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Synthesis and Characterization new 2,5- di (1,3,4-Thiadiazole)derivatives from 2,5- Thiophene Dicarboxylicacid

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Abstract

New 2,5-di-(1,3,4-thiadiazole) derivatives of thiophene are prepared .reaction of 2,5-thiophene dicarboxylic acid with excess thionyl chloride formed compound (1),then treatment with hydrazine gives thiophene-2,5-dicarbohydrazine (2).A number of prepared arylisothiocyanate was reacted with compound (2) leads to form thiosemicarbazide derivatives (3),(4) and (5) .The last compounds are addition to Conc.sulfuric acid at $0C^{o}$ with continues stirring so as to form 2,5-di-(1,3,4-thiadiazole) derivatives (6),(7) and (8) .The course of the reactions as well as the purity of products were monitored by means of T.L.C. Identification of products were achieved by elemental analysis(C.H.N), IR spectroscopy and ^{1}HN.M.R.

الخلاصة

حضرت مشتقات (4,3,1) ثياديازول على الموقعين 2و5 للثايوفين. ادخل المركب 5,2- ثايوفين ثنائي حامض الكاربوكسيلك تفاعل مع زيادة من كلوريد الثايونيل للحصول على مركب (1). ثم مفاعلة (1) مع الهيدرازين للحصول على المركب (2). مفاعلة عدد من مركبات اريل ايزوثايوسيانات المحضرة مع مشتق الهيدرازين اعطى مشتقات السميكاربازيدات (3),(4) و(5) الثنائية. بعد ذلك اضيفت هذه المشتقات المحضرة الى حامض الكبريتيك المركز في درجة الصفر المئوي ليتم الحصول على مشتقات (4,3,1) ثياديازول (6),(7) و (8) . شخصت جميع المركبات المحضرة باستخدام تقنية الأشعة تحت الحمراء وتحاليل العناصر وكذلك طيف الرنين النووي المغناطيسي.

Introduction

Thiadiazole is one of a class of organic heterocyclic compounds containing a five member diunsaturated ring structure composed of two nitrogen atoms at position (3 and 4) and one sulfur atom at position(1)[1]

The synthesis of1,3,4-thiadiazole derivatives, which were investigated for antibacterial [2-4], antifungal [5] ,cardiotonic[6], antitubercular[7,8], and antidepressant1[9,10] activities, has been reported previously.The aromatic thiadiazole nucleus is associated with a variety of pharmacological actions, such as fungicidal[11,12], controlling blood pressure[13] and can affect central nervous system[14]. The 1,3,4-thiadiazole and its derivatives are versatile ligands that can bridge over a variety of metal centers[15,16]

A number of methods for the preparation have been developed. Many synthesis of 1,3,4-thiadiazoles proceed from thiosemicarbazide or substituted thiosemicarbazide[17,18], Furthermore, heterocycles have been put to much use in the chemistry of disperse dyes, for example, a series of monoazo disperse dyes

These dyes have been found to give a wide range of color shades[19] with very good depth and levelness on fabric[20]. Therefore, thiadiazoles represent an important heterocyclic scaffold of compounds which display a wide range of different activities[21].

Experimental

Melting points were determined using an electro thermal melting point apparatus and are uncorrected. Elemental analysis was preformed using a perkin- Elmer 204E Instrument. Fourier transformer infrared spectra were recorded on a Shemadzu FT-IR 8000 spectrophotometer using KBr. ^{1}H-NMR spectra were recorded on a AVarian A 80MHz instrument using $CDCl_3$.

Thiophene - 2,5- di carbonyl di chloride (1).

A mixture of Thiophene – 2,5- dicarboxylic acid (0.01 mole) and thionyl chloride (10mL) was refluxed gently for (8 hours). Excess thionyl chloride was removed under vaccum to give compound (1) M.P (170.4) C^o

Anal. Calc. for $C_6H_2Cl_2O_2S$ C% 34.47 H% 0.96

Found C% 35.13 H% 1.17

I.R spectra (C=C) Thiophene ring (1558)cm^{-1}, (C=O) (1755) cm^{-1}, (C-S) (1180) cm^{-1}, and (C-Cl) (775) cm^{-1}

^{1}***HNMR spectrum***. (C-H) Thiophene ring δ(8.3)ppm

Thiophene - 2,5- di carbohydrazide (2).

Compound (1) (0.01 mole) which was dissolved in dry benzene (25 mL) and hydrazine (0.02 mole) was added. The reaction mixture was refluxed for 3 hours. The product was filtered and recrystallized from ethanol . M.P (182) C^o

Anal. Calc. for $C_6H_8N_4O_2S$ C% 35.99 H% 4.03 N% 27.98

Found C% 35.13 H% 4.17 N% 27.11

I.R spectra (C=C) Thiophene ring (1570)cm^{-1}, (C=O) (1735) cm^{-1}, (C-S) (1185) cm^{-1},(C-N) (1075) cm^{-1} and (N-H) (3200) cm^{-1}

^{1}***HNMR spectrum***. (C-H) Thiophene ring δ(8.1)ppm , (N-H) δ(9.4)ppm and (NH_2) δ(4.5)ppm

General procedure for preparing compounds (3),(4) and (5).

Compound (2) (0.01 mol) were dissolved in absolute ethanol (35 mL). The prepared isothiocyanate (0.01 mol) was separately dissolved in absolute ethanol (10 mL). Then the solution of the isothiocyanate was added to the solution of hydrazide with continuous stirring. The reaction mixture was then refluxed. Then , the mixture was cooled to room temperature to form a white precipitate. The crude solid was then filtered and recrystallized from the appropriate solvent to yield the compounds **(3), (4) and (5).**

Thiophene -2,5-Bis(di-(2-carbonyl)-N-P-tolyl hydrazinecarbothioamide) (3)

M.P (207.4) C^o

Anal. Calc. for $C_{22}H_{22}N_6O_2S$ C% 52.99 H% 4.45 N% 16.85

Found C% 53.32 H% 4.57 N% 17.14

I.R spectra (C=C) Thiophene ring (1560)cm^{-1}, (C=O) (1730) cm^{-1}, (C-S) (1190) cm^{-1},(C-N) (1100) cm^{-1} , (N-H) (3180) cm^{-1}, (C=S) (1620) cm^{-1}, (C=C) aromatic (1465) $cm^{-1}$and (720) cm^{-1} (C-H bending aromatic) .

Thiophene -2,5-Bis(di-(2-carbonyl)-N-P-Chlorophenyl hydrazinecarbothioamide) (4)

M.P (215.2) C^o

Anal. Calc. for $C_{20}H_{16}Cl_2N_6O_2S_3$ C% 44.53 H% 2.99 N% 15.58

Found C% 45.22 H% 3.14 N% 16.24

I.R spectra (C=C) Thiophene ring (1550)cm^{-1}, (C=O) (1740) cm^{-1}, (C-S) (1185) cm^{-1},(C-N) (1110) cm^{-1} , (N-H) (3250) cm^{-1}, (C=S) (1610) cm^{-1}, (C=C) aromatic (1480) $cm^{-1}$and (710) cm^{-1} (C-H bending aromatic) .

^{1}***HNMR spectrum***. (C-H) Thiophene ring δ(8.2)ppm , (N-H) δ(12.5)ppm and δ(2) ppm (C-H)aromatic δ(6.5-7.3)ppm

Thiophene -2,5-Bis(di-(2-carbonyl)-N-P-Nitrophenyl hydrazinecarbothioamide) (5)

M.P (219.3) C^o

Anal. Calc. for $C_{20}H_{16}N_8O_6S_3$ C% 42.85 H% 2.88 N% 19.99

Found C% 42.34 H% 2.64 N% 19.47

I.R spectra (C=C) Thiophene ring (1540)cm^{-1}, (C=O) (1730) cm^{-1}, (C-S) (1190) cm^{-1},(C-N) (1120) cm^{-1} , (N-H) (3230) cm^{-1}, (C=S) (1600) cm^{-1}, (C=C) aromatic (1485) $cm^{-1}$and (715) cm^{-1} (C-H bending aromatic) .

General procedure for preparing compounds (6),(7) and (8).

each thiosemicarbazide **(3),(4) and (5)** (0.01 mol) were added portion wise to (10mL) of conc. sulfuric acid at ($0C^0$) with continuous stirring. The reaction mixture was stirred further for (3 h) at room temperature. Then it was poured into an ice-water mixture to precipitate and neutralized by saturated Na_2CO_3 solution at room temperature. Then the solid material precipitated was filtered, washed with water, dried and crystallized to from 1,3,4-thiadiazole derivatives.

5,5'-(thiophene-2,5-diyl)bis(N-p-tolyl-1,3,4-thiadiazol-2-amine)(6)

M.P (223.2) C^o

Anal. Calc. for $C_{22}H_{18}N_6S_3$ C% 57.12 H% 3.92 N% 18.17

Found C% 57.67 H% 3.73 N% 18.55

I.R spectra (C=C) Thiophene ring (1545)cm^{-1}, (C=N) (1575) cm^{-1}, (C-S) (1185) cm^{-1},(C-N) (1120) cm^{-1} , (N-H) (3200) cm^{-1},(C-H) (2290) cm^{-1}, (C=C) aromatic (1480) $cm^{-1}$and (705) cm^{-1} (C-H bending aromatic) .

5,5'-(thiophene-2,5-diyl)bis(N-(4-chlorophenyl)-1,3,4-thiadiazol-2-amine) (7)

M.P (228.7) C^o

Anal. Calc. for $C_{20}H_{12}Cl_2N_6S_3$ C% 47.71 H% 2.40 N% 16.69

Found C% 48.12 H% 2.70 N% 16.15

I.R spectra (C=C) Thiophene ring (1540)cm^{-1}, (C=N) (1585) cm^{-1}, (C-S) (1180) cm^{-1},(C-N) (1110) cm^{-1} , (N-H) (3240) cm^{-1},(C-H) (2295) cm^{-1}, (C=C) aromatic (1490) $cm^{-1}$and (715) cm^{-1} (C-H bending aromatic) .

5,5'-(thiophene-2,5-diyl)bis(N-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine)(8)

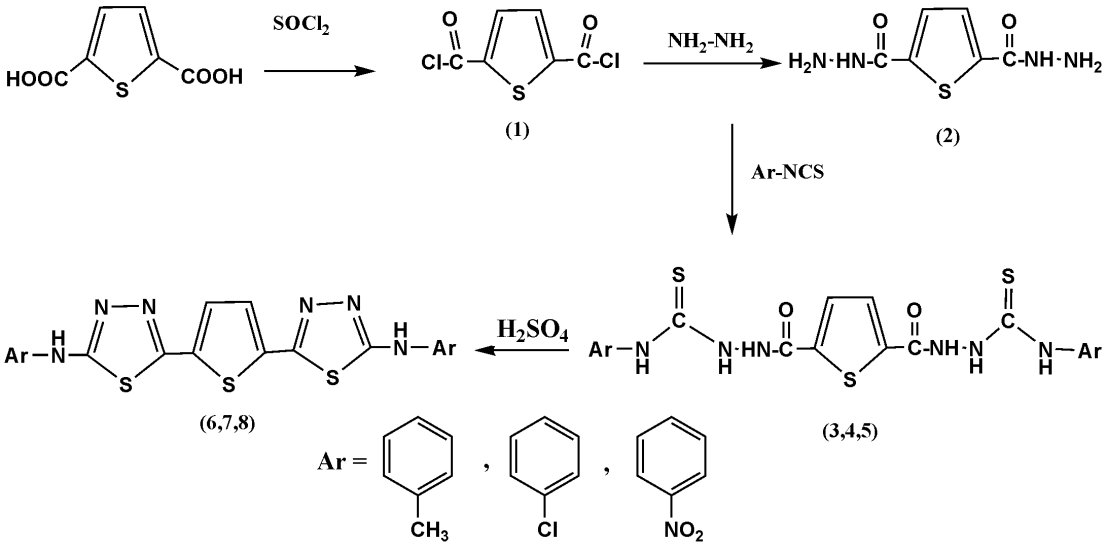
M.P (234.3) C^o

Anal. Calc. for $C_{20}H_{12}N_8O_4S_3$ C% 45.79 H% 2.31 N% 21.36

Found C% 45.92 H% 2.75 N% 21.55

I.R spectra (C=C) Thiophene ring (1558)cm^{-1}, (C=N) (1585) cm^{-1}, (C-S) (1180) cm^{-1},(C-N) (1160) cm^{-1} , (N-H) (3250) cm^{-1},(C-H) (2280) cm^{-1}, (C=C) aromatic (1470) $cm^{-1}$and (710) cm^{-1} (C-H bending aromatic) .

^{1}***HNMR spectrum***. (C-H) Thiophene ring δ(8.4)ppm , (N-H) δ(10.2)ppm (C-H)aromatic δ(6.9-7.9)ppm



Result and Discussion

The objective of this work is the synthesis of some new 2,5-di-(1,3,4-thiadiazole) derivatives of thiophene. These compounds may have biological effects beside being prepared for the first time.

First compound was synthesized by treating 2,5-thiophene dicarboxylic acid with excess of thionyl chloride . The structure of which was assigned from the I.R spectrum which showed strong absorption for (C=C) Thiophene ring (1558)cm^{-1}, (C=O) (1755) cm^{-1}, (C-S) (1180) cm^{-1}, and (C-Cl) (775) cm^{-1}. Elementary analysis showed good agreement of the calculated and found percentages.

Hydrazide derivatives (2) was synthesized by treating compound (1) with two moles of hydrazine , I.R spectra showed (C=C) Thiophene ring (1570)cm^{-1}, (C=O) (1735) cm^{-1}, (C-S) (1185) cm^{-1},(C-N) (1075) cm^{-1} and (N-H) (3200) cm^{-1}

^{1}HNMR singles showed (C-H) Thiophene ring δ(8.1)ppm , (N-H) δ(9.4)ppm and (NH_2) δ(4.5)ppm , Elementary analysis showed good agreement of the calculated and

Some aryl isothiocyanate were prepared according to literature[22] are treating with compound (2) to form thiosemicarbazide derivatives (3),(4)and(5). These compoundes are identifying by I.R spectra , C.H.N.analysis and ^{1}HNMR (all results showed in experimental part) .

1,3,4-thiadiazole derivatives (6),(7) and(8) are prepared by addition aryl isothiocyanate compoundes to Conc.sulfuric acid at $0C^o$, also These derivatives are identifying by I.R spectra , C.H.N.analysis and ^{1}HNMR (all results showed in experimental part) .

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