Synthesis of New Isoxazolin - Phenoxathiin Derivatives

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Abstract

The aim of the present work is synthesis of new phenoxathiin derivatives. The 2-(oxoalken-1-yl) phenoxathiin derivatives (3a-3j) obtained from the reaction 2-acetylphenoxathiin with different aromatic aldehyde in the presence of sodium hydroxide. The reaction of 2-(oxoalken-1-yl) phenoxathiin derivatives (3a-3j) with hydroxylamine hydrochloride in ethanolic sodium hydroxide solution to get 2-(isoxazolin-3-yl) phenoxathiin derivatives (4a-4j) which substituted at position (5) in isoxazoline ring with different aryl groups according to aromatic aldehyde used in the preparation of (3a-3j). All the synthesized compounds were characterized by different identification techniques to confirm structure which has been obtained.

Keywords: Phenoxathiin, Oxoalken derivatives,Hydroxylamine,Isoxazoline.

Introduction

Phenoxathiin is given as the preferred name by Patterson and Capell [1]. The method of preparation for phenoxathiin has been used most widely encountered is the reaction between diphenyl ether and sulfur in the presence of anhydrous aluminum chloride [2,3]. Large number has been proposed for phenoxathiin and some of its derivatives, recently addition of phenoxathiincation radical to a cyclic alkene in acetonitril (MeCN) solution occurred stereo specifically to form bis(10-phenoxathiiniumyl) alkane adducts [4]. Phenoxathiin derivatives have recently gained attention owing to their fluorescent properties [5].Ionescuand Popovici [6], studied the emission properties of 2-phenoxathiinyl-5-phenyloxazole and 5-phenoxathiinyl-2-phenyloxazole derivatives by measuring the absorption and emission spectra of the derivatives above in cyclohexane and methanol. Aly and Wasfy[7], describedthat [6-(phenoxathiin-2-yl) -2,3,4,5-tetrahydropyridazine-3-one] was successively synthesized by the condensation of [4-(phenoxathiin-2-yl)-4-oxobutanoic acid] with hydrazine hydrate in boiling ethanol. Polyamides with inherent viscosities in the range of (0.5-2.9) were readily prepared by the polycondensations of phenoxathiindiamines with aromatic diacyl chlorides and aromatic diamines with new phenoxathiindiacyl chlorides[8].Tintaru, Hillebrand andThevand [9], studied the inclusion complexes of the forms of 3-carboxy-(1) and 2-carboxy-phenoxathiin (2) with β-cyclodextrin by both one- and two-dimensional NMR spectroscopy[10]. Miguel Yus [11] described that phenoxathiin was lithiated using 4,4′-di-tert-butylbiphenyl (DTBB) as the catalyst in THF at -78ºC, so intermediate was obtained by a carbon-sulfur reductive cleavage. This specie reacted with electrophiles giving, after hydrolysis with (3M) hydrochloric acid, the corresponding compound.

Experimental

FT-IR spectra were recorded on [SHIMADZU] FT-IR 8400s spectro-photometer; Solid samples were run in KBr disc, Liquid were run as smears. UV spectra were recorded on UV-Visible Spectrophotometer [SHIMADZU] UV-160A.^{1}H-NMR spectra were recorded on ultra shield 300 MHz spectrophotometer in acetone-d_6 solutions and withwithtetramethylsilane as internal standard. Melting points were determined in a [GallenKamp] melting point apparatus with sample contained in open capillary glass tube in an electrically heated metal block apparatus.

General procedure for synthesis of phenoxathiinand itsderivatives

Phenoxathiin (1) [12,13]

A mixture of 188.6 g. (1.1 mol) of phenyl ether, 25.6 g. of sulfur and 51.0g. (0.38 mol) of anhydrous aluminum chloride, maintained on steam bath for 4 hrs. The reaction mixture

was poured slowly, with stirring, into ice bath to which (25 ml.) of concentrated hydrochloric acid was added. After the two layers were separated the water layer was discarded and the (phenyl ether-phenoxathiin) layer dried overnight with calcium chloride, this mixture was distilled under reduced pressure from a 500-ml specialClaisen flask. After removal of the phenyl ether the fraction boiling at (140-160ºC/5mm.), phenoxathiin was collected at (150-152ºC/5mm.). The product was recrystallized from methyl alcohol, m.p.(56-57)ºC,yield80%.

2-acetylphenoxathiin (2) [14]

A mixture of (22.9 g, 0.114 mol) phenoxathiin, (9.7 g, 0.155 mol, 8.8 ml) acetyl chloride and carbon disulphide (120 ml) was stirred while anhydrous aluminum chloride (15.5 g, 0.116 mol) was added in small portions. The red mixture was stirred for (2hrs.) at room temperature and refluxed on the water bath for a further (24 hours), the mixture was cooled then it poured to a mixture of ice and hydrochloric acid, the product was recrystallized once from ethanol and twice from petroleum ether b.p.(80-100)ºC, m.p. 112ºC, yield 52.5%.

2-(oxoalken-1-yl) phenoxathiin derivatives (3a-3j) [15]

A mixture of (3g, 0.013 mol) 2-acetylphenoxathiin and (1.56 g, 0.0147 mol) of appropriate benzaldehyde in (80 ml) of ethanol and (1.5ml) of (1% NaOH) solution was refluxed for (2 hrs). The reaction mixture was poured into cold water, the precipitate filtered off and recrystallized from (ethanol-water) (3:1) to give (3a-3j). Table (1) represent the physical data of compounds (3a-3j).Characteristic bands of FT-IR spectra of compounds (3a-3j) are listed in Table (2).

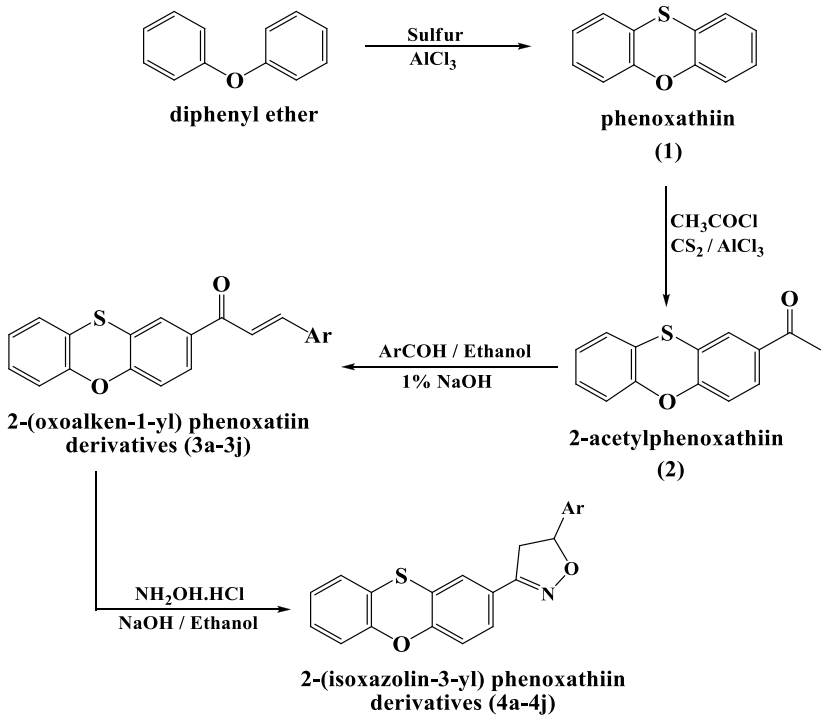
2-(5-phenylisoxazolin-3-yl) phenoxathiin derivatives (4a-4j) [16,17]

A solution of (0.33 g, 0.001 mol) of 2-(3-phenyl-1-oxypropen-1-yl) phenoxathiin (3a) and (0.07 g, 0.001 mol) of hydroxylamine hydrochloride in ethanolic sodium hydroxide solution (0.01 mol) was refluxed for (6 hrs). By concentration and cooling the product separated out, recrystallized using (ethanol-water) (3:1) to give (4a-4j) derivatives. Table (3) represent the physical data of compounds (4a-4j). Characteristic bands of FT-IR spectra of compounds (4a-4j) are listed in Table (4).

Results and Discussion

Phenoxathiin(1) was obtained from diphenyl ether and sulfur reacted in the presence of aluminum chloride, FT-IR spectrum of phenoxathiin showed a stretching band at 3063 cm^{-1} for aromatic (C-H), 1590cm^{-1} and 1450 cm^{-1} assigned to the aromatic system (C=C)str., 1219 cm^{-1} and 1026 cm^{-1} assigned to asym. and sym.(C-O-C)str. The ^{1}H-NMR spectrum showed signals between δ(6.8-7.3) ppm assigned to aromatic protons. U.V spectrum showed an absorption λ_{max} at 252 nm due to ($\pi \rightarrow \pi^*$) electronic transitions. 2-acetyl phenoxathiin (2) was prepared from reaction of phenoxathiin with acetyl chloride in dry carbon disulfide in presence of anhydrous aluminum chloride to gave compound (2) through Friedel Crafts acylation method [16].FT-IR spectrum of compound (2) showed weak bands at 3078 cm^{-1} for aromatic (C-H) str., 2962 cm^{-1}, 2931 cm^{-1} and 2877 cm^{-1} aliphatic (C-H)str. of (CH_3) acetyl group, strong bands at 1674 cm^{-1} (C=O)str., two bands at 1558 cm^{-1} and 1465 cm^{-1} aromatic system (C=C)str. and 756 cm^{-1} (=C-H) aromatic ring. The ^{1}H-NMR spectrum showed a signal at δ 2.6 ppm assigned to the three protons of the acetyl group and signals between δ (7.0-7.3) ppm assigned to aromatic protons. Through nucleophilic addition reaction of compound (2) to aldehydes and ketones, compound (2) undergoes the characteristic condensation reaction with different kinds of aromatic aldehydes in ethanol instead of 1% NaOH solution as a catalyst to afford (3a-3j) derivatives. The FT-IR spectra of compounds (3a-3j) showed absorption bands at (1674-1681) cm^{-1} (C=O)str., and (1600-1608)cm^{-1} aliphatic (C=C)str. The ^{1}H-NMR spectrum showed a signal at δ 2.6 ppm assigned to aliphatic three protons of methoxy group, signals between δ (7.0-7.3) ppm assigned to both olefinic(H1) and (H2) respectively and a signals at δ 7.5 ppm and δ 7.9 ppm assigned to aromatic protons. Table (1) represent the physical data of compounds (3a-3j). Characteristic absorption bands of FT-IR and U.V spectra of compounds (3a-3j) are listed in

Table (2). The additive property of the exocyclic (C=C) in (3) conjugated with the carbonyl group promoted us to investigate their behavior towards the action of hydroxylamine react with (3) in the presence of ethanolic sodium hydroxide solution giving 5-phenyl isoxazoline (4a-4j)as shown in the Scheme. The structure of these compounds were established from FT-IR and U.V.FT-IR spectrum showed reactivity medium weak bands at 3063 cm^{-1} and 3062 cm^{-1} aromatic (C-H)str, 1681 cm^{-1} and 1674 cm^{-1}imine (C=N)str.and bands between (817-825) cm^{-1}(N-O)str.U.V. spectrum showed an absorption λ_{max} at 252 nm due to ($\pi \rightarrow \pi^*$) electronic transitions. The ^{1}H-NMR spectra for (4e) showed a strong singlet signal at δ 2.6 ppm which was assigned to the three protons of the methoxy group. signals at δ 2.3 ppm and δ 3.9 ppm assigned to aliphatic two protons (H4) and proton (H5) of the isoxazoline ring respectively. Finally, signals between δ (7.1-7.8) ppm for aromatic protons. Table (3) represent the physical data of compounds (4a-4j). Characteristic absorption bands of FT-IR and U.V spectra of compounds (4a-4j) are listed in Table (4). Table (5) representthe^{1}H-NMR spectra for compounds (1, 2, 3e, 3h, 4eand 4j). In addition, Figs. (1, 3, 4) show FT-IR spectra for prepared comps. (2, 3a, 3f), respectively. Also, Figs. (2, 5-8) show H-NMR spectra for prepared comps. (2, 3e, 3h, 4e, 4j), respectively.



Where (Ar) is

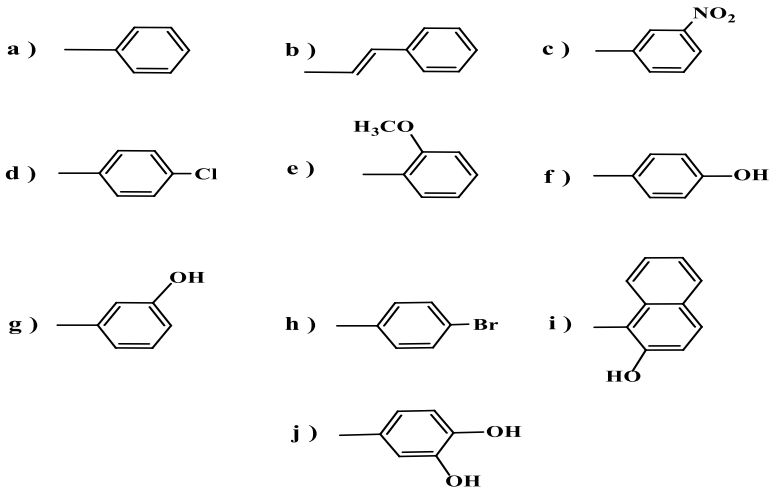
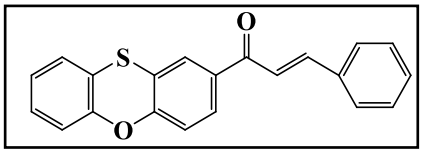


Table (1)
Represent the physical data of compounds (3a-3j).



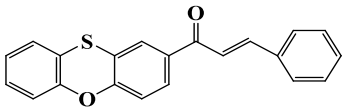
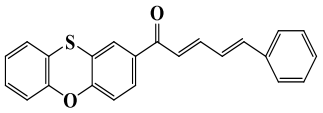
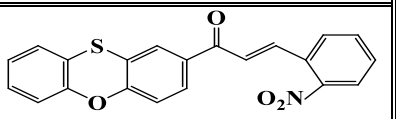
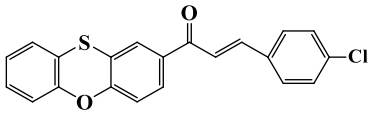
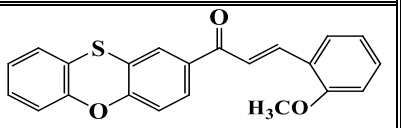
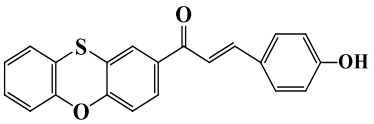
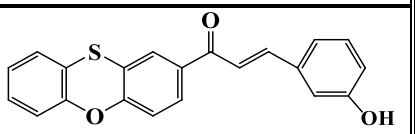
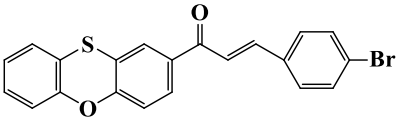
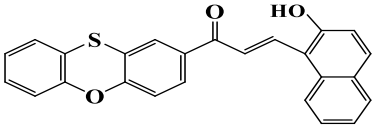
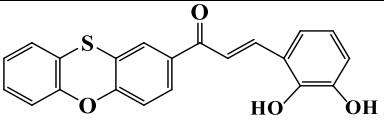
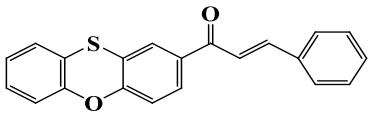
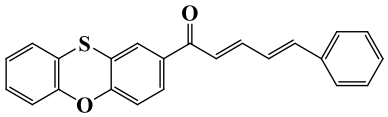
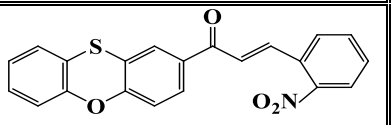
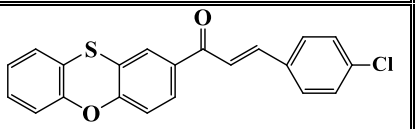
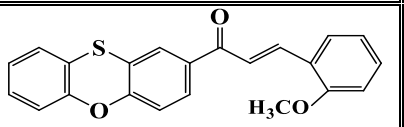
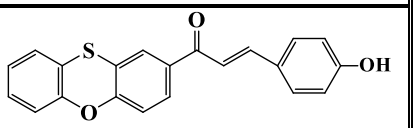
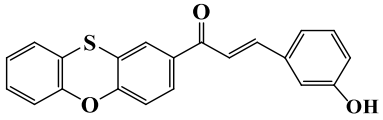
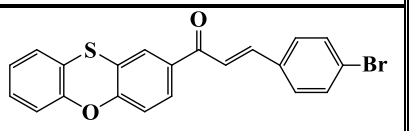
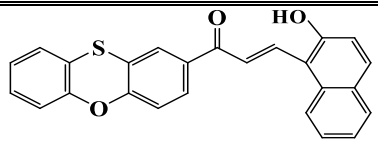
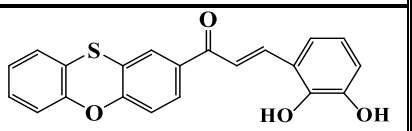
Comp. No.	*Scientific name*	*m.p. ℃*	*Yield %*	*Color of crystal*	*Chemistry structure*
3a	2-(3-phenyl-1-oxypropen-1-yl) phenoxathiin	100-102	73.0	Yellowish	
3b	2-(5-phenyl-1-oxypentadien-1-yl) phenoxathiin	102-104	53.0	Light-yellow	
3c	2-[3-(3-nitrophenyl)-1-oxypropen-1-yl] phenoxathiin	92-94	65.0	Yellow	
3d	2-[3-(4-chlorophenyl)-1-oxypropen-1-yl] phenoxathiin	94-96	45.2	Deep-yellow	
3e	2-[3-(2-methoxyphenyl)-1-oxypropen-1-yl] phenoxathiin	96-98	60.0	Deep-yellow	
3f	2-[3-(4-hydroxyphenyl)-1-oxypropen-1-yl] phenoxathiin	103-105	67.0	Reddish	
3g	2-[3-(3-hydroxyphenyl)-1-oxypropen-1-yl]phenoxathiin	102-104	67.2	Yellow-reddish	
3h	2-[3-(4-bromophenyl)-1-oxypropen-1-yl] phenoxathiin	106-108	55.9	Yellow	
3i	2-[3-(2-hydroxy-1-naphthyl)-1-oxypropen-1-yl] phenoxathiin	92-94	53.9	Black	
3j	2-[3-(3,4-dihydroxyphenyl)-1-oxypropen-1-yl] phenoxathiin	93-95	66.0	Brown	

Table (2)
Infrared absorption data for compounds (3a-3j).

Comp. No.	*Chemistry structure*	*FTIR spectral data cm^{-1}*					*U.V. (λ_{max}) nm*
		υ(C=O)	*υ(C-H) aromatic*	*υ(C-H) olefinic*	*υ(C=C)*	*Other bands*	
3a		1680	3076	3018	1608	-	249 344
3b		1681	3090	3010	1600	(C-H) olefinic 3010	248
3c		1681	3070	2977	1600	(NO_2) 1535 1350	258 300
3d		1674	3078	3009	1600	(C-Cl) 1095	249
3e		1674	3078	3008	1600	(C-O-C) 1249 1026	250 327
3f		1674	3078	3009	1600	(O-H) 3433	251
3g		1674	3075	3030	1600	(O-H) 3440	248
3h		1674	3078	3009	1600	(C-Br) 632	252
3i		1674	3078	3008	1600	(O-H) 3409	246
3j		1674	3078	3009	1600	(O-H) 3471	254 300 360

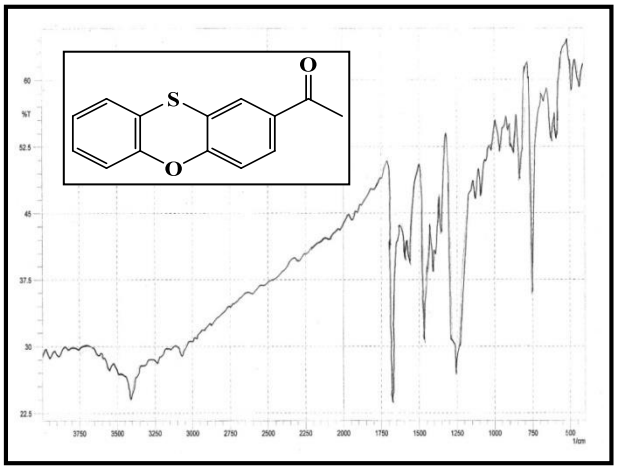


Fig.(1) FT-IR spectrum for compound (2).

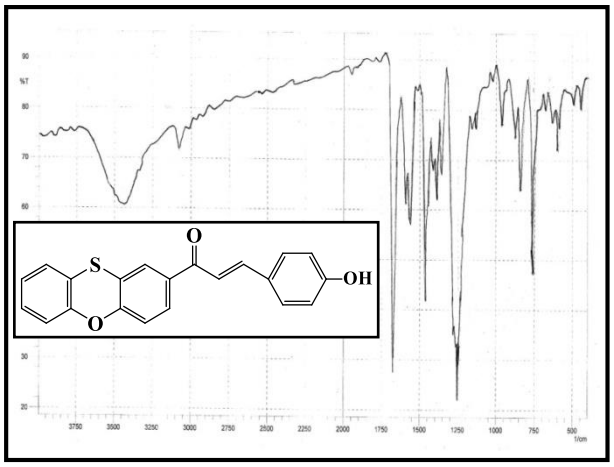


Fig.(4) FT-IR spectrum for compound (3f).

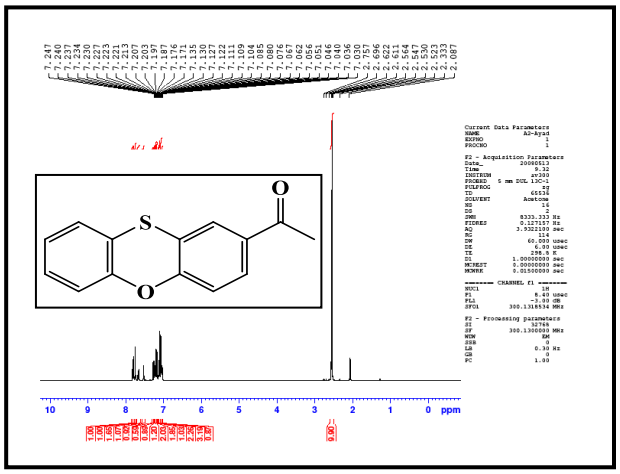


Fig.(2) ^{1}H-NMR spectrum for compound (2).

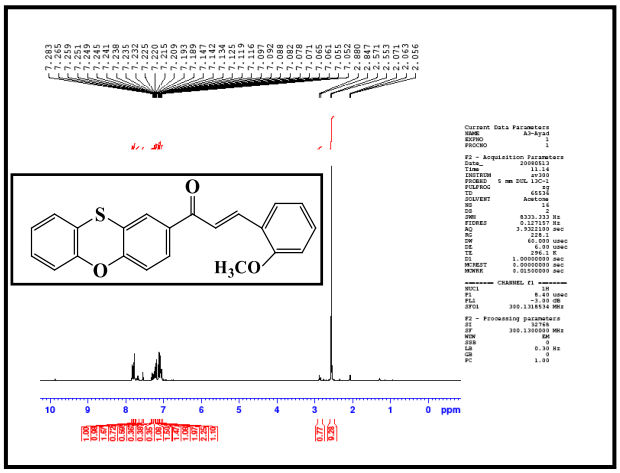


Fig.(5) ^{1}H-NMR spectrum for compound (3e).

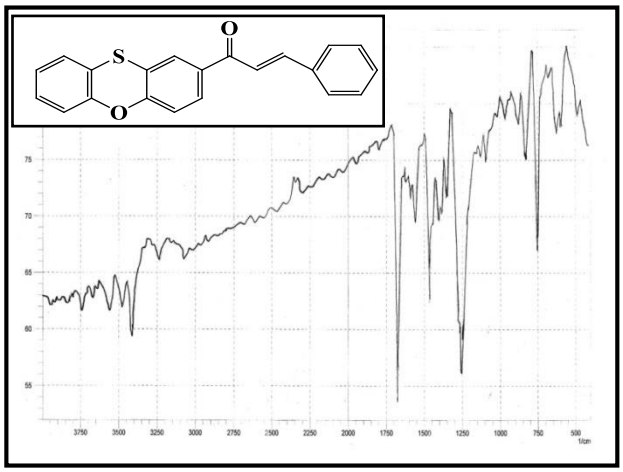


Fig.(3)FT-IR spectrum for compound (3a).

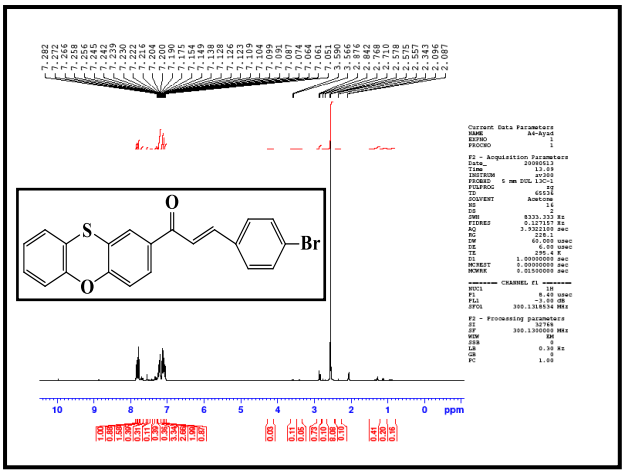
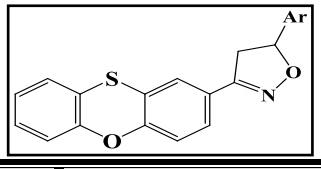


Fig.(6) ^{1}H-NMR spectrum for compound (3h).

Table (3)
Represent the physical data of compounds (4a-4j).



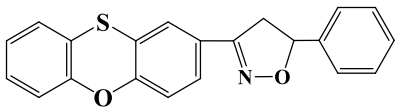
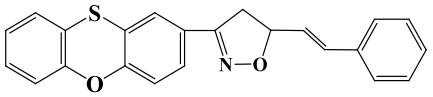
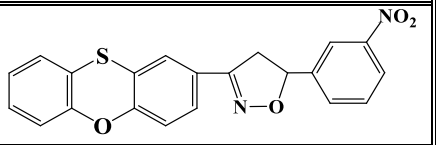
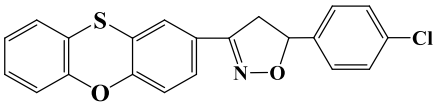
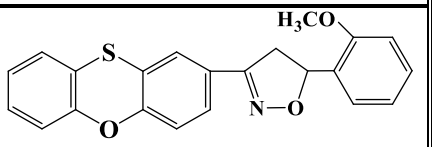
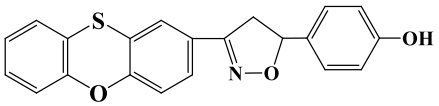
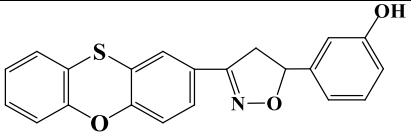
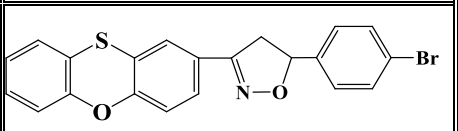
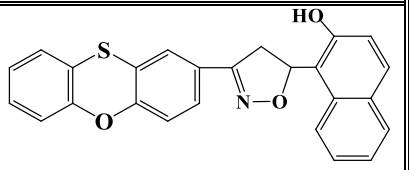
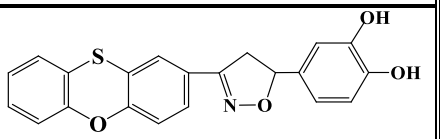
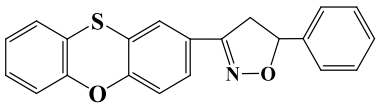
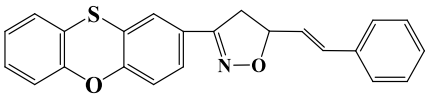
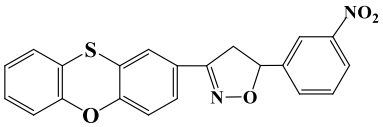
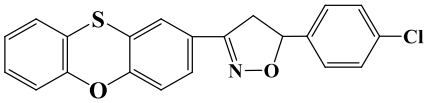
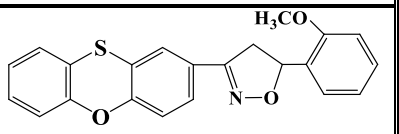
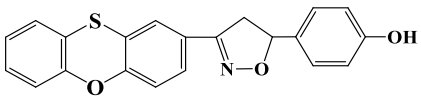
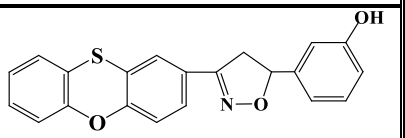
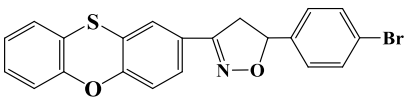
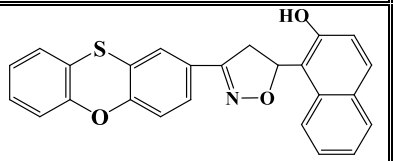
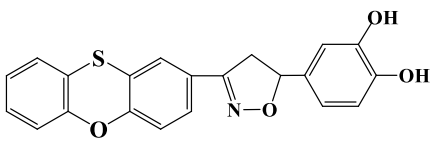
Comp. No.	*Scientific name*	*m.p. ℃*	*Yield %*	*Color of crystal*	*Chemistry structure*
4a	2-(5-phenylisoxazolin-3-yl) phenoxathiin	126-128	60.0	Yellowish	
4b	2-(5-styrenylisoxazolin-3-yl) phenoxathiin	112-114	50.0	Deep yellow	
4c	2-[5-(3-nitrophenyl) isoxazolin-3-yl] phenoxathiin	98-100	80.0	Brown	
4d	2-[5-(4-chlorophenyl) isoxazolin-3-yl] phenoxathiin	96-98	49.1	Yellow	
4e	2-[5-(2-methoxyphenyl) isoxazolin-3-yl] phenoxathiin	128-130	85.0	Deep yellow	
4f	2-[5-(4-hydroxyphenyl) isoxazolin-3-yl] phenoxathiin	110-112	47.6	Yellow	
4g	2-[5-(3-hydroxyphenyl) isoxazolin-3-yl] phenoxathiin	105-107	30.0	Yellow	
4h	2-[5-(4-bromophenyl) isoxazolin-3-yl] phenoxathiin	115-117	64.0	Yellowish	
4i	2-[5-(2-hydroxynaphthyl) isoxazolin-3-yl] phenoxathiin	143-145	66.1	Black	
4j	2-[5-(3,4-dihydroxyphenyl) isoxazolin-3-yl] phenoxathiin	165-167	70.5	Black	

Table (4)
Infrared absorption data for compounds (4a-4).

Comp. No.	*Chemistry structure*	*FTIR spectral data cm^{-1}*						*U.V. (λ_{max}) nm*
		υ(C-H) aromatic	*υ(C-H) aliphatic*	*υ(C=C) aromatic*	*υ(C=N)*	*υ(N-O)*	*Other bands*	
4a		3063	2916 2854	1600 1466	1681	825	-	244
4b		3063	2917	1600 1465	1674	818	(C-H) Olefinic 3000	244
4c		3063	2970 2924	1595 1466	1674	825	(NO_2) 1566 1358	247
4d		3063	2970 2925	1600 1465	1674	817	(C-Cl) 710	245
4e		3062	2990 2924	1595 1466	1674	825	(C-O-C) 1257 1095	247
4f		3062	2995 2940	1605 1466	1674	825	(O-H) 3402	244
4g		3063	2970 2924	1600 1466	1674	817	(O-H) 3310	243
4h		3062	2916 2880	1600 1465	1674	817	(C-Br) 640	247
4i		3062	2960 2916	1595 1465	1674	817	(O-H) 3302	244
4j		3062	2970 2924	1600 1466	1674	825	(O-H) 3310	247

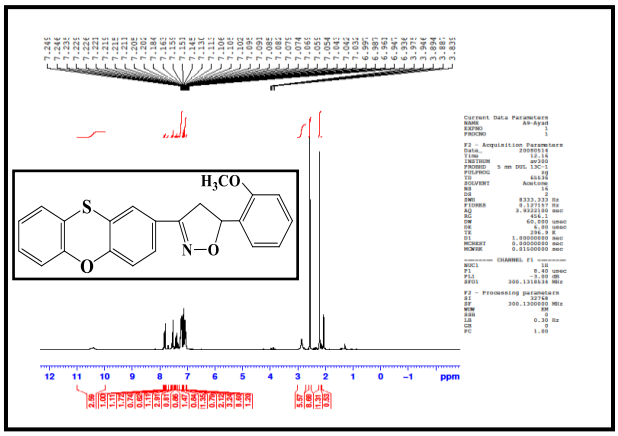


Fig.(7) ^{1}H-NMR spectrum for compound (4e).

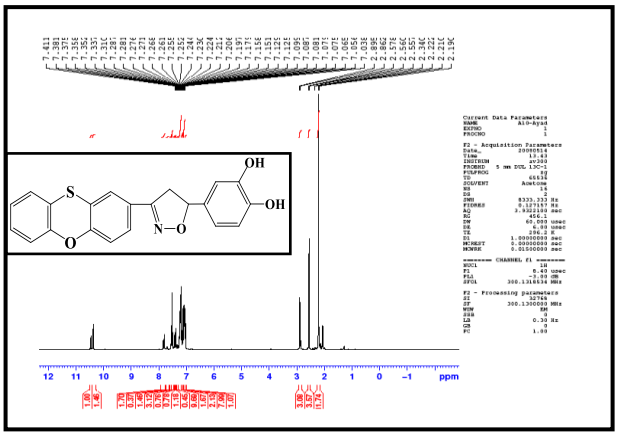
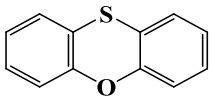
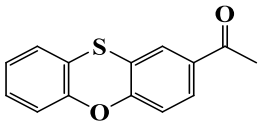
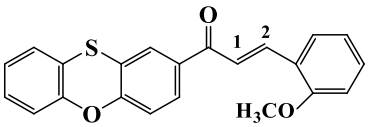
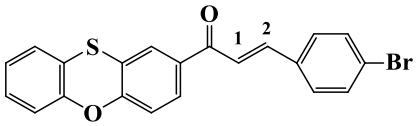
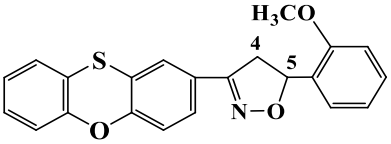
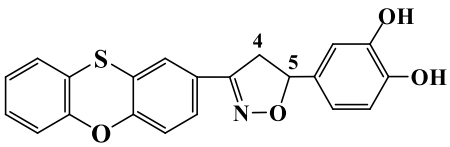


Fig.(8) ^{1}H-NMR spectrum for compound (4j).

Table (5)
^{1}H-NMR spectra for compounds (1, 2, 3e, 3h, 4e, 4j).

Comp. No.	Compound structure	δH aromatic ppm	δH other bands ppm
1		(6.8-7.3) (m,8H)	-
2		(7.0 -7.3) (m,7H)	2.6 (s,3H) acetyl protons
3e		(7.0-7.3) (m,11H)	2.6 (s,3H) methoxy protons [7.5 (s,1H) H1, 7.9 (s,1H) H2] olefin protons
3h		(7.0-7.3) (m,11H)	[7.5 (s,1H) H1, 7.8 (s,1H) H2] olefin protons
4e		(7.1-7.8) (m,11H)	2.6 (s,3H) methoxy protons [2.3 (s,2H) H4,3.9 (s,1H) H5] isoxazolin ring protons
4j		(7.0-7.8) (m,10H)	[2.6 (s,2H) H4, 2.9 (s,1H) H5] isoxazolin ring protons 10.4 (d,2H) hydroxyl protons

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الخلاصة

الهدف من هذا العمل هو تحضير مشتقات جديدةللفينوكسيثن،مشتقات لـ ٢-(أوكسو الكين-١-يل) الفينوكسيثن (3a-3j) تم الحصول عليها من تفاعل ٢-أسيتيل فينوكسيثن مع مختلف المركبات العطرية الالدهايدية وبوجود هيدروكسيد الصوديوم. المركبات (3a-3j) تم مفاعلتها مع هيدروكلوريد الهيدروكسيل أمين في محلول هيدروكسيد الصوديوم الايثانولي للحصول على مشتقات ٢-(أيزوكسازولين-٣-يل) للفينوكسيثن (4a-4j). جميع مركبات المجموعة معوضة في الموقع (٥) في حلقة الايزواوكسازولين بمجاميع أريل وحسب المركبات العطرية الالدهايدية المستخدمة في تحضير مركبات (3a-3j). كل المركبات المحضرة شخصت بتقنيات مختلفة لتاكيد التراكيب التي تم الحصول عليها.