Int.J.Curr.Microbiol.App.Sci (2016) *5*(8): 1-13

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 5 Number 8 (2016) pp. 1-13**
Journal homepage: http://www.ijcmas.com

Original Research Article http://dx.doi.org/10.20546/ijcmas.2016.508.001

Synthesis and Characterization of New Compounds containing 2-amino Thiazole Ring from Amino Benzoic Acid

Entesar O. Al-Tamimi* and Hussein F. Abdul Mahdi

University of Baghdad, college of science, Chemistry department, Baghdad, Iraq
**Corresponding author*

Keywords

Aminobenzoic acid, substituted aminobenzoate, hetrocyclic, thiazol ring.

Article Info

Accepted:
06 July 2016
Available Online:
10 August 2016

A B S T R A C T

The presented work involved the preparation of compounds containing aromatic heterocyclic (thiazol ring) derived from substituted aminobenzoic acid. The first step involved the preparation of substituted esters of aminobenzoic acid (from 1 to 9 compounds) by reaction of substitutedaminobenzoic acid withthionyl chloride then with different alcohols such as (benzyl alcohol, allylalcohol, polyvinyl alcohol).The second step includes the reaction of the prepared compounds with chloroacetyl chloride in the presence of triethylamine to give compounds from (10 to 18). The third step involves the preparation of N-(2-amio thiazole) substituted aminobenzoatefrom the refluxe of cmpounds(10 to 18) with thiourea and DMF. All the prepared compounds in this work were characterized by melting point and softening points with other physical properties, FTIR, H^1-NMR spectra.screening of the antimicrobial activity of the prepared thiazol compounds was evaluated against 2 types of bacteria.

Introduction

Heterocyclic chemistry is one of the largest branches of organic chemistry. It is particularly important in nature because of the wide variety of industrial significance and physiological activities (Bambas, 1952). Heterocyclic compounds with three to six carbons in a single ring are numerous. However, so far, only those with five or six atoms in a single ring are important, such as some of vitamin B complexes, enzymes, amino acids, drugs and the genetic material. The most common hetero atoms are (N, O, and S). Heterocyclic compounds have received much attention in the development of novel antibacterial (Azab *et al*., 2013), anthelmintic (Babu, 2013), anticancer (Kaushik *et al*., 2013) and anti-diabetic activities (Han *et al*., 2013). These compounds also have industrial applications such accelerators (Unsinn *et al*., 2013), antioxidants (Malki *et al*., 2013), copolymers (Paulo *et al*., 2013), corrosion inhibitors (Nabel *et al*., 2013) and dyes (Shihab *et al*., 2013). Thiazole derivatives are an important class of heterocyclic compounds. They occupy an important position in medicinal chemistry, presenting a wide range of bioactivities. As medicines, many of them display including antibacterial and antifungal (Ulusoy *et al*., 2002;

Kaplancikli *et al*., 2004), anti-HIV (Al-Saddi *et al*., 2008), hypertension (Tripathi *et al*., 2003), anti-inflammatory, anti-convulsant, antidepressant and tubercular activities (Karimain, 2009). Thiazoles and their derivatives have attracted continuing interest over the years because of their varied biological activities. Thiazole, particularly the 2-amino thiazole nucleus have been incorporated into a wide variety of therapeutically interesting candidates.

1. Experimental
2. Material
3. All chemicals used were of analytical grade and there where available from Aldrich and Fluka companies.
4. Instrument
5. Melting points were determined on Gallen Kamp capillary melting point apparatus and were uncorrected.
6. FTIR spectra were recorded on Shimadzu FT-IR 8400 Fourier Transform Infrared Spectrophotometer.
7. Softening points were determined on Thermal Microscope Reichert Thermover 160.
8. ^{1}H-NMR were measured in DMSO Solutions on a Bruker-500 MHz spectrophotometer using TMS as an internal standard (chemical shifts in ppm)
9. The antibacterial activity was determined by agar-well diffusion method.

Synthesis methods for the prepared compounds

General procedure for the synthesis of esters

Literature procedure was used with modifications (Karimain *et al*., 2012). Thionyl chloride ($SOCl_2$, 5 mL) was added dropwise to the used alcohol (allyl, benzyl) (5 mL, 0 °C) in a round-bottom flask. The solution was stirred for 0.5 h in ice bath. The amino acid (0.01mole) was dissolved in thionyl chloride (10ml) and then added to the round-bottom flask. The mixture was refluxed for 6 hours (50°C). At the end of the reaction, the excess of thionyl was removed under vacuum and the obtained crude product was washed with ether. The physical properties of the prepared compounds are listed in table (1).

General procedure for the synthesis of polyesters

The poly esters were prepared according to the literature with few modifications (Vogel, 1974). (0.01) mole of the amino acid was refluxed with (10ml) thionyl chloride. Upon the completion (formation of acid chloride) the mixture was transferred to a dropping funnel which is fixed on a bolt-head flask (with condenser) containing (0.01mole) of PVA dissolved in 20 ml DMF. The flask was placed in ice bath and the acid chloride was added dropwise for 30 minute with continuous stirring then the mixture was refluxed for 0.5 hour. The product was poured in water, washed with 5% sodium bicarbonate, water and then with ethanol and purified by dissolving it in DMSO and reprecipitating it from ethanol. The physical properties of the prepared compounds are listed in table (1).

General procedure for the preparation of chloroacetyl substituted amides

Literature procedure was used with modifications (21).In100 mL R.B.F the prepared esters (or poly esters) (0.02moles) were dissolved in DMF (20 mL) then was cooled to 0–5∘C and 2-3 drops of TEA were added. Chloroacetylchloride (0.02mole) in

DMF (20 mL) was slowly added to RBF with vigorous stirring for 3 hours. Upon the completion of the reaction the mixture was poured on water (50mL) and washed with 5% NaHCO3 and subsequently with water. The crude product was dried and recrystallized from ethanol. The physical properties of the prepared compounds are listed in table (2).

General procedure for the preparation of amino thiazol compounds

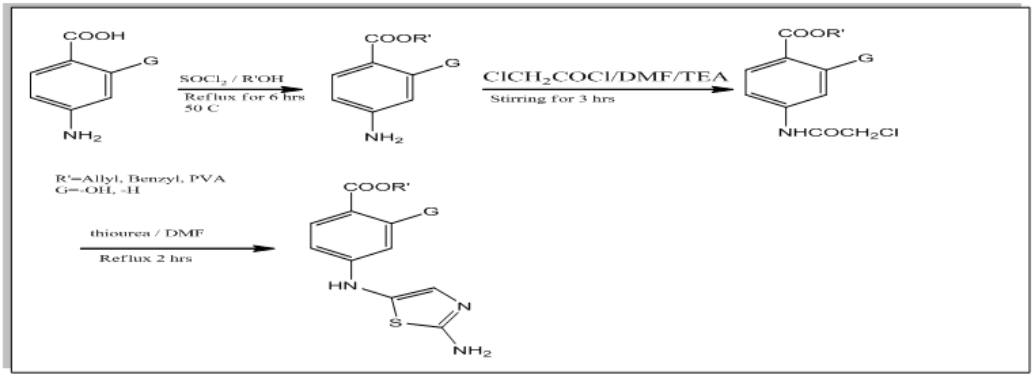
Literature procedure was used with modifications (Sujit *et al*., 2015**).** In 100 ml R.B.F (0.02mole) of chloroacetyl substituted amides and (0.02mole) of thiourea were dissolved in 20 ml DMF and the mixture was refluxed for 2 hours. Upon the completion the mixture was poured in water and the dry crude product was recrystallized from ethanol (Except the polymers were purified by DMSO). The physical properties of the prepared compounds are listed in table (3).

The Biological activity

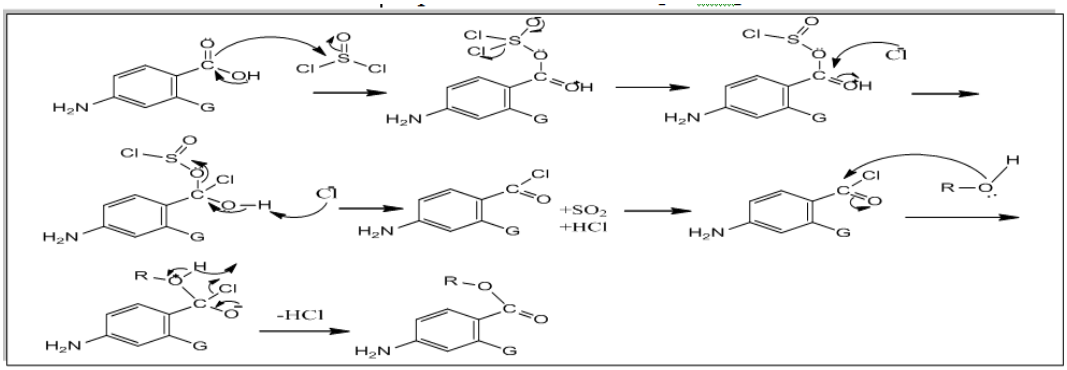
The cup plate method using nutrient agar medium was employed (Chavan *et al*., 2007; Al-Azzawi *et al*., 2010; Carey, 2010) in studying the antibacterial activity of the prepared compounds against two types of bacteria, *Staphylococcus aureous*(gram positive) and *Escherichia coli* (Gram negative) respectively using DMSO as sample solution. Using a sterilized cork borer cups were scooped out of agar medium contained in a Petri dish which was previously inoculated with the microorganisms. The test compound solution (300µl) was added in the cups and the Petri dishes were subsequently incubated at 37□ C for 24hrs. Zones of inhibition produced by each compound was measured in mm and the results are listed in Table (7).

Result and Discussion

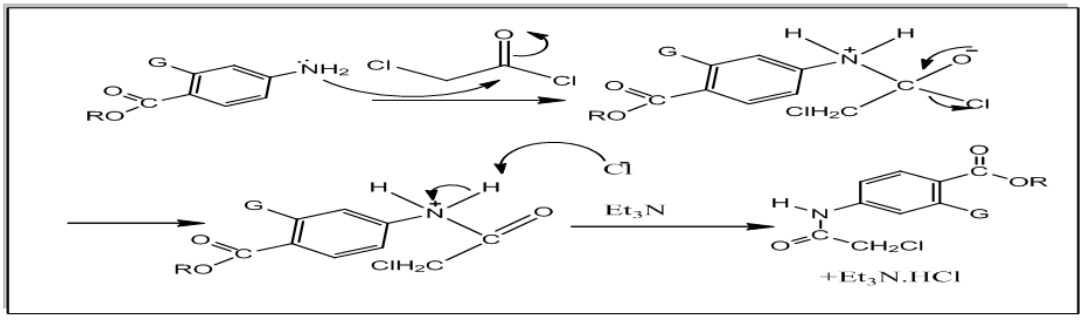
The starting material for the synthetic N-(2-aminothiazol) substituted aminobenzoate is substituted aminobenzoic acid which reacted with different alcohols and thionyl chloride then with chloroacetyl chloride in DMF and after that thiourea was added under reflux. The mechanism is shown in the schemes below.



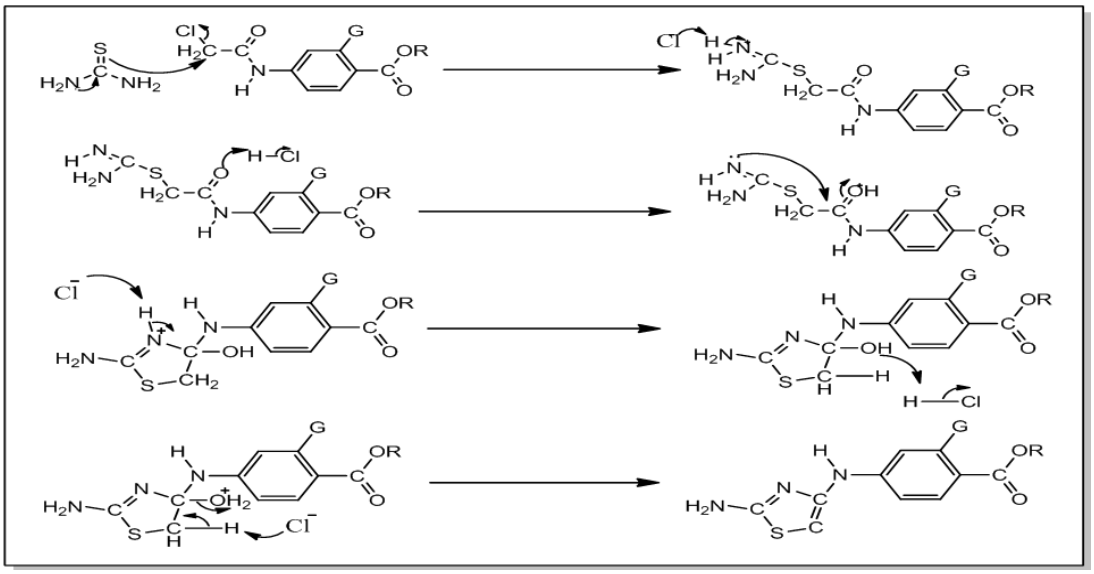
Step1. Ester formation (25,26):



Step2. Chloroacetyl substituted amide formation (27):



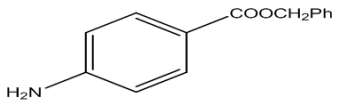
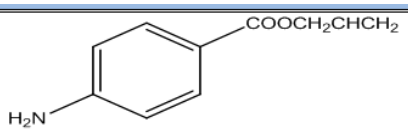
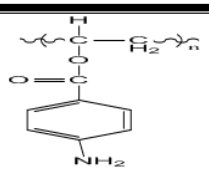
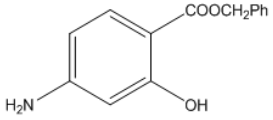
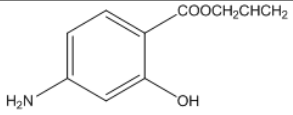
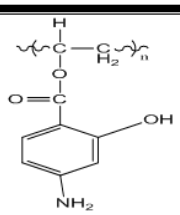
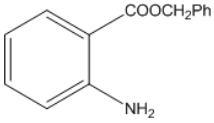
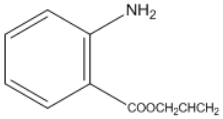
Step3. Formation of 2-aminothiazole ring (28)



Structures of the prepared compounds in the first step (1-9) were confirmed by physical properties which are listed in table (1).

FTIR spectra showed the absoribtion of the region (3419-3455) cm-1 due to (υNH_2) group, (1731-1764) cm-1 for ester, (1600-1550) cm-1for (C=C) aromatic, (3048-385) cm-1 for (C-H) aromatic, (1340-1378) cm-1 for (C-N), (2910-2952) cm-1 for (C-H)aliphatic and the absorption for (C-O) (1190-1256) cm-1. All these regions are listed in table(4).

Table.1 Physical properties of the prepared esters

Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
1	 benzyl 4-aminobenzoate	Yellow	110	-	83
2	 allyl 4-aminobenzoate	Orange	98	-	72
3	 *poly ethylene* 4-aminobenzoate	Brown	-	135	79
4	 benzyl 4-amino-2-hydroxybenzoate	Deep Yellow	175	-	65
5		Red	105	-	94
6	 *poly ethylene* 4-amino-2-hydroxybenzoate	brown	-	158	82
7	 benzyl 2-aminobenzoate	Yellow	120	-	72
8	 allyl 2-aminobenzoate	Red	105	-	76

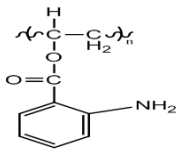
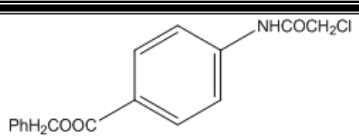
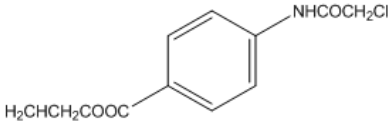
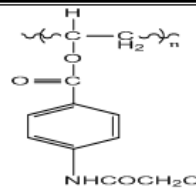
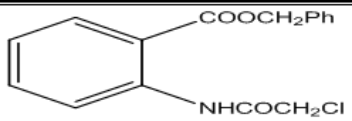
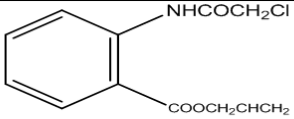
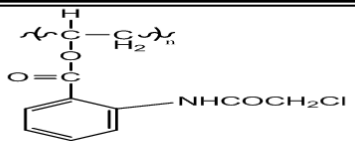
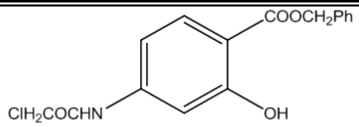
9	 *poly ethelen* 2-aminobenzoate	Brown	-	157	63

Table.2 Physical properties of the prepared chloroacetyl substituted amides

Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
10	 benzyl 4-(2-chloroacetamido)benzoate	Deep Yellow	170	-	64
11	 allyl 4-(2-chloroacetamido)benzoate	orange	155	-	78
12	 *Poly ethylene* 4-(2-chloroacetamido)benzoate	Dark Brown	-	167	63
13	 benzyl 2-(2-chloroacetamido)benzoate	Brown	-	-	80
14	 allyl 2-(2-chloroacetamido)benzoate	Orange	92	-	60
15	 *poly ethylen* 2-(2-chloroacetamido)benzoate	Dark Brown	-	136	53
16	 benzyl 4-(2-chloroacetamido)-2-hydroxybenzoate	Brown	198	-	75

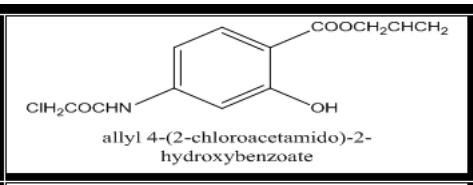
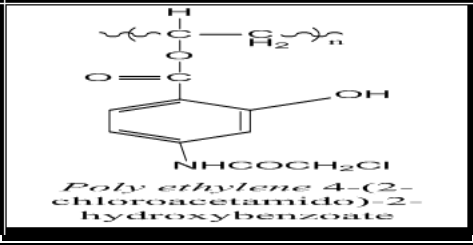
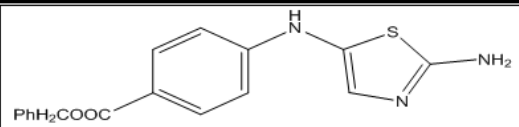
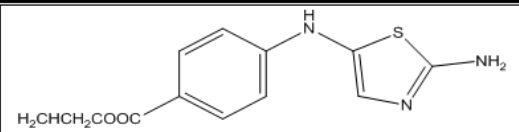
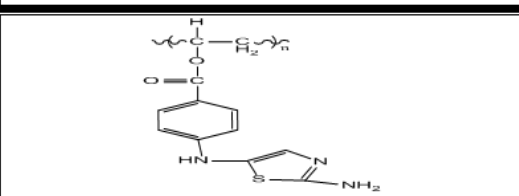
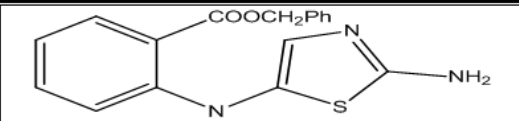
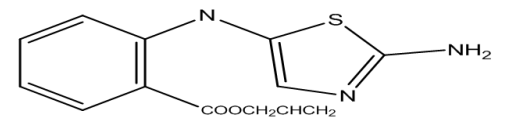
17	 allyl 4-(2-chloroacetamido)-2-hydroxybenzoate	Dark red	-	-	67
18	 *Poly ethylene* 4-(2-chloroacetamido)-2-hydroxybenzoate	Dark Brown	-	148	72

Table.3 Physical properties of the prepared thiazole compounds

Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
19	 benzyl 4-((2,,5-diaminothiazol))benzoate	Dark red	190	-	73
20	 allyl 4-(2,5-diaminothiazol)benzoate	Brown	172	-	78
21	 *poly ethylene* 4-(2,5-diaminothiazol)benzoate	Brown	-	145	87
22	 benzyl 2-(2,5-diaminothiazol)benzoate	Dark Red	108	-	76
23	 allyl 2-(2,5-diaminothiazol)benzoate	Brown	101	-	79

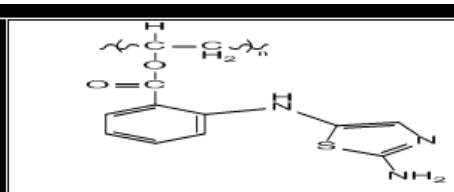
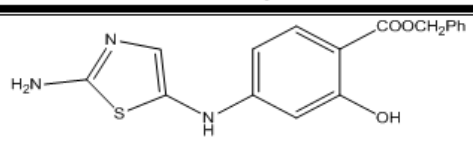
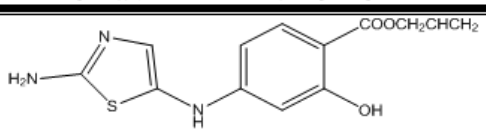
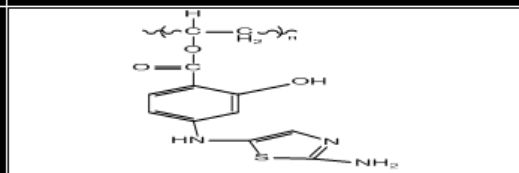
24	 poly ethylene 2-(2,5-aminothiazol)benzoate	Brown	-	107	63
25	 benzyl 4-((2,5-diaminothiazol)-2-hydroxybenzoate	Dark red	97	-	80
26	 allyl 4-(2,5-diaminothiazol)-2-hydroxybenzoate	Brown	120	-	87
27	 poly ethylene 4-(2,5-diaminothiazol)-2-hydroxybenzoate	Dark Brown	-	111	72

Table.4 FTIR spectra of the prepared esters

Comp. No.	υNH_2 1°amine	υC-H aromatic	υC-H Aliphatic	υC=O ester	υC=C aromatic	υC-N	υC-O	Others
1	3431	3052	2934	1731	1600	1364	1256	-
2	3343	3049	2932	1752	1550	1369	1245	υC=C Olef. 1608
3	3419	3053	2910	1764	1614	1377	1261	-
4	3427	3051	2952	1742	1608	1371	1243	υO-H Phenol 3558
5	3439	3029	2918	1733	1609	1340	1190	υO-H Phenol 3551
6	3455	3061	2922	1758	1602	1352	1198	υO-H Phenol 3532
7	3438	3085	2936	1746	1616	1368	1190	
8	3452	3046	2965	1743	1611	1373	1241	υC=C Olef.1617
9	3435	3072	2932	1761	1608	1378	1221	

Table.5 FTIR spectra of the chloroacetyl substituted amides

Comp.No.	υN-H 2°amine	υC-H aromatic	υC-H Aliphatic	υC=O ester	υC=O amide	υC=C aromatic	υC-N	υC-O	υC-Cl	others
10	3199	3012	2911	1735	1681	1607	1360	1250	760	-
11	3201	3065	2941	1761	1672	1610	1365	1245	745	υC=C Olef. 1607
21	3234	3013	2912	1724	1675	1606	1379	1254	767	-
13	3246	3086	2931	1743	1679	1609	1372	1247	756	-
14	3213	3034	2928	1767	1668	1617	1355	1180	781	υC=C Olef. 1611
15	3212	3025	2919	1769	1675	1606	1371	1170	777	-
16	3190	3061	2931	1773	1664	1619	1368	1154	743	υO-H Phenol 3520
17	3217	3056	2964	1763	1677	1622	1373	1234	761	υO-H Phenol 3534
18	3213	3014	2936	1764	1673	1613	1369	1257	785	υO-H Phenol 3548

Table.6 FTIR Spectra of the 2-aminothiazole compounds in cm-1

Comp.No.	υNH_2 1°amine	υNH 2°amine	υC-H aromatic	υC-H Aliphatic	υC=O ester	υC=N	υC=C aromatic	υC-N	υC-O	Others
19	3450	3210	3049	2923	1785	1632	1602	1368	1244	-
20	3332	3190	3025	2921	1781	1630	1514	1374	1263	υC=C Olef. 1600
21	3452	3224	3010	2900	1766	1637	1608	1373	1242	-
22	3444	3230	3064	2927	1762	1634	1606	1375	1238	-
23	3456	3234	3064	2923	1775	1640	1604	1323	1160	υC=C Olef.1608
24	3450	3192	3046	2916	1770	1639	1608	1369	1180	-
25	3450	3210	3085	2954	1776	1650	1612	1373	1155	υO-H Phenol 3550
26	3420	3200	3069	2989	1755	1642	1620	1370	1223	υO-H Phenol 3540
27	3422	3199	3062	2916	1760	1648	1604	1372	1265	υO-H Phenol 3542

Table.7 antibacterial activity of the prepared compounds

Comp. No.	**Inhibition Zone against *Stapylococcusaureus* (Gram positive)**	**Inhibition Zone against*Escherichia coli*(Gram negative)**
Reference Cefatoxime	48 mm	40 mm
19	30 mm	15 mm
20	21 mm	12 mm
22	22 mm	10 mm
23	20 mm	9 mm
25	25 mm	8 mm
26	18 mm	8 mm

Fig.4 1HNMR spectra of compound 11

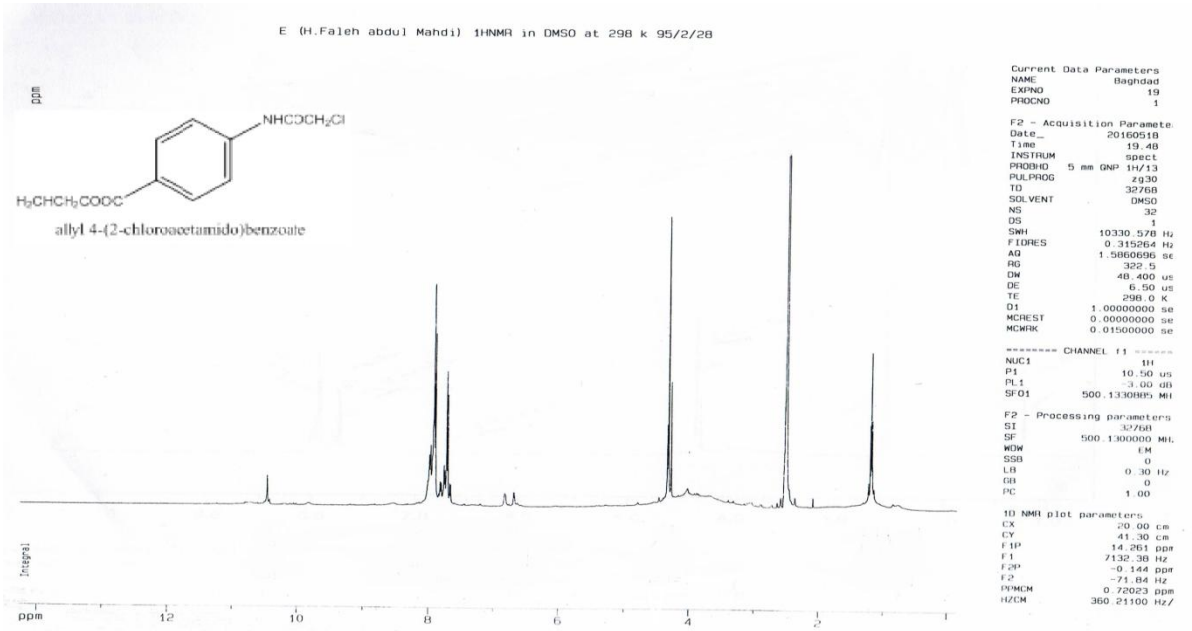
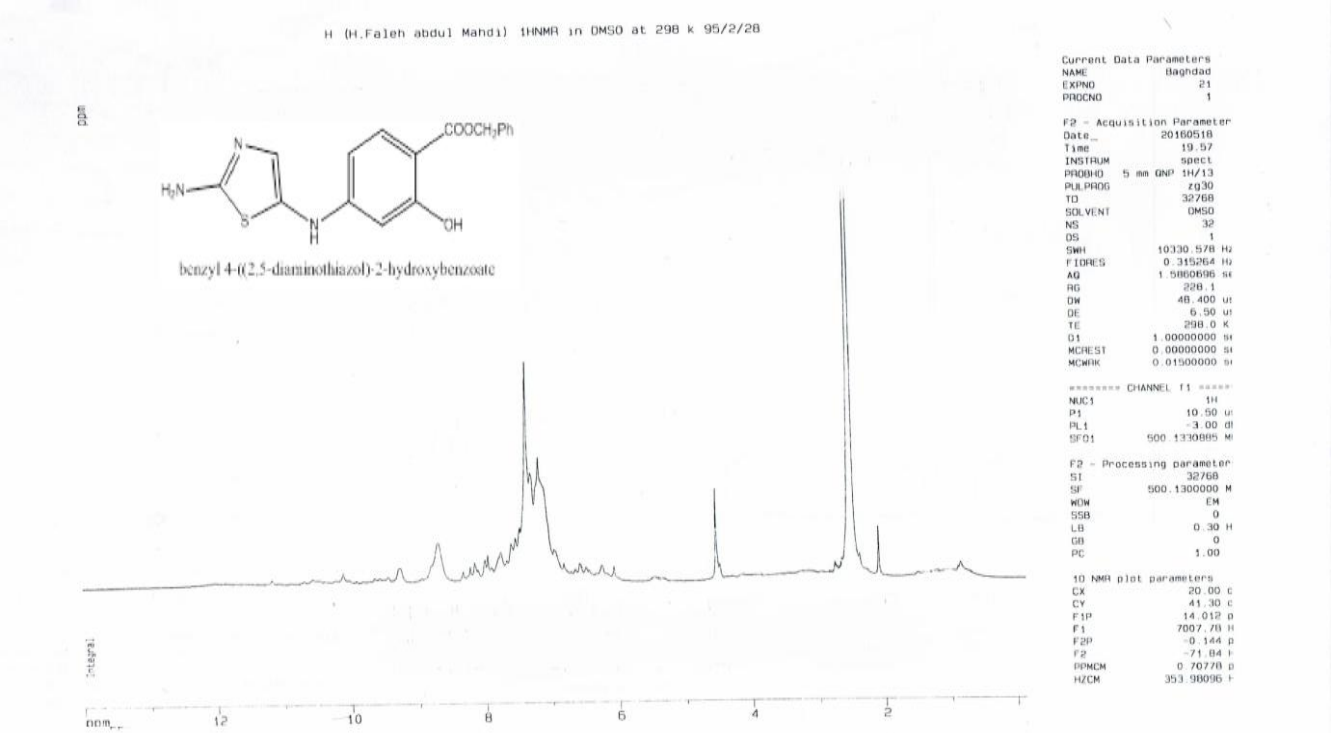


Fig.5 1HNMR spectra of compound 25



The second step involves the reaction of the prepared compounds (1-9) with chloroacetyl chloride in DMF to produce compounds (10-18). The structures were confirmed by the physical properties which are listed in table (2). FTIR spectra showed the disappearance of the absorption band at (3419-3455) cm-1 of (υNH_2) and the appearance of new region in (3190-3246) cm-1 due to (υN-H) group,(1646-1681) cm-1 for the (υC=O) amide and the absorption at (756-781) cm-1 due to the (υC-Cl) group and the other absorptions are listed in table(5).

1H-NMR spectrum of compound 11 showed signals at δ10.4 ppm of (s,1H,NH), δ7.9 ppm of (m,4H,Ar-H) ,δ7.5 ppm of (d,1H,=CH)), δ6.8 ppm for the (d,2H,$\underline{CH_2}$=CH-CH_3), δ4.3 ppm of (d,3H,CH_2=CH-$\underline{CH_3}$), δ1.3 ppm of (s,2H,CH_2Cl).

The third step included the reaction of the prepared compounds (10-18) in DMF at refluxe to produce N-(2-Aminothiazole) substituted aminobenzoate (19-27). The structures of the compounds were confirmed by the physical properties listed in table(3). FTIR of compounds (19-27) showed the disappearance of the absorption band of (υC=O) amide at (1646-1681) cm-1, absorption band of the (υC-Cl) group at (756-781) cm-1 which confirms the conversion to the final product, and the appearance of new band at (3420-3456) cm-1 of (NH_2) group and new absorption at (1630-1650) cm-1 of (υC=N) group and the other absoribtions are listed in table (6).

1H-NMR spectrum of compound 25 showed signal at δ10.1ppm for (s,1H,OH), δ9.3ppm for (s,2H,NH_2), δ8.6ppm for (s,1H,NH), 7.3ppm for (m,4H,Ar-H),δ 4.5ppm (s,1H,CH thiazole ring)

References

Al-Azzawi, A.M. and Mehdi, S.A. 2010. *Baghdad Sci. J.*, 7(1): 641.

Al-Saddi, M.S., Faidallah, H.M., Rostom, S.A.F. 2008. *Arch. Pharm. Che. Life Sci.*, 341: 424-434.

Azab, M., Youssef, M. and. El-Bordany, E. 2013. (Synthesis and Antibacterial Evaluation of Novel Heterocyclic Compounds Containing a Sulfonamido Moiety) *Mol.*, 18: 832-844.

Babu, I. and Selvakumar, S. 2013. (Synthesis and spectral characterization of some 2-((1-((substituted phenylamino)methyl)-1-benzoimidazol-2-yl) alkyl) isoindoline-1,3-diones for in-vitro anthelmintic screening) *Der. Pharma. Chemica,* 5(4): 198-206.

Bambas, L. 1952. (Five-membered heterocyclic compounds with nitrogen and sulfur or nitrogen, sulfur and oxygen (except thiazole)) 2nd ed., Parke, Davis and company, Detroit, Michigan, USA.

Baselt, T., Rehse, K. 2008. Archived der pharmazie, 24: 645-654.

Ber Dtsch. 1887. *Chem. Ges.*, 20: 3118.

Carey, F.A. 2010. "Organic chemistry", 7th Ed. RajkamalElectic press, New Delhi, PP(482,489,500,708).

Chavan, A.A. and Pai, N.R. 2007. *Mol.*, 12: 2467.

Fuson, Cruth, Morril. 1980. "the systematic identification of organic compounds"6th Ed. P.167.

Han, J., Dong, H., Xu, Z., Wang, J. and Wang, M. 2013. (Synthesis and Activity of Novel Acylthiourea with Hydantoin) Int. J. Mol. Sci., 14:19526-19539.

Jiaxi, X. 2009. "Steriochemistryin the synthesis from ketens and imines by Staudinger reaction", 5th Eurasian conference on hetrocyclic chemistry: 21-44. USA, INC.

Kaplancikli, Z.A., Zitouni, G.T., Revial, G., Guven, K. 2004. *Arch. Pharm. Res.*, 27: 1081- 1085.

Karade, H.N., Acharya, B.N., Manisha, S., Kaushik, M.P. 2008. *Med. Chem. Res.*, 19-29.

Karimain, K. 2009. *Indian J. Chem.*, 19: 369-371.

Karpov, K.A., Nazarenko, A.V., Pekarevskii, B.V., potekhin, V.M. 2001. *Russian J. Appl. Chem.*, 74: 998-1001.

Kaushik, K., Ashok, G., Swati, D., Mustafa, K. and Hiral, T. 2013. (Benzimidazole: apromising lead for anticancer drug design) *Uni. J. Pharm.*, 2(3): 57-62.

Malki, F., Touati, A. and Moulay, S. 2013. (Antioxidant Activity of Two Mesomeric Heterocyclic Betaines Containing a Pyrimidine Moiety) *J. Trop. Agric. Sci.*, 36(4): 393-402.

Modi, B.R., Vashi, D.M., and Desai, K.R. 1994. "Synthesis of 8-triazinylamino coumarin derivatives and their fluorescent properties," *Indian J. Chem. Technol.*, vol. 1, no. 5, pp. 317–318.

Nabel, A., Negm, Mona, A. and Tawfik, S. 2013. (Impact of Synthesized and Natural Compounds in Corrosion Inhibition of Carbon Steel and Aluminium in Acidic Media) *Recent Patents on Corrosion Sci.*, 3: 1-11.

Paulo, J., Coelho, A., Céu, M., Sousa, M., Cidália, R., Castro, A., Maurício, C., Fonseca, M., Manuela, M. and Raposo, P. 2013. (Fast thermal cis–trans isomerization of heterocyclic azo dyes in PMMA polymers) *Optical Materials*, 35: 1167-1172.

Shihab, N. and Intedhar, M. 2013. (Synthesis of some novel heterocyclic azo dyes for acridine

derivatives and evaluation of their antibacterial activities) *J. Chema. &Pharma. Res.*, 5(5): 345-354.

Sujit, K., Anuradha, K., Harika, M., Sarada, P. and Jenny, S. 2015. (Synthesis, Characterization and Antimicrobial Activity of Some Oxazole and Thiazole Derivatives) *J. Serb. Chem. Soc.*, 2(3): 60-66.

Tang, X., Guangxia Tang, Wang, H., LuoL, and Yang, D. 2012. *Bull. Chem. Soc. Ethiop.*, 26(3): 415-420.

Tripathi, K.D. 2003. Essential of medical pharmacology., 5th edition, 627-686.

Ulusoy, N., Kiraz, M., Kucukbasmaci. O., 2002. Monatshefte fur chemie. 133: 1305-1315.

Unsinn, A., Stefan, H., Wunderlich and Knochel, P. 2013. (Accelerated Zincations for an Efficient and Mild Functionalization of Aromatics and Heterocycles) *Adv. Synthesis & Catalysis*, 355(5): 989-995.

Vogel, A.I. 1974. "A text book in practical organic chemistry"3rd Ed Iongman group limited, London, pp.389.

How to cite this article:

Entesar O. Al-Tamimi and Hussein F. Abdul Mahdi. 2016. Synthesis and Characterization of New Compounds containing 2-amino Thiazole Ring from Amino Benzoic Acid. *Int.J.Curr.Microbiol.App.Sci.* 5(8): 1-13. doi: http://dx.doi.org/10.20546/ijcmas.2016.508.001