Synthesis of 2-Mercaptobenzimidazole and Some of its Derivatives

Mohammed R. Ahamed[*], Shetha F. Narren[**] and Amal S. Sadiq[**]
[*]Department of Chemistry, College of Science, University of Baghdad, Baghdad-Iraq.
[**]Department of Chemistry, College of Science for Women, University of Baghdad, Baghdad-Iraq.

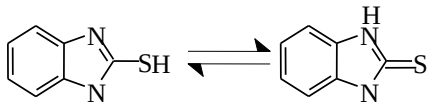
Abstract

The present work involved three steps: First step include synthesis of 2-mercaptobenzimidazole from reaction of *o*-phenylenediamine with carbon disulfide, in the second step: Alkylation of the 2-mercaptobenzimidazole with different alkyl halides or aryl to obtain thioether compounds. Third step: include oxidation of 2-mercaptobenzimidazole to disulfide, while oxidation of thioether compounds gave sulfone compounds by using hydrogen peroxide as oxidizing agent for (1-2h) with stirring at room temperature. The 2-mercaptobenzimidazole was prepared in autoclave. Structure confirmation of all prepared compounds were proved using FT-IR and elemental analysis (C.H.N.S) besides melting points.

Keyword: 2-Mercaptobenzimidazole, alkylation, oxidation.

Introduction

2-Mercaptobenzimidazole derived from benzimidazole with thiol group in the 2-position. It possesses other chemical names such as, *o*-phenylen thiourea, benzimidazol-2-thion with formula of $C_7H_6N_2S$.[1,2] Some characteristic of 2-mercaptobenzimid- azole are containing of thioamide group (-N-C=S), therefore it is considered one of thioamide compounds for its ability to react under special conditions to give derivatives having substituent at either nitrogen or sulfur atoms[3,4], 2-mercaptobenzimi- dazole possess the form dimer, because it has (C=S) group, this preferable product is the dimer[5], it is known to exist in two tautomerism forms , the thiol and thione from as represented below[6,7].



thiol form thione form

Various derivatives of 2-mercapto benzimidazole have been synthesized by several investigators and have been reported to exhibit a wide range of biological activities such as anti microbial[8] antihistamine[9] neutropic [10] and analgesic[11] activities. Although a great deal of the scientific literature concerning 2-mercapto-benzimidazole is in the area of medicinal chemistry, 2-mercaptobenzimidazole is also used in non-biological application, it serve as plant growth regulators[12] and used as corrosion inhibitor for mild steel in sulfuric acid solution[13], stainless steel in aqueous solutionsof NaCl [14], mild steel and zinc in phosphoric acid[15,16]. Also, it is widely used as an accelerator in rubber processing[17], and anti oxidant for rubber and plastics[18]. Mercaptobenzimidazole and its deriva- tives display insecticidal properties[19], it is also a well-known analytical reagent for mercury, and have been used for the determination Fe(II), Cu(II), and Cd(II) metal ions in sewage water and industrial waste waters samples[20-21].

Methods

All chemicals were high purity are used as the manufactures spilled them. The FT-IR spectra in the range (4000-200)cm^{-1} were recorded as KBr disc on a Shimadzu FT-IR 8300 spectrophoto- meter, elemental analysis (C.H.N.S) was carried out in Ministry of Oil. Melting point were recorded on stuart scientific CO-LTD melting point SMP1 and were uncorrected. Mercapto benzimidazole was prepared in outoclave, it's local mode from stainless steel with capacity (300 ml) and diameter (12.5 cm).

Experimental

Synthesis of 2-Mercaptobenzimidazole [1]

o-Phenylenediamine (5.0 g , 0.083 mol) was dissolved in absolute ethanol (75 ml) and added (35 ml) of carbon disulfide then the mixture was transferred in to autoclave with

closing it very well to get high temperature and pressure. The set-up was heated in sand both at (150 C) for (15 hours). Then the mixture was put in beaker and added (9 ml) of (10%) sodium hydroxide to get rid of *o*-phenylene diamine and some concentrated hydrochloric acid until the mixture become acidic, to precipitate 2-mercaptobenzimidazole, filtered and dried then recrystallized from ethanol and water. Table (1) shows the physical properties of compound [1].

***General procedure to prepare Thioether for 2-Mercaptobenzimida zole*[2-8][22]**

(8.4 g, 0.05 mol) of 2-MBI was dissolved in absolute ethano (15 ml) with alkyl halide (0.05 mol) and sodium hydroxide (2.0 g, 0.05 mol) in round flask (50 ml) and reflux condenser. The mixture was refluxed for (4-7 hours) and filtered directly to get rid of the precipitated salt the filtered sample was cooled and recrystallized from ethanol and water. Table (1) shows the nomenclature, physical properties of thioether .

***General Procedure to Prepare Disulfide and Sulfone* [9-16][23]**

Thiole or thioether compound (1.0 g, 0.006 mol) was added to ethanol (8.3 ml) in round flask (50 ml) hydrogen peroxide (5 ml, 30%) was added drop wise to mixture with continuous stirring for (1-2 hours) at room temperature. The precipitated was filtered and washed by distil water and dried. Table (2) shows the physical properties, nomenclature of prepared compounds.

Table (1)
The nomenclature, physical properties of compounds [1-8].

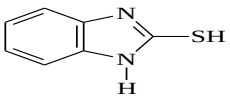
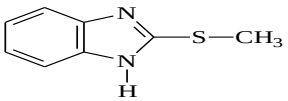
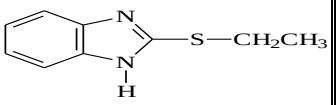
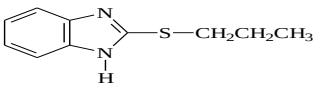
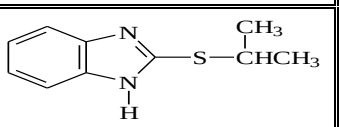
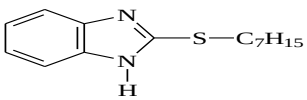
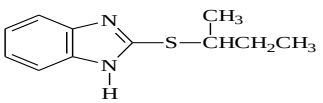
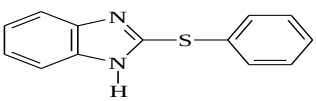
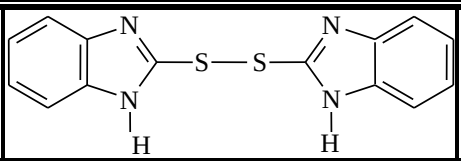
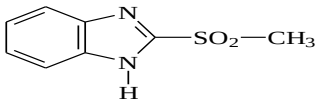
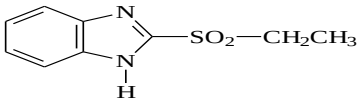
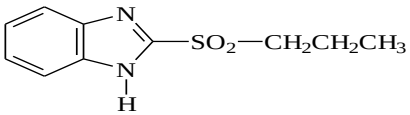
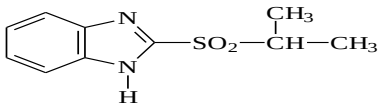
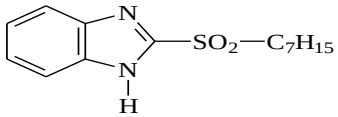
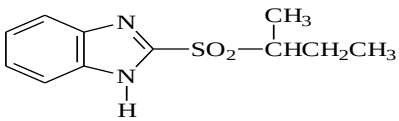
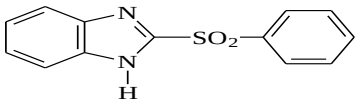
Compd. No.	*Nomenclature*	*Structure formula*	*Yield %*	*Color*	*M. P. °C*
1	2-Mercapto benzaimidazole		75	White	282-284
2	2[Methyl-mercaptobenzimidazol]		60	Yellow	130-132
3	2-[Ethyl-mercaptobenzimidazole]		54	White	145-147
4	2-[Propyl-mercaptobenzimidaole]		50	Beige	238-240
5	2-[Isopropyl-mercaptobenzimidazole]		55	White	240-242
6	2-[Heptyl-mercaptobenzimidazole]		70	White	109-111
7	2-[Isobutyl-mercaptobenzimidazoyl]		62	White	244-246
8	2-[Phenyl mercaptoobennzimidazole]		47	Beige	252-254

Table (2)
The nomenclatures, physical properties of compound [9-16].

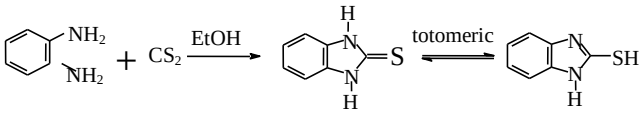
Compd. No.	*Nomenclature*	*Structure formula*	*Yield %*	*Color*	*M. P. °C*
9	[Bis(2-benzoimidazole) disulfide]		61	Yellow	218-220
10	2-[Methyl sulphonylbenzimidazole]		70	Dark Brown	120-121
11	2[Ethyl sulphonylbenzimidazole]		75	Pink	158-159
12	2-[Propyl sulphonylbenzimidazole]		94	White	149-151
13	2-[Isopropyl sulphonylbenzimidazole]		91	White	165-167
14	2-[Heptyl sulphonylbenzimidazole]		90	Light Yellow	98-100
15	2-[Isobutyl sulphonylbenzimidazole]		80	White	127-128
16	2-[Phenyl sulphonylbenzimidazole]		70	White	210-212

Results and Discussion

The present work involved three steps:

First Step

2-mercaptobenzmidazolewas obtained from the reaction of *o*-phenylene diamine with carbon disulfide in ethanol by using closed system.This method was of choice because it gives 2-mercaptobenz imidazole in good yield and high purity is shown below.

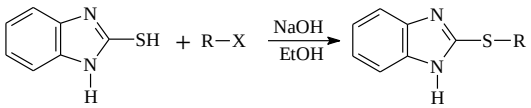


2-mercaptobenzimidazole

The structure of the compound was confirmed from its melting point Table (1) and FT-IR spectrum. Besides the C.H.N.S analysis Table (3). The FT-IR spectrum of compound [1], show the appearance stretching band at (2569) cm^{-1} of thiol group and disappearance of the two absorption band in the range (3387, 3286), (3363, 3194) cm^{-1} which could be attributed to asymmetric and symmetric stretching vibration (NH_2) group of o-phenylenediamine. These bands and other are shown in Table (4).

Second Step:

Alkylation of 2- mercaptobenzimidazole [1] under basic condition using different alkyl halides and aryl halide gave the thioethor derivatives [2-8]. As is shown below.



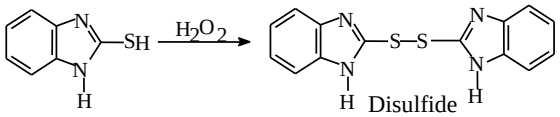
R-X=CH_3I, C_2H_5I, $CH_3CH_2CH_2Br$, CH_3CHCH_3,

$CH_3CH_2CHCH_3$, $C7H_{15}I$, C_6H_5Cl

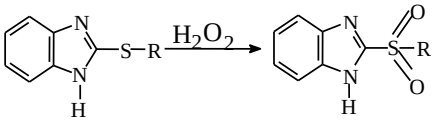
The thioether derivatives (2-8) were identified by FT-IR spectrum Table (4), melting point Table (1) and C.H.N.S analysis Table (3). The thioether derivatives showed some general FT-IR spectral, which showed a variable stretching band at (3090-3020) cm^{-1} (C-H) aromatic, (1589-1512) cm^{-1} (C=C) aromatic, (3452-3394) cm^{-1}(N-H), (1626-1616) cm^{-1} (C=N) imidazol and (695-601) cm^{-1}(C-S) .

Third Step:

Thiol compounds oxidize into disulfide easily, the weak oxidizing agent will be enough for oxidation depending on literature [24] Because the bond energy for (SH) group in thiole is (80 Kcal/mol) its very little from the bond energy for (OH) group in alcohols, therefore thiol possess ability on coupl oxidation whene it reacted with oxidizing agent to give disulfide.Oxidation of thiol compounds by hydrogen peroxide (30%) to give disulfide. As is shown below.



The structure of the compounds was confirmed from its melting point Table (2) and FT-IR spectrum. Besides the (C.H.N.S) analysis Table (3). The FT-IR spectrum of compound [9], indicated the appearance stretching band of (S-S) group at (559) cm^{-1} with disappearance the bond of (SH) at (2569), these bands and other are show in Table (5),While New compounds [10-16] were prepared by oxidation thioether to sulfone with used hydrogen peroxide. As is shown below.



R-= $-H_3$, $-C_2H_5$, $CH_3CH_2CH_2-$, $CH_3\underset{|}{C}HCH_3$,

$CH_3CH_2\underset{|}{C}HCH_3$, $-C7H_{15}$, $-C_6H_5$

The structure of the compounds were confirmed from its melting point in Table (2) and (C.H.N.S) analysis for some of them in Table (3). Besides FT-IR Table (5) shows the appearance of the two stretching bands of (SO_2) group asymmetric and symmetric at (1396-1342) cm^{-1}, (1346-1292) cm^{-1} respectively and other common bands such as: Stretching band (C-H) aromatic at (3051-3020) cm^{-1}, (C-H) aliphatic at (2966-2927) cm^{-1}, (C=C) aromatic at (1589-1582) cm^{-1} , (C=N) imidazol at (1625-1616) cm^{-1} and (C-S) at (692-617) cm^{-1}.

Table (3)
The C.H.N.S analysis of some prepared compounds.

Comp. No	*M. F.*	*C%*	*H%*	*N%*	*S%*
1	$C_7H_6N_2S$	Calc. 55.97	4.02	18.65	21.34
		Found. 55.63	3.99	18.55	20.98
2	$C_8H_8N_2S$	Calc. 58.50	4.91	17.05	19.52
		Found. 58.00	4.51	16.96	19.02
3	$C_9H_{10}N_2S$	Calc. 60.64	5.65	15.71	17.98
		Found. 60.61	5.55	15.31	17.67
6	$C_{14}H_{20}N_2S$	Calc. 67.96	8.11	12.27	12.91
		Found. 67.11	7.99	11.99	12.72
9	$C_{14}H_{10}N_4S_2$	Calc. 56.35	3.37	18.77	21.49
		Found. 56.22	3.11	18.32	20.99
12	$C_{10}H_{12}N_2SO_2$	Calc. 53.57	5.39	12.49	14.30
		Found. 53.44	5.21	12.31	14.09
15	$C_{11}H_{14}N_2SO_2$	Calc. 55.44	5.92	11.75	13.45
		Found. 55.32	5,41	11.02	12.99

Table (4)
FT-IR spectral data of compounds [1-8].

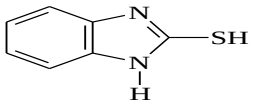
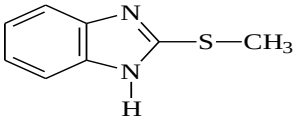
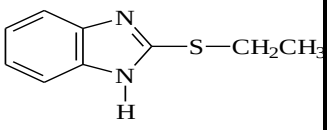
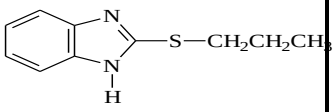
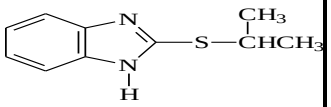
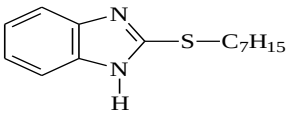
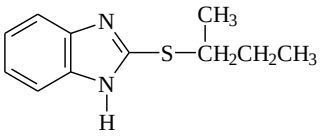
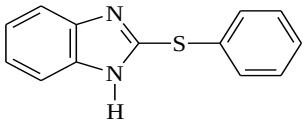
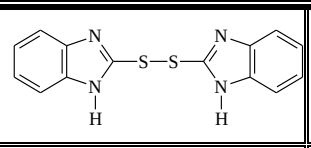
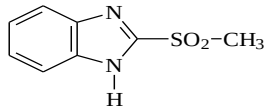
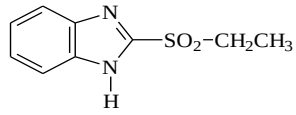
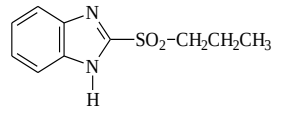
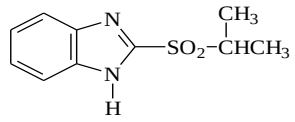
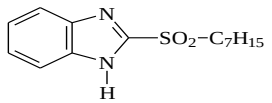
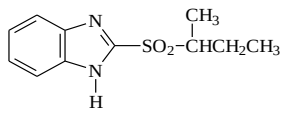
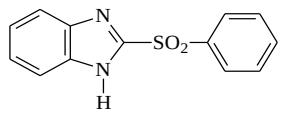
Comp. No.	*Structure*	*υ(C-H) cm^{-1} Aromatic*	*υ(C-H) cm^{-1} Aliphatic*	*υ(C=C) cm^{-1} Aromatic*	*υ(C=N) cm^{-1} Imidazole*	*υ(C-S) cm^{-1}*	*υ(N-H) cm^{-1}*	*Other Band cm^{-1}*
1		**3040**	**-**	**1512**	**1624**	**659**	**3159**	**υ(S-H) 2569**
2		**3044**	**2969**	**1585**	**1622**	**695**	**3420**	**υ(C-H) out of plane 745**
3		**3020**	**2970**	**1589**	**1616**	**659**	**3452**	**υ(C-H) out of plan 736**
4		**3055**	**2966**	**1512**	**1620**	**636**	**3394**	**-**
5		**3090**	**2952**	**1520**	**1626**	**640**	**3450**	**-**
6		**3047**	**2927**	**1585**	**1620**	**675**	**3425**	**-**
7		**3094**	**2966**	**1589**	**1616**	**601**	**3394**	**-**
8		**3059**	**2981**	**1512**	**1620**	**655**	**3398**	**-**

Table (5)
FT-IR spectral data of compounds [9-16].

Compd. No.	*Structure*	*υ(C-H) cm^{-1} Aromatic*	*υ(C-H) cm^{-1} Aliphatic*	*υ(C=C) cm^{-1} Aromatic*	*υ(C=N) cm^{-1} Imidazole*	*υ(C-S) cm^{-1}*	*υ(N-H) cm^{-1}*	*υ(C-So_2) cm^{-1}*		*Other Band*
9		3040	2954	1585	1620	617	3433	-	-	υ(S-S) 559
10		3051	2962	1585	1618	692	3432	1343	1325	-
11		3020	2966	1589	1616	659	3379	1357	1346	υ(C-H) out of plan 736
12		3051	2962	1585	1620	621	3454	1396	1342	-
13		3050	2961	1580	1622	618	3421	1342	1332	-
14		3043	2927	1585	1616	621	3414	1346	1292	-
15		3047	2966	1589	1620	664	3421	1396	1346	-
16		3042	2960	1582	1625	650	3382	1342	1330	-

References

[1] Bennamane, N.; Zaioua, K.; Akacem, Y., "Synthesis of Benzimidazole-2- thiones from Dimedone: An unexpected Cyclisation into a Five-Membered Ring"; *Org. Common*, 2:2, 49-59, 2009.

[2] Husain, A.; Varshney, M.; Rashid, M.; Akhter, A., "Benzimidazole: A valuable Insight into the Recent Advances and Biological Activities"; *J. Pharm. Rese.*, 4(2), 413-419, 2011.

[3] Korotkikh, N.; Aslanov, A.; Raenko, G., "Hetrocyclization of 2- Allylthio-benzimidazole Under the Action of Bromine"; *Russ. J. Chem*. 31, 721, 1995.

[4] Narkhede, H.; More, V; Dalal, D.; Mahulikar, P., "Solid Supported Synthesis of 2-Mercaptobenzthiazole Derivatives Using Microwaves"; *J. Scie. Indus. Rese.*, 97, 374-376, 2008.

[5] Fahmy, H.; Aboutabi, M.; Abdel Azzem, M., "On The Electrochemical Beha- viour of some 2, 3-Dihydrothiazolo [3,2-a] benzimidazol-3-one and 1-ethyl mercapto-3(4H)-Isoquinolones Derivatives"; *J. Chin., Chem., Soc.*, 33, 123-132, 1986.

[6] Hosseini, M.; Shahrabi,T.; Nichols, R., "Characterization of Mercapto benzthia-zole Adsorption on an Au(111)Electrode"; *Iran J. Sci. Tech*., 29(1), 49-63, 2005.

[7] Rangareddy, S.; Kalyani, P.; Rajes wara Roa, B.; Manikyamba,P., "Computa tion Studies and Reactivity of Nucleophiles in Benzylation Reactions"; *J. Ind. Chem.*, 47A, 236-239, 2008.

[8] Mauro,V.; Silvia, H.; Joao, V.; Marcus, V., "Synthesis of 2-Mercapto benzthiazole and 2-Mercaptobenzimidazole Derivatives Condensed with Carbohydrates as A potential Antimicrobial Agents*"; J. Sulfur, Chem*., 28, 17, 2007.

[9] Marco, M.; Claudia, B.; Rivara, S.; Valentina, Z.; Federica, V.; Uirko, R.; Elisabetta, B.; Simona, B., *Bioory, Med. Chem*., 12, 663(2004).

[10] Bakhareva, E.; Voronkov, M.; Sorokin, M.; Lopyrev, V.; Seredenin, S., *Pharm. Chem. J*., 30, 89, 1996.

[11] Anandarajagopal, K.; Timari, R.; Venkatesshan, N.; Vinothapooshan, G., "Synthesis and Characterization of 2-Mercaptobenzimidazole Derivatives as Potential Analgesic Agens"*; J. Chem. Pharm. Res*., 2(3), 230, 2010.

[12] Rebstock, T.; Ball, C.; Hamner , C.; Sell, H., "Inhibition of Plant Growth by 2-Mercaptobenzimidazole Analogs"; *J. Articale*, 1691, 382-384,1955.

[13] Makhhuf, M.; El-Shatory, S.; Said, A., *Mater. Chem. Phys*., 43(1), 76, 1996.

[14] Refaey, S.; Taha, F.; Abd El-Malak, A., "Corrosion and Inhibition of 316L StainlessSteel in Neutral Medium by 2-Mercaptobenzimidazole", *Int.J. Electrochem. Sci*., 1, 80-91, 2006.

[15] Wang, L., "Evaluation of 2-Mercaptobenzimidazole as Corrosion Inhibitor for Mild Steel in Phosphoric Acid"; *Corros. Sci*., 43, 2281,2001.

[16] Wang, L.; Pu, J.; Luo, H., "Corrosion Inhibition of Zing in Phosphoric Acid Solution by 2-Mercaptobenzimidazole"; *Corros. Sci.*, 45, 77, 2003.

[17] Norford, D.; Meaten, D.; Cullen, J.; Collins, J., "Pituitary and Thyroid Gland Lesions Induced by 2-Mercaptobenzimidazole Inhalation in Male Fischer-344 Rats"; *Soci, Toxical-Patho*., 21(5), 456, 1993.

[18] Salman, M.; Abu-Krisha, M.; El-Sheshtawy, H., "Charge Transfer Complexes of MBI with α-and Π-Electron Acceptor"; *Cand. J. Analy. Sci. Spect.*, 49(5), 282-289, 2004.

[19] Saxena, D.; Kajuria, R.; Suri, O., "Synthesis and Spectral Studies of 2-Mercaptobenzimidazole Derivatives"; *J. Hetro. Chem*., 19, 681, 1982.

[20] Berchmans, S.; Arivukkodi, S.; Yegnaraman, N., "Self Assembled Monolayer of 2-Mercaptobenzimidazole on Gold Stripping Volumetric Determination of Hg(II)"; *Electro. Commun*., 2, 226, 2000.

[21] Chalapathi, K.; Rameshbabu, L.; Madhu, P.; Maddaiah, G., "2-Mercapto benzimidazole Immobilized with Amberlite Xad-2 Using as Solid Phase Extractor for the Determination of Fe(II), Cu(II), & Cd(II*)"; Adv. Appl. Sci, Res*., 1(2), 27-35, 2010.

[22] Shoberl, A.; Waguer, A., In Houben wel, *V: IX*, P: 7-19, 97-113, 1955.

[23] Zen Al-Abideen, K.; M.Sc., Thesis University of Al-Nahrain, 2004.

[24] Karami, B.; Montazerzohori, M.; Habibi, M., "Urea- hydrogen peroxide (UHP) Oxidation of Thiols to The Corresponding Disulfides Promoted by Maleic anhydride as Mediator"; *Molecules*, 10, 1358-1363, 2005.

الخلاصة

يتضمن البحث ثلاث خطوات :

الخطوة الأولى تتضمن تحضير ٢-مركبتوبنزاميدازول من تفاعل أورثو- فنلين داي أمين مع ثنائي كبريتيد الكاربون، الخطوة الثانية يتم الكلة ٢- مركبتوبنزاميدازول مع هاليدات الكيل أو أريل لنحصل على مركبات الثايو إيثر، الخطوة الثالثة تضمنت أكسدة ٢- مركبتوبنزاميدازول إلى الداي سلفايد بينما أكسدة مركبات الثايوإيثر إلى السلفون تتم الأكسدة باستخدام بيروكسيد الهيدروجين كعامل مؤكسد لمدة (١-٢) ساعة مع التحريك بدرجة حرارة الغرفة. تم تحضير مركب ٢- مركبتوبنزاميدازول باستخدام جهاز (autoclave) . تم تشخيص المركبات المحضرة بمطياف الـFT-IR، والتحليل الدقيق لعناصر (C.H.N.S) بجانب قياس درجة الانصهار.