PHOSPHORUS HETEROCYCLES. PART I. SYNTHETIS OF THIADIAZAPHOSPHOL-2-ONES AND THIADIAZAPHOSPHOL-2-THIONES

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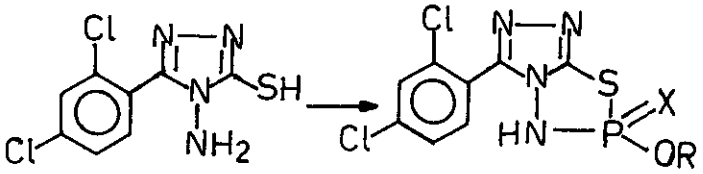
Abstract - The condensation reaction of 3-(2,4-dichlorophenyl)-4-amino-5-mercapto-1,2,4-triazole with various alkyl dichlorophosphate and alkyl dichlorothiophosphate leading to the formation of fused phosphorus heterocycles was carried out.

Cyclic phosphates or phosphorothioate esters pose as one of the important class of organophosphorus compounds as contact as well as systematic pesticides,[1] antitumor,[2] and antilukemic agents.[3] In search for new anticancer drugs, synthesis of a large number of phosphorus heterocyclic compounds is reported in literature and some of them are found to possess significant antitumour activity.[4a-d] To add to the extensive literature,[5a-c] on phosphorus heterocycles we report here the synthesis of cyclic phosphorus compounds (2,3).

In continuation of our programme of work in the chemistry of heterocycles,[6] the results obtained from these studies prompted us to synthesize some new phosphorus heterocycles from 3-(2,4-dichlorophenyl)-4-amino-5-mercapto-1,2,4-*s*-triazole (1)[7] by reacting with alkyl dichlorophosphate and alkyl dichlorothiophosphates. Exploration of these studies is principally directed towards the synthesis of new heterocyclic products. The results obtained during this attempt are reported in this paper.

The triazole (1) underwent facile condensation with various phosphorus reagents in the presence of triethylamine[5c] in methylene chloride giving 6-(2,4-dichlorophenyl)-2-alkoxy-1,2-dihydro-*s*-triazolo[4,3-*d*]-[1,3,4,2]thiadiazaphosphol-2-ones (2a-f) and 6-(2,4-dichlorophenyl)-2-alkoxy-1,2-dihydro-s-triazolo[4,3-d][1,3,4,2]-thiadiazaphosphol-2-thiones (3a-f) (Scheme 1). The structures of the new compounds (2,3) were confirmed



1 2, X=O 3, X=S

Scheme 1

on the basis of spectral studies. In the ir spectra the compounds (2a-f) showed sharp bands (ν_{max} in cm^{-1}) in the region 3270-3180 due to the -NH stretching vibration. The bands appeared[5c] in the region 1250-1150 were due to the P=O stretching vibrations. In the compounds (3a-f) the band

Table 1

Physical and spectroscopic data of Phospholes, (2,3)

Compd No	R	mp (°C)	yield (%)	ir (KBr) ν cm⁻¹		^{1}H Nmr (δppm, DMSO-d_6)	Analysis (%) Found (Calcd)		
				P=X	NH		C	H	N
2a	CH_3	185	75	1295	3210	3.8(s, 3H), 5.8(s, 1H)	32.12 (32.05	2.05 2.08	16.53 16.62)
2b	CH_2CH_3	198	70	1300	3205	1.3(t, J=7Hz, 3H), 4.4 (m, 2H), 5.7(s, 1H)	34.13 (34.19	2.50 2.56	15.91 15.95)
2c	$CH_2CH_2CH_3$	202	80	1300	3200	1.3(t, J=7Hz, 3H), 2.1 (m, 2H), 4.5(m, 2H), 5.8(s, 1H)	36.12 (36.16	3.05 3.01	15.38 15.34)
2d	$CH(CH_3)_2$	212	72	1290	3200	1.3(t, J=7Hz, 6H), 4.9 (m, 1H), 5.8(s, 1H)	36.20 (36.16	3.08 3.01	15.39 15.34)
2e	$CH_2CH_2CH_2CH_3$	206	70	1295	3205	1.4(t, J=7Hz, 3H), 2.2 (m, 4H), 4.3(m, 2H) 5.9(s, 1H)	37.92 (37.99	3.40 3.43	11.70 11.78)
2f	$CH_2CH_2CH_2CH_2CH_3$	195	75	1300	3205	1.3(t, J=7Hz, 3H), 2.2 (m, 6H), 4.5(m, 2H) 5.8(s, 1H)	39.65 (39.69	3.88 3.82	14.28 14.25)
3a	CH_3	Gummy	65	675	3200	3.7(s, 3H), 5.9(s, 1H)	30.52 (30.59	1.92 1.98	15.82 15.86)
3b	CH_2CH_3	Gummy	70	650	3200	1.2(t, J=7Hz, 3H), 4.3 (m, 2H), 5.9(s, 1H)	32.65 (32.70	2.48 2.45	15.29 15.26)
3c	$CH_2CH_2CH_3$	Gummy	65	670	3200	1.3(t, J=7Hz, 3H), 2.1 (m, 2H), 4.6(m, 2H) 5.8(s, 1H)	34.65 (34.64	2.85 2.89	14.79 14.70)
3d	$CH(CH_3)_2$	Gummy	63	700	3200	1.3(t, J=7Hz, 6H), 4.9 (m, 1H), 5.9(s, 1H)	34.60 (34.64	2.85 2.89	14.75 14.70)
3e	$CH_2CH_2CH_2CH_3$	Gummy	70	670	3200	1.2(t, J=7Hz, 3H), 2.1 (m, 4H), 4.3(m, 2H) 5.9(s, 1H)	36.42 (36.46	3.35 3.29	14.10 14.18)
3f	$CH_2CH_2CH_2CH_2CH_3$	Gummy	68	670	3200	1.3(t, J=7Hz, 3H), 2.1 (m, 6H), 4.5(m, 2H) 5.8(s, 1H)	38.19 (38.14	3.65 3.67	13.75 13.69)

appeared at 750-650 were due to the P=S vibrations. The ^{1}H nmr spectra of the compounds (2,3) showed that the signal due to the presence of -SH proton in the original triazole (1) were absent and showed signals due to the alkyl groups. The data are given in Table 1.

EXPERIMENTAL

Melting points were determined with a Buchi Oil heated apparatus in open capilaries and are uncorrected. Ir spectra were recorded with a Perkin-Elmer 580B spectrophotometer using potassium bromide discs, unless otherwise stated (ν_{max} in cm^{-1}). ^{1}H Nmr spectra were recorded in solutions stated with TMS as the internal reference in 60 MHz on a varian T-60 spectrometer (chemical shifts in δ ppm) and mass spectra were recorded on an AEIMS-30 instrument at 70 ev. 3-(2,4-Dichlorophenyl)-4-amino-5-mercapto-*s*-triazole (1) was prepared from 2,4-dichlorobenzohydrazine[8] following the method of Reid and Heindel.[9] Alkyl dichlorophosphate and alkyl dichlorothiophosphate required for condensation were prepared using the known method.[10]

6-(2,4-Dichlorophenyl)-2-alkoxy-1,2-dihydro-*s*-triazolo[4,3-*d*][1,3,4,2]thiadiazaphosphol-2-ones (2a-f)

General Method

To a well stirred solution of triazole (1)(2.61 mg, 0.01 mol) in dry methylene chloride (50 ml) and triethylamine (3 ml, 0.02 mol) added a solution of alkyl dichlorophosphate (0.01 mol) methylene chloride (50 ml) at 0-5^{o}C during 0.5 h. The mixture was stirred for another 6 h at the same temperature. The precipitated triethylamine hydrochloride was then removed by filtration. The organic phase was washed with ice cooled water and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure to give a solid which was recrystallized from ethanol. Similarly other compounds of this series were prepared.

6-(2,4-Dichlorophenyl)-2-alkoxy-1,2-dihydro-*s*-triazolo[4,3-*d*][1,3,4,2]thiadiazaphosphol-2-thiones (3a-f)

General Method

To a well stirred solution of triazole (1)(2.61 mg, 0.01 mol) in dry methylene chloride (50 ml) and triethylamine (3 ml, 0.02 mol) added a solution of alkyl dichlorothiophosphate (0.01 mol) in methylene chloride (50 ml) at 0-5^o C during 0.5 h. The mixture was stirred for another 6 h at the same temperature. The precipitated triethylamine hydrochloride was then removed by filtration. The organic phase was washed with ice cooled water and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure to give a gummy solid. Similarly other compounds of this series were prepared. The physical data of the compounds are given in Table 1.

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