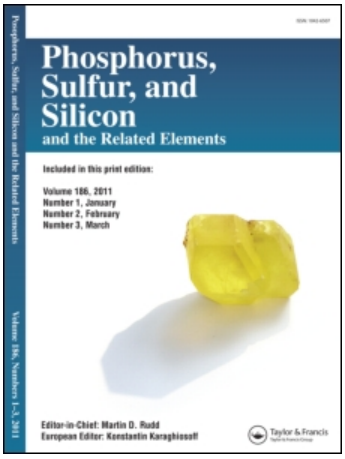

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NOVEL AND EFFICIENT ONE-POT SYNTHESIS OF PHOSPHORUS HETEROCYCLES CONTAINING THE BICYCLO [2.2.1] HEPTENE MOIETY

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NOVEL AND EFFICIENT ONE-POT SYNTHESIS OF PHOSPHORUS HETEROCYCLES CONTAINING THE BICYCLO [2.2.1] HEPTENE MOIETY

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In a convenient one-pot sequence, treatment of camphorquinone with sodium in dry tetrahydrofuran followed by addition of phosphorodichloridate and phosphorothiodichloridate yields 2-oxo-1,3,2-dioxaphospholes and 2-thioxo-1,3,2-dioxaphospholes, respectively. Similar treatment of 3-phenyliminobornan-2-one with sodium in dry THF followed by addition of phosphorodichloridate and phosphorothiodichloridate yields 2-oxo-1,3,2-oxazaphospholes and 2-thioxo-1,3,2-oxazaphospholes.

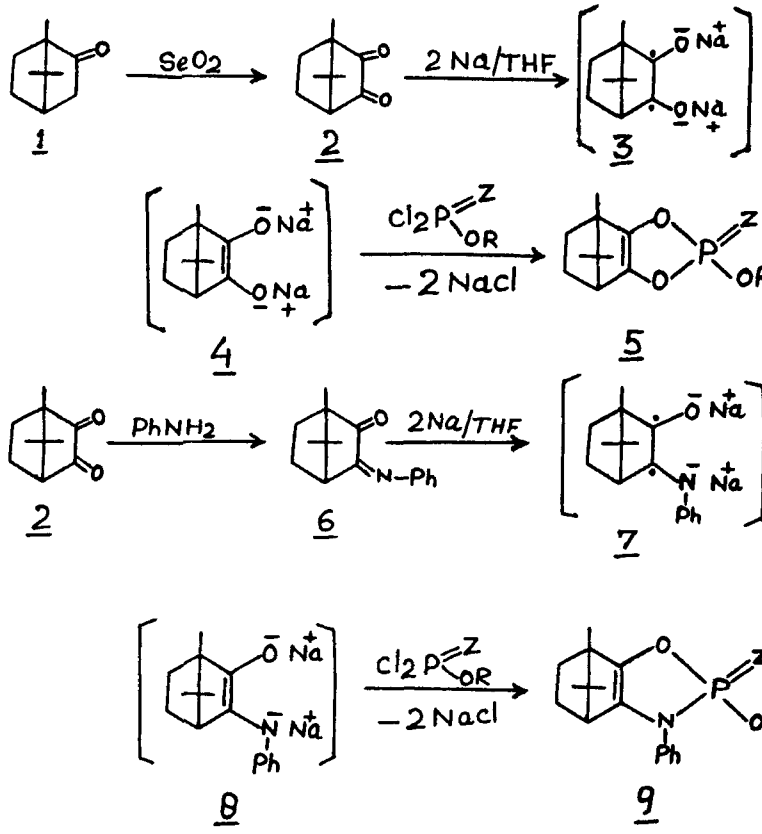
Key words: Camphorquinone, 3-phenyliminobornan-2-one, phosphorodichloridate, phosphorothiodichloridate, dioxaphospholes, oxazaphospholes.

Phosphorus heterocycles are found in the usual broad variety of ring size and ring multiplicity common to the entire field of heterocyclic chemistry. The chemistry of heterocyclic rings containing phosphorus is increasing at such an explosive rate that compounds containing phosphorus are incalculable. Potential carcinostatic[1–3] phosphorus heterocycles together with other pharmacological activities e.g. pesticides,[4] antitumoricidal[5,6] lubricant additives and coating acid[7] also have been mentioned. In continuation of our earlier work on synthesis of dioxaphospholes,[8–10] some new model heterocycles, which are not reported in the literature, have been synthesised from easily available camphorquinone.

RESULTS AND DISCUSSION

The reaction of camphorquinone (2) with sodium in dry tetrahydrofuran followed by addition of ethyl phosphorodichloridate and phenyl phosphorodichloridate gives a solid material identified as 2-oxo-2-ethoxy and 2-phenoxy-1,3,2-dioxaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 5a and 5b, respectively. The reaction of 2 with sodium in dry tetrahydrofuran followed by addition of ethyl or phenyl phosphorothiodichloridate gives 2-thioxo-2-ethoxy and 2-phenoxy-1,3,2-dioxaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 5c and 5d, respectively. Similar treatment of 3-phenyliminobornan-2-one (6) with ethyl or phenyl phosphorodichloridate and ethyl or phenyl phosphorothiodichloridates yields 2-oxo-2-ethoxy and 2-phenoxy-3-phenyl-1,3,2-oxazaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 9a and 9b and 2-thioxo-2-ethoxy and 2-phenoxy-3-phenyl-1,3,2-oxazaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 9c and 9d, respectively.

This synthesis involves the initial formation of diradical dianions 3 and 7, by the electron transfer from sodium to diketone 2 and ketoimine 6 followed by radical



	5a & 9a	5b & 9b	5c & 9c	5d & 9d
Z	O	O	S	S
R	C_2H_5	C_6H_5	C_2H_5	C_6H_5

coupling to give the dianions 4 and 8,[11] which attacks ethyl or phenyl phosphorodichloridate. Intramolecular nucleophilic attack with elimination of chloride ion (detected by the formation of silver chloride on addition of aqueous silver nitrate) leads to the formation of products 5a, 5b and 9a, 9b. The intermediates 4 and 8 react with ethyl or phenyl phosphorothiodichloridate with elimination of chloride ions to give rise to product 5c, 5d and 9c, 9d. Compounds 5 and 9 were characterized on the basis of satisfactory elemental analysis and spectral data (Tables I and II).

EXPERIMENTAL

All melting points were uncorrected. The ir and nmr spectra were recorded on a Perkin-Elmer 720 and JEOL JNM FX-90 Q Spectrophotometers, respectively. The microanalyses were carried out using

TABLE I

Compounds 5a–d and 9a–d prepared

Product	Yield[a] (%)	mp (°C)	ir[13] (Nujol) (cm^{-1}) P=O	P=S	P—O—C	^{1}nmr($CDCl_3$/TMS)(ppm)
5a	47	173–74	1275	—	1150	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.20 (t, 3H, —OCH_2CH_3); 1.35 (t, 1H, Bridging H); 1.45(m, 4H, ring CH_2); 4.30 (q, 2H, —OCH_2).
5b	52	188–190	1270	—	1210	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.35 (t, 1H, Bridging H); 1.45 (m, 4H, ring CH_2); 7.1–7.7 (m, 5H, arom).
5c	44	196–98	—	730	1160	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.30 (t, 3H, —OCH_2CH_3); 1.40 (t, 1H, Bridging H); 1.50 (m, 4H, ring CH_2); 4.40 (q, 2H, —OCH_2).
5d	48	207–09	—	720	1205	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.35 (t, 1H, Bridging H); 1.45 (m, 4H, ring CH_2); 7.2–7.8 (m, 5H, arom).
9a	54	192–94	1290	—	1040	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.25 (t, 3H, —OCH_2CH_3); 1.40 (t, 1H, Bridging H); 1.45 (m, 4H, ring CH_2); 4.30 (q, 2H, —OCH_2); 7.6–8.2 (m, 5H, arom).
9b	56	211–13	1285	—	1190	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.40(t, 1H, Bridging H); 1.45(m, 4H, ring CH_2); 7.5–8.5 (m, 10H, arom).
9c	45	181–83	—	760	1050	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.25 (t, 3H, —OCH_2CH_3); 1.45 (t, 1H, Bridging H); 1.50 (m, 4H, ring CH_2); 4.30 (q, 2H, —OCH_2); 7.6–8.4 (m, 5H, arom).
9d	43	201–03	—	740	1215	0.85 (s, 3H, gem-CH_3); 1.15 (s, 6H, gem CH_3 & ring CH_3); 1.35 (t, 1H, Bridging H); 1.45 (m, 4H, ring CH_2); 7.6–8.4 (m, 10H, arom).

[a]Yield of isolated pure product.

TABLE II

Microanalytical data for compounds 5 and 9

Compound	Molecular formula	C		H		N	
		Calc	Found	Calc	Found	Calc	Found
5a	$C_{12}H_{19}O_4P$	55.81	(55.63)	7.36	(7.14)		
5b	$C_{16}H_{19}O_4P$	62.74	(62.58)	6.21	(6.07)		
5c	$C_{12}H_{19}O_3PS$	52.55	(52.37)	6.93	(6.71)		
5d	$C_{16}H_{19}O_3PS$	59.63	(59.44)	5.90	(5.75)		
9a	$C_{18}H_{24}NO_3P$	64.86	(64.64)	7.21	(7.05)	4.20	(3.98)
9b	$C_{22}H_{24}NO_3P$	69.29	(69.08)	6.29	(6.15)	3.67	(3.45)
9c	$C_{18}H_{24}NO_2PS$	61.89	(61.71)	6.88	(6.67)	4.01	(3.86)
9d	$C_{22}H_{24}NO_2PS$	66.49	(66.38)	6.05	(5.92)	3.53	(3.37)

Coleman Carbon-Hydrogen analyser and Coleman Nitrogen analyser and were in satisfactory agreement with the calculated values which are given in Table II.

Camphorquinone (2)

Procedure: A mixture of camphor (5.0 g), selenium dioxide (6.0 g) and acetic anhydride (5 ml) was heated at 140–50°C for 3–4 hours. The cooled solution was filtered. The selenium was washed with acetic acid. The orange yellow filtrate was carefully neutralised with potassium hydroxide solution to give camphorquinone as orange-yellow needles (5.22 g), mp 190–93°C.

$C_{10}H_{14}O_2$ Calc. C, 72.29; H, 8.43
Found C, 72.12; H, 8.24%.

3-Phenyliminobornan-2-one

Procedure: Equimolar amounts of camphorquinone (2) and aniline were heated with anhyd. sodium sulphate at 100°C for 24 hr and cold water then added to mixture. Thereafter, it was extracted with chloroform, washed with 10% HCl, water, dried and freed from solvent. The residue was crystallized from ethanol or aq. ethanol to yield a solid crystalline product, mp 118–19°C, yield, 60%.

$C_{16}H_{19}NO$ Calc. C, 79.67; H, 7.88; 5.81
Found C, 79.42; H, 7.61; N, 5.64%.

2-Oxo-2-ethoxy-and 2-phenoxy-1,3,2-dioxaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 5a *and* 5b

General Procedure: Sodium pieces (1g, 0.044 mole) were slowly added to dry THF (80 ml) in a three-necked round-bottomed flask, fitted with a condenser, a mercury trap and a pressure equalizing addition funnel with constant stirring under a nitrogen atmosphere. A solution of diketone 2 (3.3 g, 0.02 mole) in dry THF (15 ml) was added dropwise. Stirring at reflux temperature was continued for 6 h and the contents were allowed to cool. Ethyl or phenyl phosphorodichloridate (4 ml) was slowly added and the mixture was heated under reflux for 2 h. The contents were allowed to stand at room temperature for about 2 h. THF was removed by distillation under reduced pressure, and the residual matter was treated with ether. The ethereal layer was washed 2–3 times with water and dried with anhydrous sodium sulphate. The ether was removed on a rotary evaporator and the residual material was crystallized from ethanol. Addition of silver nitrate solution to the aqueous layer gave a white precipitate of silver chloride.

2-Thioxo-2-ethoxy-and 2-phenoxy-1,3,2-dioxaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 5c *and* 5d

General Procedure: In place of ethyl and phenyl phosphorodichloridate in the above method ethyl or phenyl phosphorothiodichloridate (4 ml) was slowly added and the products were crystallized from ethanol.

2-Oxo-2-ethoxy-and 2-phenoxy-3-phenyl-1,3,2-oxazaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene, 9a *and* 9b

General Procedure: Ethyl or phenyl phosphorodichloridate (3 ml) was slowly added in the reaction with 3-phenyliminobornan-2-one (6; 2.4 g; 0.01 mole) following the above procedure for compounds 5a and 5b. The products were crystallized from benzene/ethanol.

2-Thioxo-2-ethoxy-and 2-phenoxy-3-phenyl-1,3,2-oxazaphospholo [4,5-b]-1,7,7-trimethylbicyclo [2.2.1] hept-2-ene. 9c *and* 9d

General Procedure: In place of ethyl and phenyl phosphorodichloridate, ethyl or phenyl phosphorothiodichloridate (3 ml) was slowly added into the reaction with 3-phenyliminobornan-2-one (6; 2.4 g; 0.01 mole) following the above procedure for compound 5c and 5d. The products were crystallized from benzene/ethanol.

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