 56.49; H, 3.83; N, 20.10%.

(E)-2-((3-Cyano-4-phenylthiophen-2-yl)amino)-N'-(4-(N-(4,6-dimethylpyrimidin-2-yl)sulfamoyl)phenyl)-2-oxoacetohydrazonoyl cyanide (**10**): Crystallization from a mixture of ethanol:benzene (3:1, *v:v*). Color: Yellow powder. Yield: 61%. M.p.: 197-199 °C. FT-IR (KBr, ν, cm^{-1}): 3243, 3235, 3212 (3NH), 2230, 2197 (2CN), 1673 (CO). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 2.25 (br, 6H, $2CH_3$), 6.76 (s, 1H, C_5-H of pyrimidine), 7.44-8.01 (m, 10H, Ar-H, C_5-H of thiophene), 11.10 (br, 1H, NH, hydrazone), 11.48 (brs., s, 1H, NHCO), 12.30 (brs., 1H, $NNHSO_2$). MS (EI, *m/z* (%)): 407 (M^+-(HCN+2-imino-4,5-dimethyl pyrimidine), 398 (33.1), 373 (23.5), 356 (25.5), 337 (28.5), 320 (31.3), 293 (30.6), 275 (25.8), 245 (35.6), 213 (42.5), 200 (83.6), 179 (54.6), 151 (28.1), 129 (34.1), 112 (41.7), 96 (58.7), 83 (93.4), 69 (100.0). Anal. calcd. for $C_{26}H_{20}N_8O_3S_2$ (556.11): C, 56.10; H, 3.62; N, 20.13. Found: C, 56.03; H, 3.71; N, 20.24%.

(E)-2-Chloro-N-(3-cyano-5-((4-(N-(4,6-dimethylpyrimidin-2-yl)sulfamoyl)phenyl)diazen-yl)-4-phenylthiophen-2-yl)acetamide (**12**): Crystallization from DMF. Color: Orange powder. Yield: 93%. M.p.: 200-202 °C. FT-IR (KBr, ν, cm^{-1}): 3353, 3197 (2NH), 2230 (CN), 1681 (CO), 1498 (N=N), 702 (C-Cl). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 2.23 (br., 6H, $2CH_3$), 4.62 (s, 2H, CH_2Cl), 6.73 (s, 1H, C_5-H of pyrimidine), 7.55-8.08 (m, 9H, Ar-H), 11.40 (brs., 1H, NHCO), 12.30 (brs., 1H, $NHSO_2$). MS (EI, *m/z* (%)): 488 (M^+-$COCH_2Cl$, 0.1), 467 (0.1), 411 (0.3), 382 (0.5), 358 (0.2), 335 (0.2), 304 (0.9), 276 (0.4), 235 (0.5), 214 (11.2), 198 (3.9), 170 (0.9), 140 (2.0), 123 (100.0), 108 (8.8), 95 (47.0), 82 (36.3), 64 (54.7), 45 (20.3). Anal. calcd. for $C_{25}H_{20}ClN_7O_3S_2$ (565.08): C, 53.05; H, 3.56; N, 17.32. Found: C, 52.96; H, 3.63; N, 17.42%.

2.2.4. Synthesis of (E)-2-(benzo[d]thiazol-2-ylthio)-N-(3-cyano-5-((4-(N-(4,6-dimethylpyrimidin-2-yl)sulfamoyl) phenyl)diazenyl)-4-phenylthiophen-2-yl)acetamide (14)

A mixture from compound **12** (2.82 g, 5 mmol) and 2-mercaptothiazole (**13**) (0.83 g, 5 mmol) in pyridine (15 mL) was refluxed for 5 h. The reaction mixture was left to cool and poured in ice cold water. The precipitated solid was filtered off, dried and crystallized from ethanol to give compound **14** (Scheme 4). Color: Black powder. Yield: 60%. M.p.: 230-232 °C. FT-IR (KBr, ν, cm^{-1}): 3342, 3262 (2NH), 2204 (CN), 1727 (CO), 1494 (N=N). ^{1}H NMR (200 MHz, DMSO-d_6, δ, ppm): 2.24 (br, 6H, $2CH_3$), 3.10 (s, 2H, CH_2), 6.74 (s, 1H, C5-H of pyrimidine), 7.29-7.99 (m, 13H, Ar-H), 11.50 (brs., 1H, NHCO), 12.48 (br., 1H, $NHSO_2$). MS (EI, *m/z* (%): 696 (M^+, 7.1), 620 (6.3), 600 (3.8), 572 (5.7), 532 (4.3), 489 (4.7), 451 (4.0), 410 (4.5), 361 (4.9), 332 (6.1), 289 (5.9), 252 (12.3), 220 (6.5), 208 (12.7), 190 (4.7), 180 (20.8), 167 (73.7), 140 (4.0), 122 (4.7), 108 (22.7), 86 (7.7), 72 (100.0), 58 (18.0). Anal. calcd. for $C_{32}H_{24}N_8O_3S_4$

(696.84): C, 55.15; H, 3.47; N, 16.08. Found: C, 55.23; H, 3.51; N, 16.17%.

2.3. Antioxidant activity

2.3.1. ABTS screening assay

Antioxidant activity determinations were evaluated from the bleaching of ABTS derived radical cations [21]. The radical cation derived from ABTS (2,2'-Azino-*bis*-(3-ethyl benzo thiazoline-6-sulfonic acid)) was prepared by reaction of ABTS (60 mL) with MnO_2 (3 mL, 25 mg/mL) in 5 mL aqueous buffer solution (pH = 7). After shaking the solution for a few minutes, it was centrifuged and filtered. The Absorbance (A control) of the resulting green-blue solution (ABTS radical solution) was recorded at λ_{max} 734 nm. The absorbance (A test) was measured upon the addition of (20 mL of 1 mg/mL) solution of the tested sample in spectroscopic grade MeOH:buffer (1:1, *v*:v) to the ABTS solution. The inhibition ratio (%) was calculated using the equation 1.

$$\text{Inhibition (\%)} = [\text{A (control)} - \text{A (test)}/\text{A (control)}] \times 100 \quad (1)$$

Ascorbic acid (20 mL, 2 mM) solution was used as a standard antioxidant (positive control). Blank sample was run using solvent without ABTS (Table 1).

Table 1. ABTS antioxidant activity assay for the thiophene derivatives.

Compound	Absorbance of samples	Inhibition %
8	0.469	1.05
9	0.445	6.11
10	0.403	14.90
12	0.452	4.64
14	0.370	21.94
Ascorbic acid	0.048	89.87
Control of ABTS	0.474	0

2.3.2. Bleomycin-dependent DNA-damage

The assay was done according to Aeschbach *et al*., [22] and Chan & Tang [23] with minor modifications. The reaction mixture (0.5 mL) contained DNA (0.5 mg/mL), bleomycin sulfate (0.05 mg/mL), and $MgCl_2$ (5 mM), $FeCl_3$ (50 mM) and the samples were dissolved in DMSO to be tested at concentration (20 mL of 1 mg/mL). L-Ascorbic acid was used as a positive control. The mixture was incubated at 37 °C for 1 h. The reaction was terminated by addition of 0.05 mL EDTA (0.1 M). The color was developed by adding thiobarbituric acid (TBA) (0.5 mL) (1%, *w*:*v*) and HCl (0.5 mL) (25%, *v*:*v*) followed by heating at 80 °C for 10 min. After centrifugation, the extent of DNA damage was measured by the increase in absorbance at 532 nm (Table 2).

Table 2. Bleomycin dependent-DNA damage of thiophene derivatives.

Compound	Absorbance of samples
8	0.135
9	0.128
10	0.119
12	0.141
14	0.112
Ascorbic acid	0.097

3. Results and discussion

3.1. Chemistry

The synthetic strategies adopted to obtain the target compounds are depicted in Schemes 1-4. Starting compounds 2-(1-phenylethylidene)malononitrile (**1**) and 2-amino-3-cyano-4-phenylthiophene (**2**) were prepared according to the reported procedures [24,25], as outlined in Scheme 1.

Cyanoacetylation of enaminonitrile derivative **2** [25] with 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-oxopropanenitrile (**3**) [26] afforded 2-cyano-*N*-(3-cyano-4-phenylthiophen-2-yl)acetamide (**4**), the reaction proceeded according to previously reported method [27]. Furthermore, reaction of compound **4** with *p*-chlorobenzaldehyde (**5**) afforded corresponding arylidene derivative **6** which further coupled with sulphadimidine diazonium salt **7** in pyridine to give the corresponding aryl azothiophene derivative **8**. Moreover, coupling of thiophene derivative **2** with diazonium salt **7** in pyridine afforded aryl azothiophene derivative **9** (Scheme 2).

Structures of compounds **4**, **6**, **8** and **9** were assessed by analytical and spectral data (IR, ^{1}H NMR and mass spectra). The IR spectra of compounds **4**, **6**, **8** and **9** showed absorption bands within ν 3361-3212 cm^{-1} due to symmetric vibrations of NH_2 and NH groups, in addition to absorption bands within ν 2242-2182 cm^{-1} corresponding to cyano functions and absorption bands within ν 1697-1670 cm^{-1} due to carbonyl groups.

The ^{1}H NMR spectrum of compound **4** displayed signals at δ 4.24 (s, 2H, CH_2), 7.60-8.42 (m, 6H, Ar-H, C5-H, thiophene), 11.12 (brs., 1H, NHCO) ppm. On the other hand, the ^{1}H NMR spectrum of compound **8** displayed signals at δ 2.24 (brs., 6H), 6.74 (s, 1H), 7.50-8.37 (m, 13H), 11.35 (brs., 1H), 12.28 ppm (brs., 1H) ppm due to two CH_3, C5-H of pyrimidine, aromatic, NHCO and $NHSO_2$ protons, respectively. Moreover, the ^{1}H NMR spectrum of compound **9** displayed signals at δ 2.23 (brs., 6H), 6.74 (s, 1H), 7.43-8.00 (m, 9H), 8.90 (br, 2H), 11.95 ppm (brs, 1H) corresponding to two CH_3, C_5-H, pyrimidine, aromatic, NH_2 and $NHSO_2$ protons, respectively.

The mass spectrum of compound **4** gave an additional evidence for structure elucidation which showed the molecular ion peaks at *m/z* 269 (M^++2), 268 (M^++1), 267 (M+) that is in agreement with the molecular formula ($C_{14}H_9N_3OS$), in addition to the base peak at *m/z* 200 attributed to (M+-[$COCH_2CN$]). Also, the mass spectrum of compound **6** showed the molecular ion peak at *m/z* 389 that is adopted with the molecular formula ($C_{21}H_{12}ClN_3OS$), in addition to the base peak at *m/z* 200 due to 2-amino-4-phenylthiophene-3-carbonitrile moiety. Moreover, the mass spectrum of compound **8** showed the molecular ion peak at *m/z* 677 (M^+-1, 0.7) which in agreement with the molecular formula ($C_{33}H_{23}ClN_8O_3S_2$), in addition to the base peak at *m/z* 570 attributed to (M^+-(dimethylpyrimidine)). Moreover, the mass spectrum of compound **17** showed four molecular ion peaks at *m/z* 492, 491, 490 and 489 corresponding to (M^++3), (M^++2), (M^++1) and (M^+), respectively, which are in agreement with the molecular formula ($C_{23}H_{19}N_7O_2S_2$), in addition to the base peak at *m/z* 123 that is related to 2-aminodimethylpyrimidine moiety.

Moreover, coupling of cyanoacetamide derivative **4** with diazonium salt **7** in ethanol containing sodium acetate afforded the corresponding hydrazone derivative **10** (Scheme 3). Assignment of structure **10** was based on analytical and spectral data (IR, ^{1}H NMR and mass spectra). The IR spectrum showed absorption bands at ν 3243, 3235, 3212, 2230, 2197, 1673 cm^{-1} corresponding to (3NH), (2CN) and carbonyl groups, respectively. Furthermore, the ^{1}H NMR spectrum displayed signals at δ 2.25 (brs., 6H), 11.10 (brs., 1H) and 12.30 ppm (brs., 1H) ppm corresponding to two CH_3, NH, hydrazone and $NHSO_2$ protons, respectively. Moreover, its mass spectrum showed four molecular ion peaks at *m/z* 407, 262, 199 and 122 corresponding to (M^+(HCN+2-imino-4,5-dimethylpyrimidine), 4-[(*N*-(4,6-dimethyl-pyrimidin-2-yl)sulfon-amide]phenyl, 2-amino-4-phenylthiophene-3-carbonitrile and 2-imino-4,5-dimethyl pyrimidine, respectively, in addition to the base peak at *m/z* 69 which is related to propiononitrile moiety.

Treatment of compound **2** with chloroacetyl chloride according to the previously reported method afforded the chloroacetamide derivative **11** [28] which coupled with diazonium salt **7** in pyridine to afforded the hydrazone derivative **12**.

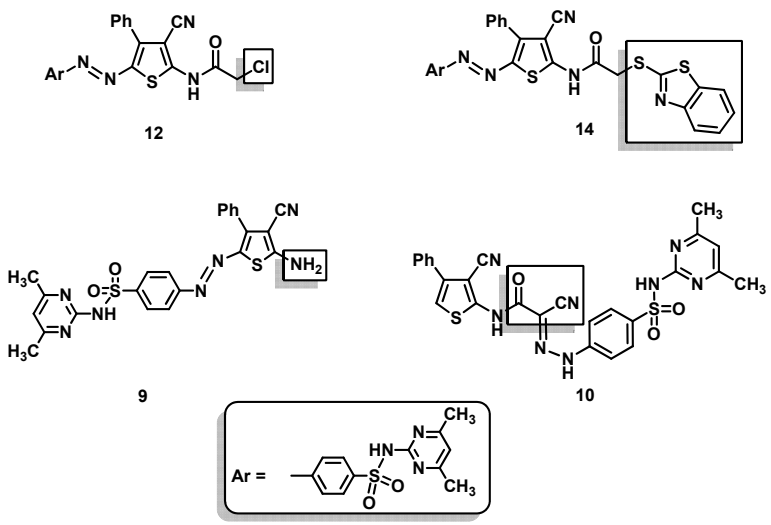


Figure 1. Structure activity relationship's (SAR's) of the more potent compounds.

Reaction of compound **12** with 2-mercapto benzothiazole **13** in refluxing pyridine yielded thiazole derivative **14** as outlined in Scheme 4. Assignment of compounds **12** and **14** was based on correct IR, ^{1}H NMR and mass spectral data. The IR spectra showed absorption bands within ν 3353-3197 and 1727-1681 cm^{-1} due to the stretching vibrations of NH and carbonyl groups, respectively, absorption bands within ν 1498-1494 cm^{-1} corresponding to symmetric vibrations of azo groups, in addition to absorption bands within ν 2230-2204 cm^{-1} are attributed to cyano groups of the coupler moieties. The ^{1}H NMR spectrum of compound **12** displayed signals at δ 2.23 (brs., 6H), 4.62 (s, 2H), 6.73 (s, 1H), 7.55-8.08 (m, 9H), 11.40 (br, 1H), 12.30 (br, 1H) ppm due to two CH_3, CH_2Cl, C5-H, pyrimidine, aromatic, NHCO and $NHSO_2$ protons, respectively. On the other hand, the ^{1}H NMR spectrum of compound **14** revealed signals at δ 2.24 (brs., 6H), 3.10 (s, 2H), 6.74 (s, 1H), 7.29-7.99 (m, 13H), 11.50 (brs., 1H), 12.48 (brs., 1H) ppm due to two CH_3, CH_2, C_5-H, pyrimidine, aromatic, NHCO and $NHSO_2$ protons, respectively. The mass spectrum of compound **12** showed the molecular ion peak at *m/z* 488 which is equivalence to (M^+-$COCH_2Cl$), in addition to the base peak at *m/z* 123 which is assigned to 2-imino-4,5-dimethylpyrimidine moiety. Moreover, the mass spectrum of compound **14** showed the molecular ion peak at *m/z* 696 (M^+) which is in agreement with the molecular formula ($C_{32}H_{24}N_8O_3S_4$).

3.2. Biological activity

3.2.1. Antioxidant activity assay

The antioxidant activities for five thiophene derivatives were evaluated as reported method by Lissi *et al*. [21]. The results outlined in Table 1 showed clearly that the investigated compounds exhibited weak activities.

3.2.2. Bleomycin-dependent DNA-damage

Five thiophene derivatives were selected for bleomycin-dependent DNA-damage screening (Table 2). Damage of DNA in the presence of a bleomycin-Fe complex has been adopted as a sensitive and specific method to examine potential pro-oxidant agents [29]. If the tested samples are able to reduce the bleomycin-Fe^{3+} and Fe^{2+} to bleomycin-Fe^{2+}, DNA degradation in this system will be stimulated, resulting in a positive test for pro-oxidant activity. Degradation of DNA is accompanied by the formation of a product similar to malondialdehyde (MDA). L-Ascorbic acid as a reducing agent can reduce Fe^{3+} to Fe^{2+}. The results outlined in Table 2 showed that all of the investigated compounds exhibited weak activities.

By comparing the results obtained of antioxidant of the compounds reported in this study to their structures, the following structure activity relationship's (SAR's) were postulated:

(i) Cyanoacetamide **10** is more potent than thiophene **9** which may be attributable to presence of cyanoacetamide moiety.

(ii) Compound **14** is more potent than chloroacetamide **12** which may be due to replacement of chlorine atom by mercaptothiazole moiety (Figure 1).

4. Conclusion

The objective of the present study was to synthesize and evaluate the antioxidant activity of some novel sulphadimidine incorporating thiophene moiety with the hope of discovering new structure leads serving as antioxidant agents. The data clearly showed that all of the investigated compounds exhibited weak anti-oxidant activities.

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