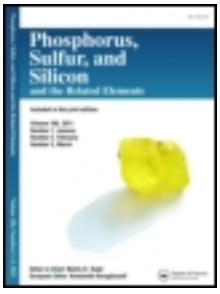

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PHOSPHORYLATION OF 5-ARYLMETYLIDENE-1-MORPHOLINOCYCLOPENTENES

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PHOSPHORYLATION OF 5-ARYLMETYLIDENE-1-MORPHOLINOCYCLOPENTENES

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The phosphorylation reaction of 5-arylmethylidene-1-morpholinocyclopentenes with various phosphorus (III) and (V) halides was studied. It was shown that the enamines react with phosphorus (III) halides giving stable halo- and dihalophosphines which are key substances for further synthesis.

Hydrolysis of the phosphorylated enamines does not afford the expected phosphorylated ketones, decomposition being observed in acidic media.

Keywords: enamines; phosphorylated enamines; 5-benzylidene-1-morpholinocyclopentene

INTRODUCTION

As many electron-rich unsaturated substances, enamines can be readily C-phosphorylated with phosphorus(III) halides affording dihalo- or halophosphines, depending on stoichiometries used. The latter are valuable starting materials for the synthesis of acyclic and cyclic derivatives of a wide variety of phosphorus-containing compounds /1/.

In the case of highly reactive enamines, the resulting halophosphines usually have a very labile C-P bond, and thus are difficult to prepare and handle. For example, halophosphines resulting from phosphorylation of cyclopentanone derived enamines are unstable and cannot be used as syn-

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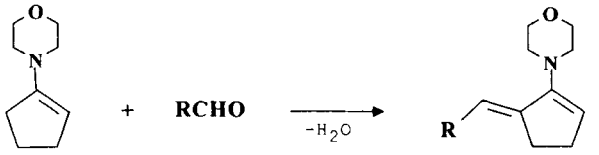
thetic intermediates /2/. However, it was reported that cyclopentanone derived enamines possessing an electron-withdrawing diphenylthiophosphoryl group can be phosphorylated smoothly to give stable dichlorophosphines which were shown to react with different nucleophiles without cleavage of the C-P bond /3/. This fact prompted us to assume that less nucleophilic enamines derived from 2-arylmethylidene substituted cyclopentanones could also be suitable substrates for phosphorylation and would hopefully lead to stable dihalo- and halophosphines.

RESULTS AND DISCUSSION

5-Arylmethylidene-1-morpholinocyclopentenes **2** were prepared using the method described for 2-benzylidenecyclopentanone /4/ which we modified to afford enamines.



1 **2**

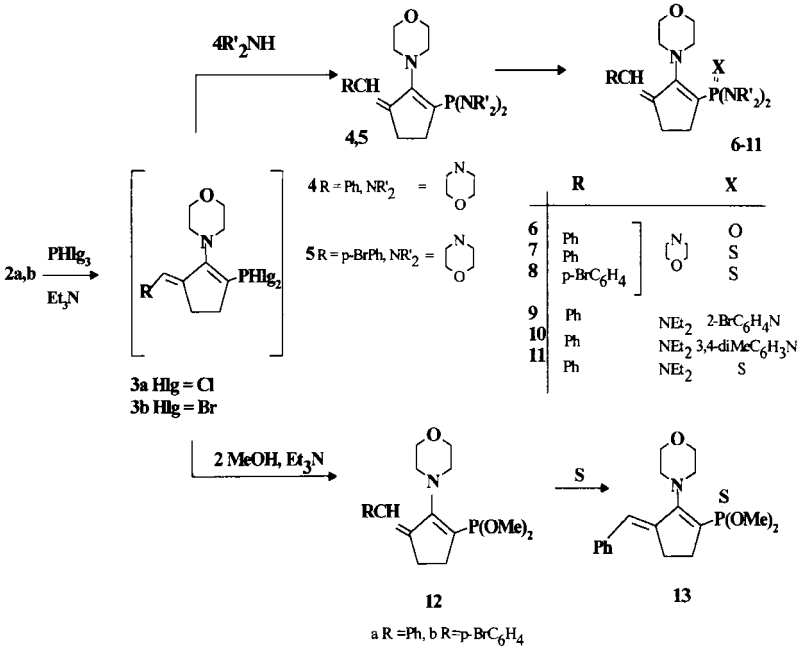
R = Ph (a), p-BrC$_6$H$_4$ (b), p-Me$_2$NC$_6$H$_4$ (c)

5-Arylmethylidene-1-morpholinocyclopentenes were easily phosphorylated with an eqiumolar amount of phosphorus trichloride or tribromide in the presence of a base in ether, dichloromethane, or benzene to give dihalophosphines **3**.The reaction was shown to be complete in several minutes by ^{31}P-NMR, no by-products being observed in the spectra. Dichloro- and dibromophosphines **3** are crystalline, highly hydrolyzable compounds which we failed to isolate in pure analytical form. Because of this, the solutions of dichlorophosphines **3** obtained were used for further synthesis without additional purification.

Dichlorophosphines **3** reacted readily with secondary amines giving stable diamidophosphonites, some of them (**4,5**) were isolated as individual

compounds while the others were oxidized to phosphorus(V) derivatives **(6–11).**

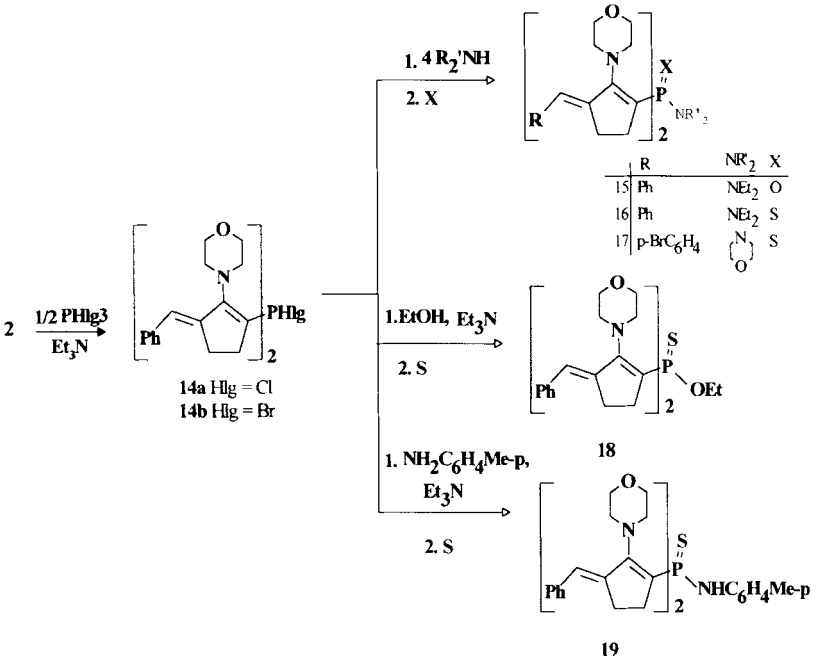
Treatment of the dichlorophosphines **3** with methanol in the presence of triethylamine resulted in the formation of phosphonites **12.** They represent viscous liquids and can be purified by distillation under high vacuum. Judging from their ^{31}P NMR spectra, the yields are high as only signals of the phosphonites **12** being observed. Solutions of **12** can be used for further transformations without any additional purification. Thus, the thiophosphonate **13** was prepared starting from **3**without isolating the intermediate phosphonite (scheme 1).



SCHEME 1

The enamines **2** react also with phosphorus (III) halides in a 2 :1 molar ratio to give halophosphines **14.** In this case the reactivity of phosphorus trichloride and phosphorus tribromide differed appreciably. Thus, the reaction with phosphorus tribromide in the presence of triethylamine in benzene was complete within 1 hr, while the analogous reaction with

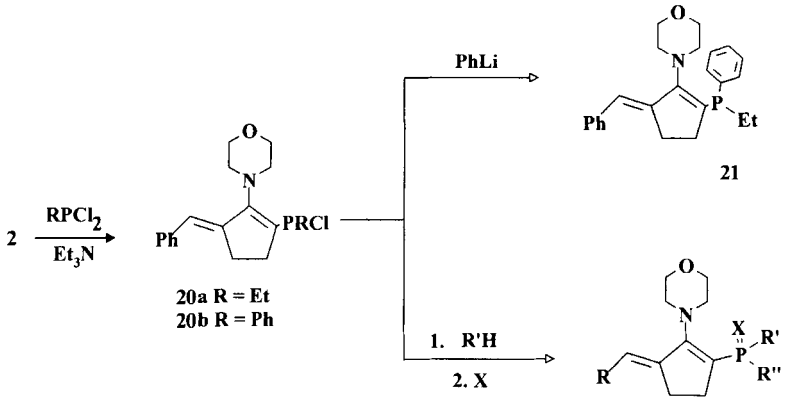
phosphorus trichloride required 4 days for completion. Both reactions proceeded selectively: only the ^{31}P-NMR signals corresponding to halophosphines **14** were observed in the reaction mixtures. They were directly used for further syntheses. The halophosphines **14** reacted easily with alcohols, secondary amines, and anilines in the presence of triethylamine. The intermediate trivalent phosphorus compounds were oxidized to pentavalent derivatives using elemental sulfur or hydrogen peroxide to give compounds **15–19** (scheme 2).



SCHEME 2

Phosphonous acids chlorides – dichlorophenylphosphine and dichloroethylphosphine can also be used successfully to phosphorylate the enamines **2.** Reaction of the enamines with the dichlorophosphines in toluene, dichloromethane, or hexane in the presence of triethylamine proceeded to completion within several days at 20 °C giving chlorophosphines **20.** The chlorophosphines **20,** like compounds **3,** are highly hydrolyzable substances. We only managed to isolate ethylchlorophosphine **20a** in analytically pure form. Compounds **20** are typical phos-

phonic acid chlorides which again can be used as key intermediates for the synthesis of a wide variety of P-substituted enamine derivatives. We carried out reactions of **20** with secondary amines, alcohols, and phenyllithium. The reaction products were then oxidized into pentavalent phosphorus derivatives to yield compounds 21 and 22 (scheme 3). They were easily isolated and purified as stable solids, although they were highly hygroscopic in some cases.

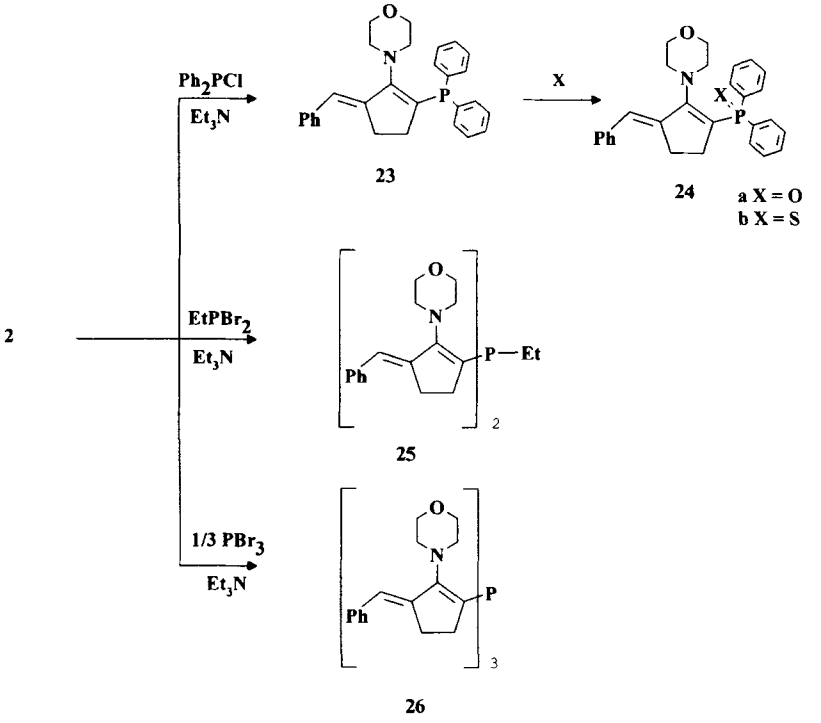


	R	R'	R''	X
a	Ph	Et	N NPh	O
b	Ph	Et	N O	O
c	Ph	Ph	N O	S
d	Ph	Ph	OMe	S
e	$pBrC_6H_4$	Ph	OMe	S

SCHEME 3

Reaction between enamines **2** and halophosphines or phosphorus tribromide can be used in the synthesis of tertiary phosphines. One, two, and three enamine residues were attached at a phosphorus atom. Thus, chlorodiphenylphosphine reacts with the enamine **2** in pyridine giving phosphine **23.** Compound **23** was readily oxidized by elemental sulphur or hydrogen peroxide affording derivatives **24.**

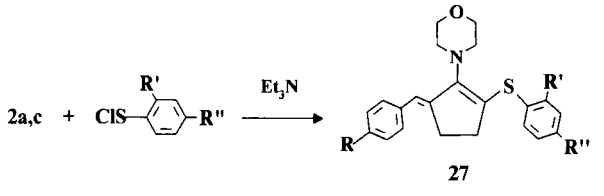
To introduce two or three enamine residues at the phosphorus atom, bromophosphines or phosphorus tribromide should be used as phosphorylating reagents. To obtain phosphine **25** the reaction was carried out in a sealed tube at elevated temperature using benzene as solvent. Phosphine **26** was synthesized in good yield with pyridine as solvent, no heating being required (scheme 4).



SCHEME 4

As can be seen from the discussion above, arylmethylidenemorpholinocyclopentenes **2** are significantly less reactive towards electrophilic phosphorylating reagents compared with the unsubstituted enamines **1**. It was of interest to examine reactions of **2** with less reactive electrophilic reagents such as $POCl_3$, $PSCl_3$ and arylsulfonic acids chlorides, which react readily with enamines **1**.

Arylsulfene acids chlorides reacted readily with enamines **2** to give sulfides **27** in high yield. The same reaction conditions applied to enamine **1** yielded a mixture of mono- and disubstituted products (scheme 5).



	R	R'	R''
a	H	NO_2	H
b	H	NO_2	NO_2
c	H	H	I
d	Me_2N	NO_2	H

SCHEME 5

Reaction of **2** with $PSCl_3$ did not proceed in dichloromethane at all. In pyridine, a number of signals can be observed in ^{31}P NMR spectrum of the reaction mixture and no individual product was isolated. $POCl_3$ did not react with the enamines **2** either, heating of the reaction mixture resulted in polymerization.

Reaction of **2** with arylsulfonic acid chlorides proceeded without regioselectivity. We were unable to isolate any individual substances from the reaction mixture. The structure of compounds synthesized was confirmed by elemental analysis (Table 1), ^{31}P and ^{1}H NMR spectroscopy (Table II).

TABLE I Yields, constants, data of elemental analyses, and ^{31}P NMR spectral parameters for phosphorylated enamines

	M.p. (°c);	*Yield, %*	*Formula*	*^{31}P, solvent*	*Found, % (Calculated,%)*	
					N	*P*
2b	93–94	74	$C_{16}H_{18}BrNO$	-	4.19 (4.37)	
2c	123–125	69	$C_{18}H_{24}N_2O$	-	9.72 (9.85)	
4	153–155	61.5	$C_{24}H_{34}N_3O_3P$	91.1 benzene	9.15 (9.47)	6.72 (6.98)
5	162–164	63	$C_{24}H_{33}BrN_3PO_3$	92.2 benzene	7.86 (8.04)	5.71 (5.93)
6	Oil	95	$C_{24}H_{34}N_3O_4P$	22.3 benzene	9.34 (9.14)	6.42 (6.74)
7	214–216	58.6	$C_{24}H_{34}N_3O_3PS$	70.9 chloroform	8.72 (8.84)	6.12 (6.51)
8	217–220	65	$C_{24}H_{33}BrN_3O_3PS$	70.3 chloroform	7.15 (7.58)	5.34 (5.59)

	M.p. (°c);	*Yield,* %	*Formula*	^{31}P, *solvent*	*Found, % (Calculated,%)*	
					N	*P*
9	120–121	56	$C_{30}H_{42}BrN_4OP$	17.7 chloroform	9.73 (9.57)	5.03 (5.29)
10	127–129	71	$C_{32}H_{47}rN_4OP$	17.2 chloroform	10.12 (10.48)	5.61 (5.79)
11	105–107	75	$C_{24}H_{38}N_3OPS$	72 chloroform	9.52 (9.39)	6.75 (6.92)
12a	160–164/ 0.001	78	$C_{18}H_{24}NO_3P$	162.6 benzene	4.02 (4.20)	9.32 (9.29)
12b	172–176/ 0.001	87	$C_{18}H_{23}BrNO_3P$	163.0 benzene	3.52 (3.40)	7.21 (7.51)
13	117–8	64.3	$C_{18}H_{24}NO_3PS$	87.9 benzene	3.75 (3.83)	8.15 (8.48)
15	77–9	52	$C_{36}H_{46}N_3O_3P$	25.3 chloroform	6.92 (7.01)	4.84 (5.16)
16	103–4	63	$C_{36}H_{46}N_3O_2PS$	54 benzene	7.01 (6.82)	4.79 (5.03)
17	128–129	43	$C_{36}H_{42}Br_2N_30_3PS$	54.7 chloroform	5.17 (5.34)	4.11 (3.93)
18	93–95	67	$C_{34}H_{41}N_2O_3PS$	72.5 chloroform	4.95 (4.76)	5.32 (5.26)
19	173–5	52	$C_{39}H_{44}N_3O_2PS$	39.7 chloroform	6.32 (6.47)	4.92 (4.77)
20a	86–90	60	$C_{18}H_{23}ClNOP$	84.7 ether	3.95 (4.17)	8.89 (9.22)
21	210/0.02	67	$C_{24}H_{28}NOP$	-28.5 ether	4.12 (4.24)	8.42 (8.21)
22a	Oil	90.2	$C_{28}H_{36}N_3O_2P$	39.1 benzene	8.89 (8.80)	6.83 (6.49)
22b	102–104	53	$C_{22}H_{31}N_2O_3P$	37.7 benzene	7.32 (6.96)	7.42 (7.70)
22c	160–161	58	$C_{26}H_{31}N_2O_2PS$	61.9 chloroform	6.11 (6.00)	6.31 (6.64)
22d	Oil	63.4	$C_{23}H_{26}NO_2PS$	81.1 chloroform	3.25 (3.40)	7.74 (7.53)
22e	124–127	72	$C_{23}H_{25}BrNO_2PS$	81.5 chloroform	2.51 (2.86)	6.66 (6.32)
23	126–129	61.4	$C_{28}H_{28}NOP$	-20.2	3.17 (3.29)	6.97 (7.28)

	M.p. (°c);	Yield, %	Formula	^{31}P, solvent	Found, % (Calculated,%) N	P
24a	174–176	57	$C_{28}H_{28}NO_2P$	23.6 acetonytrile	3.26 (3.17)	7.27 (7.02)
24b	155–6	51	$C_{28}H_{28}NOPS$	34.0 benzene	2.98 (3.06)	6.96 (6.77)
25	128–130	66.3	$C_{34}H_{41}N_2O_2P$	-44.3 benzene	4.95 (5.18)	5.54 (5.73)
26	124–125	43	$C_{48}H_{54}N_3O_3P$	-53,6 benzene	5.43 (5.59)	4.51 (4.12)
27a	132	72	$C_{22}H_{22}N_2O_3S$	-	7.01 (7.10)	8.34* (8.13)*
27b	161–162	54	$C_{22}H_{21}N_3O_5S$	-	9.11 (9.56)	6.87* (7.30)*
27c	44–45	64	$C_{22}H_{22}INOS$	-	3.05 (2.95)	6.95* (6.74)*
27d	133–135	53	$C_{24}H_{27}N_3O_3S$	-	9.73 (9.60)	7.75* (7.33)*

* Analysis for S.

TABLE II ^1H NMR spectral data (δ, multiplicity and J, Hz) for the enamines 2–27 in $CDCl_3$

N	-CH=	CH_2-CH_2	CH_2 OCH_2	CH_2 NCH_2	Ar	Other
2b	6.26	2.74, 2.38	3.76	2.84	7.36d, 7.14d, J_{HH} 8.5 Hz	
2c	6.31	2.86, 2.44	3.84	2.92	7.30d, 6.72d, J_{HH} 8 Hz	
4[1]	6.80	2.67, 2.42	3.71	3.20	7–7.5 (5H)	$PNCH_2$ 2.87, OCH_2 3.50
5[1]	6.47	2.36, 2.29	3.58	3.03	7.24d, 6.95d, J_{HH} 7Hz	$PNCH_2$ 2.75, OCH_2 3.58
6	6.76	2.83, 2.51	3.81	3.41	7.2–7.5 (5H)	$PNCH_2$ 3.14, OCH_2 3.67
7	6.70	2.77, 2.54	3.75	3.47	7.2–7.4 (5H)	$PNCH_2$ 3.10, OCH_2 3.61
8	6.69	2.77, 2.61	3.81	3.52	7.50d, 7.24d, J_{HH} 8.5Hz	$PNCH_2$ 3.16, OCH_2 3.68
9	6.59	2.87, 2.62	3.58	3.02	7.49 d(1H, J_{HH} 7.8 Hz); 7.34–7.42 m (4H); 7.2–7.28 m, (1H); 6.90 t (1H, 8Hz); 6.38–6.48 m (2H)	$\underline{CH_3}CH_2NP$ 1.13t $CH_3\underline{CH_2}NP$ 3.2 m, J_{HH} 7 Hz,

N	*-CH=*	*CH_2-CH_2*	*CH_2 OCH_2*	*CH_2 NCH_2*	*Ar*	*Other*
10	6.58	2.81, 2.63	3.57	3.03	7.2–7.4m (5H), 6.71 t (1H,J_{HH} 8Hz), 6.42d (1H, J_{HH} 8Hz), 6.21d (1H, J_{HH} 8Hz),	$\underline{CH_3}CH_2NP$ 1.10t $CH_3\underline{CH_2}NP$ 3.2 m, J_{HH} 7 Hz, 2.27 CH_3Ar, 2.26 CH_3Ar
11	6.65	2.73, 2.49	3.73	3.46	7.1–7.3m(5H)	$\underline{CH_3}CH_2NP$ 1.07t $CH_3\underline{CH_2}NP$ 3.10 m, J_{HH}7 Hz,
12a[1]	6.79	2.75, 2.64	3.64	3.19	7.36 d(2H), 7.22 t(2H), 7.07 t(1H)	POMe 3.39 d(6H, J_{PH} 11Hz)
13	6.67	2.78	3.71	3.32	7.2–7.4 (5H)	POMe 3.69 d(6H, J_{PH} 13.6Hz)
15	6.74	2.81, 2.52	3.79	3.40	7.1–7.5 (10H)	$\underline{CH_3}CH_2NP$ 1.13t $CH_3\underline{CH_2}NP$ 3.08 m, J_{HH}7 Hz,
16	6.69	2.74, 2.58	3.71	3.45	7.1–7.4 (10H)	$\underline{CH_3}CH_2NP$ 1.05t $CH_3\underline{CH_2}NP$ 3.2 m, J_{HH} 7 Hz,
17	6.63	2.68	3.73	3.42	7.42d, 7.16d, J_{HH} 8.5Hz	$\underline{OCH_2}CH_2NP$ 3.58m, $OCH_2\underline{CH_2}NP$ 3.14m
18	6.72	2.85	3.78	3.34	7.1–7.4 m(10H)	CH_3CH_2OP 1.43t, CH_3 CH_2OP 4.14 m, J_{HH} 7 Hz,
19	6.67	2.81, 2.60	3.75	3.22	7.1–7.4 m(10H), 6.96 dd (4H, J_{HH} 8.5Hz,NC_6H_4Me)	MeAr 2.19 s, NH 8.69 d(lH, J_{PH} 4.4Hz)
20a[1]	6.73	2.72, 2.52	3.55	3.19, 3.09	7.30 d(2H), 7.22 t(2H), 7.09 t(1H)	$\underline{CH_3}CH_2P$ 0.96 dt (3H, J_{HH} 7 Hz, J_{PH} 18.6 Hz), $CH_3\underline{CH_2}P$ 1.66 m(1H), 1.96 m (1H)
21[1]	6.81	2.54, 2.20	3.64	3.27	7.0–7.4 m (10H)	$\underline{CH_3}CH_2P$ 0.99 dt (3H, J_{HH} 7 Hz, J_{PH} 18 Hz), $CH_3\underline{CH_2}P$ 1.7 q (2H, J_{HH} 7 Hz)
22a	6.91	2.58, 2,23	3.72		7.1–7.4 m (7H), 6.7–6.9 m (3H)	$\underline{CH_3}CH_2P$ 1.16 dt (3H, J_{HH} 7 Hz, J_{PH} 18 Hz), $CH_3\underline{CH_2}P$ 1.5 m (2H), 3.55 m (2H), 3.39 m (2H), 2.98 m (4H), 2.82 m (4H)

N	*-CH=*	*CH_2-CH_2*	*CH_2 OCH_2*	*CH_2 NCH_2*	*Ar*	*Other*
22b	6.75	2.83, 2.54	3.70		7.2–7.4 m (5H)	$\underline{CH_3}CH_2P$ 1.21 dt (3H, J_{HH} 7 Hz, J_{PH} 17 Hz), $CH_3\underline{CH_2}P$ 1.9 m (2H), $O\underline{CH_2}$ CH_2NP 3.8m (4H), $OCH_2\underline{CH_2}NP$ 3.36m (2H), 3.48m (2H)
22c	6.63	2.72, 2.60	3.54	3.36	7.7–7.9 m (2H, PhP), 7.0–7.5 m (8H)	2.5–3.2 m (12H, CH_2)
22d	6.68	2.86, 2.73	3.50	3.11	7.9–8.1 m (2H, PhP), 7.1–7.6 m(8H)	POMe 3.52 d(3H, J_{PH} 14.2 Hz)
22e	6.59	2.81, 2.71	3.50	3.09	7.9–8.1 m (2H, PhP), 7.3–7.6 m(5H), 7.20 d(2H, J_{HH} 8 Hz)	POMe 3.53 d(3H, J_{PH} 14 Hz)
23[1]	6.85	2.53, 2.20	3.61	3.34	7.0–7.6 m(15H)	
24a	6.73	2.79, 2.31	3.58	3.21	7.1–7.9 m (15H)	
24b	6.70	2.82, 2.33	3.38	3.17	7.8–8.1 m (4H, PhP), 7.2–7.5 m(11H)	
25[1]	7,06	2,95 2,67	3,91	3,55	7.25–7.8 m(10H)	$\underline{CH_3}CH_2P$ 1.28 dt (3H, J_{HH} 8 Hz, J_{PH} 18 Hz), $CH_3\underline{CH_2}P$ 1.7 q (2H, J_{HH} 8 Hz)
26[1]	6.84	2.77, 2.52	3.69	3.34	7.44 d(6H, J_{HH} 8 Hz), 7.25 t(6H, J_{HH} 8 Hz), 7.10 d(3H, J_{HH} 8 Hz)	
27a	6.67	2.97, 2.56	3.79	3.44	7.2–7.6 m (8H), 8.23 d (1H, J_{HH} 8 Hz)	
27b[2]	6.80	2.64	3.74	3.34	9.02 s(1H), 8.48 d(1H, J_{HH} 9 Hz), 7.84 d(1 H, J_{HH} 9 Hz), 7.2–7.5 m(5H)	
27c[2]	6.65	2.89, 2.49	3.74	3.25	7.1–7.8 m (9H)	
27d[2]	6.65	2.87, 2.56	3.73	3.30	8.24 d (1H, J_{HH} 8 Hz), 7.4–7.8 m (3H, 6.77 d, 7.33d (4H, J_{HH} 8 Hz)	Me_2N 2.98 s (6H)

1-in C_6D_6; 2- in CD_3COCD_3.

One can suggest that the phosphorylated enamines could be readily hydrolyzed to obtain phosphorylated ketones. Unfortunately, we failed to isolate any compound in pure form after the hydrolysis. Attempts at

hydrolysis using hydrochloric or acetic acids resulted in decomposition. Enamine 24b simply remained intact during the hydrolysis attempts.

In conclusion, 5-arylmethylidene-1-morpholinocyclopentene can be phosphorylated with different phosphorus(III) halides giving dihalo and halophosphines which are valuable starting materials for synthesis of various trivalent and pentavalent phosphorus derivatives. The phosphorylated enamines cannot be hydrolyzed to phosphorylated ketones. Most of them decomposed in acidic medium.

EXPERIMENTAL

Melting points were measured capillary and are uncorrected. ^{1}H NMR (TMS as an internal standard) and ^{31}P NMR (85% H_3PO_4 as an external standard) spectra were recorded on a Varian instrument operating at 300 and 125 MHz respectively. The solvents were dried before use.

5-Benzylidene-1-morpholinocyclopenetene 2a

M.p. 81 °C ; M.p. 81 °C /4/, yield 76%.

5-(4'-bromobenzylidene) –2-morpholinocyclopenetene 2b

5-(4'-dimethylaminobenzylidene) –2-morpholinocyclopenetene 2c

General Procedure for synthesis of enamines 2

A mixture of 1-morpholinocyclopentene-1 (0.6 mol) and corresponding benzaldehyde (0.5 mol) in benzene (100 mL) was refluxed with a Dean-Stark adapter till the calculated amount (0.5 mol) of water was separated. The solvent was removed under reduced pressure, the enamine was crystallized from methanol.

Dimorpholide of (2-morpholino-3-benzylidenecyclopent-1-enyl) phosphonous acid 4

To a solution of phosphorus trichloride 0.48 g (3.5 mmol) in diethyl ether 15 mL cooled to – 40 °C, a mixture of 5-benzylidene-1-morpholinocy-

clopentene 0.84 g (3.5 mmol) and triethylamine 1.1 mL (8 mmol) in diethyl ether 15 mL was added with stirring. The reaction mixture was allowed to warm up to the ambient temperature. After 20 h triethylamine hydrochloride was filtered off (0.96 g). ^{31}P-NMR spectrum showed one signal 165.6 ppm assigned to dichlorophosphine **2.** A solution of morpholine 1.22 mL (14 mmol) in ether 10 mL was added to the filtrate cooled by ice water. After a day morpholine hydrochloride was filtered off, washed with ether (2*10 mL). The filtrate was evaporated, the resulting oil was triturated with hexane 10 mL, then 20 mL of hexane was added. The mixture was refluxed for 10 min and decanted. Light yellow crystals precipitated from the solution were collected by filtration.

Dimorpholide of (2-morpholino-3-(4-bromobenzylidene) cyclopent-1-enyl)phosphonous acid 5

The procedure is analogues to that described for **4.**

Dimorpholide of (2-morpholino-3-benzylidenecyclopent-1-enyl) phosphonic acid 6

To a solution of dimorpholide **4** 1.2 g (2.7 mmol) in ether 25 mL, a solution of hexachloroethane (2.7 mmol) in ether 15 mL was added with stirring. The reaction mixture was kept for 1 h, then the precipitate formed was separated by filtration, washed with ether (2*10 mL) and dried. The precipitate was dissolved in dichloromethane 15 mL and 0.04 g of water in 1 mL of triethylamine was added. The reaction mixture was stirred for 4 h. The dichloromethane was evaporated, the residue was dissolved in benzene 10 mL, the undissolved solid was filtered off and washed with benzene (3*3 mL). The combined benzene filtrate and washings were evaporated, the residue was kept in vacuo at 80 °C to obtain light yellow highly viscous oil which solidify on standing.

Dimorpholide of (2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 7

To a stirred solution of phosphorus trichloride 1.74 (12.7 mmol) in benzene 30 mL, a mixture of 1-morpholino-5-benzylidenecyclopentene 1.31 g

(12.7 mmol) and triethylamine 1.31 g (12.7 mmol) in benzene 30 mL was added. After 10 min 5.66 g (65 mmol) of morpholine was added. After next 10 min of stirring finely ground sulfur 407 mg (12.7 mmol) was added. The reaction mixture was stirred till all the sulfur was dissolved. The reaction mixture was filtered, the solution was evaporated, and the residue was crystallized from DMSO.

Dimorpholide of (2-morpholino-3-(4-bromobenzylidene) cyclopent-1-enyl)thiophosphonic acid 8

The same procedure was applied as to **7.** The product was crystallized from DMSO.

Tetraethyldiamide of (2-morpholino-3-benzylidenecyclopent-1-enyl) (2-bromophenylimino)phosphonic acid 9

To a solution of phosphorus trichloride 1.92 g (14 mmol) in toluene 25 mL a mixture of 5-benzylidene-1-morpholinocyclopentene 3.38 g (14 mmol) and triethylamine 2,1 mL (15 mmol) in toluene 25 mL was added with stirring.

The temperature was maintained below 20 °C and after 1 h diethylamine 3.1 mL (30 mmol) was added dropwise to the stirred reaction mixture. After 2 h hydrochlorides formed were filtered off, washed with toluene (2*10 mL). 2-Bromophenylazide 2,77g (14 mmol) was added to the reaction mixture which then was stirred for 2h and refluxed for 30 min afterwards. The filtrate was evaporated, the residue was triturated with hexane. The product was crystallized from heptane.

Tetraethyldiamide of (2-morpholino-3-benzylidenecyclopent-1-enyl) (3,4-dimethylphenylimino)phosphonic acid 10

The same procedure was applied as to **9.**

Tetraethyldiamide of (2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 11

The same procedure was applied as to **7.** The product was crystallized from n-octane.

Dimethyl ester of (2-morpholino-3-benzylidenecyclopent-1-enyl) phosphonous acid 12a

To a mixture of 1-morpholino-5-benzylidenecyclopentene 2.41 g (10 mmol) and triethylamine 1.01 g (10 mmol) in ether 20 mL cooled to – 30 °C, a solution of phosphorus trichloride 1.37 g (10 mmol) in ether 10 mL was added upon stirring. The reaction mixture was allowed to warm up to ambient temperature. After 1 hr the residue was filtered off and washed with ether (2*30 mL). The filtrate was evaporated to 30 mL, cooled to – 30 °C and then a mixture of methanol (20 mmol) and triethylamine 2.75 g (20 mmol) was added. The precipitate formed was filtered off, the filtrate was evaporated, the residue was dissolved in hexane (20 mL). The undissolved solid was filtered off. The hexane was evaporated and the residue was distilled.

Dimethyl ester of (2-morpholino-3-(4-bromobenzylidene) cyclopent-1-enyl)phosphonous acid 12b

The same procedure was applied as to **12a.**

Dimethyl ester of (2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 13

To a solution of phosphorus trichloride 0.96 g (7 mmol) in dichloromethane 40 mL a mixture of 1-morpholino-5-benzyledenecyclopentene 1.69 g (7 mmol) and triethylamine 0.81 g (7 mmol) in dichloromethane 20 mL was added dropwise with stirring. After 1 h a mixture of methanol 0.49 g (14 mmol) and triethylamine 1.52 g (15 mmol) was added dropwise. After 30 min finely ground sulfur was added to the reaction mixture and stirring was continued till sulfur dissolved. The reaction mixture was washed with water (3*30 mL), the organic layer was separated, dried over Na_2SO_4, the solvent was evaporated. The product was crystallized from isopropyl alcohol.

Diethylamide of bis(2-morpholino-3-benzylidenecyclopent-1-enyl) phosphonic acid 15

To a solution of phosphorus tribromide 2.7 g (0.01 mol) in benzene 70 mL, a mixture of 1-morpholino-5-benzyledenecyclopentene 4.83 g (0.02 mol) and triethylamine 2.91 mL (0.021 mol) in benzene 20 mL was added dropwise with stirring. After 1 h diethylamine 2,1 mL (0.02 mol) in 10 mL of

benzene was added dropwise. The reaction mixture was filtered, a solution of hexachloroethane 2.37 g (0.01 mol) in benzene 20 mL was added. After 1 h the resulting oil was decanted and dissolved in dichloromethane 50 mL. The solution was washed with an aqueous solution of Na_2CO_3 (10%), The organic layer was separated, dried over Na_2SO_4. The solvent was evaporated and the product was crystallized from n-heptane.

Diethylamide of bis(2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 16

To a solution of phosphorus tribromide 2.7 g (0.01 mol) in benzene 70 mL, a mixture of 1-morpholino-5-benzyledenecyclopentene 4.83 g (0.02 mol) and triethylamine 2.91 mL (0.021 mol) in benzene 20 mL was added dropwise with stirring. After 1 h diethylamine 2,1 mL (0.02 mol) in 10 mL of benzene was added dropwise.The reaction mixture was filtered and finely ground sulfur 0.32 g (0.01 mol) was added, the reaction mixture was stirred till sulfur dissolved.The solvent was removed in vacuo, the crude product was crystallized from n-octane.

Diethylamide of bis(2-morpholino-3-(4-bromobenzylidene)cyclopent-1-enyl) thiophosphonic acid 17

The same procedure was applied as to **16**.

Ethyl ester of bis(2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 18

The same procedure was applied as to 16 using absolute ethanol instead of diethylamine. The producrt was crystallized from isopropyl alcohol.

p-Toluide of bis(2-morpholino-3-benzylidenecyclopent-1-enyl) thiophosphonic acid 19

To a solution of phosphorus tribromide 2.7 g (0.01 mol) in benzene 70 mL, a mixture of 1-morpholino-5-benzylidenecyclopentene 4.83 g (0.02 mol) and triethylamine 2.91 mL (0.021 mol) in benzene 20 mL was added dropwise with stirring. After 1 h p-toluidine 1,1 g (0.01 mol) in 10 mL of benzene was added dropwise. After 10 min finely ground sulfur 0,32 g (0.01

mol) was added, the reaction mixture was stirred till sulfur dissolved.The reaction mixture was filtered, the solvent was removed in vacuo, the crude product was crystallized from methanol.

(2-Morpholino-3-benzylidenecyclopent-1-enyl)ethylchlorophosphine 20à

A mixture of 5-benzylidene-1-morpholinocyclopentene 10.3 g (0.043 mol), dichloroethylphosphine 5.6 g (0.043 mol) and triethylamine 4.8 g (0.047 mol) in diethyl ether 80 mL was heated at 50 °C for 60 h. The precipitate formed was filtered off, the filtrate was evaporated to leave brown oil 14.4 g. Hexane 20 mL was added and the reaction mixture was refluxed till almost all the oil dissolved. The solution was decanted under Ar and cooled. After 1 h settled out, hexane was decanted from the precipitate formed. The precipitate was dissolved in hexane 60 mL at reflux and the hot solution was filtered through dense filter. After 30 h the solution was decated from the precipitated crystals, the crystals were dried. The product is highly hydrolizable.

(2-Morpholino-3-benzylidenecyclopent-1-enyl)ethylphenylphosphine 21

To a stirred solution of ethylchlorophosphine 20a (6.8 mmol) in ether 25 mL at −10 °C, a solution of phenyllithium 8 mL (0.86 M solution in ether) was added dropwise over period of 5 min After 10 min the reaction mixture was allowed to warm to room temperature. After 20 min the solvent was evaporated, then benzene 10 mL and water 1 mL were added, the reaction mixture was thoroughly shaken, the benzene layer was separated, evaporated to constant weight. The residue was dissolved in ether, the solution was filtered, the filtrate was evaporated. The crude product was distilled.

4'-Phenylpiperazide of (2-morpholino-3-benzylidenecyclopent-1-enyl) ethylphosphonic acid 22à

To a stirred solution of ethylchlorophosphine **20a** 0.58 g (1.7 mmol) in benzene 5 mL, a solution of N-phenylpiperazine 0.58 g (3.4 mmol) in benzene 5 mL was added. The precipitate formed was separated by filtration, washed with benzene (3*5 mL). 31P-NMR spectrum of the reaction mixture has the only signal at 41.2 ppm . 20- % hydrogen peroxide 0.3 mL was added to the filtrate at 15 °C, the reaction mixture was stirred at room

temperature for 5 h. The benzene solution was washed with water (3*5 mL), separated, the solvent was evaporated. The residue was extracted with hot hexane 20 mL, the hot solution was decanted, hexane was evaporated and the product was kept in vacuo to constant weight. The product is an amorphous, highly hygroscopic solid.

Morpholide of (2-morpholino-3-benzylidenecyclopent-1-enyl) ethylphosphonic acid 22b

The same procedure was applied as to **22a.** The product was crystallized from toluene.

Morpholide of (2-morpholino-3-benzylidenecyclopent-1-enyl) phenylthiophosphonic acid 22c

To a stirred solution of diclorophenylphosphine 1.79 g (10 mmol) in benzene 50 mL, a mixture of 1-morpholino-5-benzyledenecyclopentene 2.41 g (10 mmol) and triethylamine 2.92 mL (21 mol) in benzene 30 mL was added dropwise. After stirring for 4 h morpholine 1.76g (0.02 mol) in 10 mL of benzene was added dropwise, and the mixture was stirred another 10 min. Finely ground sulfur 0.32 g (10 mmol) was added, the reaction mixture was stirred till sulfur dissolved.The reaction mixture was filtered, the solvent was removed in vacuo, the crude product was crystallized from methanol.

Methyl ester of (2-morpholino-3-benzylidenecyclopent-1-enyl) phenylthiophosphonic acid 22d

The same procedure was applied as to **22c** using absolute methanol instead of morpholine. The product was purified by reprecipitation from benzene with petroleum ether.

Methyl ester of (2-morpholino-3-(4-bromobenzylidene)cyclopent -1-enyl) phenylthiophosphonic acid 22e

The same procedure was applied as to **22d**.The product was recrystallized from acetonytrile.

(2-Morpholino-3-benzylidenecyclopent-1-enyl)diphenylphosphine 23

To a mixture of 1-morpholino-5-benzylidenecyclopentene 1.35 g (5.6 mmol) and triethylamine 0.9 mL (6 mmol) in pyridine 30 mL, chlodiphenylphosphine 1.24 g (5.6 mmol) was added. After 6 days the pyridine was removed under reduced pressure. The residue was dissolved in dichloromethane 30 mL and washed with water (2*20 mL). The solvent was evaporated, the resulting oil was triturated with pentane. The crude product was crystallized from n-octane.

(2-Morpholino-3-benzylidenecyclopent-1-enyl) diphenylphosphineoxide 24a

To a mixture of 1-morpholino-5-benzylidenecyclopentene (15 mmol) and triethylamine (16 mmol) in pyridine 20 mL, chlodiphenylphosphine (15 mmol) was added. After 6 days the solution of hexacloroethane (15 mmol) in dichloromethane 100 mL was added. The reaction mixture was washed with water (3*50 mL). The organic layer was separated, dried over Na_2SO_4, the solvents were removed, the crude product was crystallized from acetonitrile.

(2-Morpholino-3-benzylidenecyclopent-1-enyl) diphenylphosphinesulfide 24b

To a solution of chlorodiphenylphosphine 1.24 g, (5.6 mmol) in pyridine 20 mL, a mixture of 1-morpholino-5-benzyledenecyclopentene 1.35 g, (5.6 mmol) and triethylamine 0.84 mL, (6 mol) in pyridine 10 mL was added. After 4 days finely ground sulfur 0.182 g, (5.6 mmol) was added and the reaction mixture was stirred till sulfur dissolved. The pyridine was removed under reduced pressure, the residue was dissolved in dichloromethane 60 mL and washed with water (3*30 mL). The organic layer was dried over Na_2SO_4, the solvent was evaporated, the crude product was recrystallized from isopropanol.

Bis(2-morpholino-3-benzylidenecyclopent-1-enyl)ethylphosphine 25

An ampule was charged with 1-morpholino-5-benzylidenecyclopentene 2.4 g (0.01 mol) and triethylamine 2.7 mL (0.02 mol), the ampule was fro-

zen in liquid nitrogen under Ar and a solution of ethyldibromophosphine (5 mmol) in benzene 6 mL was added. The ampule was flushed with Ar, sealed and heated at 100 °C for 5h. Then the ampule was carefully opened, the solid was separated by filtration, the filtrate was evaporated. The residue was extracted into hexane 20 mL refluxing for 5 min, the solution was decanted under Ar. After 3 min the solution solidified, hexane 50 mL was added and the mixture was again brought to reflux. The hot solution was filtered. The precipitated solid was separated by decantation and dried.

Tris(2-morpholino-3-benzylidenecyclopent-1-enyl)phosphine 26

To a solution of phosphorus tribromide 2.2 g, (8.1 mmol) in pyridine 30 mL, a mixture of 1-morpholino-5-benzylidenecyclopentene 5.89 g, (24.4 mmol) and triethylamine 3,5 mL, (25 mmol) in pyridine 10 mL was added. After 3 days the pyridine was removed under reduced pressure, the residue was dissolved in dichloromethane 30 mL and washed with water (3*30 mL). The organic layer was separated, dried over Na_2SO_4. The solvent was evaporated, the crude product was crystallized from benzene.

(2-Morpholino-3-benzylidenecyclopent-1-enyl)2'-nitrophenylsulfide 27a

To a solution of 1-morpholino-5-benzylidenecyclopentene 1.45 g, (6 mmol) and triethylamine 1 mL (7 mmol) in benzene 30 mL, o-nitrophenylsulfenylchloride 1.14 g, (6 mmol) in benzene 10 mL was added. After 2 days the precipitated solid was filtered off, the solvent was evaporated and the crude product was crystallized from isopropyl alcohol.

(2-Morpholino-3-benzylidenecyclopent-1-enyl) 2',4'-dinitrophenylsulfide 27b

The procedure is analogous to that described for **27a** .The product was recrystallized from ethanol.

(2-Morpholino-3-benzylidenecyclopent-1-enyl)4'-iodophenylsulfide 27c

The procedure is analogous to that described for **27a.** The product was purified by reprecipitation from ethanol with water.

(2-Morpholino-3-(4-dimethylamino)benzylidenecyclopent-1-enyl) 2'-nitrophenylsulfide 27d

The procedure is analogous to that described for 27a .The product was purified by reprecipitation from ethanol with water.

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