IOP Conf. Series: Materials Science and Engineering **454** (2018) 012096 doi:10.1088/1757-899X/454/1/012096

# Synthesis, characterization and study some of physical properties of novel 1,3,4-oxadiazole derivatives

**Nour Abd Alrazzak**

Department of Chemistry, College of Science for Women, University of Babylon, Hilla, Post Box 4, Iraq.
Email: nourchem1983@gmail.com

**Abstract :** In this paper the synthesis of novel 1, 3, 4-oxadiazole derivatives in a good yield (78-86)%, starting with 1-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)naphthalen-2-ol [N1] was achieved successfully. The synthesis procedure started by reacting hydrazide derivative and carbon disulfide. Alkylation of thiol group of 1,3,4-oxadiazole [N1] by sonication using different alkyl halide [methyl iodide, allyl bromide, proprgyl chloride and benzyl chloride] gave compounds [N2-N5]. Another compound [N6] 1,1'-(((5,5'-(ethane-1,2-diylbis(sulfanediyl)) bis (1,3,4-oxadiazole-5,2-diyl))bis (4,1-phenylene))bis(diazene-2,1-diyl)) bis (naphthalen-2-ol) was prepared by the alkylation of 1,3,4- oxadiazole derivative with dibromoethane. The UV-Vis spectra of the prepared compounds N1-N5 showed red shifted absorption bands due to the effect of conjugation by the double bond of allyl group. Triple bond of proprgyl group, the aromatic double bond of benzyl group and the alkyl groups in N2-N5 compounds play an important role in changing the fluorescence properties of [N1]. The physical and the chemical properties of the novel prepared compounds N1-N6 were studied and they were characterized by $^{1}H$,$^{13}C$ NMR, FT-IR and Fluorescence techniques.

**Keywords:** 1,3.4- Oxadiazole, heterocyclic compounds, alkylation, sonication, UV-Vis, Fluorescence

## 1. Introduction

1,3,4- Oxadiazole are five membered heterocyclic compounds with two nitrogen atoms and one oxygen atom having general formula $C_2H_2ON_2$. These oxadiazole are obtained from furan by substitution of two methylene groups (=CH) with two pyridine type nitrogen's (-N=) [1]. The replacement of two methine (-CH=) groups by two pyridine type of nitrogens (-N=) reduces aromaticity of the resulting oxadiazole ring to such an extent that the oxadiazole ring exhibits character of a conjugated diene [2]. Moreover 1,3,4-Oxadiazoles are an important class of heterocyclic compounds [3] where they have been reported to have antimicrobial [4-6], anticonvulsant [7,8], antitubercular [9,10], anticancer [11] and anti-inflammatory activities [12,13]. Alkylation of thiols is a common technique for the synthesis of thioethers and usually these thioethers are prepared by the treatment of thiols with alkyl halides [14-16]. Thioether is have wide attention in medicine, pharmaceutical, agriculture, industry, bio-chemistry, heterocyclic chemistry and biological processes [17-25].

Boulerba A, Othman and Taouti M have reported that butyric oxadiazole [a] could be synthesized from the reaction of butyric hydrazide with carbon disulfide in ethanolic solution of potassium hydroxide under refluxed for (14) hour [26]. While Kushwaha and co-worker [27] have obtained the compound 5-(3-methyl-6-hydrxy benzofuran-2-yl)-2-thiol -1,3,4 oxadiazole [b] by

refluxing hydrazide derivative with ethanolic solution of potassium hydroxide and carbon disulphide for (10) hours after cooling, the reaction mixture was acidified with hydrochloric acid.

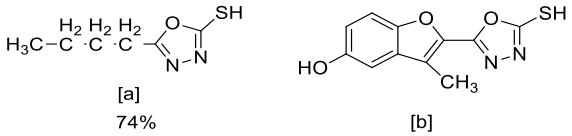



**Figure 1.** Shows 1,3,4-oxadiazole structures

Furthermore, Tien *et. al*., [28] used N-arylchloroacetamide, oxadiazole derivatives and anhydrous $K_2CO_3$ in acetone and the mixture was left to stir for (2) hours at room temperature. Then this mixture was refluxed for (3) hours to give N-Aryl-2-{5-[(2-methyl-benzimidazol-1-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanylacetamides [c 1,2].

In addition, Subimol and co-workers [29] have reported the reaction of 3-chloromethylcoumarin with 2-mercaptobenzimidazole in the presence of $Cs_2CO_3$ in DMF were this mixture was stirred for (5) hours at room temperature to give the final product [d].

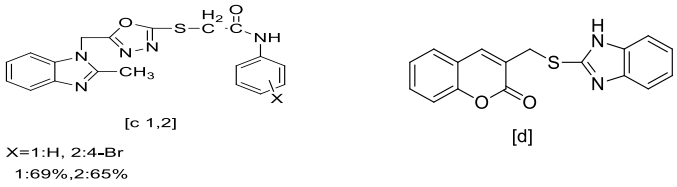



**Figure 2.** Shows alkylation 1, 3, 4-oxadiazole structures

In this paper I reported the synthesis and the characterization of novel1,3,4-oxadiazole derivatives and use of ultrasound to alkylation thiol group of 1,3,4-oxadiazole in good yield . These compounds showed red shifted emission and exhibited good fluorescence properties.

## 2. Experimental

All the starting materials that were used in this paper were purchased from Sigma Aldrich and EMD. While, the following instruments were used for the characterization of the prepared compounds: Melting points were determined on a Gallenkamp MFB-600-Melting point Stuart apparatus , FT-IR spectra were recorded on a Bruker spectrometer**.** $^{1}$H-NMR and $^{13}$C-NMR were recorded on a Bruker AC 400 NMR spectrometer, operating at 300 MHz for $^{1}$H-NMR and 75 MHz for $^{13}$C-NMR. All chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) as reference (δ=0.0 ppm). Elemental analyses were done on a C.H.N.S Elemental Analysis, Euro EA 1106. UV/VIS double beam Spectrophotometer PG CECIL- CE7200 Instruments. Spectrofluorophotometer RF-1501 (shimadzu), 220-900 nm.

*2.1 Preparation of 1-((4-(5-mercapto-1,3,4-oxadiazol-2-yl) phenyl)diazenyl) naphthalen-2- ol [N1][30]:*

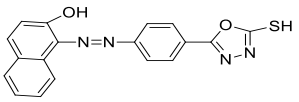
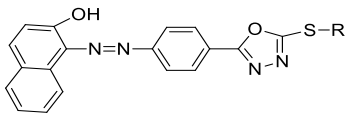


**Figure 3.** Shows structure of compound [N1]

(0.01 mole, 0.56g) Potassium hydroxide was added to (0.01 mole, 3.06g) hydrazide and excess of carbon disulfide in absolute ethanol was added. The mixture was refluxed for (14) hour and the solvent was evaporated, after that distill water was added and the residue was dissolve in with 30% HCl solution, until maintain on PH 5-6, the precipitate was filtered and washed with water four times.

Compound [N1]: molecular formula: $C_{18}H_{12}N_4O_2S$, colour: brown, yield: 86%, m.p.= 121-123 °C .IR (V=cm): 3311.30 (N-H), 3097.64(C-$H_{Ar.}$), 2990(C-$H_{alph.}$), 1637.88 (C=N.), 1637.88(C=$C_{Ar.}$), 1602.62(N=N), 937.12(C-O-C) (figure 6). $^1$H-NMR (δ, ppm): 1.274 (s,H, SH ), 4.256 (s,H, Ar-OH), 6.716-8.201 (m,10H, Ar-H) (figure 7). $^{13}$C-HNMR (δ, ppm): 110.362-146.630 (16C, Ar-C), 165.344(2C, CH) (figure 8).

*2.2 Preparation of 1-((4-(5-(methylthio)-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)naphthalen-2-ol [N2-N5] [31]:*




R= methyl iodide, allyl chloride
proprgyl chloride, benzyl chloride

**Figure 4.** Shows structure of compounds [N2-N5]

Compound [N1] (0.001 mole, 0.349g) was dissolved in a mixture of (3.5 mL) ethanol and 10% NaOH (3 ml). Alkyl halides (0.001 mole) [(0.06 mL) methyl iodide, (0.08 ml) allyl chloride, (0.07 ml) proprgyl chloride, (0.11 mL) benzyl chloride] was added and the solution was sonicated for (45) minute, then add (7mL) distill water and extracted by chloroform afforded the target compounds [N2-N5].

*2.2.1 Preparation of 1-((4-(5-(methylthio)-1,3,4-oxadiazol-2-yl)phenyl) diazenyl)naphthalen-2-ol [N2]:* molecular formula: $C_{19}H_{14}N_4O_2S$, colour: brown, yield: 84%, m.p. >280 °C . IR (V=cm): 3418.91 (O-H), 3066.62 (C-$H_{Ar..}$), 2982.85 (C-$H_{alph.}$), 1593.83 (C=N.), 1548.01 (C=$C_{Ar.}$), 1510 (N=N),(C-O-C) (figure 9).$^1$H-NMR (δ, ppm): 3.916 (s,3H, $CH_3$ ), 5.117 (s,H, Ar-OH), 6.488-8.814(m,10H, Ar-H) (figure 10).

*2.2.2Preparation of 1-((4-(5-(allylthio)-1,3,4-oxadiazol-2-yl)phenyl) diazenyl)naphthalen-2-ol [N3]:* molecular formula: $C_{21}H_{16}N_4O_2S$, color: dark brown, yield:78%, m.p. >98 °C . IR (V=cm): 3353.88 (O-H), 3080 (C-$H_{Ar..}$), 2090 (C-$H_{alph.}$), 1599.38 (C=N.), 1561.89 (C=$C_{Ar.}$), 1492.69 (N=N) (figure 11). $^1$H-NMR (δ, ppm): 2.2 (d,2H, $CH_2$ ), 2.5(p,H,CH), 4.5 (d,2H, $CH_2$), 6.611-9.090 (m,10H, Ar-OH) (figure 12).

*2.2.3 Preparation of 1-((4-(5-(prop-2-yn-1-ylthio)-1,3,4-oxadiazol-2-yl) phenyl) diazenyl) naphthalen-2-ol [N4]:* molecular formula: $C_{21}H_{14}N_4O_2S$, colour: dark brown yield: 80% , m.p. >223 °C . IR (V=cm): 3295.04 (N-H), 3059.90 (C-$H_{Ar..}$), 2916.31 (C-$H_{alph.}$), 2112.94 (—C≡C—), 1706.72 (C=N.), 1603.09 (C=$C_{Ar.}$), 1492.62 (N=N) (figure 13). $^1$H-NMR (δ, ppm): 1.615 (s,H, CH ), 3.3 (s,2H,$CH_2$), 6.7(s,H, OH), 7.317.98 (m,H, Ar-H) (figure 14). $^{13}$C-HNMR (δ, ppm): 24(C, $CH_2$), 60.663 (C, CH), 68.603(2C, —C≡C—), 109.631-127.333 (C, Ar-C) (figure 15).

*2.2.4 Preparation of 1-((4-(5-(benzylthio)-1,3,4-oxadiazol-2-yl)phenyl) diazenyl)naphthalen-2-ol [N5]:* molecular formula: $C_{25}H_{18}N_4O_2S$, colour: black, yield:79%, m.p. >275 °C. IR (V=cm): 3343.45 (O-H), 3185.06 (N-H), 3080 (C-$H_{Ar.}$), 2780 (C-$H_{alph.}$), 1644.90 (C=N.), 1594.36 (C=$C_{Ar.}$), 1550.49 (N=N),( C-O-C) (figure 16). $^1$H-NMR (δ, ppm): 4.562 (s,2H, $CH_2$), 4.835-7.989 (m,10H, Ar-H) (figure 17).

*2.3 Preparation of 1,1'-(((5,5'-(ethane-1,2-diylbis(sulfanediyl))bis (1,3,4-oxadiazole-5,2-diyl))bis(4,1-phenylene))bis(diazene-2,1-diyl))bis(naphthalen-2-ol) [N6] [32]:*

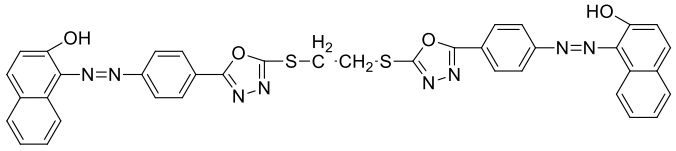
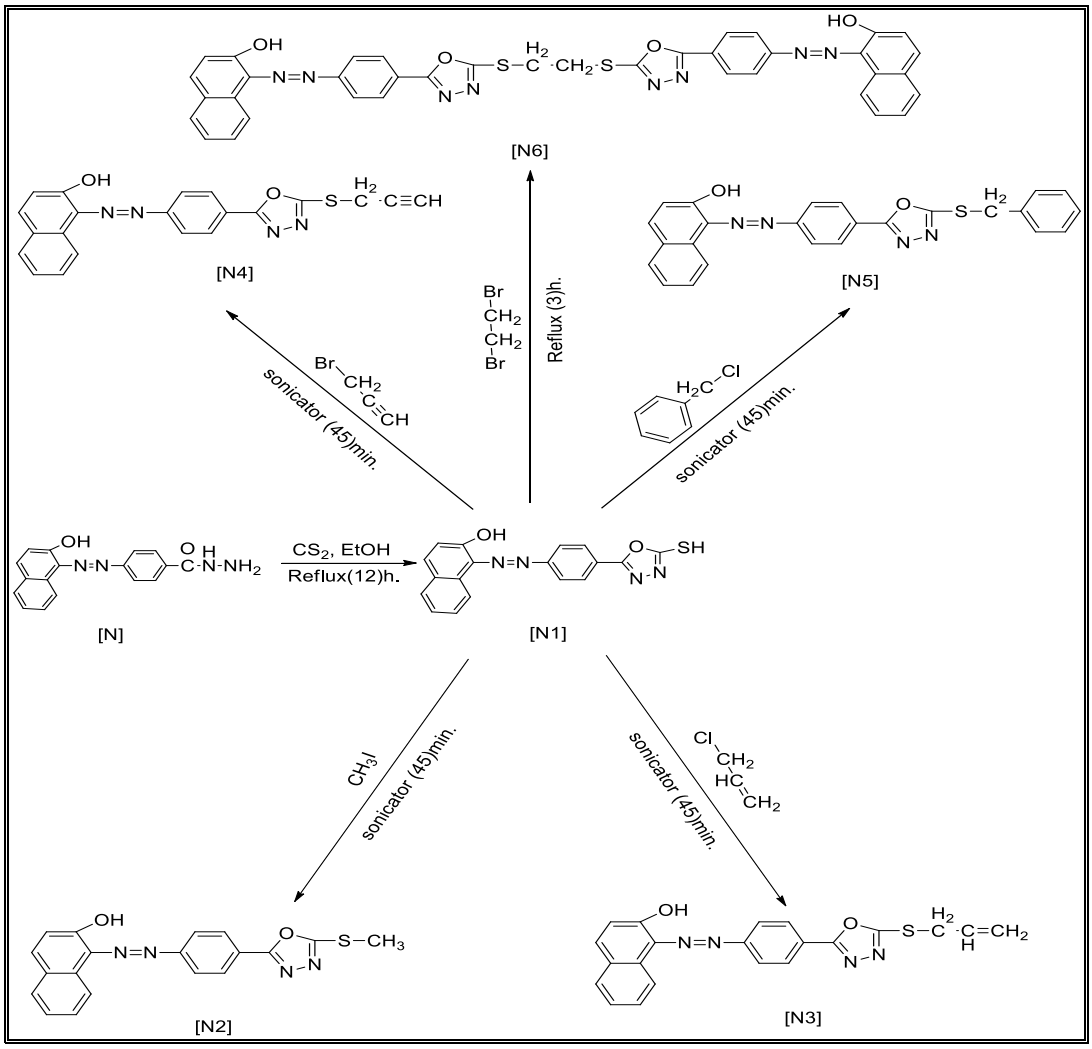


**Figure 5.** Shows structure of compound [N6]

Dissolve (0.001 mole,0.34g) of compound [N1] in (4mL) DMSO, (0.2)mL NaOH add as drops, after that (0.08 ml) dibromoethane was add, reflux for (3)hours at (50-60)C$^{o}$, then (4mL) $H_2O$ was add, extracted by ethyl acetate.

Compound [N6]: molecular formula: $C_{38}H_{26}N_8O_4S_2$, colour: black, yield:81%, m.p. >95 °C . IR (V=cm): 3293.37 (O-H), 3057.59 (C-$H_{Ar.}$), 2976.97- 2851.48 (C-$H_{alph.}$), 1767.37 (C=N.), 1596.35 (C=$C_{Ar.}$), 1492.42 (N=N),( C-O-C) (figure 18). $^{1}$H-NMR (δ, ppm): 4.5 (s,4H, 2$CH_2$), 5.7 (s,2H, 2OH), 7.080-8.283 (m,20H,Ar-H) (figure 19). $^{13}$C-HNMR (δ, ppm): 61.053 (2C, $CH_2$), 116.917-124.250 (2C, Ar-C), 152 (2C, $CH_2$), 158.622(2C, CH), 163.5(2C, CH) (figure 20).




**Scheme 1**. Synthesis rout of compounds [N1-N6]

## 3. Results and Discussion

Hydrazide was react with carbon disulfide and cyclization by potassium hydroxide, followed by acidification by hydrochloric acid to give 1,3,4-oxadiazole derivative [N1].

The I.R spectrum of compound [N1] exhibited absence absorption band of $NH_2$ at (3399.76, 3286.29) $cm^{-1}$ and absence of absorption band of N-H at (3221.10) $cm^{-1}$, and appearance absorption band for S-H at (2680.17, 2636.27) $cm^{-1}$ and absorption band at (1076.35) $cm^{-1}$ for C-O-C $_{heterocyclic}$ ; $^{1}$H-NMR (δ, ppm) spectrum exhibited disappearance single signal at 1.2 for (2H,$NH_2$), and at 5.964 for (H,NH) .and appearance single signal at 1.274 for (H, SH ); $^{13}$C-NMR (δ, ppm) spectrum showed disappearance signal at 165.828 for (C, C=O). and appearance signal at 165.344 for (C, C=S).

Alkylation of thiols occur by using different alkyl halides and ethanolic basic solution, where the reaction mixture was sonicated for (45) min. in the absence of the solvent to give the desired compounds.

Methylation of compound [N1] to give compound [N2] where its IR spectra showed disappearance peak of stretch S-H at (2680.17, 2636.27) $cm^{-1}$ and appearance C-$H_{aliphatic}$ at (2982.85) $cm^{-1}$. $^{1}$H-NMR (δ, ppm) spectrum exhibited disappearance single signal at 1.274 for (H, SH ), and appearance single signal at 3.916 for (3H, $CH_3$ ).

The IR spectra of alkylation of oxadiazole by allyl chloride exhibit a new absorption band at (2923.86) $cm^{-1}$ for C-$H_{aliph.}$ and absorption band at (1651.10) $cm^{-1}$ for C=C $_{aliph.}$ and disappearances thiol group at (2680.17, 2636.27) $cm^{-1}$; $^{1}$H-NMR (δ, ppm) spectrum exhibit disappearance single signal at 1.274 for (H, SH ), and appearance signals at 2.2 for (d,2H, $CH_2$ ), at 2.5 for (d,2H, $CH_2$) and at 4.5 for (p,H,CH),.

1,3,4-oxadiazole-3-thiol upon alkylation with proprgyl chloride gave compound [N4] which showed the appearance absorption band for alkyne group at (3295.04) $cm^{-1}$ and the absence of thiol group absorption band of at (2680.17, 2636.27) $cm^{-1}$. $^{1}$H-NMR (δ, ppm) spectrum exhibited disappearance single peak at 1.274 for (H, SH ), and appearance new single signal at 1.190 for (H, CH ), and appearance a new single signal at 3.713 for (2H,$CH_2$); $^{13}$C-NMR (δ, ppm) spectrum showed appearance new signal for (2C, $CH_2$) at 25, and the presence new signal at 61.146 for (C, CH), and at 62.526 for —C≡C—.

The IR spectra for Compound [N5] show appear new peak at for C-$H_{aliphatic}$ at (2928.61) $cm^{-1}$ and disappearance peak for stretch S-H of compound [N1] at (2680.17, 2636.27) $cm^{-1}$. $^{1}$H-NMR (δ, ppm) spectrum exhibited disappearance single signal at 1.274 for (H, SH ), and appearance new signal at 4.562 for (H, $CH_2$).

The I.R spectrum of compound [N6] exhibited absorption band for C-H $_{aliphatic}$ at (2976.97, 2922.03) $cm^{-1}$ and disappearance the absorption band for thiol at (2678.97)$cm^{-1}$.$^{1}$H-NMR (δ, ppm) spectrum exhibited disappearance single signal at 1.274 for (H, SH ), and appearance single signal at 4.5 for (4H, 2$CH_2$ ).$^{13}$C-NMR (δ, ppm) spectrum showed appearance new signal at 61.053 for (2C, 2$CH_2$).

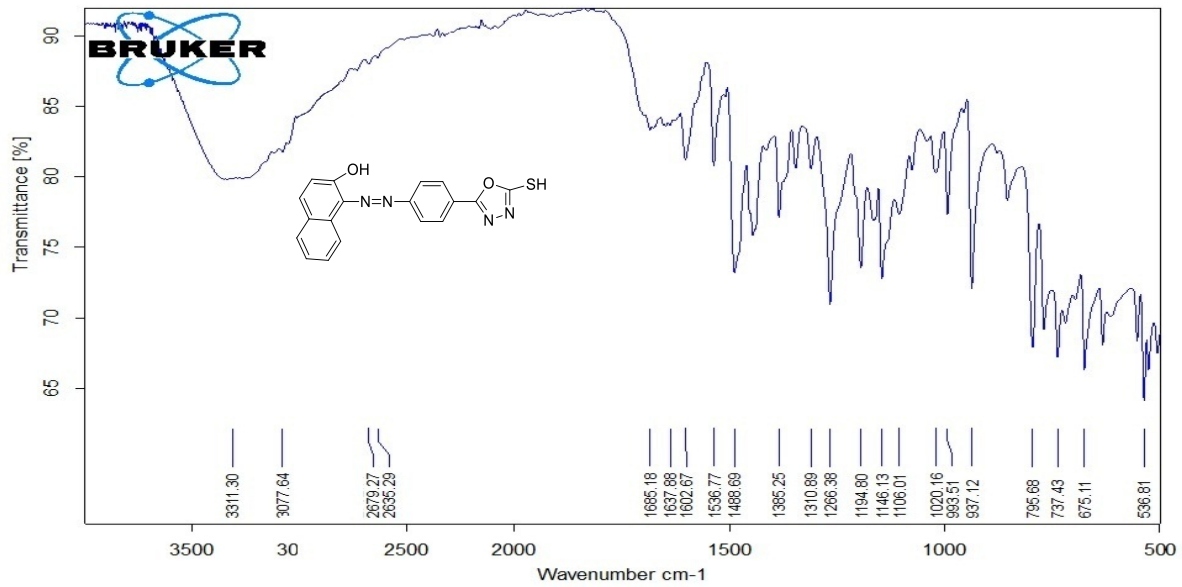



**Figure 6.** F.T-IR spectrum of compound [N1]

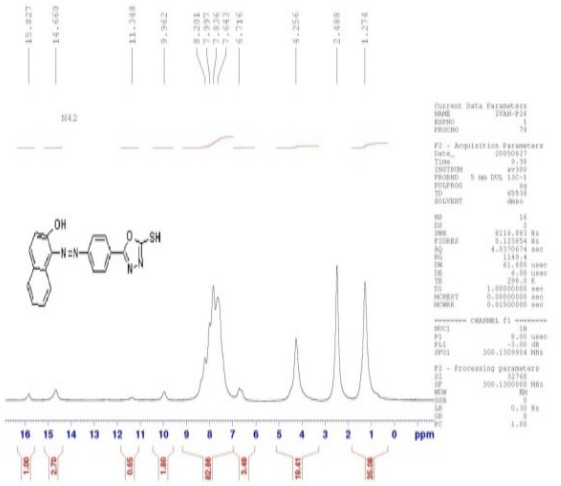



**Figure 7.** [1]HNMR spectrum of compound [N1]

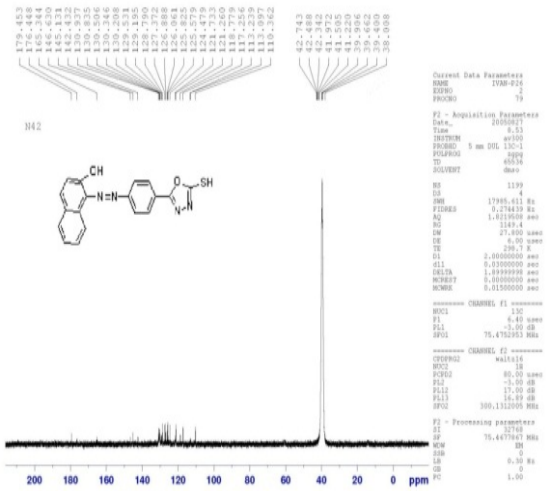



**Figure 8.** [13]CNMR spectrum of compound [N1]

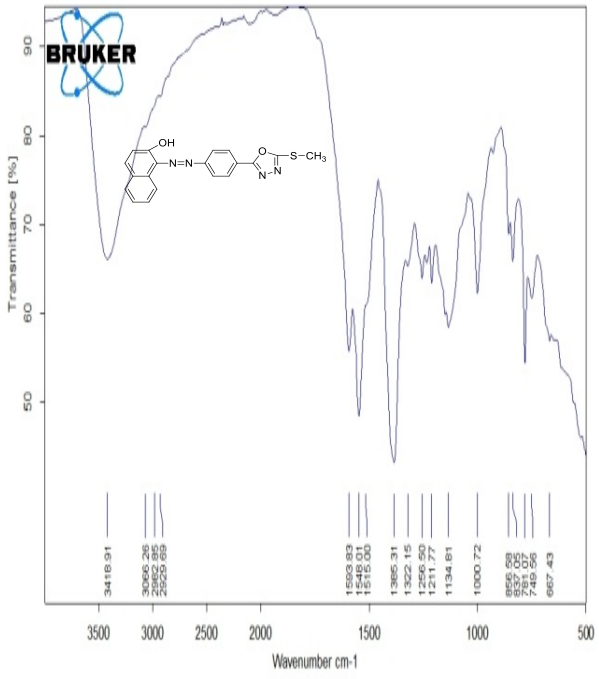



**Figure 9.** F.T-IR spectrum of compound [N2]

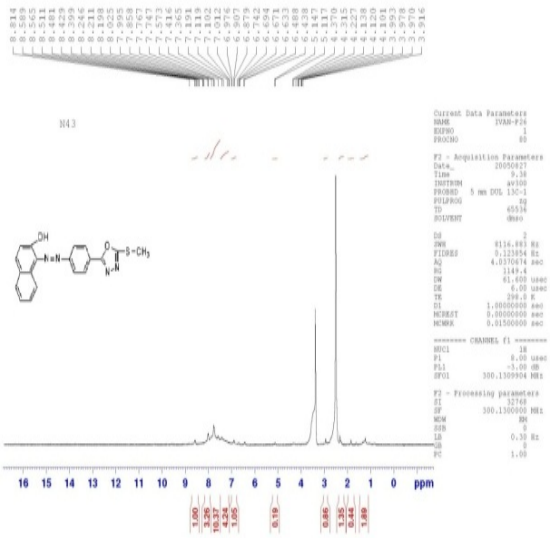



**Figure 10.** $^{1}$HNMR spectrum of compound [N2]

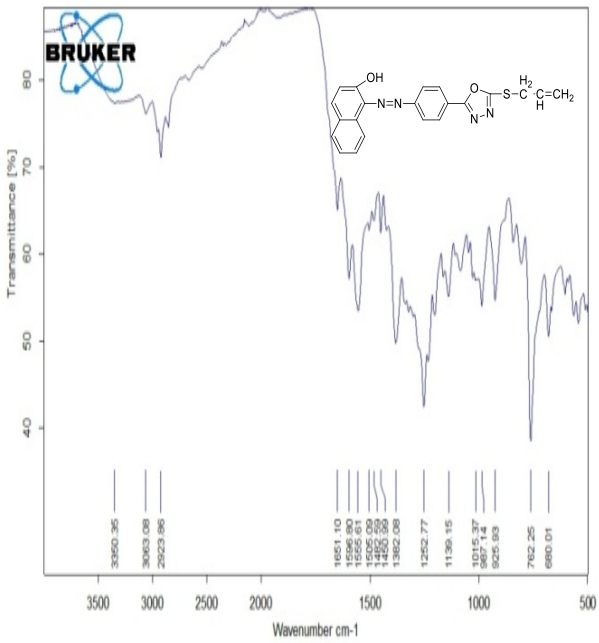



**Figure 11.** F.T-IR spectrum of compound [N3]

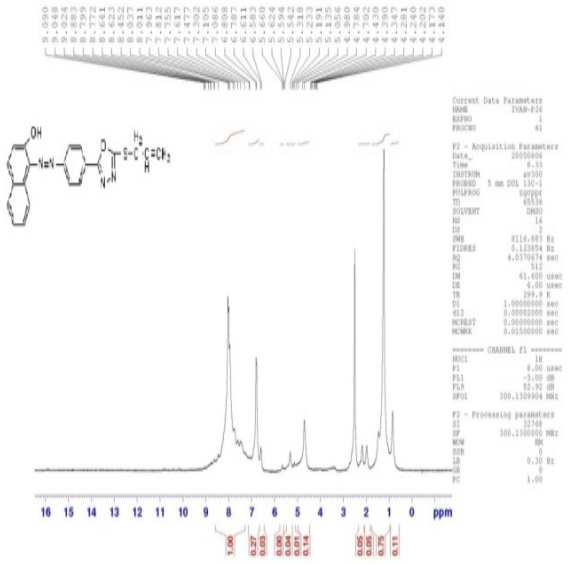



**Figure 12.** $^{1}$HNMR spectrum of compound [N3]

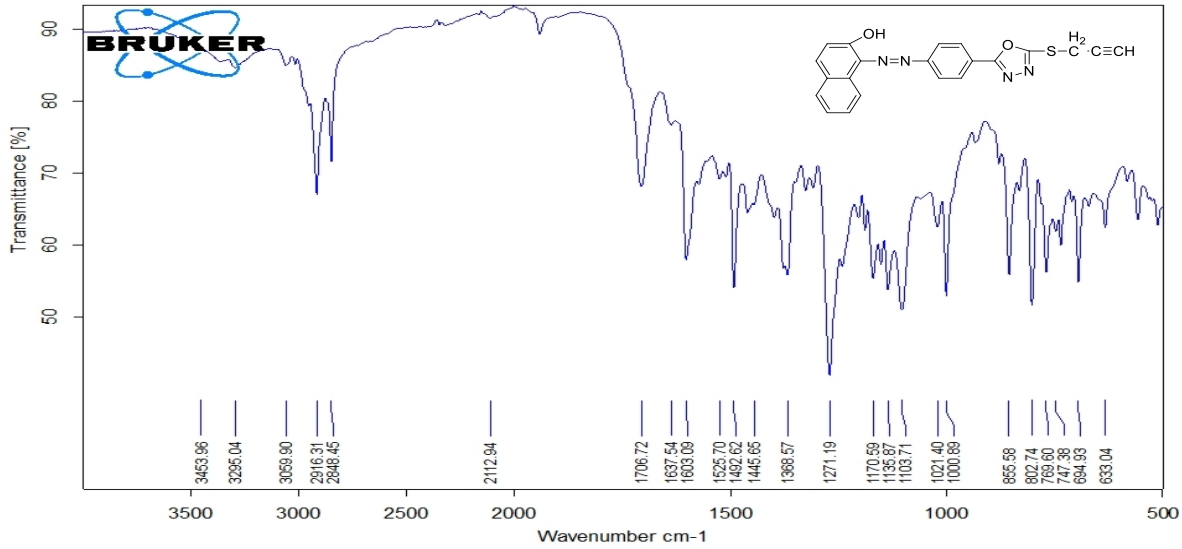



**Figure 13.** F.T-IR spectrum of compound [N4]

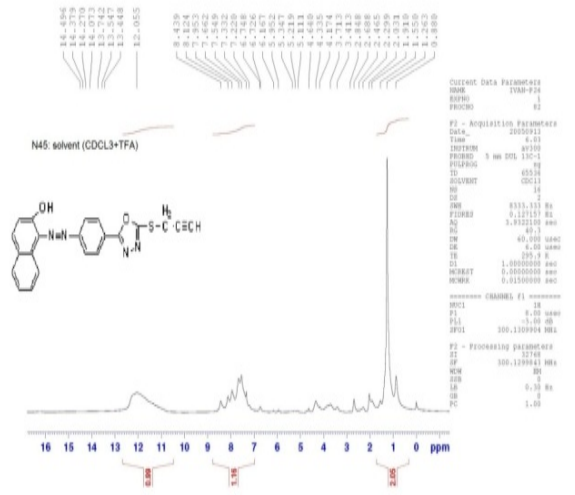



**Figure 14.** [1]HNMR spectrum of compound [N4]

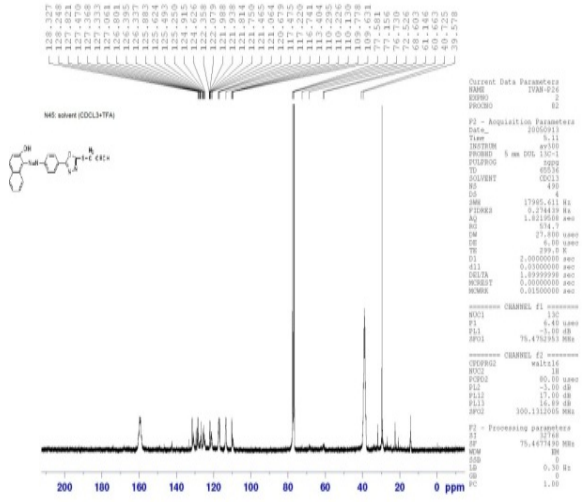



**Figure 15.** [13]CNMR spectrum of compound [N4]

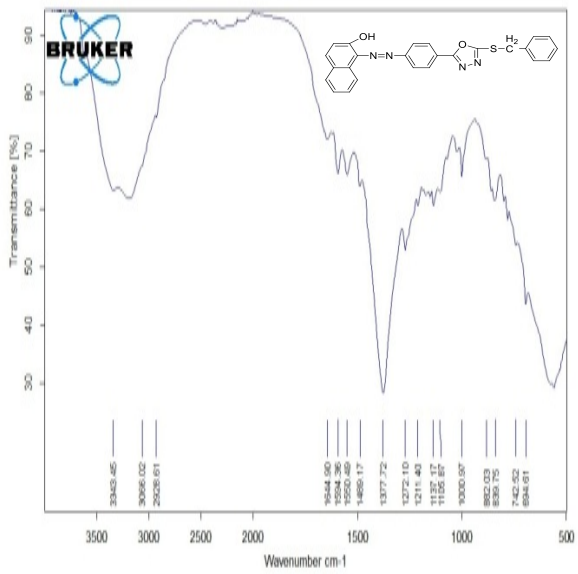



**Figure 16.** F.T-IR spectrum of compound [N5]

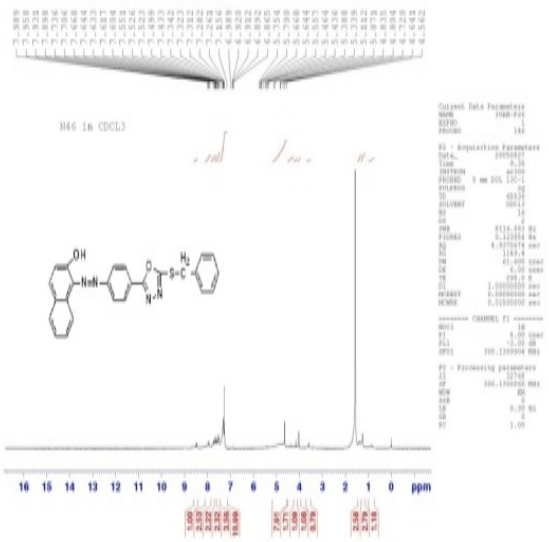



**Figure 17.** $^{1}$HNMR spectrum of compound [N5]

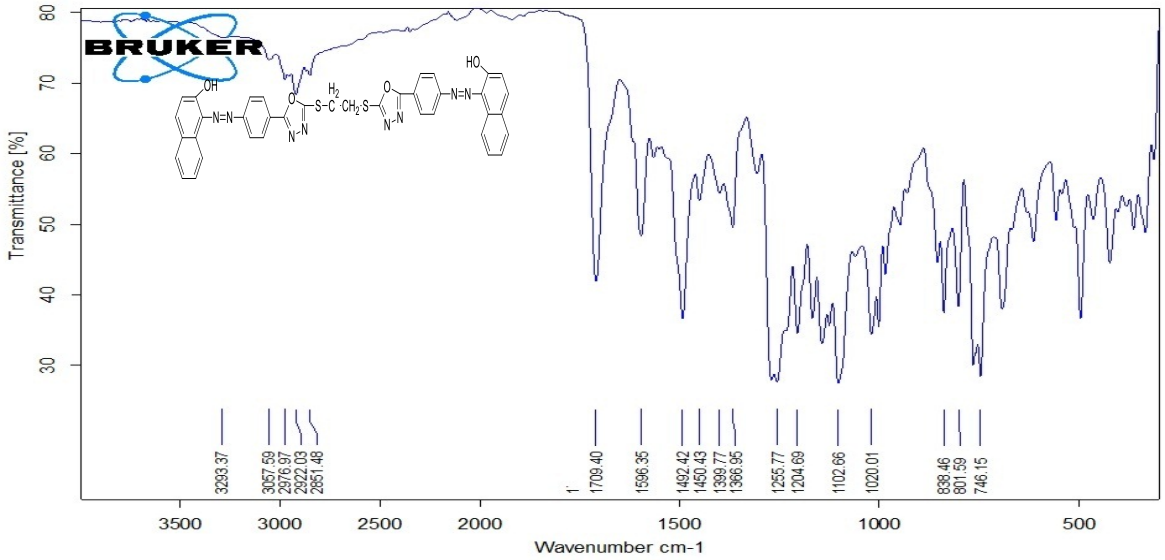



**Figure 18.** F.T-IR spectrum of compound [N6]

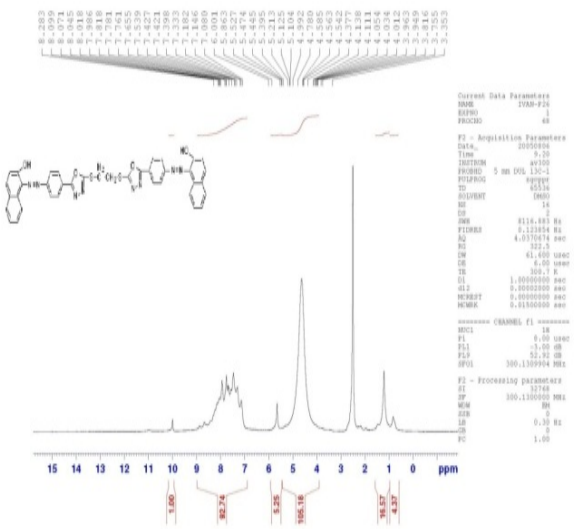


**Figure 19.** [1]HNMR spectrum of compound [N6]

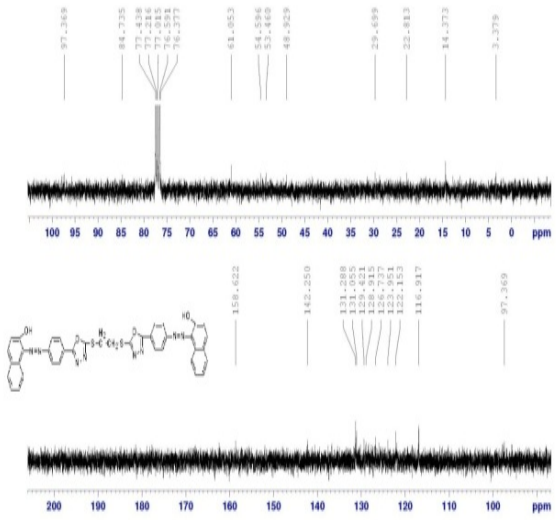


**Figure 20.** [13]C-NMR spectrum of compound [N6]

The UV-Vis spectra of compounds N2-N5 were recorded in (DMSO) and they displayed broad charge-transfer bands with end absorptions reaching closely into the near infrared in comparison with compound [N1] reflecting the effective of conjugation. Red shift (12-34 nm) absorption spectra occurred in DMSO, as shown in figure 21. While in the fluorescence spectra, it could be seen that alkyl group in compounds N2-N5 plays an important role in modulating the fluorescence properties of compound [N1] as shown in figure 22:

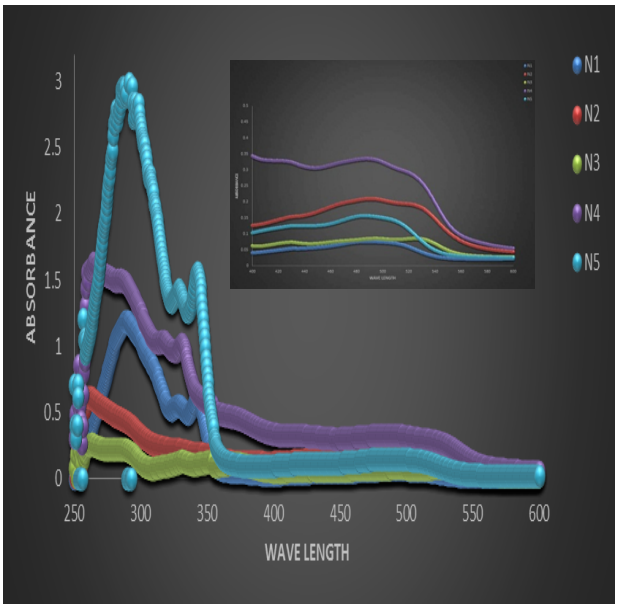



**Figure 21.** UV-Vis of compounds N1-N5 recorded in DMSO (1x10$^{-4}$M)

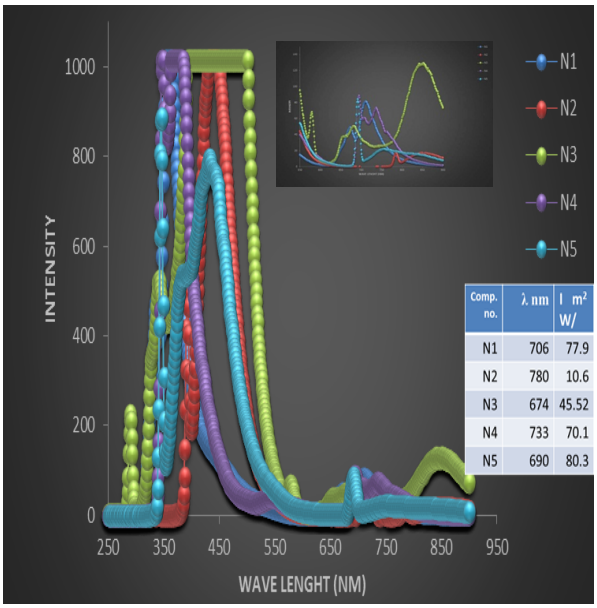



**Figure 22.** Fluorescence spectra for compounds N1-N5 recorded in DMSO (1x10$^{-4}$M)

**Table 1.** Physical properties of compounds [N1-N6]:

| Comp. NO. | Melting Point | Yield | Colour | MWt | M.F | TLC | |
|---|---|---|---|---|---|---|---|
| | | | | | | Solvent | $R_f$ |
| N1 | 121-123 | 86 | Brown | 340 | $C_{18}H_{12}N_4O_2S$ | Petrolum ether:DCM 4:2 | 0.65 |
| N2 | >280 | 84 | brown | 362 | $C_{19}H_{14}N_4O_2S$ | Hexane:ethylacetate 3:3 | 0.71 |
| N3 | >89 | 78 | Dark brown | 388 | $C_{21}H_{16}N_4O_2S$ | Hexane:ethylacetate 3:2 | 0.61 |
| N4 | >223 | 80 | Dark brown | 386 | $C_{21}H_{14}N_4O_2S$ | Hexane:chloroform 3:3 | 0.44 |
| N5 | >275 | 79 | black | 438 | $C_{25}H_{18}N_4O_2S$ | Petrolum ether:ethylacetate 3:3 | 0.57 |
| N6 | >95 | 81 | Black | 722 | $C_{38}H_{26}N_8O_4S_2$ | Petrolum ether:$CHCl_3$ 3:3 | 0.77 |

## 4. References

[1] Revarthy S, Amruyha U, Sneha J, Shalumol A and Leena K; 2017 *Research Journal of Pharmaceutical, Biological and Chemical Sciences*; **8** 2 468.
[2] Rama D, Rao P, Ashok D, Raju Bm , Satla Shobha R, Vasudha B and Swathia G 2017 *Int. J. of Pharmacy and Analytical Research*, **6** 2 396.
[3] Partha P, Shalini B, Tapan M and Jagadish S 2017 *Indian Journal of pharmaceutical Education and Research*, **51** 2.
[4] Naveena C, Boja P and Kumari N 2010 *Eur. J. med Chem.*, **45** 4708.
[5] Ramaparasad G, Kalluraya B and Kumar B 2010 *Eur. J. med Chem*, **45** 4587.
[6] Kumar G, Rajendraprasad Y and Mallikarjuna B 2010; *Eur. J. med Chem*, **45** 2063.
[7] Almasird A, Tabatabai S and Faizi M 2004 *Bioorg Med Chem Lett*;, **14** 6057.
[8] Rajak H, Deshmikh R and Veerasamy R 2010 *Bioorg Med Chem Lett*;, **20** 4168.
[9] Mamolo M and Zampieri D 2005 *Bioorg Med Chem Lett*;**13** 3797.
[10] Shashikant P, Rabara P and Jayashir P 2009 *Ind. J. Chem.* , **48** 1453.
[11] Sundaree K and Johnson E 2009 *Bioorg Med Chem Lett*; **19** 4492-94.
[12] Jayashnkar B, Rai M and. Baskaran N 2009 *Eur. J. Med, Chem.*, **44** 3898-3902.
[13] Singh A. parthsarthy M 2013 *Iran J. pharm Res.*, **12** 319-23.
[14] Kabalka W, Reddy G and Yao M 2009 *Tetrahedron let.*, **50** 7340.
[15] Drabowicz J, lewkowski J and Kudelska W 2008 *T. Girek; Synth.*, **39** 154.
[16] Drabowicz J, lewkowski J and Kudelska W 2008 *T. Girek; Synth.*, **39** 173.
[17] Giri S and Pandey B 2013 *Industry Bioresource Technol*., **142** 420.
[18] Yi Z Wang X and Sheng G 2008 Agri. *Ecosyst. Environ*, , **123** 116.
[19] Shaabani A and Rezayan A 2007 *Catal Commun*;, **8** 1112.
[20] B. Huang, W. B. Yi, C. Cai 2011 *J. Fluorine Chem*; **132** 554.
[21] Bahrami Y, Khodaei M and Soheilizad M 2010 *Tetrahydron let.*, **51** 4843.
[22] Hejaz S Iqbal B AlSalmani N Al-Ghafri N and Rahhman S 2013 *Pharm. Analy*;, **3** 248.
[23] Malmstrom J Gupta V and Engman L 1998*J. Org. Chem.*;, **63** 3318.
[24] Blanchard P Jousselme B. Frere P and. Roncali J 2002 *J, Org, Chem*, **67** 3961.
[25] Yang W and Drueckhammer D 2001 *J. Am. Chem. Soc.*, **123** 1004.
[26] Boulerba A, Othman and Taouti M 2017 *Chemical Science International Journal*,**18** 4, 1.

[27] Kushwaha D, Mishra K and chaturvedi A 2017*Oriental Journal of Physical Sciences*; **2** 1, 63.
[28] Tien C, Cam D, Buimanh H and Dangs D 2016 *Journal of Chemistry*, **6**.
[29] Subimol K, Antony S, Jegatheesan K and Kumars K 2016 *Journal of Advanced Chemical Sciences*; **2** 2 251-254.
[30] Ghoneim A and Mohamed S 2013 *Oriental Journal of chemistry*; **29** 2.
[31] Foks H, Ksepko D, Janoweic M, Zwolska Z and Kopec E 2004 *Acta polonia pharmacetiueal- drug research*; **61**, 6.
[32] Nazarbahjat N, Abdullah Z, Abdullah M and Arrifin A 2014 *Asian Journal of Chemistry*; **26** 24.