Synthesis of novel azaarene derivatives and its biological evaluations

Mohammed S. Muftah

Chemistry department , faculty of sciences, Bani Walid University –Libya

Abstract : the 5,6,7triethyl – 2,3-bis (2^{-}-pyridyl) quinoxaline was synthesized by reaction of 2,2^{-} pyridil with phenylenediamine . The new compounds (c-1) and (c-2) were characterized by elemental analysis , ^{1}H-NMR ,infrared and mass spectroscopy .

The Synthesized compounds were screened for their antibacterial activity against one gram positive bacteria , one gram negative bacteria and two fungi.

The biological significance was compared with amikacin as standard

Keywords : 5,6,7 triethyl -2,3-bis (2^{-} –pyridyl) quinoxaline (c-1) , molybdenium complex (c-2).

Introduction:

The C-H bond functionalization is aconvenient and atom economical synthetic strategy to obtain functionalized azaarene derivatives [1-9] . The benzoquinazoline ring system is present as a substructure in various natural product alkaloids of therapeutic

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Corresponding author

E-mail : msm_Libya@yahoo.com

importance such as rutecarpin [10] (I) and ardeemin [11](II) .

Benzimidazo (2,1-b) benzo (F) isoquinoline (III) ring system [12] is present in pharmacologically active compounds These polyazaarenes display pronounced biological activities [13-15] as anticancer , diuretic , anticonvulsant and antihypertensive agents.

Quinolines are notorious to inhibit DNA synthesis by promoting cleavage of bacterial DNA gyras and type IV topoisomerase which causes rapid bacteria death [16-18].

Numerous Quinoline derivatives have been proposed as therapeutic agents against bacterial infections [19] malaria [20] , HIV[21] ,and tumor [22]. Most metabolites of azaarene (dihydrodiols and diolepoxides) are highly carcinogenic in experimental animals [23-26] . The azaarene unit is an extremely important pharmacopher which exists in many natural and synthetic bioactive compounds [27]. Tranisition metal complexes of azaarene derivatives especially quinoxallin have important uses as models for bioinorganic system [28].

Experimental procedures

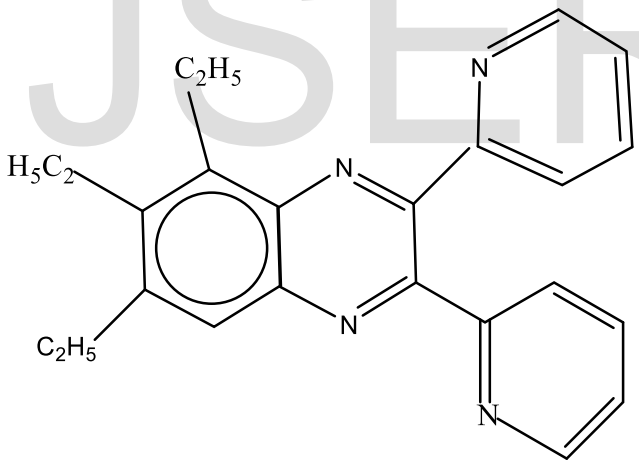
Instrumentation

Infrared measurements were carried out on a UnicamMattson 1000 FTIR spectrometer using KBr pellets . Nuclear magnetic resonance measurments were performed on a spectrospin – Bruker AC 200 MHz spectrometer samples were dissolved in DMSO of using TMS as internal reference .

Mass spectra of the compounds (c-1) and (c-2) (70 ev,EI) were carried out on a shimadzu QP-2010 plus spectrometer : Elemental analysis were performed on perkin – elmer 2400 CHN elemental analyzer.

Synthesis of 5,6,7 triethyl -2, 3-bis (2^{-} - pyridyl) quinoxaline (c-1).

(0.1 mole) of $2,2^{-}$ pyridil and (0.1 mole) of 3,4,5 triethyl 1,2 phenylendiamine were mixed together in 100ml ethanol . The mixture was heated to reflux for 8 hrs at which a brown residue was separated . the reaction mixture was cooled and the brown residue was separated by filtration . The solid was recrystallized from ethyl alcohol to give brown crystals.



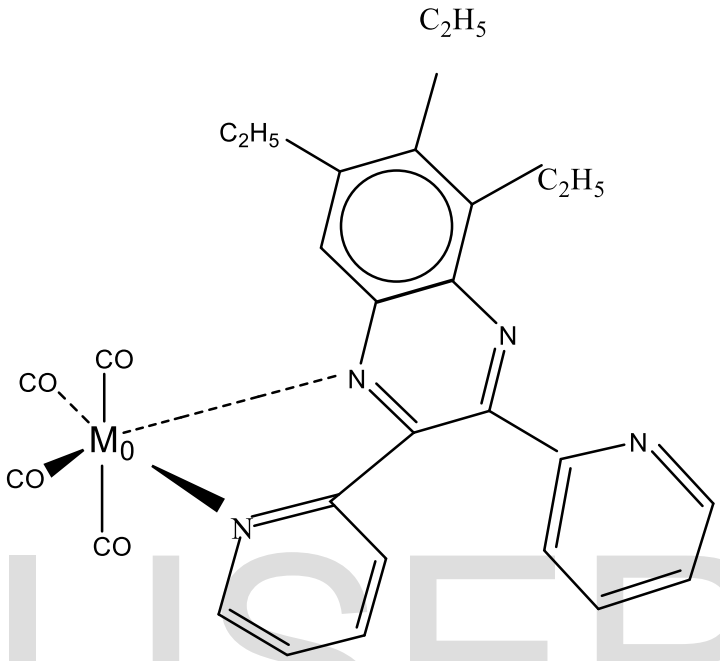
[C-1]

Reaction of $Mo(co)_6$ with (c-1)

A mixture of $Mo(co)_6$ (0.45 mmole) and (c-1) (0.45 mmole) dissolved in 25ml THF in glass (pyrix) round bottom flask (250 ml) and left in sunlight for 3 days in summer time (850-1000 w/m^2) .

The color of the solution changed from brown to dark brown with formation of brown precipitate . The solvent was evaporated

under reduced pressure using rotatory evaporator to give a solid residue which was washed several times with boiling petroleum ether (60/80) filtered off and dried to give (c-2) . The solid was recrystallized from ethanol.



structure of[c-2]complex

Results and discussion

Infrared and NMR studies of the ligand (c-1):

The infrared spectrum of the (c-1) ligand (table 2) exhibited a strong band at 1580 cm^{-1} due to ν c =n stretching frequency . Also the IR spectrum displayed a strong band at 1476cm^{-1}due to ν c= c. The ^{1}HNMR spectrum of (c-1) in deuterated DMSO showed a three multiplets at 8.12, 7.96 , 7.83 ppm due to the protons of pyridyl rings. Also the ^{1}HNMR spectrum exhibit singlet signal at 6.24 ppm is due to the protons in phenyl ring of quinoxaline as well as quartet signal at 4.30 ppm due to protons (q,2H ,CH_2-CH_3) and triplet signal at 1.81ppm due to protons (t ,3H,CH_2-CH_3) .

The mass spectra for compound (c-1) shwed the molecular ion peak at m/z 340 (83.19 %) and base peak at m/z 64 (100%) . infrared and NMR studies of (c-2)complex (table1) $Mo(co)_6$ reacted with (c-1) in THF under sunlight irradiation to form the mononuclear complex $Mo(CO)_4$ (c-1). The IR spectrum of the complex showed a pattern containing ɣc=N and ɣc=c at 1620 and 1461 cm^{-1} respectively , similar to those of the ligand with the appropriate shifts(table2). furthermore,the IRspectrum displayed a pattern of three strong and one medium bands in the terminal metal carbonyl region with symmetry $2a_1+b_1+b_2$, which indicated the presence of four CO groups in an octahedral environment (two axial and two equatorial) the ^{1}HNMR spectrum of $Mo(CO)_4$ (C-1) in DMSO , d_6 displayed three multiplets at 8.08 ,7.91 ,7.80 ppm with slight shift relative to those of the ligand due to complex formation . therefore , it can be concluded that the complex might have the Mo atom in an octahedral environment and coordinated to a (c-1) molecule in two equatorial positions as well as four CO ligands in the other two equatiorial and the two axial positions . The mass spectrum showed a molecular ion peak at m/z = 578 corres ponding to the parent peak (table2).

Table 1 : physical characterization of compounds

Compound NO	M.P.C° (color)	Solvent Yield%	MF(M.wt)	Elemental analysis Calc/found		
				C%	H%	N%
C -1	210-212 Brown	Ethanol 86	$C_{24}H_{24}N_2$ 340,467	84.66 84.20	7.10 6.79	8.22 7.96
C-2	>280 Brown	Ethanol 74	$C_{28}H_{24}O_4N_2Mo$ 578.448	63.37 62.85	4.18 3.62	4.84 4.15

Table 2 ; spectroscopic for (C-1)and (C-2)

Compound number	IR(KBr)scm^{-1}	^{1}H-NMRS(ppm)	MS;m/z(%)relevant fragments
C-1	ν C=N 1580 ν C=C 1476	8.12,7.96,7.83(m,pyridylrings) 6.24(s,phenyl ring) 4.30(q,CH_2) 1.81(t,CH_3)	340(83.19%),(M-1)339(68.10%), 312(35.29%) 284(43.08%),263(57.23%),256(28.62%) ,184(35,79%),64(100%)
C-2	ν C=N 1620 ν C=C 1461	8.08,7.91,7.80,(m,pyridylrings) 6.20(s, phenyl ring) 4.35 (q,CH_2) 1.73 (t,CH_3)	578(67.31%),552(48.24%) ,526(50.33%),1500(26.18%) ,472(71.29%) ,444(19.65%) , 367(100%).

Table 3; the inhibition zone diameters of some azaarene derivatives

Sample /standard	Inhibition zone diameter (mm/mg sample)			
	Escherichia coli (G-)	Staphylococcus Aureus (G+)	Aspergillus flavus (fungus)	Candida albicanus (fungus)
C-1	21	19	16	11
C-2	25	20	19	14
amikacin	28	18	21	16

Biological activity:

Antibacterial and antifungal of compound (c-1) and (c-2) were screened using the disc diffusion method . The experiments were performed using test bacterial organisms belonging to the gram negative and gram positive groups namely Escherichia coli and staphylococcus aureus respectively as well as candida albicans and aspergillus flavus as tested fungi .The results of antimicrobial studies are given in table 3 and figure 1.

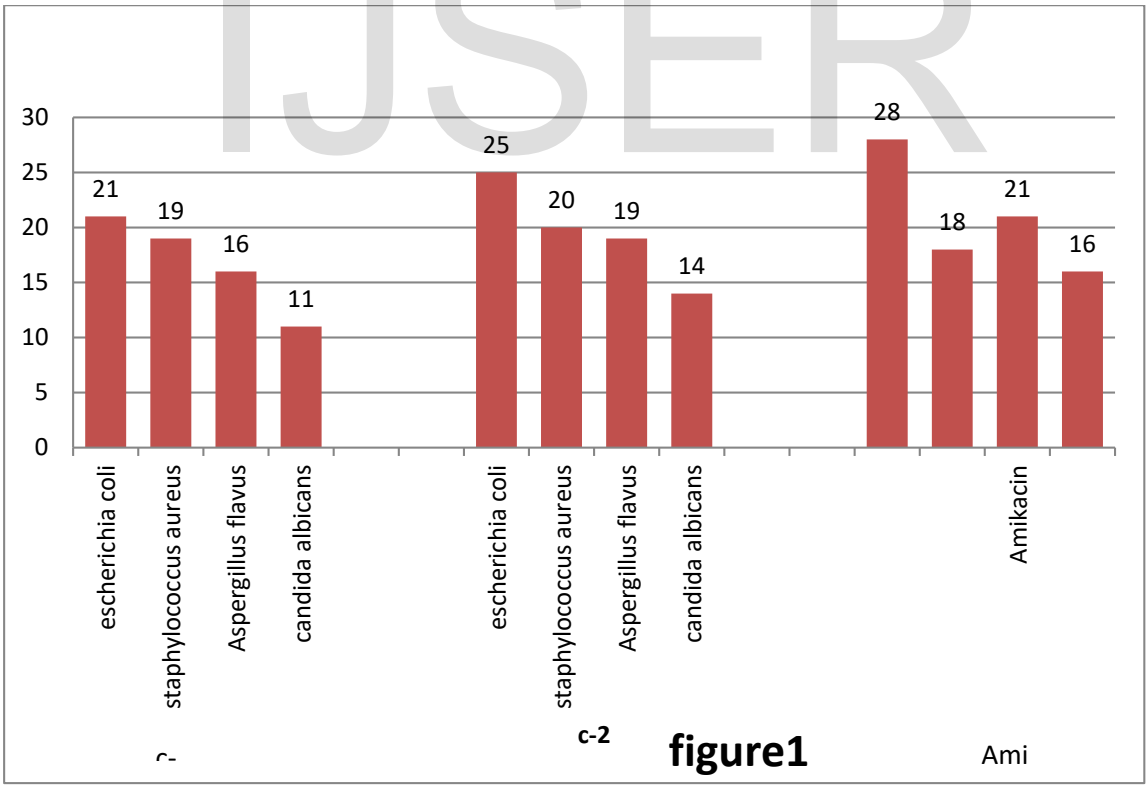


figure1

Figure 1 : the effect of compounds (c-1) , (c-2) and amikacin on inhition zone diameters against tested organisms.

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