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Synthesis of Several New Schiff Bases Linked to Sulfonamido Naphthalimide Moiety with Expected Biological Activity.

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ABSTRACT

Several new Schiff bases linked to sulfonamidonaphthalimide moiety have been synthesized. The first step in this work involved introducing of 4-(N-naphthalimidyl) phenyl sulfonylchloride in amination reaction with hydrazine hydrate producing 4-(N-naphthalimidyl) phenyl sulfonylhydrazine. Introducing of the prepared sulfonyl hydrazine in condensation reaction with different substituted aromatic aldehydes in the second step afforded the target new Schiff bases. Structures of the prepared compounds were elucidated on the basis of FTIR, ^{1}HNMR, ^{13}CNMR spectral data which agreed with the proposed structures. The newly synthesized compounds are expected to have biological activity scince they are built from biologically active components including naphthalimide, sulfonylimide and Schiff base.

Introduction

Schiff bases which contain azomethin group attract much interest in synthetic chemistry (1,2). They are used as substrate in the preparation of industrial and biologically active compounds .Moreover they are also known to have biological activities such as antibacterial, antifungal, anti-tumor and antioxidant activities (3-6).

On the other side naphthalimides first discovered by Brana and coworkers have been found to exhibit divers biological activities, some of them have shown high anticancer activity against a variety of murine and human tumor cells while others have shown analgesic properties (7-9).

Besides sulfonylimide drugs were the first effective chemotherapeutic agents to be employed systemically for the prevention and cure of bacterial infection in human beings (10,11).

Encouraged by all these observations it was thought worthwhile to synthesize new Schiff bases linked to naphthalimide through sulfonylimido group with expected biological activity.

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NATERIALS AND METHODS

Melting points were determined on Thomas Hoover apparatus and were uncorrected. FTIR spectra were recorded on SHIMADZU FTIR-8400 Fourier Transform Infrared spectro-photometer using KBr discs. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker 300MHz instrument in Al-Albate University in Jordan using DMSO-d_6 as a solvent and trimethyl-silane (TMS) as internal reference.

Synthesis of 4-(N-naphthalimidyl) phenyl sulfonylhydrazine [1]

To a solution of (0.01 mol, 3.71g) of 4-(N-naphthalimidyl)phenyl sulfonyl-chloride in (15 mL) of absolute ethanol , (0.01 mol) of hydrazine hydrate was added dropwise with stirring and keeping temperature at zero C^{o} (12) .

The resulted mixture was refluxed for six hours then cooled to room temperature before pouring on crushed ice with stirring . The resulted precipitate was filtered , washed with cold water, dried and finally recrystallized from ethanol.

synthesis of Schiff bases [2-10]

A mixture of 4-(N-naphthalimidyl) phenyl sulfonylhydrazine (0.01mol , 3.67g) of aromatic aldehyde (0.01 mol) and (2-3) drops of glacial acetic

acid in absolute ethanol (20 mL) was refluxed for 6 hours (13).

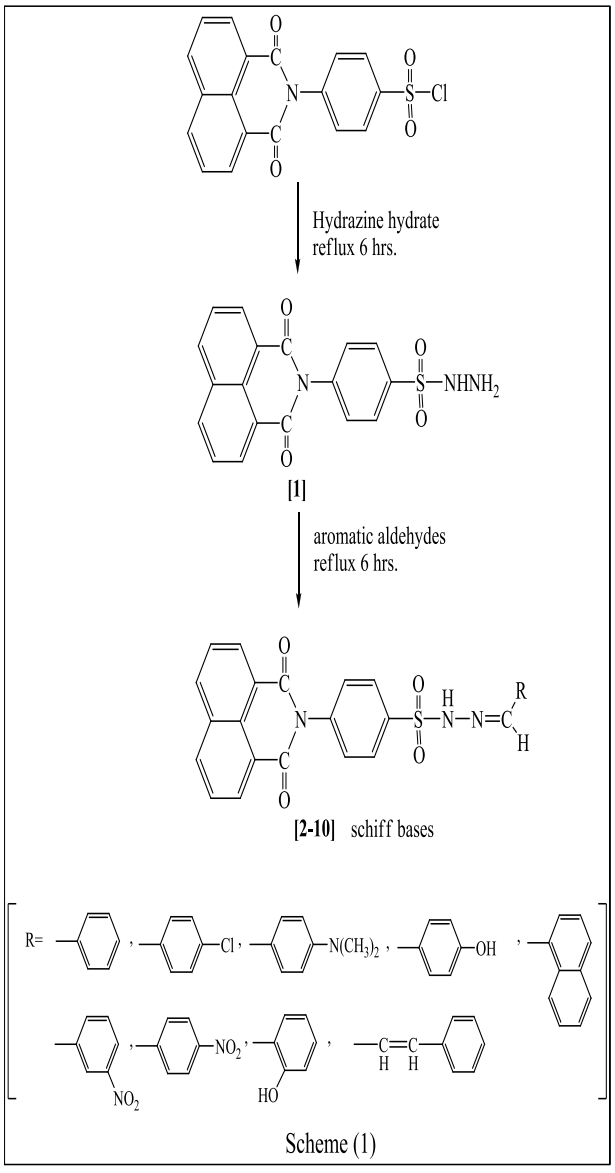
After cooling the obtained precipitate was filtered then washed with cold ethanol , dried and recrystallized from a suitable solvent.

Physical properties of Schiff bases [2-10] are listed in Table (1).

RESULT AND DISSCUTION

Since both naphthalimides and Schiff bases belong to a widely used group intermediates important for production of many types of pharmaceuticals and have wide spectrum of biological applications the target of the present work is synthesis of new molecules containing these two active moieties naphthalimide and Schiff base linked together through phenyl sulfonamide component.

Steps for performing this target are shown in scheme (1).



Scheme (1)

The first step involved preparation of 4-(N-naphthalimidyl)phenylsulfonyl- hydrazine [1] via reaction of 4-(N-naphthalimidyl)phenyl sulfonylchloride with hydrazine hydrate under reflux conditions.

The starting compound 4-(N-naphthal-imidyl)phenyl sulfonylchloride was prepared via reaction of N-phenyl- naphthalimide with chlorosulfonic acid according to literatures (14).

Compound [1] was purified by recrys-tallization from ethanol and was afforded as off-white crystals in (87%) percent yield and having melting point (>300)C^{o} .

In the second step compound [1] was Introduced in condensation reaction with different aromatic aldehydes producing the desired Schiff bases [2-10]. Physical properties of Schiff bases [2-10] are listed in Table (2).

Structures of the prepared compounds were confirmed by FTIR, ^{1}HNMR and ^{13}CNMR spectra data.

FTIR spectrum of compound [1] showed clear absorption bands at 3417 cm^{-1} and 3309 cm^{-1} due to asym. And sym. ν (NH_2). Absorption bands belong to ν(N-H) amide ,ν(C-H) aromatic and ν(C=O) imide appeared at 3236 cm^{-1} and 3062 cm^{-1} and 1705 cm^{-1} while absorption bands due to ν(C=C) aromatic , ν(C-N) imide ,asym. ν(SO_2) and sym. ν(SO_2) appeared at 1620 cm^{-1}, 1361 cm^{-1} ,1381 cm^{-1}and 1180 cm^{-1} respectively (15).

^{1}HNMR spectrum of compound [1] showed clear signal at δ = 2.27 ppm belong to (N-H) amide proton, signals at δ= (7.38-7.53)ppm belong to phenyl ring protons, signals at δ= (7.84-8.51)ppm belong to naphthyl ring protons and signal at δ=(8.71)ppm belong to (NH_2) protons.

^{13}CNMR spectrum of compound [1] showed signals at δ = (122.14-134.95) ppm belong to aromatic

carbons and signal at δ=(160.95) ppm belong to (C=O) imide carbons.

FTIR spectra of prepared Schiff bases [2-10] showed clear absorption bands at (3230-3260) cm^{-1}, (3040-3113) $cm^{-1}$and (1701-1740) cm^{-1}which are belong to ν(N-H) amide ,ν(C-H) aromatic and ν(C=O) imide respectively (15).

Other absorption bands were appeared at (1660-1680) cm^{-1}, (1585-1596) $cm^{-1}$and (1290-1350) cm^{-1} belong to ν(C=N) imide , ν(C=C) aromatic and ν(C-N) imide respectively while absorption bands due to asym. ν(SO2) and sym. ν(SO2) were appeared at (1342-1390) cm-1 and (1178-1192)cm^{-1} respectively (15).

FTIR spectrum of compound [3] showed clear absorption bands at (1087) cm^{-1} belong to ν(C-Cl) ,while FTIR spectra of compound [4] and [5] showed absorption bands at (1508 ,1523)cm^{-1} and(1435,1438)cm^{-1}belong to ν(C-NO_2) and FTIR spectra of compounds [7] and [9] showed absorption bands at (3417, 3411) cm-1belong to ν(OH) . All details of FTIR spectral data of Schiff bases [2-10] are listed in Table (2).

^{1}HNMR spectrum of compound [3] showed clear signal at δ = 5.8 ppm belong to (N-H) amide proton, signals at δ= (7.65-8)ppm belong to phenyl ring protons, signals at δ= (8.43-8.7) ppm belong to naphthyl ring protons and signal at δ= (8.79)ppm belong to imine proton.

^{13}CNMR spectrum of compound [3] showed signals at δ=(122.13-137.79) ppm belong to aromatic carbons present in two phenyl rings and naphthyl ring. The spectrum showed also signals at δ= (160.73-161)ppm belong to (C=N) carbon and signal at δ= (171.16)ppm belong to (C=O) imide carbon.

^{1}HNMR spectrum of compound [5] showed signal at δ = 5.79 ppm belong to(N-H) amide proton, signals at δ=(7.38-7.89)ppm belong to phenyl rings protons, signals at δ=(8.29-8.54)ppm belong to aromatic proton in naphthyl rings and signal at δ= (8.69) ppm belong to imine proton.

^{13}CNMR spectrum of compound [5] showed signals at δ=(111.91-134.98) ppm belong to aromatic carbons present in two phenyl rings and naphthyl ring, signal at δ= (160.0)ppm belong to (C=N) carbon and signal at δ= (172.2)ppm belong to (C=O) imide carbon.

^{1}HNMR spectrum of compound [6] showed two clear signals at (δ = 2.98 ppm and δ = 3.04 ppm) belong to two methyl groups protons and signal at δ= (5.80)ppm belong to (N-H) amide proton. Signals appeared at δ= (7.62-8.45)ppm are belong to aromatic protons in two phenyl ring and naphthyl rings while the signal appeared at δ= (8.5)ppm is belong to imine proton.

^{13}CNMR spectrum of compound [6] showed two signals at δ=(19.3 and 24.64) ppm belong to carbons of two methyl group and signals at δ= (118.13-148.14)ppm are belong to aromatic carbons of two phenyl rings and naphthyl rings. Other signals appeared at δ= (159.5-160.42)ppm and at δ= (179.66)ppm which are belong to (C=N) and (N=O) imide carbons respectively.

CONCLUSION

A series of new Schiff bases containing two biologically active components was synthesized successfully by performing two steps synthesis. The newly synthesized compounds were expected to possess high biological activity since they contain three known biologically active moieties cyclic imide, sulfonamide and Schiff base.

ACKNOLDEGMENT

Authors are thankful to all who help in this work or share their knowledge.

Table (1) physical properties of Schiff bases [2-10]

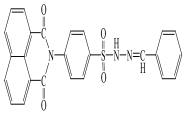
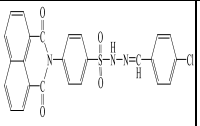
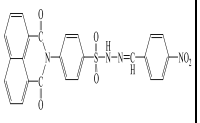
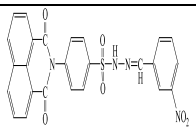
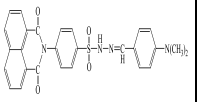
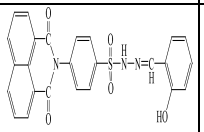
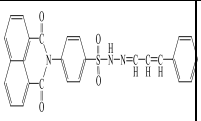
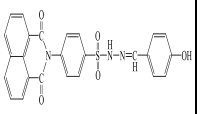
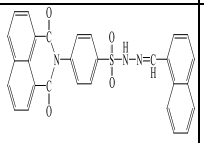
Comp.No.	Compound structure	Yield%	Color	Melting point C°	Recrystall. solvent
2		87	yellow	232-233	Acetone
3		85	Light brown	183-185	Acetone
4		78	yellow	207-209	Ethanol
5		75	yellow	210-212	Ethanol
6		87	Red	239-241	Acetone
7		72	Brown	235-237	Dioxane
8		85	Brown	202-204	Acetone
9		80	Redish Brown	205-207	Dioxane
10		70	Deep yellow	223-225	cyclohexane

Table (2) FTIR spectral data (cm^{-1}) of Schiff bases [2-10]

CompNo.	2	3	4	5	6	7	8	9	10
ν(NH) Amide	3230	3236	3260	3236	3255	3234	3260	3238	3255
ν(C-H) Aromatic	3040	3066	3040	3078	3103	3113	3060	3110	3105
ν(C=O) Imide	Asym.1740 Sym.1700	1701	Asym.1725 Sym.1700	1705	Asym.1740 Sym.1700	1705	1708	1708	1708
ν(C=N) Imide	1670	1662	1680	1674	1660	1674	1668	1675	1665
ν(C=C) aromatic	1590	1585	1590	1589	1596	1593	1587	1588	1590
Asym.νSO_2 Sym. νSO_2	1390 1185	1381 1188	1385 1185	1342 1188	1363 1178	1346 1192	1375 1188	1348 1190	1345 1189
ν(C-N) Imide	1315	1330	1346	1290	1332	1292	1350	1295	1345
Others	-	ν(C-Cl) 1087	ν(C-NO_2) 1508 1435	ν(C-NO_2) 1523 1438	ν(C-H) Aliphatic 2912	ν(O-H) 3417	-	ν(O-H) 3411	-

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تحضير عدد من قواعد شيف الجديدة المرتبطة بمكونة سلفون اميدونفثال ايمايد ذات فعالية بايولوجية متوقعة

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الخلاصة

تم في هذا البحث تحضير عدد من قواعد شيف الجديدة المرتبطة بمكونة سلفن اميدو نفثال ايمايد. تضمنت الخطوة الاولى من التحضير ادخال المركب 4-(N – نفثال ايميديل) فنيل كلوريد السلفونيل في تفاعل مع الهيدرازين وبذلك تم الحصول على المركب 4-(N- نفثال ايميديل) فنيل سلفونيل هيدرازين. اما الخطوة الثانية فقد تضمنت ادخال المركب المحضر 4-(N- نفثال ايميديل) فنيل سلفونيل هيدرازين في تفاعل تكاثف مع الديهايدات اروماتية مختلفة لانتاج قواعد شيف الجديدة.تم اثبات صحة تراكيب المركبات المحضرة من خلال الاعتماد على مطيافية الاشعة تحت الحمراء والرنين النووي المغناطيسى بنوعيه ^{1}HNMR, ^{13}CNMR حيث كانت النتائج المستحصلة مطابقة للتراكيب المقترحة. من المتوقع ان تكون قواعد شيف الجديدة ذات فعالية بايولوجية سيما وان جزيئاتها قد بنيت اساسا من مكونات فعالة بايولوجيا وهي النفثال ايمايد والسلفون امايد وقواعد شيف.