Noor Y. Jaber et al /J. Pharm. Sci. & Res. Vol. 10(12), 2018, 3189-3193

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Synthesis and Modification of New Derivatives from Thiophenol

Noor Y. Jaber[1,*], Mohammed R. Ahmed[1]
[1]*Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq.*

Abstract:
This work includes oxidation of thiophenol to their derivatives of disulfide and sulfone by using hydrogen peroxide as oxidation agent and tert-amine (tri-ehtylamine) as acatalyst. Also the reaction of thiophenol with alkyl and aryl halides to their thoiether derivatives and oxidize the products to sulfone. All synthetic compounds were definite by their melting point, FT-IR spectra and ^{1}H-NMR spectra for some of them.
Keywords: Thiophenol, disulfide, sulfone, thioether.

1. INTRODUCTION:

Thiols (R-SH) can be defined as a group of compounds rich in (–SH) moieties. This moiety is highly reactive and is often found conjugated to other both organic and inorganic molecules [1]. The total thiol status in the body, specially thiol (-SH) groups present in protein are considered as major plasma antioxidants in vivo and most of them are present over albumin and they are the major reducing groups present in our body fluids [2]. By determining the serum levels of thiols the calculation of thiol status in the body can be performed easily [3]. Also, the aromatic thiols (thiophenols) are much more toxic than aliphatic thiols for example, in fish; thiophenols have a median lethal concentration (LC_{50}) of 0.01–0.4 mm and a median lethal dose (LD_{50}) of (46.2) $mg.kg^{-1}$ in a mouse [4]. The oxidation of thiols to disulfides or sulphonic acid in the absence and presence of catalysts has been the subject of several recent investigations [5]. Disulfides are relatively more stable toward organic reactions, such as oxidation, alkylation, and acylation, compared to the corresponding free thiols; the thiol group can conveniently be protected as a disulfide. These compounds are useful reagents in organic synthesis and essential moieties of biologically active compounds for peptide and protein stabilization [6]. While molecules such as thioethers are commonly found in biochemical, organic synthesis and materials chemistry [7]. They are very efficient and valuable compounds in various areas such as medicine, pharmaceutical, agriculture, industry and heterocyclic chemistry [8]. Also, they serve as useful building blocks for various organosulfur compounds [9]. The S-alkylation reactions for the synthesis of these compounds are very important from an industry point of view, biology, notably in the amino acid methionine and the cofactor biotin [10]. They are valuable key intermediates in various organic syntheses, precursors for sulfoxides and sulfones. Chiral sulfoxides are useful auxiliaries in asymmetric syntheses [11]

Chemicals and Instruments:

Chemicals: All chemicals were purchased from Fluke and BDH.

Instruments:

1- Melting point were recorded using Gallenkamp capillary melting point apparatus.
2- FT-IR spectra were recorded using KBr disc on shimadzu FT-IR8400 Fourier Transform Infrared spectrophotometer.
3- Some of the prepared compounds were characterized by ^{1}H-NMR spectra that recorded on nuclear magnetic resonance in 400 MHz (Laboratory of Isfahan University) and ^{1}H-MNR at 300 MHz (University of Al-Albayt in Jordan) and DMSO as solvent.

2. EXPERIMENTAL

(2-1) oxidation of thiophenol to disulfide (a). [12]

(2 ml, 0.019 mol) of thiophenol was put in a round bottom flask, then added (4 ml) of (50%) hydrogen peroxide gradually with continuous shaking and (1-2) drops of tert-amine (tri-ethylamine).The mixture stirred for (3 hr) at room temperature. Then the precipitate was filtered and washed with distilled water.

(2-2) oxidation of disulfide to sulfone (b). [12]

(1.5 gm., 0.0068 mol) of disulfide dissolved by (6 ml) of absolute ethanol in around bottom flask, then added (4 ml) of (50%) hydrogen peroxide gradually with continuous shaking and (1-2) drops of tert-amine (tri-ethylamine). The mixture refluxed on water bath at (40-50)
C° for (3 hr). Then the precipitate was filtered and wished with distilled water.

(2-3) Synthesis of thioether derivatives (1-10). [13]

To (2 ml, 0.019 mole) of thiophenol, (2 ml) of (30%) sodium hydroxide was added with continuous shaking for (15 min), then (0.019 mol.) of alkyl or aryl halides dissolved by (10 ml) of ethanol added gradually to the stirred mixture, this mixture refluxed for (6 hr) at (70-80) C°. The hot reaction mixture filtered to get free of precipitated salts. Then, the product filtered after cooling if it was solid, and if it s liquid the organic layer separated by separating funnel. Physical properties of compounds (1-10) are listed in Table (3-1).

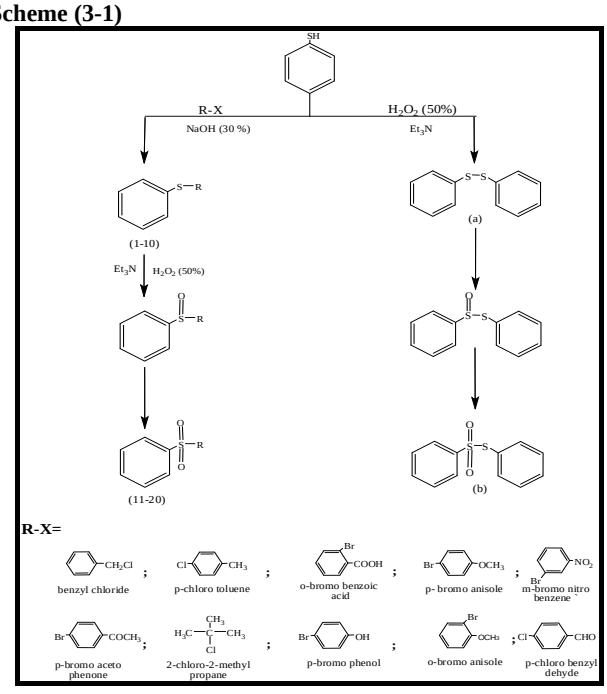
(2-4) oxidation of thioether derivatives to sulfone (11-20).

The same procedure for synthesis of compound (b) was flowed. Physical properties of compounds (11-20) are listed in Table (3-1).

3. RESULTS AND DISCUSSION

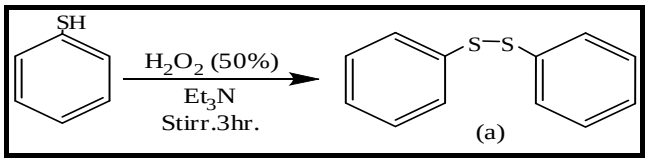
Present work includes reaction and synthesis new derivatives of aromatic thiols as show in scheme (3-1).

Scheme (3-1)



(3-1)- oxidation of thiophenol to disulfide (a).

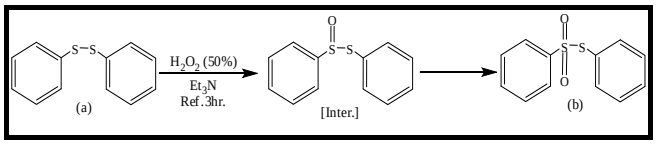
Aromatic thiophenol oxidizes by hydrogen peroxide (50%) and tri-ethylamine as catalyst to prepare compound (a) as shown in equation (3-1). Off white, M.P (50-51) C° yield (70%). FT-IR spectra data of compound (a) show the appearance of characteristic absorption band at (505) cm^{-1} belong to ν (S-S) and disappearance of the absorption band at (2567) cm^{-1} due to ν(S-H).



Equation (3-1)

(3-2)- oxidation of disulfide to sulfone (b).

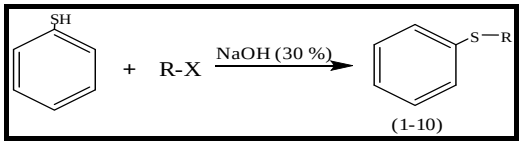
The oxidation reaction of compound (a) produced compound (b) by using the same oxidation reagent, and the same conditions that used to prepared compound (a) as shown in equation (3-2). White, M.P (58-60) C° yield (64%). FT-IR spectra data of compound (b) show the appearance of characteristic absorption bands at (1145) and (1326) cm^{-1} belong to symmetric and asymmetric ν (SO_2). ^{1}H-NMR Spectrum of compound (b) showed signals at (7.2-7.5) ppm belong to aromatic protons.



Equation (3-2)

(3-3)- Synthesis of thioether derivatives (1-10).

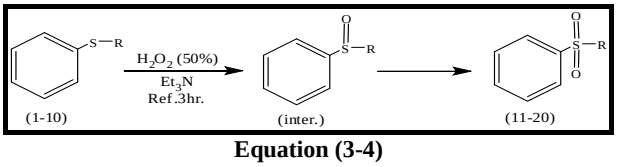
The prepared compounds produce when thiophenol react with alkyl halides in alkali medium as show in equation (3-3). Physical properties of these compounds are listed in Table (3-1). FT-IR spectrum data of compounds (1-10) show appearance of characteristic bands at (600-700) cm^{-1} belong to ν(C-S) and disappearance of the absorption band at (2567) cm^{-1} due to ν(S-H). All other details of FT-IR spectral data of compounds (1-10) are listed in Table (3-2).



Equation (3-3)

(3-4)- oxidation of thioether derivatives to sulfone (11-20).

The oxidation process to prepare compound (b), is the same for compounds (11-20) to synthesis sulfone derivatives as show in equation (3-4). Physical properties of these compounds are listed in Table (3-1). FT-IR spectrum data of compounds (11-20) show appearance of characteristic bands at (1150) and (1300) cm^{-1} belong to symmetric and asymmetric ν (SO_2). All other details of FT-IR spectral data of compounds (11-20) are listed in Table (3-2). ^{1}HNMR Spectrum of compound (11) showed signals at (4.23) ppm belongs to aliphatic protons and (7.03-7.69) ppm belongs to aromatic protons.



Equation (3-4)

CONCLUSION:

In this work we report the synthesis of new thiophenol derivatives. The FT-IR and ^{1}H-NMR data for some of them gave good evidence for the formation of the prepared derivatives.

Physical properties of thiophenol compound:

Formula	M.Wt gm/mol.	B.P C^0	Color
C_6H_5SH	110.18	169	colorless

FT-IR spectral data (cm^{-1}) of thiophenol compound:

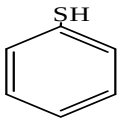
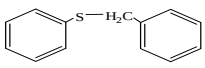
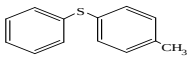
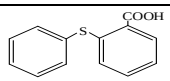
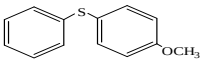
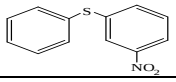
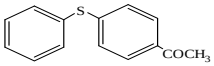
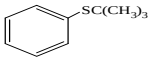
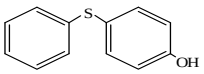
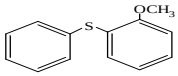
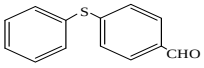
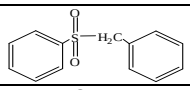
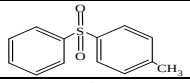
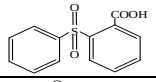
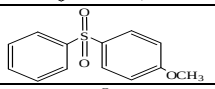
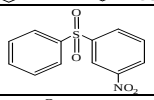
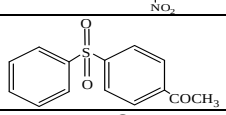
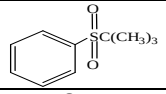
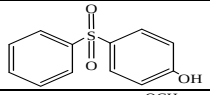
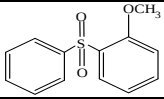
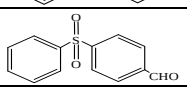
Compound structure	FT-IR spectral data, cm^{-1}
	ν (S-H)=2567, ν (C=C)= 1581, ν (C-H)= 3068

Table (3-1): physical properties of compounds [1-20]

NO.	Formula	M.Wt g/mol	M.P C^0	B.P C^0	Color	Yield (%)
1	$C_{13}H_{12}S$	200	44-46		white	90
2	$C_{13}H_{12}S$	200	40-42		white	60
3	$C_{13}H_{10}O_2S$	230	50-52		white	73
4	$C_{13}H_{12}OS$	216		214-216	Light yellow	62
5	$C_{12}H_9NO_2S$	231		88-90	Dark red	87
6	$C_{14}H_{12}OS$	228	Oily		Dark red	92
7	$C_{10}H_{14}S$	166	42-44		Off white	56
8	$C_{12}H_{10}OS$	202	50-52		white	56
9	$C_{13}H_{12}OS$	216		230-233	yellow	75
10	$C_{13}H_{10}OS$	214		90-92	yellow	95
11	$C_{13}H_{12}O_2S$	232	110-111		white	86
12	$C_{13}H_{12}O_2S$	232	46-48		white	86
13	$C_{13}H_{10}O_4S$	262	128-130		white	62
14	$C_{13}H_{12}O_3S$	248		226-227	yellow	75
15	$C_{12}H_9NO_4S$	263	oily		Brown	81
16	$C_{14}H_{12}O_3S$	260	42-44		yellow	62
17	$C_{10}H_{14}O_2S$	198	50-51		white	92
18	$C_{12}H_{10}O_3S$	234	41-43		white	82
19	$C_{13}H_{12}O_3S$	248		210-212	Light yellow	85
20	$C_{13}H_{10}O_3S$	246		228-230	yellow	71

Table (3-2): FT-IR spectral data (cm^{-1}) of compounds [1-20]

NO.	Compounds structure	FT-IR spectral data, cm^{-1}
1		ν (C-S)= 694, ν (C-H)= 2921
2		ν (C-S)= 688, ν (C-H)= 2918
3		ν(C-S)= 688, ν (C=O)= 1635, ν (O-H)= 3415
4		ν (C-S)= 688, ν (C-O)= 1245, ν (C-H)= 2935
5		ν (C-S)= 688, ν (NO_2)= asym.(1531) and sym.(1346)
6		ν (C-S)= 690, ν (C=O)= 1683, ν (C-H)= 2958
7		ν (C-S)= 686, ν (C-H)= (2930-2871)
8		ν (C-S)= 686, (O-H)= 3452
9		ν (C-S)= 659, (C-O)= 1249, ν (C-H)= 2937
10		ν (C-S)= 661, ν (C=O)= 1722, (C-H) ald.=2858
11		ν (C-S)= 692, ν (C-H)= 2962, ν (SO_2)= asym.(1307sd) and sym.(1149)
12		ν (C-S)= 686, ν (C-H)= 2925, ν (SO_2)= asym.(1367) and sym.(1153)
13		ν (C-S)= 686, ν (C=O)= 1689, ν (O-H)= 3413, ν (SO_2)= asym. (1311) and sym.(1149)
14		ν (C-S)= 688, ν (C-O)= 1245, ν (C-H)=2937, ν (SO_2)= asym. (1326) and sym.(1147)
15		ν (C-S)= 690, ν (NO_2)= asym.(1531) and sym.(1348), ν (SO_2)= asym.(1301) and sym.(1159)
16		(C-S)= 688, ν (C=O)= 1683, ν (C-H)= 2958, ν (SO_2)= asym.(1298) and sym.(1155)
17		ν(C-S)= 688, ν (C-H)=(2928-2873), ν (SO_2)= asym.(1328) and sym.(1149)
18		ν (C-S)= 686, ν (O-H)= 3406, ν (SO_2)= asym.(1296) and sym.(1149)
19		ν (C-S)= 659, ν (C-O)= 1249, ν (C-H)= 2962, ν (SO_2)= asym.(1296) and sym.(1124)
20		ν(C-S)= 663, ν (C=O)= 1722, ν (C-H) ald.= 2858 ν (SO_2)= asym.(1303) and sym.(1166)

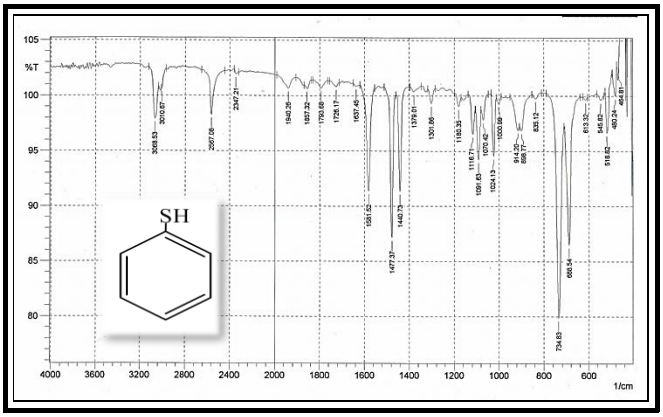


Figure 1: FT-IR spectral of thiophenol compound

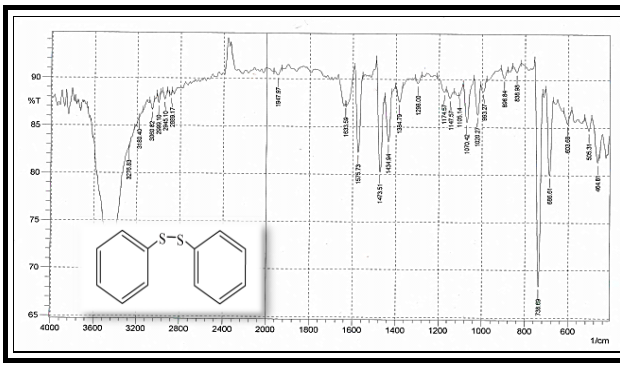


Figure 2: FT-IR spectrum of compound (a).

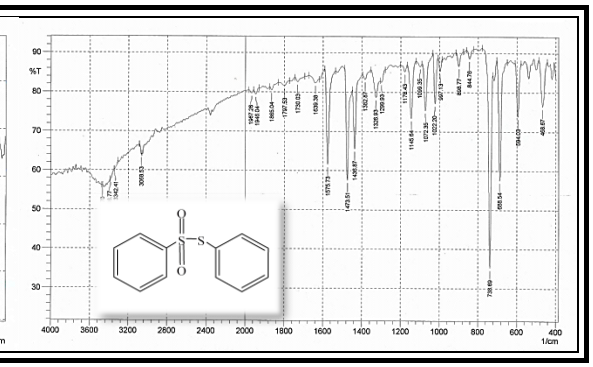


Figure 3: FT-IR spectrum of compound (b).

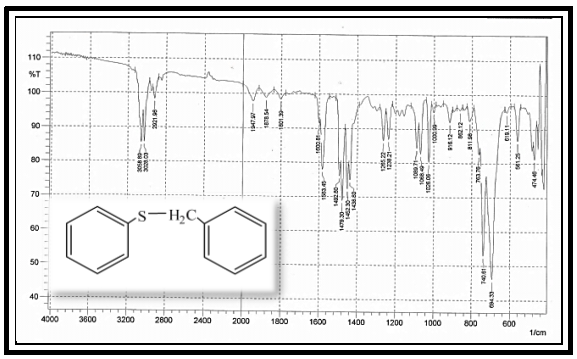


Figure 4: FT-IR spectrum of compound (1).

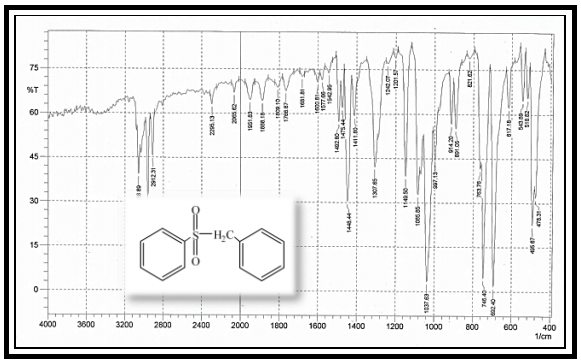


Figure 5: FT-IR spectrum of compound (11).

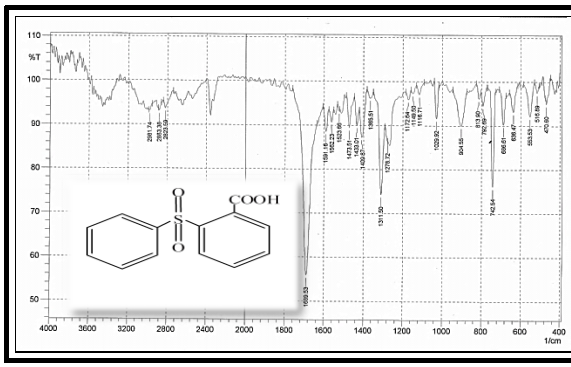


Figure 6: FT-IR spectrum of compound (13).

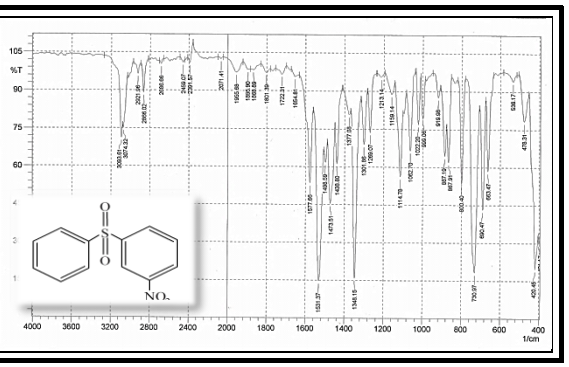


Figure 7: FT-IR spectrum of compound (15).

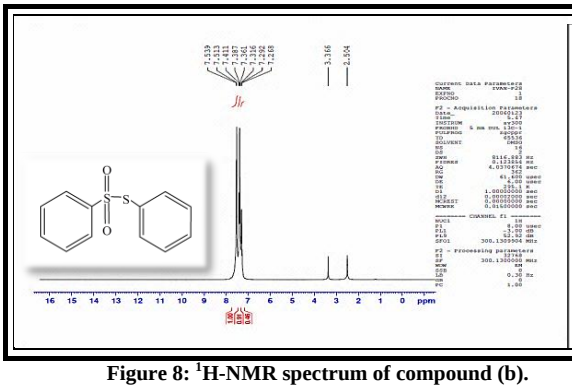


Figure 8: ^{1}H-NMR spectrum of compound (b).

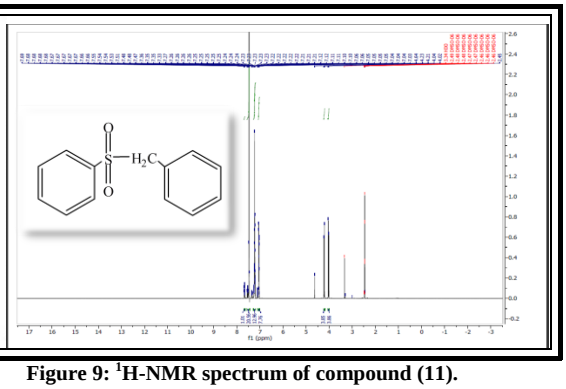


Figure 9: ^{1}H-NMR spectrum of compound (11).

REFERENCES

1. Beklova, M., Adam, V., Mares, P., Zeman, L., Dolezal, P., Pikula, J., Trnkova, L. & Kizek, R.(2008) Employing voltammetry for determination of low molecular mass thiols and metallothionein in blood of pig (Sus scrofa domestica). *Nat .Croat .* ;*17*:293-301.
2. Mungli Prakash, Jeevan K Shetty, Sambit Dash, Bijay K Barik, Abhirup Sarkar, Sharanabasappa M Awanti and Ravindra Prabhu.**(2008)** Urinary protein thiols in different grades of proteinuria. *Indian Journal of Clinical Biochemistry* ;*23*(4):404-406,.
3. Mungli Prakash, Mahesh S Shetty, Prasiddha Tilak and Naureen Anwar.**(2009)** Total thiols: biomedical importance and their alteration in various disorders. *Online journal of health and allied sciences* ;*8*(2):1-9.
4. Hyunsu Kim,K. M. K Swamy,Nahyun Kwon, Yonghee Kim, Sungsu Park, and Juyoung Yoon.(2017) Colorimetric Detection of Thiophenol Based on a Phenolphthalein Derivative and Its Application as a Molecular Logic Gate. *Chem .Phys .Chem .* ;*18*(13):1752-1754,.
5. Hosein Imanieh , Shahriar Ghamami and Mohammad kazem Mohammad.(2006) Oxidation coupling of organic thiols to disulphides with Tetramethylammonium Fluorochromate (VI)(TMAFC). In *Proceedings of ECSOC-10, International Electronic Conference on Synthetic Organic Chemistry ;10th*(p. a001).
6. Samuel Thurow, Vanda A. Pereira, Débora M. Martinez, Diego Alves, Gelson Perin, Raquel G. Jacob and Eder J. Lenardão.(2011) Base-free oxidation of thiols to disulfides using selenium ionic liquid. *Tetrahedron letters* ;*52*(5):640-643.
7. Chin-Fa Lee, Yi-Chen Liu, and Satpal Singh Badsara.(2014) Transition-Metal-Catalyzed C-S Bond Coupling Reaction. *Chemistry–An Asian Journal* ;*9*(3): 706-722.
8. Mosstafa Kazemi, Homa Kohzadi and Omran Abdi.(2015) Alkylation of thiols in green mediums. *J. Mater. Environ. Sci.* ;*6*:1451-1456.
9. Subhash Banerjee, Jayanta Das, Richard P. Alvarez and Swadeshmukul Santra. (2010)Silica nanoparticles as a reusable catalyst: a straightforward route for the synthesis of thioethers, thioesters, vinyl thioethers and thio-Michael adducts under neutral reaction conditions. *New Journal of Chemistry* ;*34*(2):302-306.
10. Krishnakant. T. Waghmode, Ganesh. S. Pathre and Nandini R. Pai. S- (2012)Alkylation of thiophenol under biphasic versus triphasic PTC condition using Tetrabutyl Ammonium Bromide as a Phase Transfer Catalyst. Journal of Chemical and Pharmaceutical Research ;4(3):1589-1591.
11. Deniz Gunes, Okan Sirkecioglu and Niyazi Bicak. Aliphatic thioethers by S-alkylation of thiols via trialkyl borates. *Phosphorus, Sulfur, and Silicon*2010*; 185*(8) 1685-1690,.
12. K. W. zen Al-Abideen , (2004)M. Sc., Thesis Universty of Al-Nahrain, .
13 Schobler A. and . Wagure A. , (1995)In Houben Wel ;V : IX , P: 7-19 ,97-113.