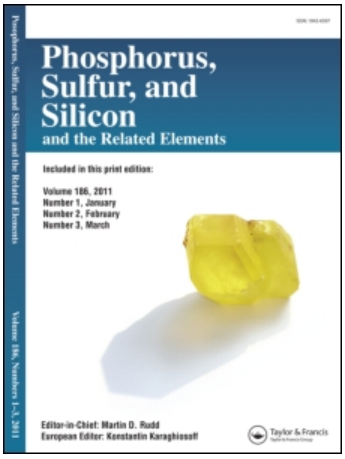

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STAUDINGER REACTION BETWEEN BICYCLIC PHOSPHITES AND AZIDES†

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Staudinger reaction of 4-isopropyl bicyclic phosphite **1** with azides **2–5** to N-substituted bicyclic iminophosphates **8–11** is described. Attempts to obtain the corresponding bicyclic iminophosphates from **1** with azides **6** and **7** were unsuccessful. The microanalytical data, i.r., Raman, ^{31}P n.m.r. and mass spectra of these bicyclic iminophosphates are also reported. The results show that the Staudinger reaction of bicyclic phosphites is more difficult than that of acyclic phosphites, bicyclic phosphites react only with azides (R—N_3) in which R are strong electron-attracting groups. The mechanism of the reaction is discussed.

Key words: Staudinger reaction; bicyclic phosphite; iminophosphate.

INTRODUCTION

Staudinger reaction of phosphites with covalent azides is a common method for obtaining iminophosphates. Although it has been well studied,[1,2] little knowledge is available on the reaction of bicyclic phosphites with azides.[3] The skeleton structure of bicyclic phosphites is stericly defined, their Staudinger reaction may be different from that of acyclic phosphites. We wish to report the results on this reaction and discuss the affecting factors.

RESULTS AND DISCUSSION

4-Isopropyl phosphite **1**, which was prepared by Wadsworth's procedure,[4] reacts with alkoxy carbonyl azides **2** at 60–80°C in dry benzene losing a molecule of nitrogen. The reaction is finished when nitrogen evolution ceases and *N*-alkoxy carbonyl-4-isopropyl bicyclic iminophosphates **8** are obtained in high yields (60–99%). Compound **8b** will decompose above 80°C when it is purified by recrystallization.

Compound **1** interacts with azidophosphates **3** similarly. The reaction proceeds over a period of 48–54 hrs at 80°C and affords the products **9** in 60–90% yields. **9a** is also obtained by a combination of the Atherton-Todd and Staudinger reaction,[5] in which pyridine and triethylamine are used as catalysts:

† It was accepted at the 10th International Conference on Phosphorus Chemistry in Bonn, Germany 1986.

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1 **2** R=C(O)OR^1 **8** R=C(O)OR^1

R^1= a) Me; b) Ally; c) Pr-i; d) Pr; e) Bu-n; f) Bu-t; g) Pent-n; h) Ph; i) CHMeC(Me)$_3$; j) Octyl-n

3 R=P(O)R^{2}R^3 **9** R=P(O)R^{2}R^3

a) R^2=R^3=OMe; b) R^2=R^3=OEt; c) R^2=CH$_3$; R^3=OBu-i

4 R=C(O)R^4 **10** R=C(O)R^4

a) R^4=Ph; b) R^4=CH=CHPh; c) R^4=C≡CPh

5 R=C(O)NMe$_2$ **11** R=C(O)NMe$_2$

6 R=CH$_2$CH$_2$NMe$_2$ ———

7 R=SiMe$_3$ ———

TABLE I

Synthetic conditions and physical data for bicyclic iminophosphates

Compd no.	Yield (%)	M.P. (°C)	Synthetic Condition Solv./Tempt./Time	Microanalysis found(calc.)% C	H	N	P
8a	93	172-173.5	C_6H_6/80°C/5hrs	43.14 (43.37)	6.62 (6.42)	5.70 (5.62)	12.39 (12.45)
8b	91	109-110.5	C_6H_6/60°C/6.5hrs	47.33 (48.00)	6.78 (6.55)	5.09 (5.09)	10.83 (11.27)
8c	98	105-107	C_6H_6/80°C/7.5hrs	47.37 (47.65)	7.50 (7.22)	4.75 (5.05)	11.29 (11.19)
8d	99	150-151.5	C_6H_6/80°C/8hrs	47.88 (47.65)	7.00 (7.22)	5.02 (5.05)	11.04 (11.19)
8e	84	129-131	C_6H_6/80°C/5hrs	49.49 (49.48)	7.09 (7.52)	4.51 (4.81)	10.92 (10.56)
8f	99	169-171	C_6H_6/80°C/7.5hrs	48.96 (49.48)	7.78 (7.52)	4.45 (4.81)	10.81 (10.56)
8g	95	129-131	C_6H_6/70°C/10hrs	50.52 (51.15)	7.77 (7.87)	4.04 (4.59)	10.16 (10.16)
8h	60	127-129	C_6H_6/80°C/7.5hrs	53.58 (54.02)	5.85 (5.78)	4.36 (4.50)	9.67 (9.97)

TABLE I (*Continued*)

Compd no.	Yield (%)	M.P. (°C)	Synthetic Condition Solv./Tempt./Time	Microanalysis found(calc.)% C	H	N	P
8i	35	184-185	C_6H_6/70°C/10hrs	52.39 (52.66)	5.88 (5.79)	4.36 (4.50)	9.96 (9.73)
8j	91	100-102	C H /70°C/10hrs	55.00 (55.33)	8.90 (8.65)	3.80 (4.03)	9.01 (8.93)
9a	90	135-135.5	C6H6/80°C/54hrs	36.21 (36.12)	6.58 (6.35)	4.49 (4.68)	20.60 (20.74)
9b	73	132-133.5	C6H6/80°C/48hrs	40.07 (40.39)	7.30 (7.03)	3.68 (4.28)	19.10 (18.96)
9c	62	105-105.5	C6H6/80°C/54hrs	44.36 (44.31)	8.02 (7.69)	4.04 (4.31)	18.84 (19.08)
10a	59	215-215.5	C6H6/40°C/3.5hrs	57.25 (56.95)	6.34 (6.10)	4.54 (4.75)	10.55 (10.51)
10b	28	208-210	C6H6/40°C/24hrs	59.87 (59.81)	6.40 (6.23)	4.09 (4.36)	9.18 (9.66)
10c	14	182-184	C6H6/40°C/10hrs	59.45 (60.19)	5.82 (5.64)	3.91 (4.38)	9.60 (9.69)
11	70	152-153	C6H6/80°C/9hrs	45.78 (45.60)	7.58 (7.25)	10.65 (10.69)	11.78 (11.83)

$$\mathbf{1} + HP(O)(OMe)_2 + NaN_3 + CCl_4 \xrightarrow[Et_3N]{Py.} \mathbf{9a} + CHCl_3 + NaCl\downarrow + N_2\uparrow$$

1 has to be treated with excessive amount of aryl carbonyl azides **4** at 40°C to give *N*-aryl carbonyl 4-isopropyl bicyclic iminophosphates **10a–c**. Attempts to obtain the corresponding bicyclic iminophosphates from compound **1** with alkyl carbonyl azides **4** (R^4 = alkyl) are unsuccessful, because alkyl carbonyl azides rearrange slowly to isocyanates.[6] The trans configuration of **10b** is proved by ^{1}H. n.m.r. spectroscopy. Generally, the configurations of cinnamides (Ar—CH_b=CH_a—C(O)NR_2) were determined by coupling constants of Ha and Hb protons ($^4J_{HaHb}$) in the ^{1}H n.m.r. spectra.[7] When $^4J_{HaHb}$ were larger than 13 Hz, the cinnamides were trans; when $^4J_{HaHb}$ were smaller than 13 Hz, they were cis. In the ^{1}H n.m.r. spectrum of **10b** can be seen a doublet in which $^4J_{HaHb}$ is 15.8 Hz, which we ascribe to the Hb proton, and a quadruplet of Ha proton in which $^4J_{HaHb}$ is 15.8 Hz and $^5J_{HaP}$ is 6 Hz.

Compound **1** does not react with alkyl azide **6** or trimethylsilyl azide **7** in benzene at 80°C or in mesitylene at 150°C, while acyclic phosphites did react with **6** and **7** on gentle heating.[8,9]

It was reported that acyclic phosphites react with azides under gentle conditions.[2,8–10] From our experiments, we find that the Staudinger reaction of bicyclic phosphites with azides is more difficult than that of acyclic phosphites, bicyclic phosphites react only with azides R—N_3, where R is a strong electron-attracting group, Kozlov *et al.*[3] reported the synthesis of *N*-ethyl carbonyl-4-ethyl bicyclic iminophosphate and explained that it was the increase of *s*-electron density in the

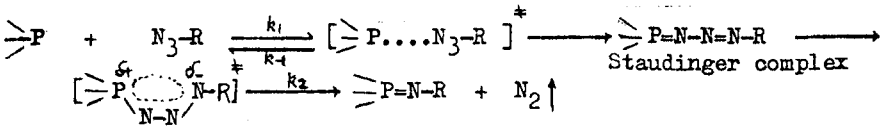
TABLE II

Spectral data for bicyclic iminophosphates

Compd no.	I. R. (cm^{-1}) (KBr film)	^{31}P-NMR P^r† P^s†($J_{P^rP^s}$Hz)	Raman (cm^{-1})	Ms (m/e)
8a	1690 1460 950 4.65 C=O P=N C-O(P)		853 760 649 P(O)3 P-O C(CH2)3	249
8b	1660 1580 1480 1000 5.34 C=O C=C P=N C-O(P)			275
8c	1650 1410 1020 4.39 C=O P=N C-O(P)			277
8d	1660 1410 980 5.00 C=O P=N C-O(P)		845 760 625 P(O)3 P-O C(CH2)3	277
8e	1600 1410 1050 5.40 C=O P=N C-O(P)		870 763 626 P(O)3 P-O C(CH2)3	291
8f	1600 1410 1000 4.73 C=O P=N C-O(P)		870 783 626 P(O)3 P-O C(CH2)3	291
8g	1650 1400 980 4.88 C=O P=N C-O(P)			305
8h	1680 1580 1460 900 6.25 C=O Ph P=N C-O(P)		870 749 635 P(O)3 P-O C(CH2)3	311
8i	1660 1410 1020 4.71 C=O P=N C-O(P)			319
8j	1660 1420 1020 5.01 C=C P=N C-O(P)			347
9a	1350 1240 1010 -7.06 -0.09(82.2) P=N P=O C-O(P)			299
9b	1360 1220 960 -7.69 -2.73(81.4) P=N P=O C-O(P)		857 709 600 P(O)3 P-O C(CH2)3	327
9c	1360 1210 1020 -8.88 20.93(47.4) P=N P=O C-O(P)			325
10a	1610 1580 1410 980 8.86 C=O Ph P=N C-O(P)		875 745 619 P(O)3 P-O C(CH2)3	295
10b	1640 1595 1410 1000 6.70 C=O C=C P=N C-O(P)			321
10c	2180 1600 1400 1000 4.44 C≡C C=O P=N C-O(P)			319
11	1620 1400 1030 5.24 C=O P=N C-O(P)		871 754 630 P(O)3 P-O C(CH2)3	262

† P^r is the chemical shift of phosphorus in the bicyclic skeleton, P^s is that in the substituents.

electron cloud around phosphorus of bicyclic phosphites which caused reduced reactivity. The mechanism of Staudinger reaction is:



The reason that bicyclic phosphites react with azides difficultly is probably that the electron-donating ability of bicyclic phosphites descends when compared with that of acyclic phosphites.

The electronic charge distribution of phosphites was calculated by CNDO/2 method:[11] δ- of P(III) in $P(OMe)_3$ was 1.791, δ- of P(III) in $RC(CH_2O)_3P$ was 1.718.

Thus, the electron-donating ability of bicyclic phosphites descends obviously. Rational explanation is that, firstly, there is an important degree of d_π—p_π bonding in the phosphorus-ester oxygen link of phosphites, and the overlap will favor electron delocalization of oxygen to phosphorus. Therefore, the electron-donating ability of phosphorus will increase. Because of hard steric restriction of the bicyclic skeleton, the favorable overlap will be destroyed; Secondly, the oxygen lone pairs of electrons on esters will depart further from the lone pair of electrons of phosphorus, "α electron repulsion effects will be reduced. As a result, the negative charge of P(III) in bicyclic phosphites will decrease and their electron-donating ability will decrease.

EXPERIMENTAL

Melting points were measured on a SM-Lux micromelting meter made by West Germany and were uncorrected. ^{31}P and ^1H n.m.r. spectra were obtained on a Varian FT-800A spectrometer, respectively in $CDCl_3$ solvent (H_3PO_4—D_2O as an internal standard) and in $CDCl_3$ solvent ($SiMe_4$ as an internal standard). The IR and Raman spectra were done as KBr pellets respectively on a BE 599B spectrometer and on a R-500 laser Raman spectrometer made by Japan Spectroscopic Co. Mass spectra were determined on a JEOL JMS-300 spectrometer, using the direct-insertion method and electron-impact at an ionizing voltage of 70 eV. Azides were prepared according as previously described. All solvents were dried.

N-alkoxy carbonyl-4-isopropyl bicyclic iminophosphates **8**: A solution of 11 mmol of alkoxy carbonyl azides **2** in 2 ml of benzene was added slowly to a stirred solution of 10 mmol of 4-isopropyl bicyclic phosphite **1** in 3 ml of benzene at 80°C. Stirring was continued until nitrogen evolution ceased. The white solid was filtered and purified by recrystallization. The detailed synthetic conditions and spectral data of Compound **8** are summarized in Tables I and II.

Solvent for recrystallization: **8a,d** ethanol; **8b,i** 1,2-dichloroethane-ether; **8c** tetrachlorocarbon-ethanol; **8e,f** isopropanol-*n*-hexane; **8g** tetrachlorocarbon; and **8h** ethanol-trichlorohydrocarbon; **8j** benzene-petroleum ether.

N-phosphate-4-isopropyl bicyclic iminophosphates **9**: Method A: Compound **9a–c** were synthesized by above method.
Recryl. solvent: **9a** benzene-ether; **9b** tetrachlorocarbon-hexane-*n*
9c was purified by column chromatography on silica gel ($CHCl_3$: ethyl acetate 1:1 as eluent). Method B: 0.525 g (3.44 mmol) of tetrachlorocarbon was added slowly to a solution of 0.55 g (3.13 mmol) of **1**, 3.13 mmol of dimethyl phosphite, 0.28 g (4.31 mmol) of sodium azide, 2 drops of triethylamine and 15 ml of dry CH_3CN at 80°C about 30 minutes. Stirring was continued for 2 hrs, then 4 drops of pyridine was dropped to the solution, the reaction continued for 48 hrs. After cooling, solids (NaCl + NaN_3) were filtered off, and the solution was evaporated. The residue was recrystallized from benzene and ether.

N-aryl carbonyl-4-isopropyl bicyclic iminophosphates **10**: Compound **10a–c** were synthesized by a method similar to **8**.
Recryl. solvent: **10a** benzene-ether; **10b** ethanol
10c was purified by column chromatography on silica gel ($CHCl_3$: ethyl acetate 1:1 as eluent).

N-dimethylamide-4-isopropyl bicyclic iminophosphate **11**: Compound **11** was synthesized by a method similar to **8**. It was purified by recrystallization in benzene and ether.

The detailed synthetic conditions, physical properties and spectral data of Compound **9–11** are summarized on Tables I and II.

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