International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.2, pp 742-748, 2017

New Imidazolidine-dione Derivatives: Synthesis, Characterization and Spectroscopic study

Mohammed Ridha Al-Haideri* and Shireen Ridha Rasool

Department of Chemistry, College of Science, University of Babylon, IRAQ

Abstract : Different N-heterocyclic substituted derivatives of 5,5-dimethylhydantoin have been synthesized. The two nitrogen atoms have been alkylated to form N-carboxymethyl derivatives followed by cyclization reaction to form heterocyclic/substituted aryl group (oxazole, pyrazole and oxadiazole derivatives) and Prepared New Schiff base compounds. Prepared compounds have been identified by using FT-IR and ^{1}HNMR.$\lambda_{exc.}$, $\lambda_{em.}$ and the compounds absorption at $\lambda_{exc.}$ have been found. The fluorescence quantum yields of these compounds are calculated.

Keywords: 5,5-substituted imidazolidine-Dione, Hydantoin derivatives, 1,3-Oxazole, pyrazole, Oxadiazole, Schiff baseand Fluorescencec ompounds.

Introduction:

Imidazolidine-Dione (hydantoin) derivatives are reported to show the wide range of biological activitiesanticonvulsant[1], antimalarial agents[2], anticancer[3] and antiarrhythmic[4,5]. Oxazole derivatives have activities such as antibacterial[6], antifungal[7],anti-tuberculosis[8],anti-inflammatory[9] and antitumor[10]. Imidazole is the main structure of some well-known components of human organisms such as amino acid histidine, histamine, purines, biotin, Vit-B12[11] and used Antiprotozoal,antibacterial[12].1,3,4-Oxadiazole derivatives are reported to show the wide range of biological activities, which include anti- antibacterial[13], antifungal[14,15], anti-oxidant activity[16], antitumor agent[17] and haemolytic activity[18].Fluoresces compounds have many applications such as Biochemistry and medicine[19],spectroscopy[20],Microscope [21]and Forensics[22].The ratio of the number of fluorescence photons emitted to the number of photons absorbed called the quantum yield of fluorescence Φf [23].

Materials and Methods

All the chemical were purchased from Sigma Aldrich, BDH, CDH and Merck. Melting point determinations were performed by the open capillary method using a SMP30 melting point apparatus and are reported uncorrected. The F T - IR spectra (KBr-discs) were recorded with a IRAFFINITY-1CE Shimadzu spectrometer.^{1}HNMR spectra were recorded on a Jeol 400-Hz NMR spectrophotometer operating at 400 MHz for ^{1}H measurements. UV-6100 PC Double beam Spectrophotometer, EMCLAB, Germany. Spectrofluorophotometer RF-1501 (Shimadzu).Thin layer chromatography was performed on pre-coated sheets with a 0.25 mm layer of Silica Gel GF254 of the Merck company.

Synthesis of diethyl2,2'-(4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene)bis(4-argio-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carboxylate) (M3-M4):

(0.01 mole) of Compound (M1 and M2)[23]respectively dissolved in solution of ((0.04 mole) of Sodium hydroxide dissolved in ethanol (50mL)).Then(0.02mole,2.6g)athyl aceto acetate have been added, The mixture was refluxed for(6hrs).This reaction was monitored by TLC. Then, the mixture was cooled to room temperature, The cooled Water (400 mL) added wit stirring, the product was collected and recrystallized from absolute ethanol.

Synthesis of 1,3-bis((4-argio-3-oxo-3,3a,4,8-tetrahydro-2H-oxazolo[4,5-f]indazol-6-yl)methyl)-5,5-dimethylimidazolidine-2,4-dione. (M5-M6):

Compounds (M3-M4)(0.01 mole)respectively dissolved in solution of absolute ethanol (60 mL) and hydrazine hydrate (80%) (0.02 mol,0.64g).The mixture was refluxed for(10hrs).This reaction was monitored by TLC. Then, the mixture was cooled to room temperature, the product was collected and recrystallized from absolute ethanol.

Synthesis of 2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-argio-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide). (M7-M8):

Compounds(M3-M4)(0.01 mole)respectively dissolved in solution of absolute ethanol (60 mL) and hydrazine hydrate (80%) (0.02 mol,0.64g), The mixture was refluxed for(5hrs).This reaction was monitored by TLC. Then, the mixture was cooled to room temperature, the product was collected and recrystallized from absolute ethanol.

Synthesis of 2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-argio-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide). (Schiff base) (M9-M10):

Compounds(M7-M8)(0.01 mole) respectively mixed with(p-bromobenzaldehyde and p-N, N-dimethyl amino benzaldehyde) (0.02mole)respectively dissolved in absolute ethanol (40 mL), The mixture was refluxed for(3 hrs).This reaction was monitored by TLC. Then, the mixture was cooled to room temperature, the product was collected and recrystallized from absolute ethanol.

Synthesis of (N'Z,N'''Z)-2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-argio-N'-(argiomethylene)-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide). (M11-M12):

Compound (M9-M10)(0.01 mole) respectively dissolved in acetic anhydride (40 mL), The mixture was refluxed for(20 hrs).This reaction was monitored by TLC. Then, the mixture was cooled to room temperature, the product was collected and recrystallized from acetone.

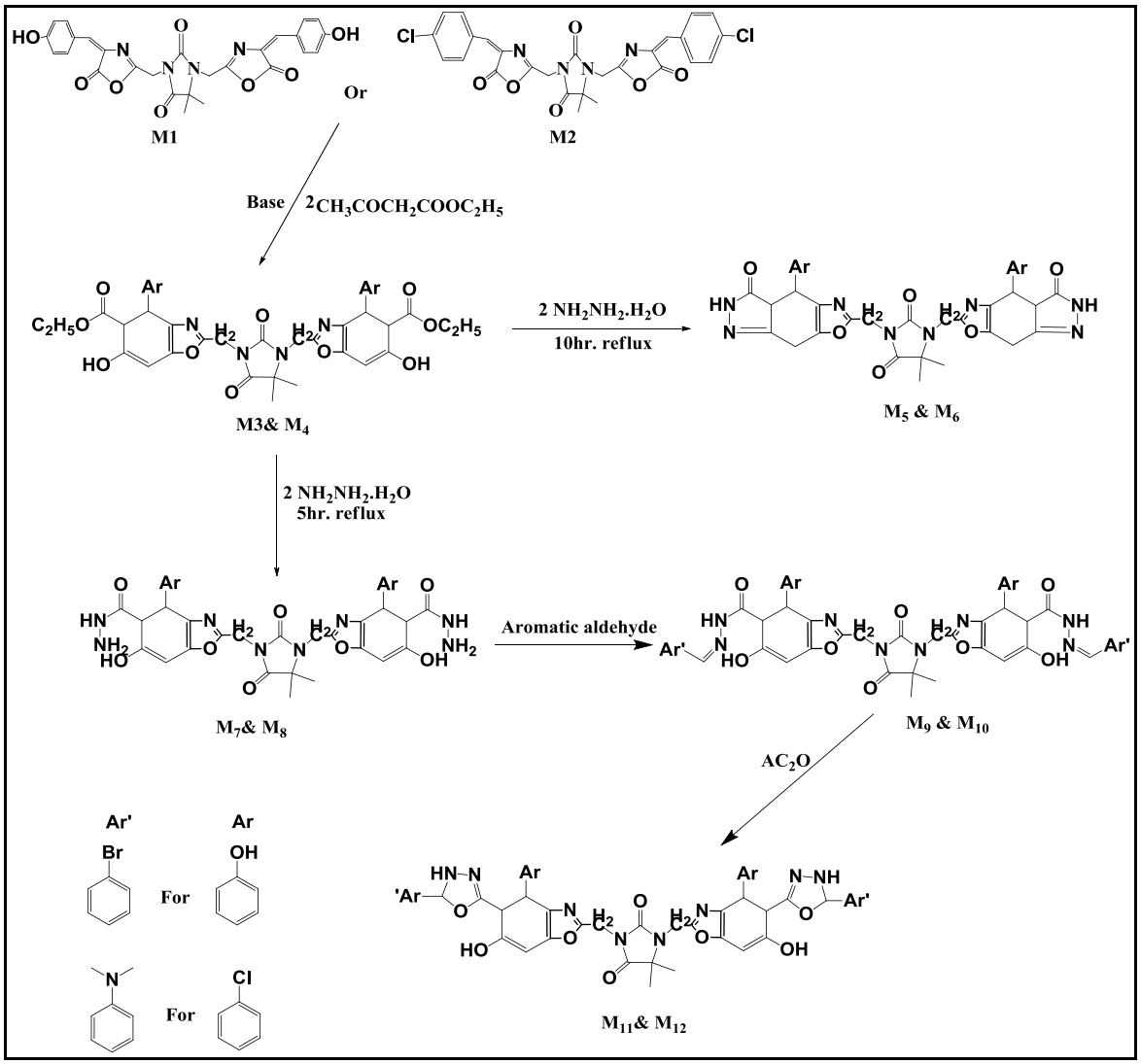
Table (1) Show The Physical Properties of Compounds.

Compounds	M.Wt	Color	Yields%	M.P.	TLC	
					Solvent	R*f*
M3	754.74	Brown	83	166-168	DMF:DCM	0.80
M4	791.63	White	76	184-186 DC	n-hexane:$CHCl_3$	0.63
M5	690.66	Dark Brown	65	119-120	n-hexane:DCM	0.50
M6	727.55	Yellow	60	Gamy	n-hexane:$CHCl_3$	0.45
M7	726.69	Black	54	Oily	n-hexane:DCM	0.89
M8	763.58	Reddish Brown	48	85-86	n-hexane:DCM	0.77
M9	1060.69	Brown	70	208-209	n-hexane:DCM	0.41
M10	1025.93	Pale Brown	76	95-96	n-hexane:$CHCl_3$	0.78
M11	1060.70	Brown	45	63-65	n-hexane:DCM	0.46
M12	1025.93	Black	54	85-86	Petroleum ether :$CHCl_3$	0.34

DC=decomposed

Results and Discussion

The designated compounds were synthesized according to Scheme1:



Scheme 1.The synthesis of compounds M3-M12.

Spectral Data Analysis Compound M3:

IUPAC name: diethyl 2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(6-hydroxy-4-(4-hydroxyphenyl)-4,5-dihydrobenzo[d]oxazole-5-carboxylate).

IR (KBr)cm^{-1}:3,410-3,282brod (OH) ,1,618(C=O), 1,720(C=Oester) ,3,050(C-Har),2,939–2,877(C-Haliph).

Spectral Data Analysis Compound M4:

IUPAC name: **diethyl 2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-(4-chlorophenyl)-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carboxylate)**.

IR (KBr)cm^{-1}:3,365-3,207brod (OH) ,1,672(C=O) ,1,734(C=Oester),3,068(C-Har),2,933–2,856(C-Haliph.).

1H-NMR(δppm):10.88(S,2H,-OH),1.28(t,4H,O-CH_2),4.00(q,6H,-CH_3 ester),3.67 (d, 2H, -CH ring) , 4.19 (d, 2H, Ar-CH), 7.9 (s, 2H, =CH_{ring}), 7.94-7.36(d ,8H,CH)ar,4.15(s,4H,N-CH_2),1.32(s,6H,-CH_3).

Spectral Data Analysis Compound M5:

IUPAC name:
1,3-bis((4-(4-hydroxyphenyl)-3-oxo-3,3a,4,8-tetrahydro-2H-oxazolo[4,5-f]indazol-6-yl)methyl)-5,5-dimethylimidazolidine-2,4-dione.

IR (KBr)cm^{-1}:3,500-3,200brod (OH), 3,331(NH),1,660(C=O pyrazol) , 3,050(C-Har),2,933,2,891(C-Haliph).

Spectral Data Analysis Compound M6:

IUPAC name:
1,3-bis((4-(4-chlorophenyl)-3-oxo-3,3a,4,8-tetrahydro-2H-oxazolo[4,5-f]indazol-6-yl)methyl)-5,5-dimethylimidazolidine-2,4-dione.

IR (KBr)cm^{-1}:3,323(NH) , 1,674(C=O pyrazol), 3,074(C-Har),2,924,2,854(C-Haliph).

1H-NMR(δppm):7.99(s,2H,-NH),3.53 (d, 2H, Ar-CH), 2.34 (s, 4H, CH_{2ring}), 2.91 (d,2H,CH-CO),7.37-7.27(d ,8H,CH)ar,3.83(s,4H,N-CH_2), 1.21(s,6H,-CH_3).

Spectral Data Analysis Compound M7:

IUPAC name:**2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(6-hydroxy-4-(4-hydroxyphenyl)-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide).**

IR (KBr)cm^{-1}:3,400-3,100brod (OH),3,410-3,275(NH_2), 3,215(NH) ,1,664(C=O), 3,061(C-Har),2,943, 2,899(C-Haliph).

1H-NMR(δppm):1.87(d,4H,-NH_2),7.97(t,2H,-NH),4.00 (d, 2H, Ar-CH), 7.69 (s, 2H, =CH_{ring}), 3.50(d,2H,CH-C=O),7.67-7.09(d ,8H,CH)ar,4.11(s,4H,N-CH_2), 10.00(s,2H,OH), 6.67(s,2H,OH ph.), 1.25 (s,6H,-CH_3).

Spectral Data Analysis Compound M8:

IUPAC name:
2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-(4-chlorophenyl)-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide).

IR (KBr)cm^{-1}:3,400-3,000brod (OH),3,317-3,230(NH_2), 3,265(NH) ,1,668(C=O), 3,062(C-Har),2,931,2,858 (C-Haliph).

1H-NMR(δppm):1.87(d,4H,-NH_2),7.98(t,2H,-NH),3.57 (d, 2H, Ar-CH), 7.70 (s, 2H, =CH_{ring}), 3.46 (d,2H,CH-C=O), 7.39-7.27(d ,8H,CH)ar,4.00(s,4H,N-CH_2), 9.00(s,2H,OH), 1.25(s,6H,-CH_3).

Spectral Data Analysis Compound M9:

IUPAC name:
(N'Z,N'''Z)-2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(N'-(4-bromobenzylidene)-6-hydroxy-4-(4-hydroxyphenyl)-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide).

IR (KBr)cm^{-1}:3,392(OH),3,246(NH) ,1602(C=N) ,1,660(C=O),3,084(C-Har),2,967–2,852(C-Haliph).

1H-NMR(δppm):10.01(s,2H,-NH),8.72(s,2H,N=CH),3.47 (d, 2H, Ar-CH), 7.88 (s, 2H, =CH_{ring}), 3.45(d,2H,CH-CO),7.75-7.49(d ,16H,CH)ar,3.98(s,4H,N-CH_2), 4.22(s,2H,OH),11.3(s,2H,OHph.), 1.28 (s,6H,-CH3).

Spectral Data Analysis Compound M10:

IUPAC name:**(N'Z,N'''Z)-2,2'-((4,4-dimethyl-2,5-dioxoimidazolidine-1,3-diyl)bis(methylene))bis(4-(4-chlorophenyl)-N'-(4-(dimethylamino)benzylidene)-6-hydroxy-4,5-dihydrobenzo[d]oxazole-5-carbohydrazide)**.

IR (KBr)cm^{-1}:3,406(OH),3,273(NH) ,1624(C=N) ,1,703(C=O),3,047(C-Har),2,924,2,852(C-Haliph).

1H-NMR(δppm):2.47(s ,12H,$N(CH_3)_2$),10.00(s,2H,-NH),8.00(s,2H,N=CH),3.50 (d, 2H, Ar-CH), 7.91 (s, 2H, $=CH_{ring}$), 3.30(d,2H,CH-CO),7.40-7.33(d ,16H,CH)ar,4.35(s,4H,N-CH_2), 4.16(s,2H,OH),1.25(s,6H,-CH_3).

Spectral Data Analysis Compound M11:

IUPAC name:
1,3-bis((5-(5-(4-bromophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-hydroxy-4-(4-hydroxyphenyl)-4,5-dihydrobenzo[d]oxazol-2-yl)methyl)-5,5-dimethylimidazolidine-2,4-dione.

IR (KBr)cm^{-1}:3,473(OH),3,226(NH) ,1,664(C=N) , 1,707(C=O),3,061(C-Har),2,933,2,856(C-Haliph).

1H-NMR(δppm):8.72(d,2H,-NH),7.88(d,2H,CH_{ring}),3.47 (d, 2H, Ar-CH), 3.45 (s, 2H, $=CH_{ring}$), 4.19 (d,2H,$CH_{Oxadiazol}$),7.86-7.51(d,16H,CH)ar,3.49(s,4H,N-CH_2), 10.1(s,2H,OH),3.92(s,2H,OH ph.),1.28 (s,6H,-CH_3).

Spectral Data Analysis Compound M12:

IUPAC name:**1,3-bis((4-(4-chlorophenyl)-5-(5-(4-(dimethylamino)phenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-6-hydroxy-4,5-dihydrobenzo[d]oxazol-2-yl)methyl)-5,5-dimethylimidazolidine-2,4-dione**.

IR (KBr)cm^{-1}:3,444(OH),3,406(NH) ,1,600(C=N) ,1,660(C=O),3,068(C-Har),2,926–2,854(C-Haliph).

1H-NMR(δppm):2.47(S,12H,$N(CH_3)_2$),8.00(d,2H,-NH),3.36(d,2H,CH_{ring}),4.1 (d, 2H, Ar-CH), 7.91 (s, 2H, $=CH_{ring}$), 5.60(d,2H,$CH_{Oxadiazol}$),7.40-7.39(d ,16H,CH)ar,4.3(s,4H,N-CH_2), 10.1(s,2H,OH),1.25(s,6H,-CH_3).

Application:

The process of the internal conversion and intersystem crossing of fluorescence or phosphorescence process was not found the efficiency of 100%, thereby it's become necessary to calculate the quantum yield.

Quantum yields of the compound calculated by the equations below:[23]

$$\frac{F2}{F1} = \frac{I°\varepsilon C d\Phi 2}{I°\varepsilon C d\Phi 1} = \frac{(area)}{(area)}$$

$$\Phi_{sample} = \frac{(area)\ standerd \times Asample}{(area) sample \times Astanded} \times \Phi_{standerd}$$

Prepare solution ($1x10^{-3}$ M) of a prepared compounds in (10 mL) absolute ethanol and scan solution by (Spectroflurophorphotometer) to find λexc. ,λem. and area under the peak after find absorbance of the same concentration of compound by (Uv/Vis Spectrophotometer),Then quantum yield of compounds calculated by Comparison with Rhodamine 6G.

Table (2) Shows λexc.,λem. and Quantum Yield of Compounds

Compound	$\lambda_{exc.}$(nm)	$\lambda_{em.}$(nm)	ϕf
M3	341	379	0.42
M5	336	421	0.21
M6	348	408	0.47
M7	274	324	0.38
M8	372	427	0.45
M9	380	452	0.31
M10	454	508	-
M11	321	374	0.28
M12	419	467	0.58

λexc.&λem.= Excitation and emission maxima in nanometers
ϕf = quantum yields
- =ϕf<0.05

References:

1. Botros S, Khalil NA, NaguibBH , El-Dash Y. Synthesis and anticonvulsant activity of new phenytoin derivatives. *Eur. J. Med. Chem.***60,** 57–63 (2013).
2. Zhang L, Sathunuru R, Luong T, Melendez V, Kozar MP, Lin AJ.New imidazolidinedione derivatives as antimalarial agents. *Bioorganic Med. Chem.***19,** 1541–1549 (2011).
3. Shankaraiah N, Nekkanti S, Chudasama JK, Senwar KR,Sharma P, Jeengar MK, Naidu VG, Srinivasulu V, Srinivasulu G, Kamal A. Design, synthesis and anticancer evaluation of tetrahydro-β-carboline-hydantoin hybrids. *Bioorganic Med. Chem. Lett.***24,** 5413–5417 (2014).
4. Singh N,Sinha JN, Rastogi SK, Dua PR , Kohli RP.An Experimental Investigation on the Antiarrhythmic Activity of Antiepileptic Agent.Japan J. Pharmacol.29,755-761 (1971).
5. Czopek A, Byrtus H, rska AZ, Siwek A, Kazek G, Marek Bednarski M, Sapa J, Pawłowski M. Design, synthesis, anticonvulsant, and antiarrhythmic properties of 4 novel N-Mannich base and amide derivatives of b-tetralinohydantoin. Pharmacological Reports.68,886-893 (2016).
6. Shamsuzzaman, Khan MS, Alam M, Tabassum Z,Ahmad A, Khan AU. Synthesis, antibacterial and antifungal activities of 6,5 fused steroidal oxazoles in cholestane series. European Journal of Medicinal Chemistry. 45, 1094–1097(2010).
7. Ryu C, Lee R, Kim NY, Kim YH , Song AL. Synthesis and antifungal activity of benzo [d] oxazole-4 , 7-diones. Bioorg. Med. Chem. Lett. 19, 5924–5926 (2009).
8. Li D , Gao N , Zhu N , Lin Y, Li Y, Chen M, You X, Lu Y , Wan K, Jiang W, Si S. Discovery of the disubstituted oxazole analogues as a novel class antituberculotic agents against MDR- and XDR-MTB. Bioorganic & Medicinal Chemistry Letters.24,466-472 (2015).
9. Shakya AK, Kaur A, Al-Najjar BO,Naik RR. Molecular modeling, synthesis, characterization and pharmacological evaluation of benzo[d]oxazole derivatives as non-steroidal anti-inflammatory agents. Saudi Pharmaceutical Journal.24,616-624 (2015).
10. UMADEVI P,DEEPTI K,SRINATH I,VIJAYALAKSHMI G, TARAKARAMJI M. SYNTHESIS AND IN-VITRO ANTIBACTERIAL ACTIVITY OF SOME NEW UREA,THIOUREA AND THIOSEMICARBAZIDE DERIVATIVES. International Journal of Pharmacy and Pharmaceutical Sciences.4, 379-383 (2012).
11. Kleeman A, Engel J, Kutscher B, Reichert D. Pharmaceutical Substances, Syntheses, Patents and Applications of the Most RelevantAPIs, Thieme Medical, New York, NY,USA, 3rd edition, 1999.
12. Novikov OO, Pokrovskii MV, Konovalenko.Prooxidant Effects of Nitrofurantoin .Bulletin of Experimental Biology and Medicine.134,148-150 (2002).
13. Patel MB, Modi NR, Raval JP , Menon SK.Calix[4]arene based 1,3,4-oxadiazole and thiadiazole derivatives: Design,synthesis, and biological evaluation.Org. Biomol. Chem.. 10, 1785–1794 (2012).
14. HASAN A,GAPIL S, KHAN I. Synthesis, Characterization and Antifungal Activity of Some New 5-Substituted 1,3,4-oxadiazole-2-thiols.Asian Journal of Chemistry.23, 2007-2010 (2011).

15. Patel PK, Patel RK, KumariP, Rajani DP, Chikhalia KH. Synthesis of benzimidazolyl-1,3,4-oxadiazol-2ylthio-N-phenyl (benzothiazolyl) acetamides as antibacterial, antifungal and antituberculosis agents.European Journal of Medicinal Chemistry. 53,41-51(2012).
16. Kerimov I, Ayhan-Kılcıgil G, Ozdamar ED, Can-Eke B, Coban T,Ozbey S, Kazak C.Design and One-Pot and Microwave-Assisted Synthesis of 2-Amino/5-Aryl-1,3,4-oxadiazoles Bearing a Benzimidazole Moiety as Antioxidants.Arch. Pharm. Chem. Life Sci. 000, 1–8 (2012).
17. KAVITHA S, GNANAVEL S, KANNAN K. BIOLOGICAL ASPECTS OF 1,3,4-OXADIAZOLE DERIVATIVES. Asian J Pharm Clin Res.7, 11-20 (2014).
18. Gul S, Rehman A, Abbasi MA, Khan KM, Nafeesa K, siddiqa A, Akhtar MN, Shahid M,Subhani Z. Journal of Saudi Chemical Society.1-23 (2014).
19. Nhat KP, Watanabe T, Yoshikoshi K, Hohsaka T. Antibody-based fluorescent and fluorescent ratiometric indicators for detection of Phosphotyrosine. Journal of Bioscience and Bioengineering.122, 146–154(2016).
20. Yuan Y, Fu S, Xu Q, Yang J, Hu X, Liu S. The fluorescence and resonance Rayleigh scattering spectral study and analytical application of cerium (IV) and cefoperazone system. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy.162, 93–97 (2016).
21. Oida T, Sako Y, Kusumi A.Fluorescence lifetime imaging microscopy (flimscopy)Methodology development and application to studies of endosome fusion in single cells.Biophys. J. .64,676-685 (1993).
22. Zapata F, Ossa MA, Garcia-Ruiz C.Emerging spectrometric techniques for the forensic analysis of body fluids. Trends in Analytical Chemistry.64, 53-63(2015).
23. Abood MR, Rasool SR. Synthesis, Characterization and study of Some New Heterocyclic Compounds For Imidazolidine-dione Derivatives. Research Journal of Pharmaceutical, Biological and Chemical Sciences.7,617-623 (2016).

*****