Egypt. J. Chem. **Vol. 65,** No. 3 pp. 179 - 183 (2022)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Synthesis and characterization of new N- Aryl sulfonyl hydrazone compounds

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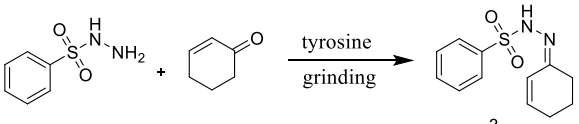
Abstract

In this paper we report synthesis of new substituted benzene sulfonohydrazone by the reaction of aniline with furo [3,4-b] pyridine-5,7- dione to give 2-(phenylcarbamoyl) nicotinic acid (1) which can be convert to 6- phenyl -5H- pyrrolo[3,4-b] pyridine -5,7(6H)- dione (2) by its reaction with acetic anhydride in the presence of sodium acetate. This compound was treated with chlorosulfuric acid to give 4-(5,7- dioxo-5,7- dihydro-6H- pyrrolo [3,4-b] pyridine 6-yl) benzenesulfonyl chloride (3). The compound (3) was reacted with hydrazine hydrate to give hydrazone (4). Lastly, the resulted hydrazone (4) was handled with numbers of aromatic aldehydes and ketones to give substituted benzene sulfonohydrazones (5- 12).

Keywords: Nicotinic acid, Sulfono, Hydrazone, imine

1. Introduction

N-aryl sulfonohydrazone compounds were reported in many recent papers due to its expected biological activities and shortage of prepared compounds, although chemistry of these compounds are known. In 2019 Qian Yang[1] has reported a green synthesis using tyrosine as a catalyst (scheme 1). In addition, in the last decade there are several of researchers used to synthesize number of these compounds and other Schiff base for different purposes [2-6].



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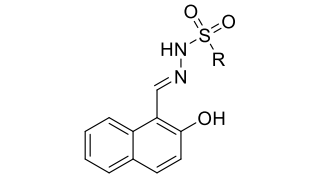
Biological activity of these compounds has a broad spectrum of active property. In 2002 Dmitrienko [5] and coworker have reported group of compounds as Inhibitors of IMP-1 Metallo β-Lactamase (4). In addition, Sartorelli [7] has prepared 2- Formyl pyridine N-oxide and proved their activity as antineoplastic activity (5).



R= Ph(4-CH), Ph(4-$C(CH_3)_3$, Ph(4-NO_2), Ph(4-OMe), Ph(4-OCH_3)

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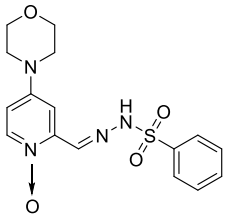

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2. Experimental

All chemicals and solvents were purchased from commercially available known source and used directly without more purification. IR spectra (*v*max in cm^{-1}) were verified utilizing Shimadzu FT- IR 8400 spectrophotometer with KBr disc. ^{1}H-NMR Bruker at 300 MHz, using DMSO -d^6 and TMS as a standard shift**.**

Synthesis of 2-(phenyl carbamoyl) nicotinic acid (1)[8]

to a solution of 0.01 mole 1.5 gm of furo [3,4-*b*] pyridine -5,7-dione melt in 25 ml of acetone. 0.01 mole of aniline was dropped wisely and stirring with cooling for two hours at room temperature. The produced precipitation was filtered, dried and recrystallized from ethanol to give a white solid

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EJCHEM use only: Receive Date: 14 August 2021, Revise Date: 31 August 2021, Accept Date: 12 September 2021
DOI: 10.21608/ejchem.2021.90637.4320

powder 80% (m.p. 193-194 ˚c); IR cm^{-1} 3405, 3134, 3082, 1720, 1643, 1606, 1242; ^{1}HNMR (300 MHz, DMSO d^6) δ 8.10- 7.75(m, 3 H), 7.64- 7.29 (m, 5 H).

Synthesis of 6-phenyl-5H -pyrrolo [3,4-b] pyridine - 5,7(6H)- dione (2)[9].

A mixture of (0.01 mole), 2.5 gm of (1) melt in 25 ml of acetic anhydride with 5% by weight of anhydrous sodium acetate, the resulted solution was refluxed with stirring for two hours. The homogenous product solution cooled to room temp. and pouring into crushed ice, the resulted precipitation was filtered, dried and recrystallized from acetone to give yellow solid powder 82% (m.p. 208- 210 ˚c); IR cm^{-1} , 3101, 1724, 1620, 1394; ^{1}HNMR (300 MHz, DMSO -d^6) δ 7.99-7.94 (m, 3 H), 7.7-7.73 (m, 5 H).

2. Synthesis of 4-(5,7-dioxo-5,7-dihydro-6H-pyrrolo[3,4-b] pyridine-6-yl)benzenesulfonyl chloride (3)[10-12].

Chlorosulfonic acid (4ml) was added dropwise to (0.01 mole, 2.23 gm) of (2). during two hours with stirring and keeping temp. at 0 ˚C then the temperature raised to room temp., and the stirring was continued for ten hours, the resulted mixture was poured on to crushed ice carefully with stirring. The obtained precipitate was filtered, dried, and recrystallized from acetone to give brown solid powder in 90% m.p.= 270-272 ˚c., cm^{-1} 3053, 1700, 1583, 1250; ^{1}HNMR (300 MHz, DMSO -d^6) δ 8.13-7.81 (m, 3H), 7.31-7.26 (d, 4H).

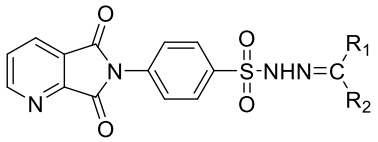
3. Synthesis 4-(5, 7-dioxo-5,7-dihydro-6H- pyrrolo [3, 4-*b*] pyridine-6 -yl) benzenesulfonohydrazide (4)[13]

To a solution of (0.01 mole, 3.227gm) of (3) in 5ml of absolute ethanol, (0.01 mol) of hydrazine hydrate was added dropwise with stirring and keeping temp. to 0 ˚C. after that, the resulted mixture was refluxed for six hours, then cooled to room temp. and pouring in crushed ice with stirring. The resulted wet powder filtered, washed with cold water, dried and finally recrystallized from ethanol to give pale yellow solid powder in 71% m.p.= 184d. ˚c., cm^{-1} 3390, 3295, 1714, 1704, 1600, 1172; ^{1}HNMR (300 MHZ, DMSO - d^6) δ 9.99 (s, 1H), 8.1- 7.8 (m, 5H), 7.40-7.37 (d, 2H).

Synthesis N- arylidene -4- (5 ,7-dioxo-5 ,7-dihydro-6H-pyrrolo [3 ,4-*b*] pyridine-6-yl) benzenesulfonohydrazide (5- 12)[14]

A mixture of (4) (0.01mol, 3.1831gm) with 0.01mol of aromatic aldehyde or ketone and two to three drops of glacial acetic acid in abs. ethanol (20ml) was refluxed for six hours then, the mixture cooled to room temp. after that, the resulting precipitate filtered, washed with cold ethanol, dried, and recrystallized from suitable solvent. Table (1), show the physical properties, table (2) the IR spectra result and table (3) the HMNR shifts.

Table (1) the physical properties of (5- 13)



Comp. No.	R1	R2	Yield%	m.p. C˚	Color	Recry. solvent
5	H	O-Me-Ph	54	160-161	Orange	Acetone
6	Ph	Ph	86	201- 202	Dark yellow	Ethanol
7	H	p-OH-Ph	70	119-120	Orange	Acetone
8	CH_3	m-NO_2-Ph	61	120- 121	White	Ethanol
9	Ph	o-NO_2-Ph	54	207-208	White	Ethanol
10	H	m-OMe-Ph	91	114-116	Brown	Acetone
11	H	o-OMe-Ph	93	176-178	White	Acetone
12	CH_3	p-Cl-Ph	71	160- 162	yellow	Acetone

Table (2) the IR wavenumbers cm^{-1} (5- 13)

Comp. No.	N--H	C—H aromatic	C==O amide	C==N	S=O	Other
5	3499	3100	1720	1665	1372	C-H aleph. 3000
6	3221	3108	1730	1627	1328	-
7	3284	3100	1714	1630	1336	O-H Phenol 3340
8	3406	3105	1714	1641	1315	Asy.NO_2 1504
9	3221	3100	1718	1661	1338	Asy. NO_2 1522
10	3310	3100	1720	1665	1306	Bent CH alepha. 1300
11	3300	3100	1707	1638	1344	St. CH aleph. 3033
12	3300	3100	1715	1620	1340	St.C-H aleph. 2950

Table (3) ^{1}HNMR Shift of (5- 13)

Comp. No.	N-H (s, 1H)	Aromatic ring (m. 11-17 H	N=C-H (s, 1H)	CH_3 (s, 3H)	other
5	8.99	8.21-7.31m, 11H	7.55 s, 1H	3.42	-
6	9.50	8.31- 7.21 17H	-	-	-
7	٩.81	8.4-7.4 11H	7.62	-	OH phenol 9.10-901 (S, 1H)
8	9.99	8.41-7.72	-	3.42	-
9	9.59	8.61- 7.55 16H	-	-	-
10	10.01	8.29- 7.32 13H	7.62	3.92	-
11	10.01	8.29- 7.32 11H	7.61	3.92	-
12	10.01	8.52- 7.67 11H	-	3.42	-

3-Result and discussion

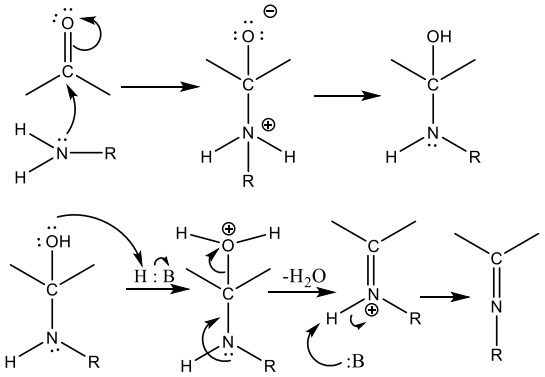
One of the interesting fields of organic chemist is to prepare new compounds. These compounds could solve one or more problem in different aera scheme (2). In this paper we used to make acetylation reaction of furo [3, 4-*b*] pyridine-5,7- dione as starting material with aniline as nucleophile to form acetanilide (1)in 80%. The resulted product was confirmed by IR signals in 1720 and 1643 cm^{-1} which belong to acid and amide groups respectively. In addition, ^{1}H NMR spectra miss the protons of (N-H) and (O-H) disappear due to the expected use of wet DMSO d_6 and the ability of these proton to exchange with deuterium in DMSO d_6 up fielded the signal of the solvent [15].

The dehydration of compound (1) with acetic anhydride was afforded (2). The structure was confirmed by ^{1}HNMR the two signals at δ 7.99-7.73 ppm multiplit corresponding to pyridine and phenyl protons. After protected of aniline with two acetyl group, at this moment (2) was ready to proceed to the next step which was chloro sulfonation reaction through electrophilic aromatic substitution reaction. Because of ortho and para orientation of amino group, two compounds were expected to obtained but the

steric effects increased the desired product (para) (3). The structure was confirmed by IR spectra which showed band at 1700 cm^{-1} related to amid group and by ^1H NMR (300 MHZ, DMSO -d^6) δ which showed signal at 7.13-7.26 as a doublet corresponding to four protons while, the fifth one was substituted by SO_2Cl group.

The next step was the reaction of compound (3) with hydrazine hydrate to give benzene sulfono hydrazide (4). The electron pair of nitrogen attacks the sulfur by SN^2 reaction reaction mechanism and bonded to the sulfur atom instead of chlorine. The structure was confirmed by IR spectra which showed signals at 3390, 3295 cm^{-1} belong to N-H and NH_2 respectively. The ^1H-NMR also confirmed the formation of the structure. Signal at δ 9.99 ppm belong to NH proton while the protons of NH_2 were exchange with the expected wet DMSO d_6 at 3.3 ppm.

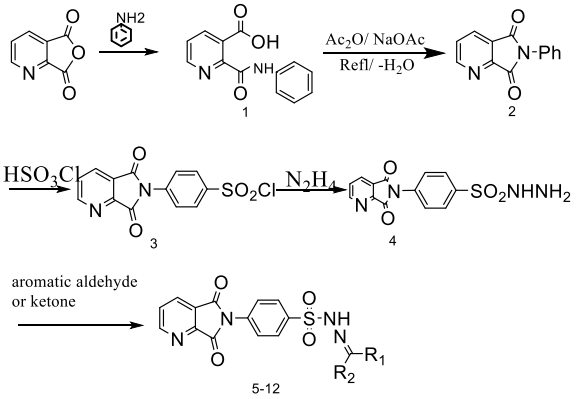
The final step was the reaction of compound(4) with number of substituted aldehydes and ketones to form substituted benzene sulfonohydrazones (5- 12), the mechanism of the reaction start when the nucleophile electron pair of the nitrogen of the primary amine attack the carbonyl of the aldehyde or ketone, then the next step was the proton transfer to give cabinolamine, then the final step was dehydration catalyzed by acid to form the new nitrogen carbon double bond. The scheme (1) below describes the mechanism [16].



Scheme (1) Mechanisim of formation (5- 12)

the resulted compounds (5- 12) identified by IR spectra, Table (1) shows different functional groups, belong to one compound. This may cause dragging the range to right or lift of the IR spectrum due to the exchanging effect between these groups. N-H absorbs from 3499 to 3221 cm^-, C—H aromatic from 3100 to 3108, C=O amid from 1707 to 1730, C=N 1600 to 1665 and S=O 1372 to 1306 with other specific groups. The IR spectroscopy confirmed the resulted compounds (5-12) [17].

Table (3) shows the ^1HNMR data of the resulted compounds (5-12), the expected chemical shifts at δ 10.01 to 8.99 ppm were appeared as a singlet signals which belong to the proton of N—H, while the multiplet signal appeared in the region 8.21 to 7.21 belongs to aromatic protons, these two signals belong to all resulted compounds (5- 12). The N=C-H proton gave singlet bands between 7.55 to 7.62 in compounds (5, 7, 10, 11), while the CH_3 protons in (5, 8, 12) gave singlet at δ 3.42 ppm and in (10, 11) shift at 3.92 due to the methoxy group. In compound 7 the proton of hydroxyl group appeared at δ 9.2 ppm [18].



Scheme (2)

4. Conclusions

We prepared several new substituted benzenesulfonohydrazides with few steps from available chemicals. The biological activity of these compounds seems to be promised, in addition the resulted compounds can be converted to many other products via the active imine group.

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

we would like to thank the College of Education for Pure Science University of Mosul/ Iraq to their permission to work in their labs.

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