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Synthesis of New Organophosphorus Compounds Derived from 2-Arylidenecyclohexan-1-ones

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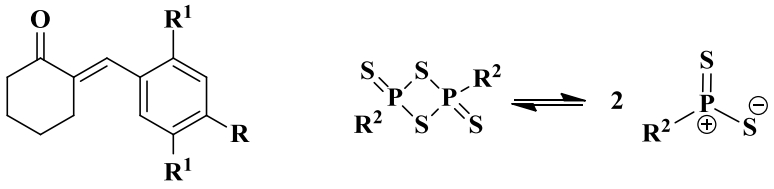
Abstract: 2-(4-Arylidene)cyclohexane-1-one derivatives react with 2,4- *bis* (phenylthio) -1,3-dithia,2,4-diphosphetane-2,4-disulphide (JR) to give a mixture of the benzodithiadiphosphi-nine -2-sulphides and dithiadispirotetradecanes. The same reaction was carried out using Lawesson's reagent to yield the 4-methoxyphenylbenzodithiaphosphinine sulfides. A putative reaction mechanism involves an initial thiation of arylidenecyclohexane-1-one derivatives then Michael addition by sulfide anion of Lawesson's reagents followed by intramolecular cyclization, and resulting in the formation of new heterocyclic compounds containing phosphorus moiety. Biological activities for some of the new compounds are also reported.

Keywords: Japanese and Lawesson's reagents; Phosphorus Compounds; Cyclohexan-1-one derivatives.

Introduction

Arylidene cyclohexanones attract great attention of many investigators effective class of α-β unsaturated carbonyl compound [1]; for synthesis of saturated and partially saturated heterocyclic ring systems.[2-4] Diverse biological and pharmacological properties were also reported for these analogues as antimicrobial [4,5], antitubercular [6], antioxidant [7], anti-angiogenic [8,9], cytotoxic [10,11], cholesterol-lowering [12], pesticidal [13], and HIV- integrate inhibitory [14] activities. Additionally, phosphorus compounds such as Japanese (JR, **2a**) and Lawesson's reagents (LR, **2b**) are considered as selective reagents in the realm of sulfur chemistry due to their ability to convert the carbonyl groups into their thiocarbonyl functions [15]. They can also be utilized in the construction of heterocycles containing either sulfur or phosphorus atoms which are of particular interest in industrial and pharmacological fields [16-19].

This together with our interest in the organophosphorus chemistry of carbocyclic and heterocyclic compounds [4,26,27] have prompted the present study directing towards investiga-tion of the behavior of 2-arylidenecyclohexanones **1a,b** with **2a**,**b** (Scheme 1). Antimicrobial properties of the newly synthesized compounds will be also considered against Gram- positive, Gram-negative and fungi.



1a; R = $N(CH_3)_2$, R^1 = H
1b; R = Cl, R^1 = H
1c; R = H, R^1 = OCH_3

2a; R^2 = SC_6H_5
2b; R^2 = 4-$C_6H_4OCH_3$

Scheme 1. Starting materials

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Experimental Section

Materials and equipment

Melting points were determined in open glass capillaries using an Electrothermal IA 9100 series digital melting point apparatus (Electrothermal, Essex, U.K.). IR spectra were recorded (KBr pellets) on a Perkin- Elmer 1650 FT-IR spectrophotometer. The ^{1}H-, and ^{13}C-NMR spectra were recorded in $CDCl_3$ on a Joel spectrometer (^{1}H:500 , ^{13}C: 125 MHz). Chemical shifts were recorded in δ values relative to TMS as internal reference. The coupling constants (*J*) are given in Hertz (Hz). Mass spectra were recorded at 70 eV on a JEOL JMS/AX-500 spectrometer.

Cyclohexanone, 4-chlorobenzaldehyde, and 4-dimethylaminobenzaldehyde were obtained from Sigma-Aldrich. Thiophenol, and anisole from Merck AR grade.

General procedure for the synthesis of 3a-c, 4a-c and 5a-b

A mixture of equimolar amounts of 2-arylidenecyclohexanone **1a**,**b** (1mmol) and 1,3,2,4-dithiadiphosphetane-2,4-disulfide **2a** /or **2b** was refluxed for 1h in 30 ml dry toluene. After removal of toluene under reduced pressure, the given crude material was subjected to column chromatography, using ethyl acetate / petroleum ether (40-60 ^{0}C) as an eluent giving **3a-c, 4a-c, 5a,b.**

4-[4-(Dimethylamino)phenyl]-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphinin-2-sulfide 3a

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 45:55 (v/v).
Yield: 60 %; mp= 171^{o}C
FT- IR (KBr) ν, cm-1: 2910, 2854 (CH_2 stretching), 1170 (P-S- stretching), 1650 (C=C, stretching), 680 (P=S, stretching).
H^{1} NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.79-1.76 (m, 2H, *J* = 2.3, CH_2), 1.90-1.88 (m, 2H, *J* = 2.3 ,CH_2), 2.51-2.86 (t, 4H, *J* =3.5, $2CH_2$), 3.00 [s, 6H, N $(CH_3)_2$], 4.39 (d, 1H, $^{3}J_{HP}$ = 4.4, HC-S-P), 6.70 - 6.67 (d, 2H**,** *J* = 8.4, aromatic**),** 7.40-7.38 (d, 2H, *J* = 8.4, aromatic**),** 7.53(d, 2H, *J* = 8.4, aromatic), 7.73-7.75 (m, 3H, aromatic)
^{13}C NMR: ($CDCl_3$, 125 MHz) (δ: ppm)34.1 (*d*, $^{2}J_{CP}$ = 29.02, HC-S-P), 22.9, 24.4, 24.8, 23.9 (CH_2), 41.7(N-CH_3), 112.7,125.8,127.1, 127.8, 128.9,131.0,132.6, 148.0 (C-aromatic).
Anal.Calc. for $C_{21}H_{24}NPS_4$ C, 56.09%, H 5.38%, N, 3.11%, P, 6.89%, S, 28.52 %. Found: C, 56.30%, H, 5.54%, N, 3.25%, P, 6.90%, S, 28.32 %.

4-[4-Chlorophenyl]-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphinin-2-sulfide 3b

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 60:40 (v/v).
Yield 62%, mp=183^{o}C.
FT-IR (KBr) ν, cm-1: 2990, 2845 (CH_2 stretching), 750(C-Cl), 665 (P=S), 1540, 1665(C=C-, stretching of aromatic), 1150 (P-S-).
H^{1} NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.71-1.63 (m, 2H, CH_2), 1.95-1.81 (m, 2H, CH_2), 2.01, 2.48 (t, 4H, *J* = 3.6, $2CH_2$), 4.21 (d ,1H, $^{3}J_{HP}$ = 3.9, CH-S-P), 6.70-6.67 (d, 2H**,** *J* = 8.4, aromatic**),** 7.40-7.38 (d, 2H, *J* = 8.4, aromatic**),**7.73-7.74 (d, 2H, *J* = 8.0, aromatic**),**7.75-7.76 (m, 3H, aromatic).
^{13}C NMR ($CDCl_3$, 125 MHz) (δ: ppm): 34.7 (*d*,$^{2}J_{CP}$ = 26.02, HC-S-P), 22.9, 24.4, 24.8, 27.4 (CH_2), 112.7,125.8, 127.3, 127.6, 128.7, 131.4, 132.4, 148.3(C-aromatic).
Anal.Calc for $C_{19}H_{18}ClPS_4$ C, 51.74%, H 4.11%, Cl, 8.04%, P, 7.02%, S, 29.08 %. Found: C,51.97%, H, 4.41%, Cl, 8.33%, P, 7.42%,S, 13.32 %.

4-[2,5-Dimethoxyphenyl]-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphinin-2-sulfide 3c

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 55:45 (v/v).
Yield 70 %, mp=178 ^{0}C.
FT- IR (KBr) ν, cm-1: 2960,2840 (CH_2 stretching), 1180 (P-S-), 1650(C=C, aromatic), 680 (P=S).
H^{1} NMR: ($CDCl_3$, 500 MHz) (δ: ppm): 1.79-1.76 (m, 2H, *J* = 2.3, CH_2), 1.90-1.88 (m, 2H, *J* = 2.3 ,CH_2), 2.51-2.86 (2t, 4H, *J* = 3.5, $2CH_2$), 3.41, 3.45 [2s, 6H, $(OCH_3)_2$], 4.52 (d, 1H, $^{3}J_{HP}$ = 4.4, HC-S-P), 6.70 - 6.67 (d, 2H**,** *J* = 8.4, aromatic**),** 7.53 (1H, s, aromatic), 7.74-7.75(d, 2H, *J* = 8.5, aromatic), 7.76-7.77 (m, 3H, aromatic).
^{13}C NMR ($CDCl_3$, 125 MHz) (δ: ppm): 28.1 (d, $^{2}J_{CP}$ = 29.02, HC-S-P), 22.9, 24.8, 23.9 (CH_2), 53.7 (OCH_3), 112.7,125.8, 127.1, 127.8, 128.9, 131.0, 132.6, 160.0 (C-aromatic).
Anal. Calc for $C_{21}H_{23}O_2PS_4$ C, 54.05%, H, 4.97%, P, 6.64%, S, 27.49 % Found : C, 54.22%, H, 4.79%, P, 6.61%, S, 27.40 %.

1,9-[4-(Dimethyamino)phenyl]-7,14-dithiadispiro[5.1.5.1]tetradecane 4a

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 40:60 (v/v).
Yield: 30%; mp= 153^{o}C.
IR (KBr) ν, cm^{-1}: 2994, 2845 (CH_2 stretching), 1630 (C=C- stretching), 1225 (CH_2SCH_2 stretching), 1609 (=CH stretching).
H^{1} NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.89-1.88 (m, 4H , $2CH_2$), 1.65-1.57(m, 4H, $2CH_2$), 2.92 (t, 4H, *J* = 3.0 ,$2CH_2$), 2.52 (t, 4H, *J* = 3.0 , $2CH_2$), 3.01, 3.10 [*s*, 12H, 2N $(CH_3)_2$], 6.71, 6.68 (2d, 4H**,** *J* = 8.4, aromatic**),** 7.45,7.43 (2d, 4H, *J* = 8.4, aromatic), 7.75(s, 1H, =CH), 7.78 (s, 1H, =CH).
^{13}C NMR: ($CDCl_3$, 125 MHz) (δ: ppm): 22.9, 24.4, 42.4(CH_2), 35.0 (spiro-C), 39.3(N-CH_3), 112.7, 125.8, 127.1, 127.8, 128.9,131.0, 132.6, 148.0 (C- aromatic).
Anal. Calc for $C_{30}H_{38}N_2S_2C$, 73.42%, H 7.80%; N, 5.71%, S, 13.07% . Found: C ,73.79%, H,7.68%, N, 5.91%, S,13.32 %.

1,9-[4-(Chloro)phenyl]-7,14-dithiadispiro[5.1.5.1]tetradecane 4b

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 35:65 (v/v).
Yield; 30%; mp =171^{o}C.

FT-IR (KBr) ν, cm-1: 2920, 2850(CH_2, stretching), 1530, 1460 (C=C-, stretching), 1230 (CH_2SCH_2, stretching), 1620 (=CH).
H^1 NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.89-1.88 (m, 2H, CH_2), 1.65-1.57 (m, 2H, CH_2), 2.92 (t, 4H, *J* = 3.0 , $2CH_2$), 3.01 [s, 6H, $N(CH_3)_2$], 6.71, 6.68 (2d, 4H**,** *J* = 8.4, aromatic**),** 7.45-7.43 (2d, 4H, *J* = 8.4, aromatic), 7.75 (s, 1H, =CH), 7.80 (s, 1H, =CH);
^{13}C NMR ($CDCl_3$, 125 MHz) (δ: ppm) : 22.9, 24.4, 24.8, 42.4(CH_2), 35.0 (spiro-C) ,112.7, 125.8, 127.1, 127.8, 128.9, 131.0, 132.6, 147.0 (C-aromatic).
Anal. Calc for $C_{26}H_{26}Cl_2S_2$ C, 65.95% , H, 5.53% ,Cl, 14.97%, S,13.54%. Found: C, 65.79%, H,5.62%, Cl,14.81%, S,13.32%.

1,9-[2,5-(Dimethoxy)phenyl]-7,14-dithiadispiro[5.1.5.1]tetradecane 4c

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 30:70 (v/v).
Yield: 30%; mp= 160 ^{o}C.
FT-IR (KBr) ν, cm-1: 2960, 2845 (CH_2 stretching);1220 (CH_2SCH_2 stretching); 1609 (=CH) ;1660 (C=C-, stretching of aromatic ring).
H^1 NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.89-1.88 (m, 4H, $2CH_2$), 1.65-1.57 (m, 4H, $2CH_2$), 2.92 (t, 4H, *J* =3.4, $2CH_2$), 2.52 (t, 4H, *J* =3.4, $2CH_2$), 3.45, 3.40 [2s, 12H, 2 $(O\text{-}CH_3)_2$], 3.56, 3.53 [2s, 12H, $2(OCH_3)_2$], 6.71, 6.68 (d, 2H**,** *J* =8.4, aromatic**),**7.35, 7.40 (2s, 2H, aromatic**),** 7.45,7.43 (d, 2H, *J* =8.4, aromatic),7.75 (s, 1H, =CH), 7.79 (s, 1H, =CH).
^{13}C NMR ($CDCl_3$, 125 MHz) (δ: ppm): 22.6, 24.8, 42.4(CH_2), 35.7(spiro-C), 56.3($O\text{-}CH_3$), 112.7, 125.8, 127.1, 127.8,128.9, 131.0, 132.6,162.0 (C-aromatic).
Anal. Calc for $C_{30}H_{36}O_4S_2$ C, 68.67%, H, 6.92%, S, 12.22%. Found: C, 68.59%, H, 6.86 %, S, 12.15%.

4-(5,6,7,8-Tetrahydro-2-(4-methoxyphenyl)-2-sulfanyl-4H-benzo[d][1,3,2] dithiaph-sphinin-4-yl)-N,N-dimethylbenzenamine 5a

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 70:30 (v/v).
Yield 62%; mp=168^{o}C.
FT-IR (KBr) ν, cm-1: 3060, 3015(C-H stretching of aromatic ring) ; 2964, 2840 (CH_2 stretching) ;1660(C=C stretching) ;675 (P=S)**.**
H^1 NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.71-1.63 (m , 2H, CH_2), 1.95-1.81 (m, 2H, CH_2), 2.01, 2.48 (2t, 4H, *J* = 3.2, $2CH_2$), 3.00 [s, 6H, N $(CH_3)_2$], 3.5 (s, 3H, O- CH_3) 4.21 (d , 1H, CH, $^3J_{HP}$ = 3.9, HC-S-P), 6.70,6.67 (2d , 4H**,** *J* = 8.4, aromatic**),** 7.40,7.38 (2d , 4H, *J* = 8.4 Hz, aromatic**).**
^{13}C NMR: ($CDCl_3$, 125 MHz) (δ: ppm)**:** 34.1 (*d*, J_{CP} = 24.8 Hz, HC-S-P), 54.0 (p-OCH_3), 22.9, 24.4, 24.8, 27.4 (CH_2), 39.3 (N-CH_3), 112.7, 125.8, 127.1, 127.8, 128.9, 131.0, 132.6, 162.0 (C-aromatic).
Anal. Calc for C_{22} H_{26} NO PS_3 C, 59. 03%, H 5.85%, N, 3.13%, P, 6.92%, S, 21.49%; Found: C, 59.45%, H, 5.65% N, 3.43%, P, 6.72%, S, 21.61 %.

4-(4-Chlorophenyl)-2-(4-methoxyphenyl)-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphin-ine-2-sulfide 5b

Eluent solution : ethyl acetate / petroleum ether (40-60 ^{0}C); 75:25 (v/v).
Yield: 62 %: mp=179^{o}C;
FT-IR (KBr) ν, cm-1: 2964; 2840 (CH_2 stretching);760(C-Cl); 660 (P=S)**.**
H^1 NMR ($CDCl_3$, 500 MHz) (δ: ppm): 1.61-1.63 (m, 2H, CH_2), 1.85-1.81 (m, 2H, CH_2), 2.01, 2.40 (2t, 4H, *J* = 3.8, $2CH_2$), 3.20 (s, 3H, OCH_3), 4.21 (d, 1H, $^3J_{HP}$ = 3.9, CH-S-P), 6.70,6.67 (2d, 4H**,** *J* = 8.4**,** aromatic**),** 7.40, 7.38 (2d ,4H, *J* = 8.4, aromatic**)**;
^{13}C NMR: ($CDCl_3$, 125 MHz) (δ: ppm): 39.3(d, J_{CP} = 34.7 Hz, HC-S-P), 52.1 (p-OCH_3), 23.1, 24.4, 24.8, 24.4 (CH_2), 112.7, 125.8, 127.1,127.8, 128.9, 132.6, 141.7, 161.9 (C-aromatic).
Anal. Calc. for $C_{20}H_{20}ClOPS_3$: C, 54.72%, H 4.59%, Cl, 8.08%, P, 7.06%, S, 21.91 %, Found: C, 54.97%, H, 4.41%,Cl, 8.23%, P,7.22%, S,21.76 %.

Biological Methods:

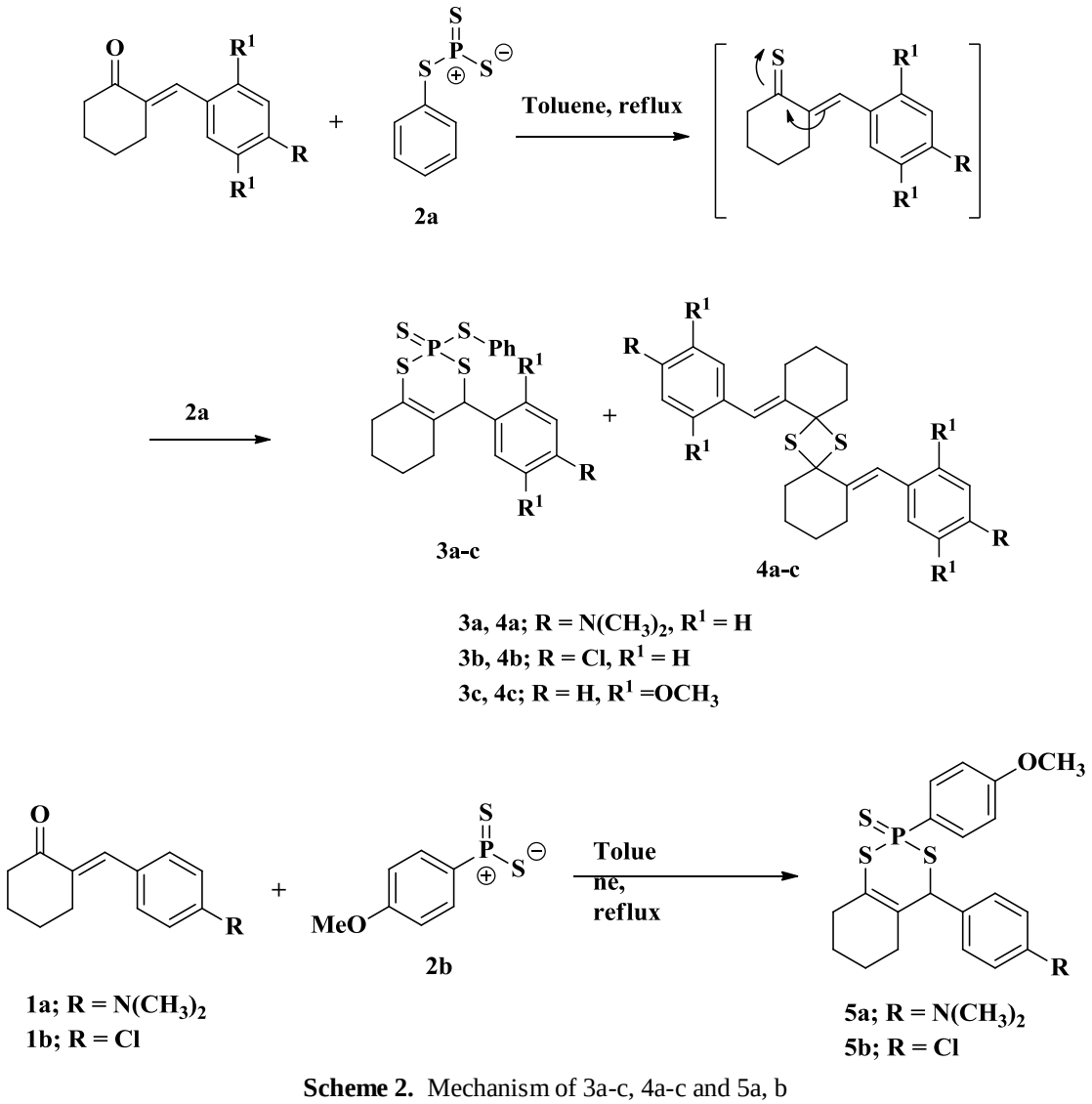
The antibacterial and antifungal activities were carried out in the Microbial Department, National Research centre, using the diffusion plate method. A solution of each of the tested compound (5, 2.5, 1 mg/ml) was placed onto sterile 5 mm filter paper discs and allowed to dry, then the discs were placed onto a plate (9 cm diameter) containing a solid bacterial medium (nutrient agar) or a fungal medium (potato dextrose agar) which has been seeded with the spore suspension of the test organism. After incubation at 37^{o}C for 24 h for bacteria (in case of fungi, at 25^{o}C for 72 h), the diameter of the clear zone of inhibition surrounding the sample is taken as a measure of the inhibitory power of the sample against the particular test organism (% inhibition = sample inhibition zone (cm) / plate diameter x 100). All measurements were done in methanol as a solvent which has zero inhibition activity. The antimicrobial activities of the tested compounds were examined with Gram-positive bacteria, *Bacillus cereus*, *Staphylococcus aureus* ATCC 6538, *Salmonella typhimurium ATCC 25566* and Gram-negative bacteria *Escherichia coli* NRRN 3008 , *Pseud*o*monas aeruginose* ATCC 10145 and fungus *Candida albicans* EMCC105. The obtained results are compared with the Cephradine antibiotics that were purchased from Egyptian markets. [28-31]

Results and Discussion

Reaction of equimolar quantities of 2-[4-dimethylaminobenzylidene]cyclohexan-1-one (**1a)**, and 2,4-*bis* (thiophenoxy)-1,3,2,4- dithiadiphosphetane -2,4-disulfide (JR, **2a**) in refluxing toluene afforded a mixture of benzodithiaphosphinin-2-sulfide **(3a**) and dithiadispiro-tetradecane (**4a**) (Scheme 2). Compounds **3b**,**c** and **4b**,**c** were similarly produced through reaction of **1b,c** and **2a**. Meanwhile, arylidenecyclohexanones (**1a,b)** reacted with 2,4-bis (methoxyphenyl)-1,3,2,4- dithiadiphosphetane -2,4-disulfide (LR, **2b**) in 1:1 molar ratio in boiling toluene giving the respective dithiaphosphetan-2,4-disulfides (**5a**,**b**).

The structure of 4[4-(dimethyamino)phenyl]-5,6,7,8-tetrahydro-4*H*-1,3,2-benzodithiaphos-phinin-2-sulfide **3a** is deduced from its spectroscopic data. ^{1}H NMR spectrum of **3a** exhibits the P-S-CH as a doublet signal (δ_H = 4.39 ppm, $^{3}J_{HP}$ = 4.4 Hz). The remaining methylene protons of benzodithia-phosphinin system were revealed at multiplet signals at δ_H = 1.79, 1.90, 2.51, 2.86.[16,20-24] ^{13}C NMR spectrum of **3a** shows the P-S-CH- at δ_C = 34.1 ppm. IR spect-rum of **3a** reveals bands at ν = 680 (P=S), 2910 (CH_2) and 1170 (P-S-) cm^{-1} [22]. Structures of **3b-c** and **4a-c** have also been supported by spectral data (^{1}H-, ^{13}C- NMR, Mass, IR). Structures of dithiaphosphininyldimethylbenzenamine (**5a**) and dithiaphosphinine-2-sulfide (**5b**) are confirmed by the presence of molecular ion peaks in their mass spectra m/z 447 and 438, respectively, in addition to compatible ^{1}H- and ^{13}C- NMR spectral data (Experimen-tal) [20, 21].

The reaction proceeded via thiation of compounds **1a,b** due to the effect of dithiadiphosphetane-2,4-disulfide **2** forming the unstable thioxo intermediates, followed by nucleophilic attack of the sulphide anion of **2a,b**, and cyclization affording isolated **3a-c** and **5a-b** (Scheme 2)**.** Whereas, formation of dithiadispiro [5.1.5.1] tetradecanes **4a-c** is due to dimerization of the dipolar form of **1a**.



Scheme 2. Mechanism of 3a-c, 4a-c and 5a, b

Antimicrobial properties

The Antimicrobial activities of compounds **3a-c** and **5a,b** were investigated against Gram-positive Gram- negative bacteria and yeast. The results (Table 1) show that the compounds are highly effective against the negative bacteria *E-coli* , *Pseudomonas aeruginose*, and *Salmonella sp*. with inhibitory power exceeding or equals to that of the reference antibiotic (Cephradine), weak activity against the yeast (*Candida albicans*). On the other hand moderate antibacterial effect was achieved against Gram-positive bacteria.

Table 1. The antibacterial and antifungal activity of the synthesized compounds

Compd.		Zone of inhibition in mm					
		Gram negative bacteria			Gram positive bacteria		*Candida*
	C*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Salmonella sp*	*Bacillus cereus*	*Staphylococcus aurous*	
Cephradine	5	15	20	15	30	30	40
	2.5	10	15	8	12	12	20
	1	---	---	--	--	--	--
3a	5	11	22	15	--	25	7
	2.5	5	10	--	--	15	--
	1	--	--	--	--	--	--
3b	5	12	15	11	10	8	13
	2.5	6	7	--	6	--	--
	1	--	--	--	--	--	--
3c	5	15	18	20	15	10	14
	2.5	10	8	--	7	---	--
	1	--	--	--	--	--	--
5a	5	8	13	10	8	7	--
	2.5	--	--	--	--	--	--
	1	--	--	--	--	--	--
5b	5	10	14	8	12	10	10
	2.5	6	--	--	--	--	--
	1	--	--	--	--	--	--

N.B. Cephradine was used as standard , *Concentration of the sample in mg/ml ; data are from single experiments and the antimicrobial properties of the test compounds are tentative.

Conclusions

From all the above it can be concluded that, the reaction of 2-(4-arylidene)cyclohexane-1-one derivatives with 1,3,2,4 –dithiadiphosphetane- 2,4-disulphides**,** affords new heterocyclic ring systems containing phosphorus moiety**.** Furthermore dithia-dispiro[5.1.5.1] tetradecanes are formed due to dimerization of 2-arylidenecyclohexanthione. The antimicrobial activity of 1,3,2-benzodithiaphosphinine-2-sulfide derivatives were examined with Gram-positive bacteria, *Bacillus cereus*, *Staphylococcus aureus* and Gram-negative bacteria *Escherichia coli* ,*Pseud*o*monas aeruginose*, *Salmonella sp* and fungus *Candida albicans*. Thus 4-[4-(dimethylamino)phenyl]-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphinin-2-sulfide, higher concentration (5 mg/ml), exhibited maximum activity against *Pseudomonas aeruginos.*, in the mean time 4-[2,5-dimethoxyphenyl]-5,6,7,8-tetrahydro-4H-1,3,2-benzodithiaphosphinin-2-sulfide exhibited maximum activity against *Salmonella sp*. Whereas,4-[2,5-dimethoxy-phenyl]-1,3,2-benzo-dithia-phosphinin-2-sulfide resulted in 50% inhibition effect of the Cephradine antibiotic against *Bacillus cereus*.

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