CHEMISTRY OF PHOSPHORUS YLIDES 20[1]
NOVEL SYNTHESIS OF PHOSPHORANYLIDENE-CYCLOBUTYLIDENE DERIVATIVES FROM THE REACTION OF N-PHENYLIMINOVINYLIDENE -, 2-OXOVINYLIDENE- AND 2-THIOXOVINYLIDENE-TRIPHENYLPHOSPHORANE WITH α-DIKETONES.

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ABSTRACT

Naphtho [2,1-b] furan -1,2-dione(**1**), isatin (**8a**), N-methylisatin (**8b**) and/or N-acetyl isatin (**8c**) can be converted by reaction with N-phenyliminovinylidene-(**2a**), 2-oxovinylidene-(**2b**) and/or 2-thioxovinylidentriphenylphosphorane (**2c**) into the corresponding phosphoranylidene-cyclobutylidene derivatives (**5a-c**) and (**9a-i**) respectively. The structure of the new cyclobutylidenes was confirmed on the bases of elemental analysis and spectral studies.

Key words : Phosphacumulenes, α-diketones, cyclobutylidenes

INTRODUCTION:

In the scope of enhanced reactivity and versatility of their nucleophilic reactions, phosphacumulenes (**2a-c**), are the most important phosphorus compounds were used recently, for the synthesis of heterocycles[1,2] . Therefore, it was of interest to study the reaction of the active phosphacumulene ylides, namely, (N-phenyliminovinylidene)- **2a**, (2-oxovinylidene)- **2b** and/or (2-thioxovinylidene)-triphenylphosphorane (**2c**) with some α-diketones, such as, naphtho[2,1-b]furan-1,2-dione (**1**) and isatins (**8a-c**) and compare the reactivity of these active phosphacumulene ylides (**2a-c**) with the reactivity of the stabilized phosphonium ylides (**6a,b**), towards the above mentioned α-diketones.

RESULTS AND DISCUSSION:

When naphtho[2,1-b]furan-1,2-dione (**1**) was treated with two mole equivalents of active phosphacumulene ylides, namely, (N-phenyliminovinylidene)-**2a**, (2-oxovinylidene)-**2b** and/or (2-thioxovinylidene)-triphenylphosphorane (**2c**) in tetrahydrofuran at room temperature for six hrs in case of **2a**, nine hrs with **2b** and/ or twelve ~~hrs with~~ **2c**, triphenylphosphine oxide together with the corresponding phosphoranylidene-cyclobutylidene derivatives (**5a-c**), were obtained repectively. Structural support for 1-[2,4-bis(phenylimino)-3-(triphenylphosphoranylidene)cyclobutylidene]naphtho[2,1-b]furan-2(1H)-one (**5a**) was based upon correct elemental analysis and spectroscopic data. The IR spectrum of 5a (in KBr, cm^{-1}) showed strong absorption bands at 1735 (C=O), 1640 (C=N), 1610 (C=P)[3] and 1440 (P-phenyl)[4] .In the ^{13}C-NMR spectrum of 5a, a signal was observed at δ 192.89 which is attributed to the carbonyl-lactone and there is no absorption band for the ketocarbonyl-function, which appeared in the starting material at δ 190.16[5] . A signal at δ 12.23 was observed in the ^{31}P-NMR of **5a** which fits with phosphorane in a four-membered ring.[6]

2-(2-Oxonaphtho[2,1-b]furan-1(2H)-ylidene)-4-(triphenylphosphoranylidene)-1,3-cyclobutanedione (**5b**) revealed the presence of strong absorption bands at 1720 (C=O, lactone), 1660 (C=O, cyclobutanedione),[7] 1620 (C=P) and 1440 (P-phenyl), in its IR spectrum. In the ^{13}C-NMR spectrum, it showed signals at δ 194.00 (C=O, cyclobutanedione). and 160.00 (C=O, lactone). Moreover, a signal at δ 8.13 was obseved in its ^{31}P-NMR.

In case of 1-[2,4-dithioxo-3-(triphenylphosphoranylidene) cyclobutylidene]naphtho[2,1-b]furan-2(1H)-one (**5c**) strong absorption bands at 1740 (C=O), 1660 (C=P), 1440 (P-phenyl) and 1200 (C=S)[4] was found in its IR spectrum. The distinguishing features of ^{13}C-NMR spectrum of **5c** were presence of signals at δ 197.02 (C=S) and 193.77 (C=O) and the ^{31}P-NMR, shift was recorded at δ 10.01.

The reaction of active phosphacumulene ylides was studied with the bifunctional isatin **8a**, too. When two mole equivalents of (N-phenyliminovinylidene)triphenylphosphorane (**2a**) was allowed to react with one mole of isatin **8a** in tetrahydrofuran at ambient temperature for three hrs, the corresponding 1-hydro-3-[2,4-bis-(phenylimino)-3-(triphenylphosphoranylidene)cyclobutylidene]-2-indolinone (**9a**) and triphenylphosphine oxide were isolated. Carrying out the reaction using four moles of the phosphorane **2a** instead of two, led to the formation of the same phosphoranylidene-cyclobutylidene **9a**, together with triphenylphosphine oxide. The structure of compound **9a** was verified through elemental analysis and spectroscopic results. The IR spectrum showed bands at 3421 (NH), 1716 (C=O, lactam), 1620 (C=P) and 1440 (P-phenyl) cm^{-1}. The ^{1}H-NMR of **9a** showed signals at δ 4.4 (H, NH, s) exchangeable with D_2O and 7.7-7.5 (29H, aromatics, m). Its ^{31}P-NMR shift recorded at δ 15.45.

When isatin **8a** was treated with (2-oxovinylidene)-**2b** or (2-thioxovinylidene)-triphenylphosphorane (**2c**), in dry boiling tetrahydrofuran for six hrs in case of **2b** and/or ten hrs with **2c**, orange and brown crystals of **9b** and **9c** were obtained respectively. The IR spectrum of 1-hydro-3-[2,4-dioxo-3-(triphenylphosphoranylidene)cyclobutylidene]-2-indolinone (**9b**) revealed the presence of strong absorption bands at 3400 (NH) 1720 (C=O, lactam), 1640 (C=O, cyclobutanedione),[7] 1620 (C=P) and 1440 (P-phenyl) Presence of carbonyl groups in **9b** was also attested by signals at δ 198.5 (C=O, cyclobutanedione) and 179.4 (C=O, lactam), in its ^{13}C-NMR spectrum. Moreover, ^{1}H-NMR showed signal at δ 4.25 (H, NH, s) exchangeable with D_2O and 7.7-7.4 (19H, aromatics, m). The ^{31}P-NMR shift recorded for compound **9b** was δ 11.50. On the other hand, absorption bands were shown by the IR spectrum of 1-hydro-3-[2,4-dithioxo-3-(triphenylphosphoranylidene)-cyclobutylidene]-2-indolinone (**9c**) at 4321, 1718, 1440 and 1184 which were attributed to the N-H, C=O, P-phenyl and C=S groups respectively. The ^{1}H-NMR spectrum of **9c** disclosed the presence of signal at δ 4.8 (H, NH, s) exchangeable with D_2O.

The reaction of N-methyl isatin and N-acetyl isatin (**8b,c**) was also performed with the active ylides (**2a-c**). The reaction was stirred in THF at room temperature for three hrs in case of **2a**, six hr with **2b** and/or ten hr with **2c**. The phosphoranylidene-cyclobutylidene derivatives (**9d-i**) were isolated together with triphenylphosphine oxide. Analytical and spectroscopic data for these compounds are recorded in Tables (I) and (II).

CONCLUSION

It could be concluded that the reaction of active phosphacumulene ylides (**2a-c**), with α-diketones **1** and **8a-c** occurs by [2+2]-cycloaddition of the reactive carbonyl group, rather than the lactone[5,8] in naphtho[2,1-b]furan-1,2-dione (**1**) or lactam[9] in isatins **8a-c**. Initial nucleophilic attack by the carbanion centre in the active phosphacumulene ylides (**2a-c**) furnishes the oxaphosphetane **3**, as an intermediate.[10] Expulsion of triphenylphosphine oxide from **3** affording the unstable ketene **4**,[11] which is followed immediately by [2+2]-cycloaddition to a second molecule of the active phosphacumulenes **2**, giving the four-membered ring phosphoranylidene-cyclobutylidenes **5a-c** and **9a-I** (scheme 1). Besides, the difference in the nucleophilic character of (N-phenyliminovinylidene)-**2a**, (2-oxovinylidene)-**2b** and/or (2-thioxovinylidene) triphenylphosphorane (**2c**) can be noticed, too (**2a**>**2b**>**2c**).[12] While ,(N-phenyliminovinylidene)triphenylphosphorane **2a** reacts smoothly with **1** and **8a-c**, the oxo- and thioxo-analogue react less rapidly, respectively. On the other hand, we have previously reported[13]that the reaction of the stabilized phosphonium ylides, namely, methoxy-**6a** and/or ethoxycarbonylmethylenetriphenylphosphorane (**6b**) with naphtho[2,1-b]furan-1,2-dione (**1**), afforded the α,β-unsaturated compounds **7a,b**. Therefore, it could be concluded that the active and stabilized phosphonium ylides behave differently towards α-diketones. These reactions represents a convenient method for the preparation of the cyclobutylidene derivatives **5a-c, 9a-i**, by one step process, and can be considered as a new trend supplements to the wide utilization of active phosphacumulenes in preparative work.[13]

EXPERIMENTAL

All melting points are uncorrected. The solvents were dried and distilled by usual techniques. Reactions were carried out under nitrogen atmosphere. Elemental analyses were carried out at the "Microanalysis Department", National Research Center. The IR spectra were measured in KBr, on a Perkin-Elmer infracord Spectrometer Model 157 (Crating). The ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Spectrometer at 90 MHz, using TMS as an internal reference. ^{31}P-NMR spectra were run, relative to extermal H_3PO_4 (85%), with a Varian FT-80 Spectrometer, Mass Spectra were obtained on a Varian MATCH-4B instrument.

The reaction of naphtho[2,1-b]furan-1,2-dione(1)with (N-phenyliminovinylidene)-2a,(2-oxovinylidene)-2b, and/or (2-thioxovinylidene)-triphenylphosphorane(2c).Preparationof the new phosphoranylidene-cyclobutylidene derivatives (5a-c).

To a solution of naphtho[2,1-b]furan-1,2-dione (**1**)[14] (0.01 mol) in 20 ml of tetrahydrofuran was added dropwise, with stirring at room temperature, a solution of (N-phenyliminovinylidene)- 2a,[15] (2-oxovinylidene)- **2b**[16] and/or (2-thioxovinylidene)-triphenylphosphorane (**2c**)[16] (0.02 mol) in 30 ml THF. The reaction mixture was left for six hrs in case of **2a**, nine hrs with **2b** and/or twelve hrs with **2c**, during which the colour was changed from orange to brown. After THF has been distilled off under reduced pressure, the residue that left behind was dissolved in 20 ml of chloroform followed by addition of 20 ml of n-hexane, and the new solution was left overnight in the refrigerator. The precipitate that formed was filtered off and crystallized from the appropriate solvent to give phosphoranylidene-cyclobutylidene derivatives (**5a-c**). The chloroform/n-hexane filterate was chromatographed on alumina, affording triphenylphosphine oxide, m.p. and mixed m.p. 151°C[17].. Yields, analytical and physical data are shown in Table (I) and (II)

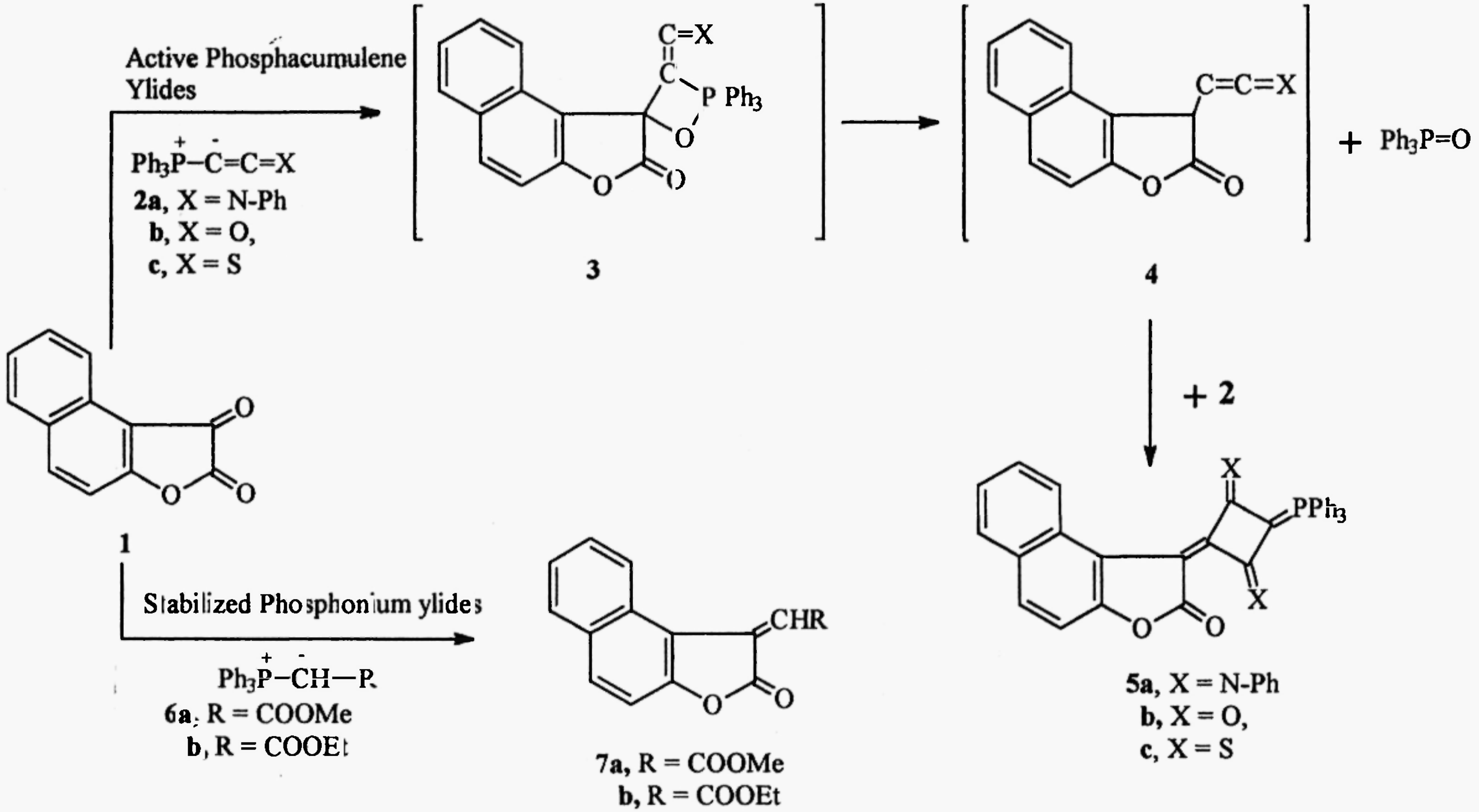
.The reaction of isatin (8a) with (N-phenyliminovinylidene)-triphenylphosphorane (2a). Synthesis of 1-hydro-3-[2,4 –bis-(phenylimino)-3-triphenylphosphoranylidene)cyclobutylidene]-2-indolinone (9a)

To a solution of isatin (**8a**) (0.01 mol) in 20 ml THF, was added dropwise at room temperature, a solution of (N-phenyl-iminovinylidene)triphenylphosphorane (**2a**) (0.02 mol) in 20 ml THF. The reaction mixture was stirred for three hrs, during which the colour changed from orange to brown . After the solvent was distilled off, The residue that left behind , was crystallized from benzene to give the phosphoranylidene-cyclobutylidene (9a).

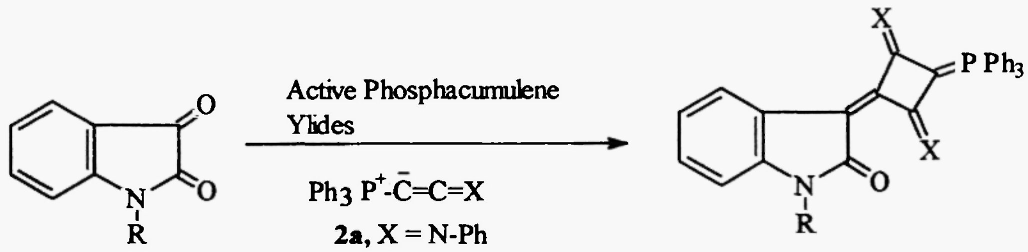
When the reaction was performed using one mole of the isatin (**8a**) and four moles of the phosphorane (2a). The same phosphoranylidene-cyclobutylidene **9a**, together with triphenylphosphine oxide were obtained. Yields, analytical and physical data of compound (**9a-i**) are shown in Table (I) and (II) .

Table (I) : ***Physical and Analytical data for Phosphoranylidene Cyclobutanediones (5a-c) and (9a-l)***

No	Mol.wt	m.p° C	Yield% crystallization	Analyses Calc / Found				
				C	H	N	P	S
5a	674		80%	81.89	4.59	4.15	4.59	-
	$C_{46}H_{31}N_2O_2P$	194	Ethanol	81.75	4.62	4.05	4.62	-
5b	524		70%	77.86	4.00	-	5.91	-
	$C_{34}H_{21}O_4P$	160	Ethanol	77.75	4.13	-	5.80	-
5c	556		65%	73.38	3.77	-	5.57	11.51
	$C_{34}H_{21}O_2PS_2$	232	Ethanol	73.53	3.80	-	5.62	11.70
9a	623		75%	80.89	4.82	6.74	4.98	-
	$C_{42}H_{30}N_3OP$	300	Ethanol	80.75	4.53	6.84	4.95	-
9b	473		80%	76.10	4.23	2.96	6.55	-
	$C_{30}H_{20}NO_3P$	190	chloroform/ Pet.ether	76.32	4.12	2.75	6.46	-
9c	505		75%	71.29	3.96	2.77	6.14	12.67
	$C_{30}H_{20}NOPS_2$	175	Ethyl acetate/ Pet.ether	70.15	3.76	2.56	6.02	12.58
9d	637		72%	81.00	5.01	6.59	4.86	-
	$C_{43}H_{32}N_3OP$	210	chloroform/ Pet.ether	80.52	5.25	6.65	4.65	-
9e	487		75%	76.38	4.51	2.87	6.36	-
	$C_{31}H_{22}NO_3P$	145	chloroform/ Pet.ether	76.23	4.50	2.66	6.25	-
9f	519		80%	71.67	4.23	2.69	5.97	12.33
	$C_{31}H_{22}NOPS_2$	190	Ethyl acetate /n-hexane	71.58	4.43	2.57	5.85	12.22
9g	665		75%	79.39	4.81	6.31	4.66	-
	$C_{44}H_{32}N_3O_2P$	190	Benzene/ Pet.ether	79.26	4.70	6.20	4.54	-
9h	515		79%	74.56	4.27	2.71	6.01	-
	$C_{32}H_{22}NO_4P$	200	Benzene/ Pet.ether	74.73	4.16	2.56	6.14	-
9i	547		65%	70.20	4.02	2.55	5.66	11.70
	$C_{32}H_{22}N_2O_5PS_2$	165	Methylene chloride/ n-hexane	70.42	4.33	2.45	5.54	12.55


Active Phosphacumulene Ylides
$Ph_3\overset{+}{P}-\overset{-}{C}=C=X$
2a, X = N-Ph
b, X = O,
c, X = S
C=X
P Ph3
O
3
C=C=X
4
+ Ph3P=O
+ 2
X
PPh3
5a, X = N-Ph
b, X = O,
c, X = S
1
Stabilized Phosphonium ylides
$Ph_3\overset{+}{P}-\overset{-}{C}H-R$
6a, R = COOMe
b, R = COOEt
CHR
7a, R = COOMe
b, R = COOEt

(Scheme 1)



8a, R = H
b, R = Me
c, R = COMe

9a, R = H X = N-Ph
b, R = H X = O
c, R = H X = S
d, R = Me X = N-Ph
e, R = Me X = O
f, R = Me X = S
g, R = COMe X = N-Ph
h, R = COMe X = O
i, R = COMe X = S

Scheme 2

Table (II) : ***NMR & IR Data for Phosphoranylidene Cyclobutanediones (9d-i)***

Cpd No	I.R	NMR ^{1}H-NMR	 ^{31}P-NMR	 ^{13}C-
9d	1716 (C=O), 1436 (P-phenyl)	2.8 (s, 1H, N-CH$_3$) 7.2-7.7 (m, 29H, Ar)	δ 13.94	δ 179 (C=O)
9e	1704 (C=O), 1440 (P-phenyl)	3.2 (s, 3H, CH$_3$) 7.3-7.9 (m, 19H, Ar)	δ 15.81	δ 193(C=O, lactone,178.5 (C=O, cyclobutandione)
9f	1740 (C=O), 1440 (P-phenyl), 1335 (C=S)	3.7 (s, 3H, CH$_3$) 7.3-8.3 (m, 19H, Ar)	δ 25.57	δ 198(C=S) δ 193(C=O)
9g	1718 (C=O), 1645 (C=N), 1438 (P-phenyl)	2.9 (s, 3H, COCH$_3$) 7-7.8 (m, 29H, Ar)	δ 16.36	—
9h	1700 (C=O, lactone), 1633 (C=O, cyclo)	2.7 (s, 3H, COCH$_3$)	δ 20.82	δ165(C=O, cyclobutandione, δ165 (C=O, lactone
9i	1680 (C=O), 1436 (P-phenyl), 1160 (C=S)	3.7 (s, 3H, CH$_3$) 7-7.4 (m, 19H, Ar)	—	δ192(C=S), δ168(C=O)

Reaction of (2-Oxovinylidene)- 2b and/or (2-Thioxovinylidene)-triphenylphosphorane (2c) with Isatin 8a. Synthesis of Phosphoranylidene-cyclobutylidene Derivatives 9b and c.

A mixture of isatin (**8a**) (0.01 mol), (2-oxovinylidene)-**2b** and/or (2-thioxovinylidene)-triphenylphosphorane (**2c**) (0.02

mol) in THF (40 ml) was refluxed for six hrs in case of **2b** and/or ten hrs with **2c**. THF was distilled off and the residue was crystallized from benzene to give the cyclobutylidene derivatives **9b,c**, respectively. The benzene filterate, afforded upon concentration and addition of n-hexane, triphenylphosphine oxide.

When the reaction was performed using four moles of the phosphorane (**2a**, b and **c**) and one mole of the isatin (**8a**) the phosphorane reacted with only one carbonyl group in isatin (8a) together with unchanged phosphorane(**2a**, b and **c**) were obtained.

The Reaction of N-Methyl Isatin 8b and/or N-Acetyl Isatin 8c with Phosphacumulenes 2a-c. Preparation of Phosphoranylidene-cyclobutylidenes 9d-i.

A solution of N-methyl isatin **8b** and/or N-acetyl isatin **8c** (0.01 mol) in 20 ml of tetrahydrofuran was added dropwise with stirring, to a solution of the active phosphacumulene ylides **2a-c** (0.02 mol) in 30 ml THF. The reaction mixture was kept at room temperature for three hr in case of **2a**, six hr with **2b** and/or ten hr with **2c**. After the solvent was distilled off, the residue was dissolved in 20 ml chloroform followed by addition of 30 ml n-hexane and the new solution was left overnight in the refrigerator. The precipitate that formed was filtered off and crystallized from the appropriate solvent.

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Received on March 7, 2002