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Synthesis and characterization of 1,3,4-Oxadiazoles Derivatives from 4-Phenyl-Semicarbazide

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Abstract

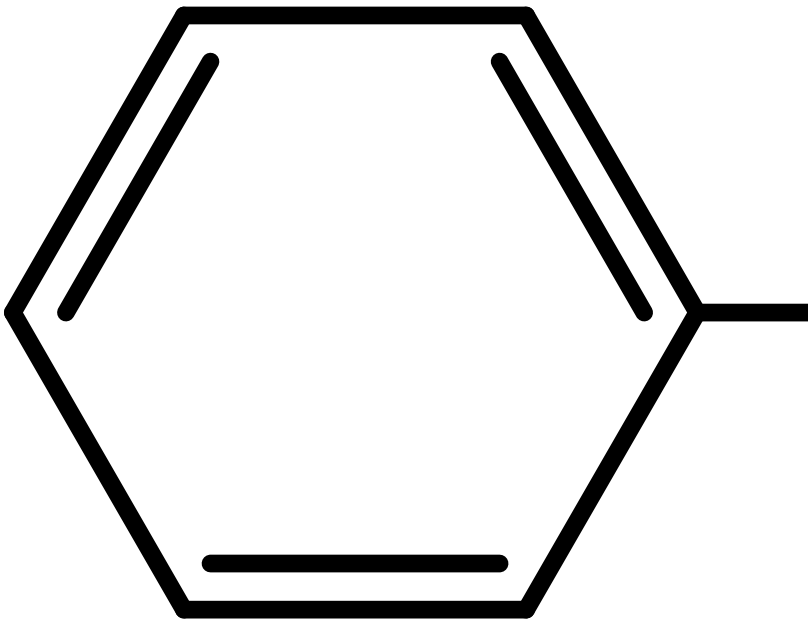
In this work, a series of novel 1-(2-(4-xphenyl)-5-(phenylamino)-1,3,4- oxadiazole-3(2H)-yl) ethanone (X=H,OH,Cl,NO_2,N(CH_3) (4a-e) were prepared from the condensation of Schiff base (3a-e) with acetic acid. The azomethines were prepared from the corresponding 4-phenyl semi carbazide(1) with aryl aldehydes (2a-e). This convenient method benefits from its broad applicability, ease and safety reagent handing, simple product isolation. All the reaction was routinely monitored and purity was determined, on thin layer chromatography using coated aluminum plates and spots were visualized by exposing the dry plates in iodine vapours. The structure elucidation of synthesized compound is based on the ^{1}HNMR, FTIR, U.V spectral data, mass spectroscopy , melting points and computational methods **.** Our results indicate that the energy differences between the lowest unoccupied molecular orbit and the highest occupied molecular orbit are predominantly affected by the terminal groups of the Oxadiazoles compounds.

Keywords : Synthesis, Oxadiazoles, Semicarbazide

Introduction

A wide variety of heterocyclic systems has been explored for developing pharmaceutically important molecules. Among them the derivatives of oxadiazoles have played an important role in the medicinal chemistry [(1,2)] . The oxadiazole a five- membered nitrogen and oxygen containing heterocyclic which has been commonly used as a privileged scaffold to produce various novel pharmaceutical drug such as : antitumor[(3)], anti cancer agents[(4)] and anti prostate[(5)]. This class of material also has gained the worth of modern application such as scintillators ,

fluorescence and photographic materials[6] . The development of simple and general routes for widely used organic compounds from the readily available reagents is one of major challenges in organic synthesis. Because of these interesting features, several routes to synthesis of oxadiazoles derivatives have been developed. Oxidative cyclization of the aldehyde N-acyl hydrazones is the most known method to prepare oxadiazoles derivatives and several reagents have been reported in the literature which includes oxidation with ceric ammonium nitrate[7], trimethylsilyl[8], dicylohexyl carbodiimide[9], potassium permanganate [10] and hyper valent iodine reagents[11]. The other oxadiazoles derivatives have been synthesized from cycldehydration of diaceyl hydrazines. This method of synthesis usually involves rigorous condition or use of harsh reagents $SOCl_2$,$POCl_3$[12] , propylophosphoric anhydride [13], liquid sulfuric acid[14] and phosphorous pent oxide[15]. By a similar approach but in a non-oxidative media. As part of our efforts to explore the utility of novel methods for the synthesis of oxadiazoles derivatives. Here we report our efficient preparation of 1-(2-(4-x-phenyl) -5- (phenylamino)-1,3,4-oxadiazole-3(2H)-yl) benzylidene)-N-phenylhydrazine carboxamide with acetic acid. The synthetic route and the sequence of reaction are depicted in scheme 1:



Scheme 1 : Synthetic route to 1,3,4- Oxadiazoles derivatives

Experimental

All chemicals used were of (BDH. Fluka, Merk). All melting points were determined using Electro thermal (Gallen Kamp) apparatus were uncorrected. Thin layer chromatography (TLC) using performed throughout the reaction on aluminum sheets using mixture of different polar and non polar solvents in varying proportions and spots were observed using iodine as visualizing agent. ^{1}HNMR spectra were recorded on a Bruker's 500 FT MHz NMR instrument using DMSO-d6 as solvent and TMS as internal reference (chemical shift in δ ppm) in Iran. IR spectra were recorded on Shimadzu FTIR-8400S spectrophotometer in Iraq. Electronic spectra were measured by using T 80$^+$ Spectrometer in the region (200-600nm) for solution ethanol in Iraq. Mass spectra were recorded on MSD direct probe using Acq method test dp.M.in Iran.

Preparation of Schiff bases (3a-e)

General method[16]

The corresponding aryl aldehyde (2a-e) (0.003 mol) was added to a solution of 4-Phenyl semicarbazide (1) (0.003 mol) in absolute ethanol (15ml) and the mixture was refluxed for 3hrs. After cooling, the solvent was filtered off, evaporated under vacuum and the formed precipitate was filtered and recrystallized from ethanol. It was obtained 63-82% yield.

Preparation of 1-(2-(4-X-Phenyl) -5-(Phenyl amino)-1,3,4-Oxadiazole 3(2H)-yl) ethanone(4a-e)

General method[17]

Anhydrous acetic acid (10 ml) was added to appropriate Schiff bases (3a-e) (0.0025 mol). The mixture was refluxed for 3 hrs, then the solvent was evaporated and the corresponding product was collected and recrystallized from ethanol absolute , yield 43-60%. The characterization data for 1,3,4-Oxadiazole derivatives is given in table 1.

Geometry Optimization

All calculations were performed with GAUSSIAN 03 package [18]. The geometry optimization with the semi empirical AM1 Hamiltonian. The MOs calculation the values dipole moment, total Energy, HOMO, LUMO and HOMO-LUMO gap of studied compounds .

Results and Discussion

The physical properties of Schiff bases and novel 1,3,4-Oxadiazole derivatives are presented in table 1. The compounds are quite stable in dry air and they are soluble in most organic solvent. Synthetic routes leading to target compounds are summarized in scheme 1. The structure of these compounds were proven on the basis of melting points and spectral data.

^{1}HNMR spectra

^{1}HNMR spectra of Schiff bases (3a-e), a singlet corresponding to one proton characteristic of the (1HCH=N) group was observed in between δ 8.64-8.70 ppm, (m,9H,Ar-H) at δ7.02-8.34 ppm and a singlet at δ 3.31 ppm integrating for one proton of (1H,NH) groups [19]. ^{1}HNMR spectra of 1,3,4-Oxaiazoles derivatives (4a-e) show the absence of singlet at δ 8.64-8.70 ppm due to (1H,CH=N) groups, the appearance singlet at δ 10.38 ppm due to (1H,NH) and the appearance singlet corresponding to one proton of the (1H,CH) group of oxadiazole cyclie at δ 8.09 ppm [20] and singlet at δ 2.03 ppm due to (3H,CH_3) groups.

FT IR spectra

The IR spectra of all compounds and the study are recorded in the solid state using KBr disk. Selected bands of diagnostic importance are collected in table 2. The formation of Schiff bases (3a-e) was indicated by their IR spectra from appearance of azomethane CH=N stretching band at 1650- 1674 cm^{-1} combined with the absence of IR band in region 3236 cm^{-1} and 1710 -1780 cm^{-1} corresponding to NH_2 group and C=O group of 4-Phenyl semicarbazide and 4-X-benzaldehyde respectively [21]. While 1,3,4-

Oxadiazole derivatives (4a-e) display in their IR new carbonyl and C=N absorption near 1690-1697 cm^{-1} and 1640-1672 cm^{-1} respectively, in addition two band at 1230 – 1271 cm^{-1} and 1150-1197 cm^{-1} for the C-O-C group asymmetric and symmetric stretching respectively[22].

Mass spectra

The mass spectra of 1-(2-(4-x phenyl)-5-(phenyl amino)-1,3,4-oxadiazole-3(2H)-yl) ethanone (4c) exhibit parent peak m/z 316. As per the even electron rule the 316 ion cleaves to fragment with even mass at fragment peaks at m/z 180 formed by the loss of ph-NH from the base peak, m/z 239 due to the removal of ph^+ and m/z 135 due to fragment of $C8N_2^+ClH5$ [23]. The other peaks of mass prove the structure of compound, Scheme 2.Fragmentation pattern of compound (4c)

Table 1: Physical properties and analytical data of compounds synthesis

Comp.	X	M.p(°C)	Colour	M.Wt	M. Formula	Yield%	λ(nm)	ε max(L. mol^{-1}.cm^{-1})
3a	H	179-181	Buff	239	$C_{14}ON_3H_{13}$	82	255	5100000
3b	OH	165-170	Orange	255	$C_{14}O_2N_3H_{13}$	74	250	5000000
3c	Cl	215- 218	Yellow	273	$C_{14}ON_3H_{12}Cl$	73	250	5000000
3d	NO2	197-199	Pale Yellow	284	$C_{14}O_3N_4H_{12}$	63	255	5100000
3e	$N(CH_3)_2$	187-190	Buff	282	$C_{16}ON_4H_{18}$	66	290	5800000
4a	H	164-168	Pale Yellow	281	$C_{16}O_2N_3H_{15}$	51	255	5100000
4b	OH	201-205	Red	297	$C_{16}O_3N_3H_{15}$	60	235	4700000
4c	Cl	189-192	Yellow	315	$C_{16}O_2N_3H_{14}Cl$	48	295	5900000
4d	NO_2	190-192	Brown	326	$C_{16}O_4N_4H_{14}$	43	255	4500000
4e	$N(CH_3)_2$	192-194	Red	324	$C_{16}O_2N_3H_{15}$	46	225	4500000

Table 2:Major IR absorption bands (cm^{-1}) of compounds synthesized

Comp.	υ(OH) max.	υ(NH) max.	υ(CH) max. aromatic	υ(CH) max. aliphatic	CO-CH3 amide	υ(C=O)	υ(CH=N)	υ(C=N)	υ(C-N)	υ (C-O-C)
3a	-	3379	3095	2968	-	1689	1657	-	1363	-
3b	3350	-	3018	2970	-	1695	1660	-	1350	-
3c	-	3339	3089	2979	-	1692	1654	-	1325	-
3d	-	3391	3107	2944	-	1694	1674	-	1349	-
3e	-	3330	3085	2870	-	1680	1650	-	1360	-
4a	-	3373	3101	2962	1697	-	-	1654	1366	1235
4b	3355	-	3013	2932	1690	-	-	1640	1342	1230
4c	-	3242	3017	2842	1690	-	-	1658	1325	1240
4d	-	3389	3108	2954	1690	-	-	1672	1349	1271
4e	-	3335	3095	2942	1693	-	-	1642	1340	1237

Scheme 2: Fragmentation pattern of compound (4c)

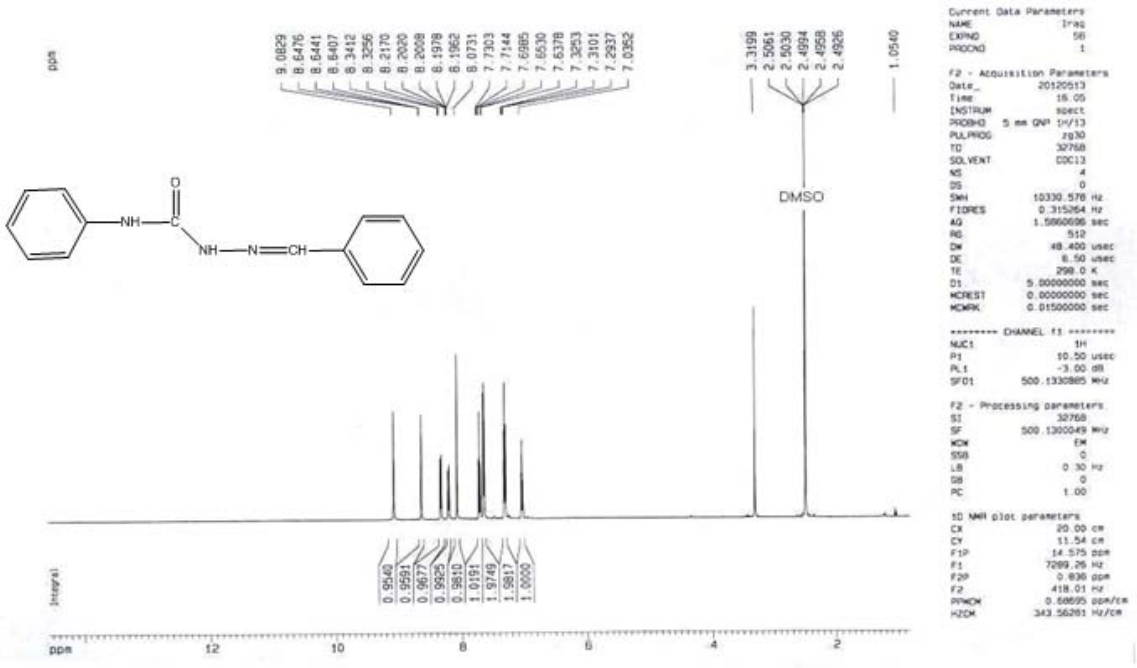


Fig 1. [1]HNMR of Compound 3a.

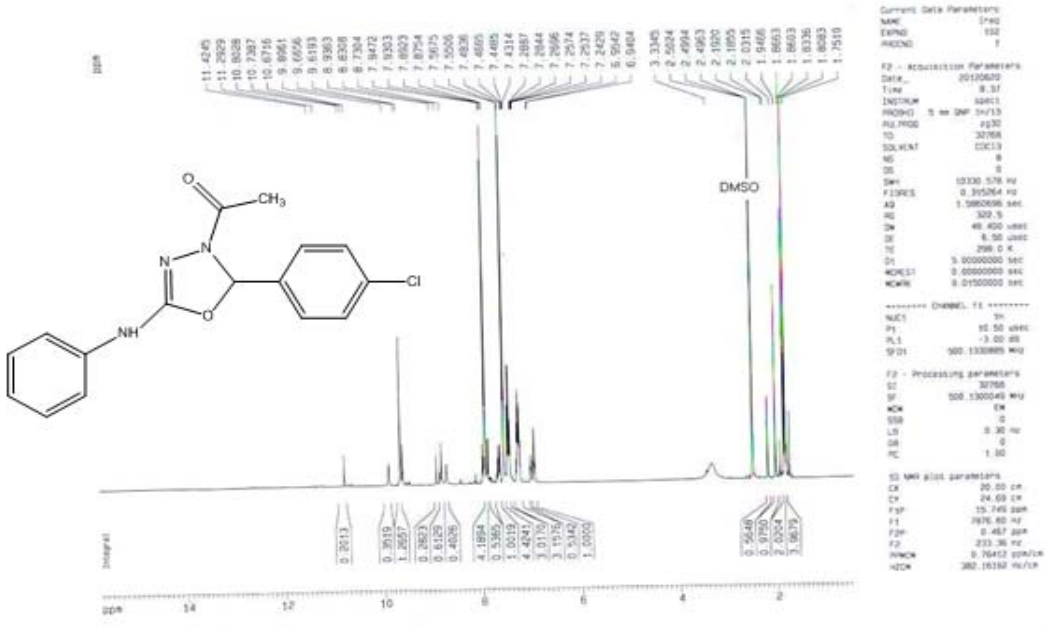


Fig 2 . [1]HNMR of Compound 4c.

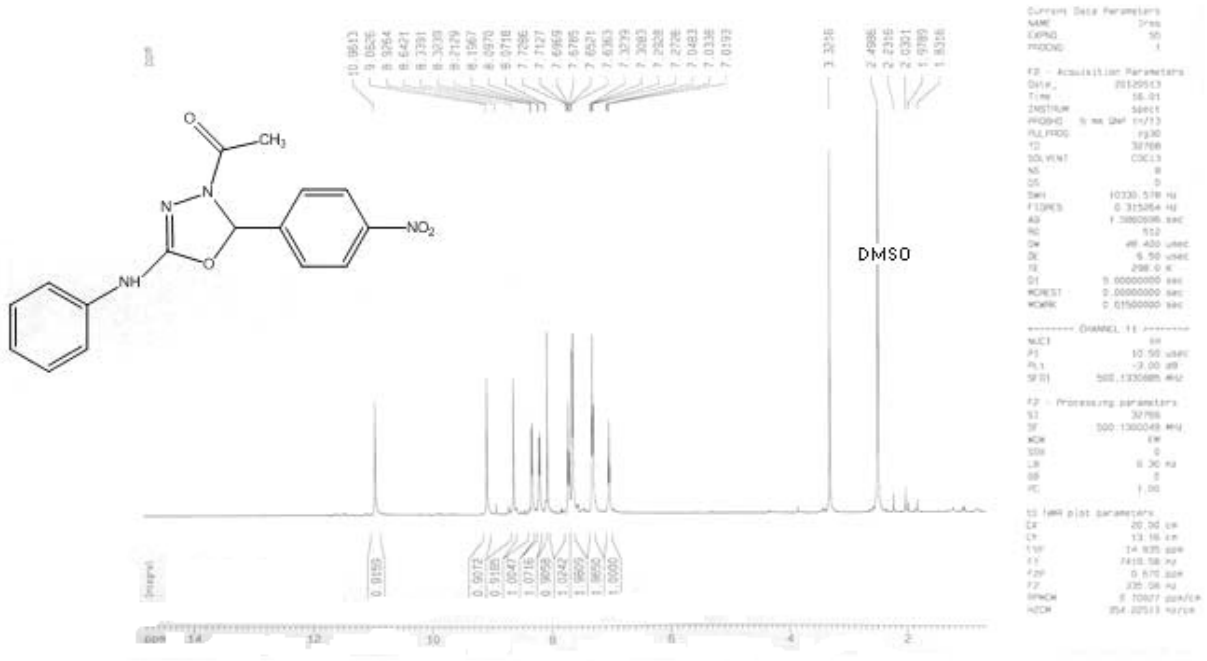


Fig 3. [1]

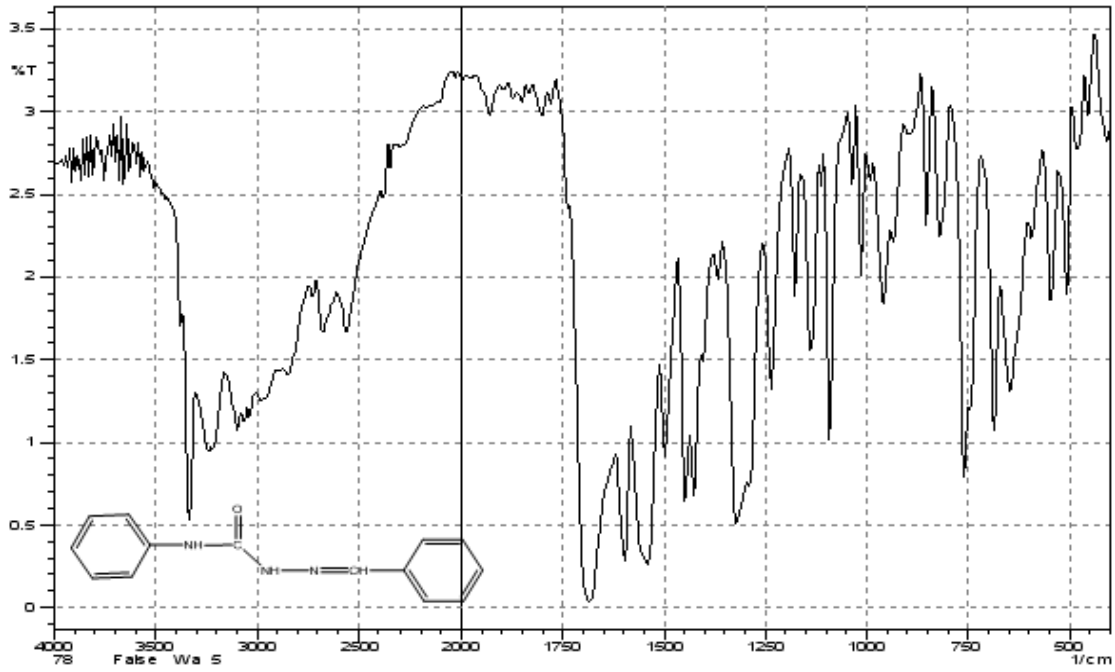


Fig 5. FT- IR of Compound 3a.

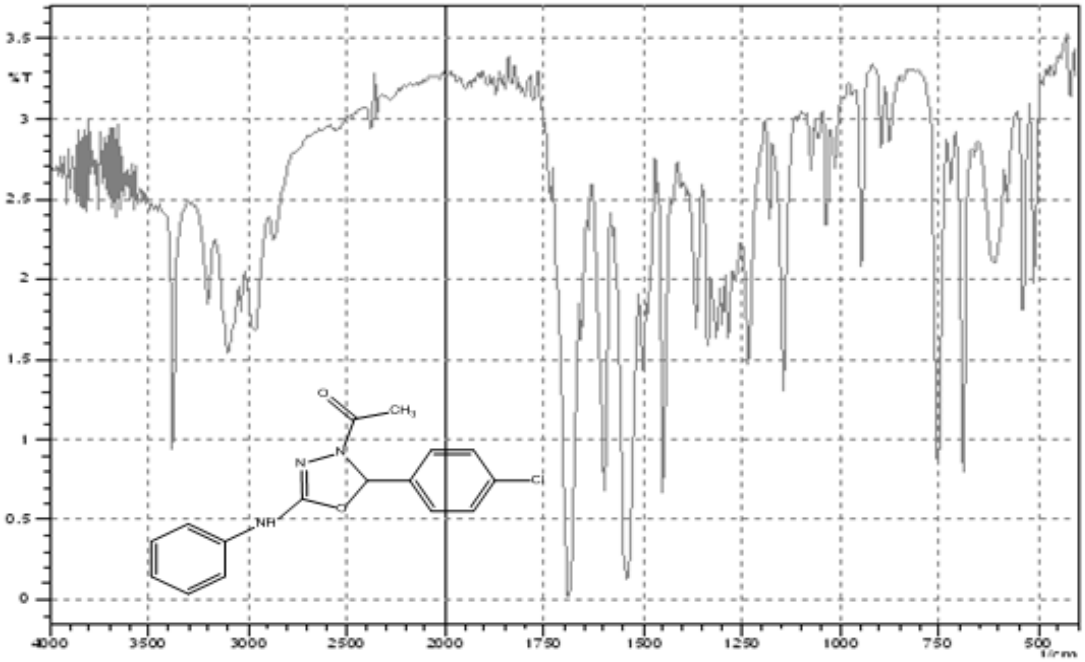


Fig 6. FT- IR of Compound 4c.

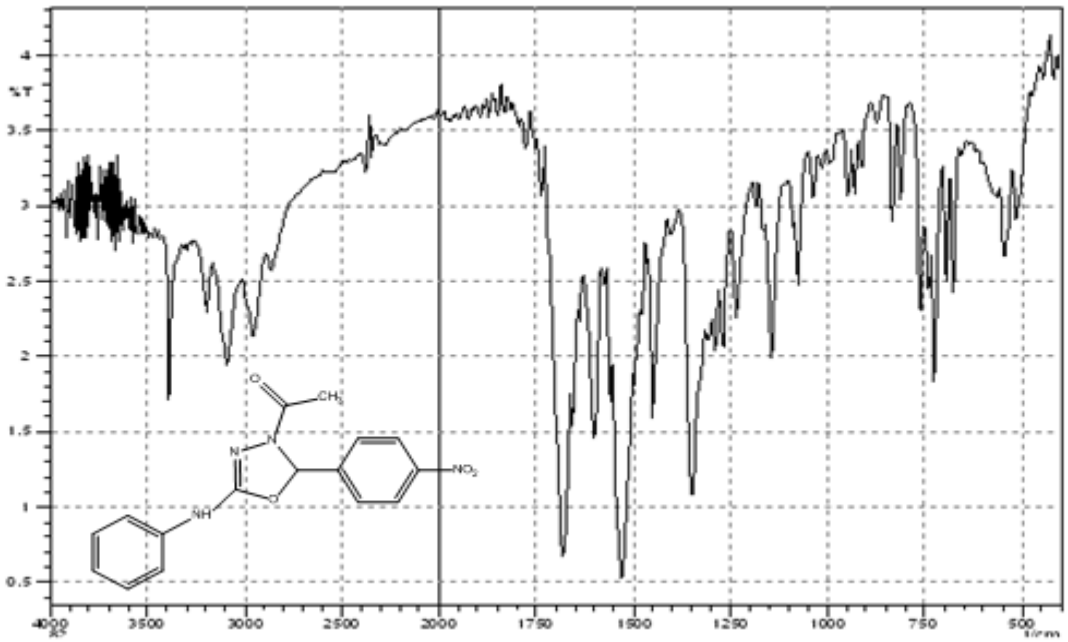


Fig 7. FT- IR of Compound 4d

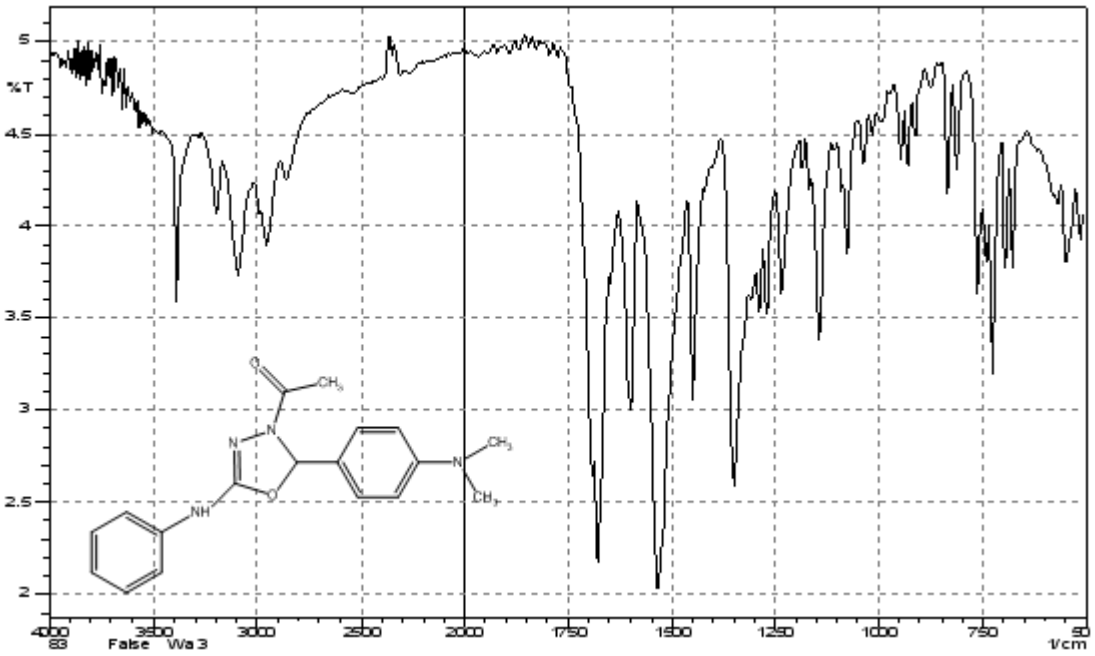


Fig 8 . FT- IR of Compound 4e.

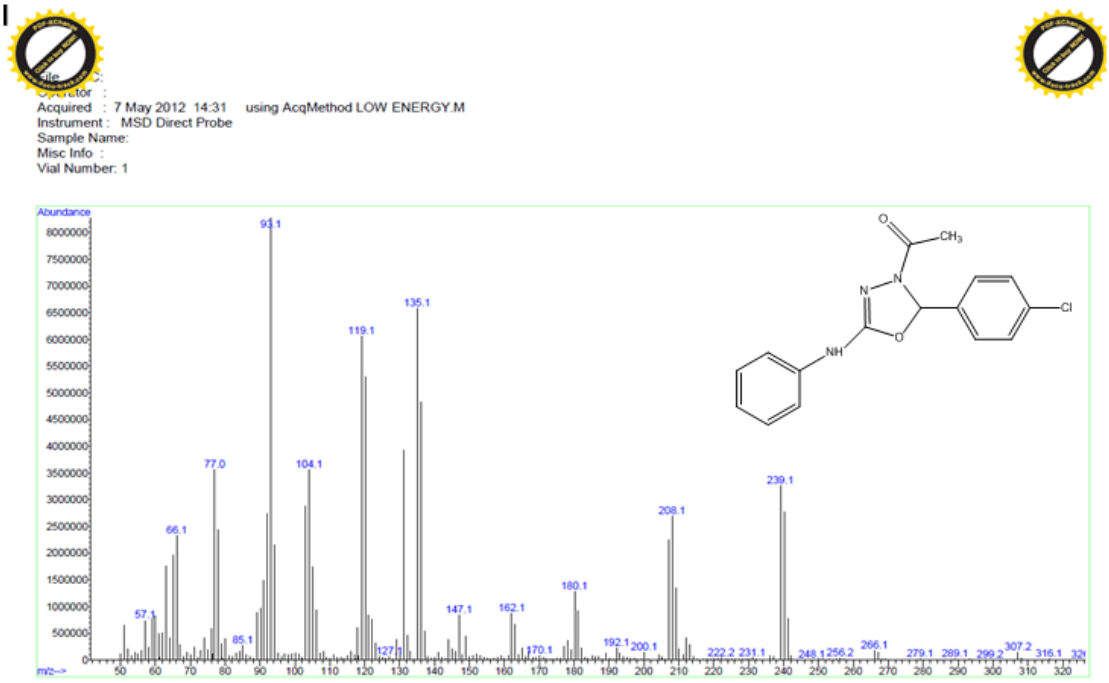


Fig. Mass Spectra of Compound 4c.

Computational Details

The highest occupied molecular orbital (HOMO), the lowest unoccupied molecular orbital (LUMO) and HOMO-LUMO energy gaps for (4a,4b,4c,4d and 4e) are calculated at semi empirical AM1. Results are presented in table 3. Representation of the HOMO and LUMO orbitals of molecules 4A-4E are determined with the semi empirical AM1 in Figure 4. The smaller the LUMO and HOMO energy gaps, the easier it is for the HOMO electrons to be excited; the higher the HOMO energies, the easier it is for HOMO to donate electrons; the lower the LUMO energies, the easier it is for LUMO to accept electrons. From the resulting data shown in table 3, it is obvious that the HOMO energies of 4d are higher than other compounds studies and the energy gap of 4d is smaller than other compounds studies. Consequently, the electrons transfer from HOMO to LUMO in 4d is relatively easier than that in other compounds studies. With the decrease of the LUMO energies, LUMO in 4c accepts electrons easily. The same methods were employed to study other compounds studies, also leading to the above stated conclusions and confirming the obtained results. Furthermore, according to semi empirical calculation frontier molecular orbital energy gap, namely the HOMO – LUMO gap[24]

Table 3: The calculated amounts of HOMO and LUMO energies, dipole moment (Debye) with the semi empirical AM1 .

Compounds	Dipole moment (Debye)	Total Energy (a.u.)	HOMO (a.u.)	LUMO (a.u.)	(HOMO-LUMO) Gap ΔE-L (a.u.)
4a	**3.9722**	**0.08820**	**-0.31714**	**-0.00596**	**0.31118**
4b	**5.0409**	**0.01911**	**-0.32019**	**-0.00433**	**0.31586**
4c	**3.8457**	**0.07900**	**-0.32320**	**-0.01487**	**0.30836**
4d	**4.0783**	**0.09753**	**-0.33182**	**-0.05218**	**0.27964**
4e	**6.0624**	**0.10338**	**-0.3175**	**-0.00045**	**0.31705**

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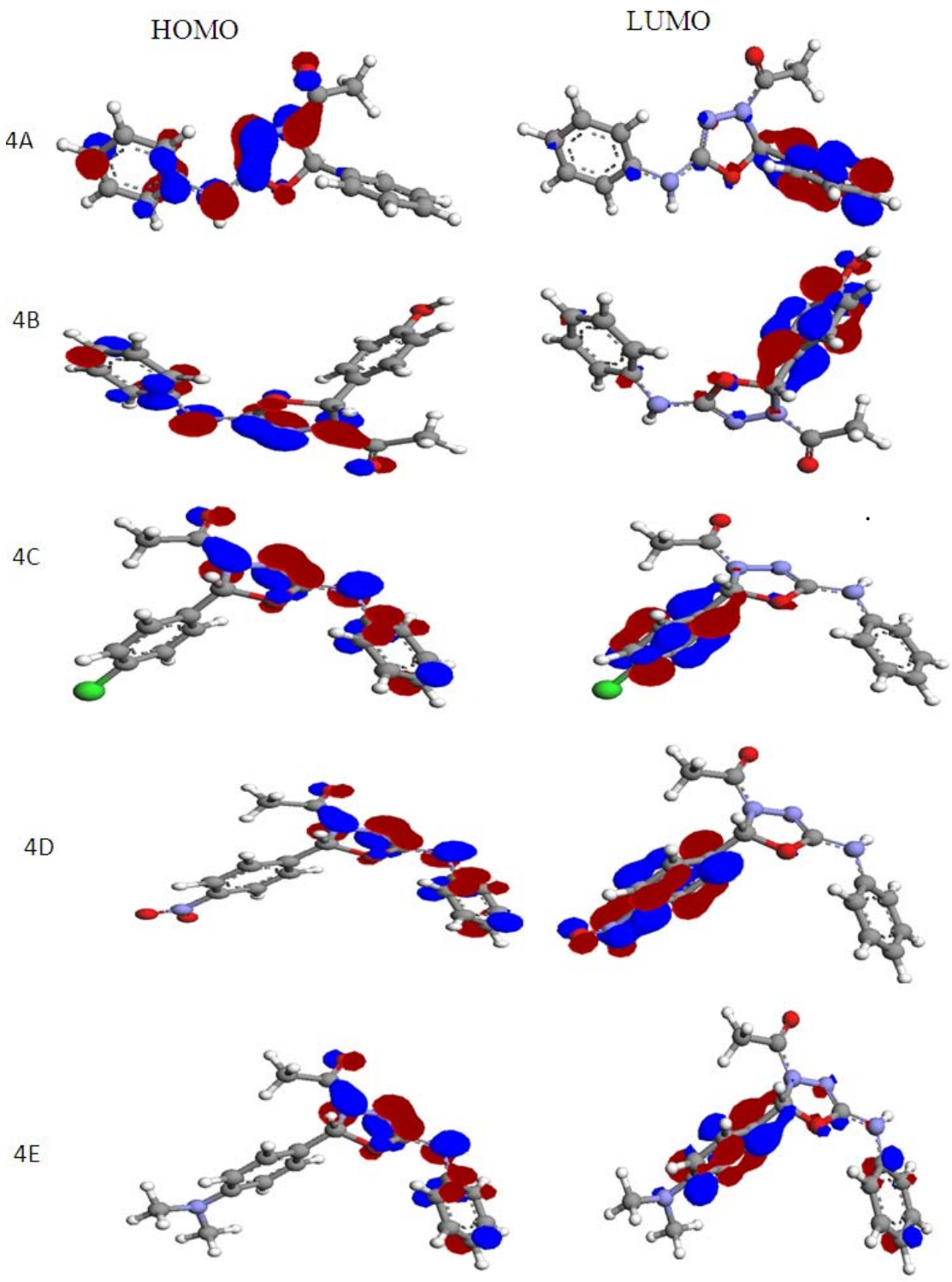

Figure 4. Representation of the HOMO and LUMO orbitals of molecules 4A-4E determined with the semi empirical AM1.

References

1. A.B. Raut and M.R.M. Matto, *Acta.Chim.solv.*,55,448, 2008.
2. K. Babak and M. Leila, *Tetrahedron lett.*,52,6424-6426, 2011.
3. I.Z. Noha, S .Fabio and F. Stefamo, *European.J.Med.Chem.*,45,4523,2010.
4. P. Dali,.P. Gautum and K.C. Angpla, *European.J.Med.Chem.*,46,3085-3092, 2011.
5. L.K. Gopal,.K. Jasmine and k. Varnm, *Bio.Organic.Med.Chem let.,* 22,1912-1916, 2012.
6. M. Nasser and R.M. Kurosh, *Chinese.Chem.Lett.* ,19,1143-1146,2008.
7. M. Dabbiri, P. Salehi and M. Baghbanddeh ,*Tetrahedron lett.*,47,6983-6986,2006.
8.V.Z. Evgenij, I.P.Igor and S.M. Anatolij, *Tetrahedron Lett.*, 64,10431-10442,2008.
9. R. Abdul, S. Shweta and G. Saloni ,*Chinese .Chem.Lett*,19,5-8,2008.
10. S. Rosstamizadeh and S.H. Ghasem, *Tetrahedron.Lett.*, 34,8753-8756, 2004.
11. P. Om,.R.K. Manojkumar and S. Chatan , *European.J.Med.Chem*,45,4252-4257,2010.
12. P.R. Neithnadka and P.K. Venugo, *European .J .Med.Chem.*, 44,4522-4527,2009.
13. K.A. John, V.P. Veeramani and N.S. Sharmila, *Tetrahedron lett*, 65,9989-9996, 2009.
14. R. Shahnaz and S.A. Haseml tousanini,*Tetrahedron.lett,*.45.8753-8756, 2004.
15..P.H. Carlsen and J. Jorgensen, *J .Hetero cycl.Chem*., 31,805, 1994.
16.K. Navjeet and K. Dharma, *J.Chem.Pharm.Res*,4,991-1015,2012.
17. I.A. Redha, J.L. Saud and S.A.A. Almustansiriya, *J.Sci*,2009,20,47-58.
18. M.J. Frisch et al Gaussian 03,Revision C.02. Gaussian Inc. , Wallingford,2004.
19. K.M. Shaabank, A.A. Antar and A.M. Maharumor, *J.Chem. Pharm.Res* ,4, 966-971, 2012.
20. T.C. Frank, A.E. Karem and L.G. Todd , *Tetrahedron.lett.*,45,3257,2004.
21. G.V. Suresh,Y. Rajendraprajad, B.P. Mallikarjuna,S.M. Chandrasxekav and C. Kistayya, *European.J.Med. Chem.* ,45,2063-2074, 2010.
22. N.F. Nida,.R.B. Mudasir and A. Anis, *Bio organic.Med.Chem.lett.*,20,1933-1938, 2010.
23. A. K. Kanli and Ö. Ates , *II farmaco.*,56,975, 2001.
24. U.J. AL-Hamdani, *J. Chem. Pharm. Res*, 4(1):932-938, 2012.

تحضير مشتقات جديدة لـ1،3،4- اوكسادايزول من مركب 4-فنيل- سيماكاربازايد وتشخيصها

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المستخلص

في هذا البحث حضرت سلسلة من مشتقات جديدة لمركب 1-(2-(x- فنيل)-5- (فنيل امينو)- 4،3،1- اوكسادايزول بوساطة تكاثف قاعدة شف مع حامض ألخليك الثلجي، بينما حضرت قاعدة شف من تكاثف 4- فنيل سيماكاربازايد مع الالديهايدات الاروماتية المعوضة بموقع بارا. حيث تمت متابعة التفاعلات باستخدام تقنية كَروماتوغرافيا الطبقة الرقيقة وشخصت المركبات المحضرة بوساطة أطياف الرنين النووي المغناطيسي للبروتون، الأشعة تحت الحمراء، الأطياف المرئية وفوق البنفسجية وطيف الكتلة بالإضافة إلى استخدام الكيمياء الحاسوبية في حساب عزم ثنائي القطب، طاقات HOMO و LUMO والطاقات الكلية للمركبات المحضرة.