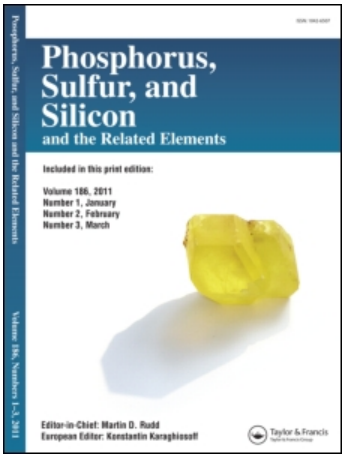

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SYNTHESIS OF FUSED PHOSPHORUS HETEROCYCLIC COMPOUNDS(III)

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SYNTHESIS OF FUSED PHOSPHORUS HETEROCYCLIC COMPOUNDS(III)

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Mannich-type reaction of 5-amino-1,2,4-triazole **1**, containing guanidine substructure, with the arylphosphonyl dichloride and aromatic aldehyde using cation exchange resin (D72, Amberlyst-15) to afford 6-phospha-4,5,6-trihydroimidazolo[2,3-e]1,2,4-triazole **4** is described. The microanalytical data, IR ^{1}H NMR, ^{31}P NMR and mass spectra of 6-phospha-4,5,6-trihydroimidazolo[2,3-e]1,2,4-triazole **4** are reported. The mechanism of the reaction is discussed.

Key words: Synthesis, Mannich-type reaction, guanidine, 1,2,4-triazole, cation exchange resin, imidazolo[2,3 e]1,2,4-triazole.

INTRODUCTION

Because various fused heterocyclic compounds that contain more nitrogen atoms tend to have higher biological activity, we attempted to synthesize a new kind of phosphorus and nitrogen-containing fused heterocyclic compound in order to find new pesticidal lead compounds.[1–3]

Recently, R. Chen noted that 1,4,2-diazaphospholidin-5-one could be prepared by the Mannich-type cyclization of phenylureas with phenylphosphonyl dichloride and aldehyde or ketone under acidic conditions.[4] However, only ureas and thioureas worked well in the transformation.[4–7] Under the same conditions, a Mannich-type cyclization of 5-amino-1,2,4-triazole and its analogue, which contain a guanidine (—N=C(N)—NH_2—) group in the molecule, failed to give the expected fused heterocyclic compound. Possibly this is because the 5-amino-1,2,4-triazole may easily form a salt with arylphosphonyl dichloride. We found that in the presence of cation exchange resin (D72 Amberlyst-15) the reaction could proceed successfully to yield 6-phospha-4,5,6-trihydroimidazolo[2,3-e]1,2,4-triazole **4**.

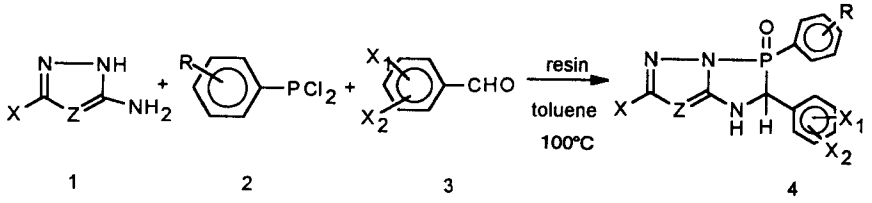
RESULTS AND DISCUSSION

5-Amino-1,2,4-triazole **1** was reacted with the arylphosphonyl dichloride and aromatic aldehyde at 100°C for 20 h in the presence of cation exchange resin (D72 Amberlyst-15) and with blowing N_2 to remove HCl to accelerate the transformation. The resin was removed by filtration. The solvent was evaporated and the residue was subjected to flash chromatography on a silica gel column using acetone/petroleum ether as eluent. The fused heterocyclic compound **4** was obtained as white prisms. The experimental results are summarized in Table I.

TABLE I
Characterization data for **4**

No.	Solvent of VLC or recry.	Yield (%)	m.p. (°C)	Formula	Elemental Analysis Calc./(Found)		
4a	A:P=2:1*	85	229-230	$C_{22}H_{18}ClN_4OPS$	58.34 (58.49)	3.98 (4.00)	12.38 (12.11)
4b	A:P=2:1*	81	198-200	$C_{22}H_{19}N_4OPS$	63.16 (63.20)	4.55 (4.61)	13.40 (13.57)
4c	CH_3CN**	75	207-209	$C_{23}H_{19}N_4O_3PS$	59.74 (59.91)	4.11 (4.12)	12.12 (12.09)
4d	THF**	86	218-219	$C_{23}H_{20}ClN_4OPS$	59.16 (59.00)	4.29 (4.19)	12.00 (12.31)
4e	THF**	79	190-192	$C_{23}H_{21}N_4OPS$	63.89 (63.91)	4.86 (4.69)	12.96 (13.00)
4f	THF**	78	166-168	$C_{24}H_{21}N_4O_3PS$	60.50 (60.72)	4.41 (4.18)	11.76 (11.91)
4g	A:P=2:1*	69	251-253	$C_{24}H_{18}ClN_4OPS$	60.44 (60.27)	3.78 (3.51)	11.75 (11.74)
4h	THF**	65	205-207	$C_{24}H_{19}N_4OPS$	65.16 (65.10)	4.30 (4.11)	12.67 (12.49)

* eluting solvent: A=acetone, P=petroleum (60–90°C); ** solvent of recrystallization.



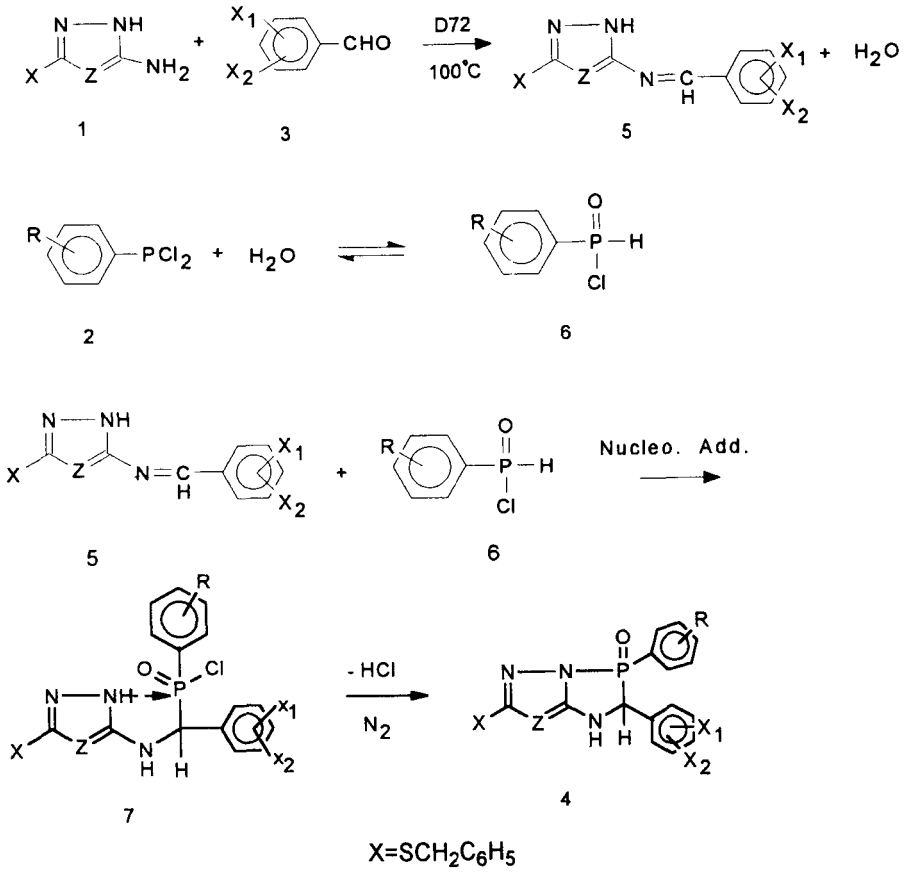
1 2 3 4

X=$SCH_2C_6H_5$

SCHEME I

4	a	b	c	d	e	f	g	h
X1	4-Cl	H	2,3-OCH_2O	4-Cl	H	2,3-OCH_2O	4-Cl	H
X2	H	H		H	H	H	H	H
R	H	H	H	4-CH_3	4-CH_3	4-CH_3	H	H
Z	N	N	N	N	#N	#N	CCN	CCN

The structures were assigned on the basis of mass spectrometry, ^1H NMR, ^{31}P NMR, and IR spectroscopy and are supported by satisfactory elemental analyses. The ^1H NMR spectrum of 2-benzylthio-5-(4-chlorophenyl)-6-phenyl-6-oxo-6-phospha-4,5,6-trihydroimidazolo[2,3e]1,2,4-trizole **4a** shows a doublet of doublets at



SCHEME II Proposed mechanism

5.52–5.63 ppm with the coupling constant $^2J_{PCH}$ = 14.8 Hz, J_{HNCH} = 8.9 Hz. The magnitude of $^2J_{PCH}$ (14.8 Hz) relates to the smaller of the dihedral angle (θ_{OPCH})[8] and this suggests that the oxygen on P-6 and the proton on C-5 are *cis*. The signal for NH mixes with the signal of the aryl group. In the ^{31}P NMR spectrum one singlet at 37.63 ppm indicated only one isomer was formed. The IR spectrum suggests the presence of a P=O group. Based on the above analysis, *trans*-configuration can be proposed.

The mechanism of the reaction may be rationalized as follows: The condensation of 3-benzylthio-5-amino-1,2,4-triazole **1** and the aromatic aldehyde **3**, promoted by a catalytic amount of D72, lead to the imine **5** (Scheme II). The formed H_2O from the condensation reaction partially hydrolyzes the arylphosphonyl dichloride **2** to form **6**, which then undergoes an addition reaction with the imine **5** to yield intermediate **7**. Then the final product **4** is formed by intramolecular nucleophilic substitution. The proposed mechanism was supported by the following fact. The addition reaction of the imine **5g**, isolated from the reaction system, with phenylphosphonyl dichloride **2** could not proceed; when trace H_2O was added to the above reaction system, the reaction proceeded smoothly to give the addition-cyclization production

TABLE II

IR, ^1H, ^{31}P NMR and MS data of **4** prepared

No.	IR(KBr) (cm^{-1})	^1H NMR(DMSO-d6, TMS) (δ, ppm; J, Hz)	^{31}P NMR (85% H_3PO_4)	MS m/z (M^+)
4a	3327(NH) 1289.5(P=O)	4.02(s 2H CH_2), 5.52-5.63(q CHAr $^2J_{PCH}$=14.8 J_{HNCH}=8.9), 7.01-8.00(m 15H ArH C_6H_5 NH)	37.63	452
4b	3310(NH) 1309(P=O)	4.04(s 2H CH_2), 5.31-5.36(b 1H NCHP), 6.91-7.80(m 16H C_6H_5 NH)	37.26	418
4c	3297(NH) 1290(P=O)	4.02(s 2H CH_2), 5.35-5.48(b 1H NCHP), 5.99 (s 2H OCH_2O), 6.79-7.91(m 14H ArH C_6H_5 NH)	35.91	462
4d	3318(NH) 1302(P=O)	2.31(s 3H CH_3), 4.01(s 2H CH_2), 5.51-5.63(q 1H NCHP $^2J_{PCH}$=16.0 J_{HNCH}=7.1), 7.00-7.95 (m 14H ArH C_6H_5 NH)	37.08	466
4e	3293(NH) 1301(P=O)	2.32(s 3H CH_3), 4.01(s 2H CH_2), 5.29-5.41(q 1H NCHP $^2J_{PCH}$=18.0 J_{HNCH}=6.4), 6.91-7.81 (m 15H ArH C_6H_5 NH)	36.78	432
4f	3296(NH) 1303(P=O)	2.31(s 3H CH_3), 4.08(s 2H CH_2), 5.34-5.41(b 1H NCHP), 5.99(s 2H OCH_2O), 6.88-8.00(m 13H C_6H_5 ArH NH)	36.63	476
4g	3381(NH) 2302(C=N) 1301(P=O)	4.05(s 2H CH_2), 5.17-5.29(q 1H NCHP $^2J_{PCH}$ =16.0 J_{HNCH}=8.8),6.92-7.73(m 15H ArH C_6H_5 NH)	33.64	476
4h	3289(NH) 2237(C=N) 1295(P=O)	4.02(s 2H CH_2), 4.91-5.06(b 1H NCHP), 6.84 -7.67(m 16H C_6H_5 NH)	34.57	442

2-benzylthio-5-(4-chlorophenyl)-6-phenyl-6-oxo-6-phospha-4,5,6-trihydroimidazolo-[2,3e]pyrazole **4g**.

In conclusion, a Mannich-type reaction of the 5-amino-1,2,4-triazole and its analogues, which may be applicable to other heterocyclic systems, offers a very efficient route to a new kind of fused phosphorus heterocyclic compounds. However, aliphatic aldehydes or ketones do not react in the same way. Further study is in progress.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were run on a Shimadzu-IR 435 infrared-spectrometer using KBr pellects. ^1H NMR and ^{31}P NMR were obtained using a Brucker AC-P200 spectrometer and were referenced to TMS and 85% H_3PO_4 respectively. EI-MS were measured on a Finniga 4201 mass spectrometer (70 ev). Elementary analyses were obtained using a CHN corder MT-3 elemental analyser. 5-Amino-3-benzylthio-1,2,4-triazole and 5-amino-3-benzylthiopyrazole **1** and arylphosphonyl dichloride **2** were prepared according to the literature.[9-11] D72 resin from Nankai University factory was activated at 80–90°C before use. The aromatic aldehydes were freshly distilled or recrystallized before use.

General procedure for the preparation of 2-benzylthio-5,6-diaryl-6-oxo-6-phospha-4,5,6-trihydroimida-

zolo[2,3e]1,2,4-triazole and its analogues: To a solution of 5-amino-3-benzylthio-1,2,4-triazole or its analogue **1** (5 mmol), arylphosphonyl dichloride **2** (5 mmol) and 50 mg D72 (Amberlyst-15) in 10 ml toluene, a solution of the aromatic aldehyde **3** (5 mmol) in 5 ml toluene was added dropwise at room temperature. The reaction mixture was stirred at 100°C for 20 h with slowly blowing N_2 (TLC indicated the completion of the reaction), and was then filtered. Toluene was removed under reduced pressure and the residue was purified by column chromatography (silica gel H) or recrystallization.

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