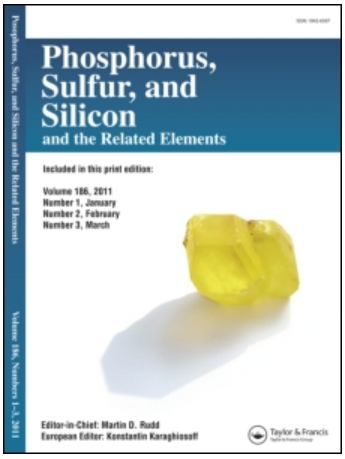

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STUDIES ON CHIRAL THIOPHOSPHORIC ACIDS AND THEIR DERIV ATIVES 16.-THE ASYMMETRIC CYCLIZATION OF L-( )- PROLINOL WITH (THIO)PHOSPHORO(-NO)DICHLORIDATES

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STUDIES ON CHIRAL THIOPHOSPHORIC ACIDS AND THEIR DERIV ATIVES 16.—THE ASYMMETRIC CYCLIZATION OF L-(+)-PROLINOL WITH (THIO)PHOSPHORO(-NO)DICHLORIDATES

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The cyclizations of L-(+)-prolinol **5** with (thio)phosphoro(-no)dichloridates **6** give 1,2,3-azaphosphaoxabicyclo[3.3.0]octanes **7** consisting of unequal amounts of diastereoisomers, eight pairs of which have been successfully resolved by silica gel column chromatography or recrystallization. The influences of reaction temperature, solvent and substrate concentration upon the asymmetric induction have also been investigated.

Keywords: Asymmetric Cyclization; L-prolinol; (Thio)phosphoro(-no)dichloridate; Azaphosphaoxabicyclooctane; Diastereoisomer

INTRODUCTION

It was reported previously that (+)-cis-1,2,2-trimethyl-1,3-diaminocyclopentane **1** derived from D-camphor reacts with thiophosphorodichloridates **2** or O-(4-nitrophenyl) thiophosphorochloridates **3** to form a diastereoisomeric mixture of (+)-2,4,5-diazaphosphabicyclo[3.2.1]octane **4**.[1,2] In that paper,[2] the difference in stereochemical outcome between the cyclization of (+)-**1** with phosphorus reagent **2** and that of (+)-**1** with phosphorus reagent **3** had been investigated and explained rationally according to a trigonal bipyramid(TBP) intermediate and Berry pseudorotation(BPR) concept. In this paper, the cyclization of L-(+)-

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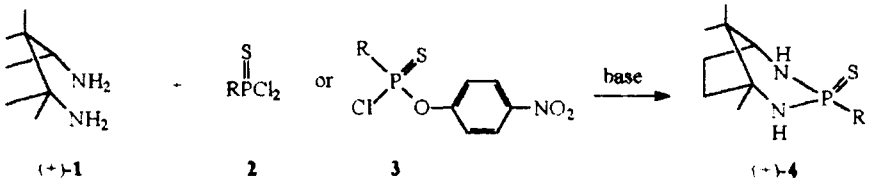


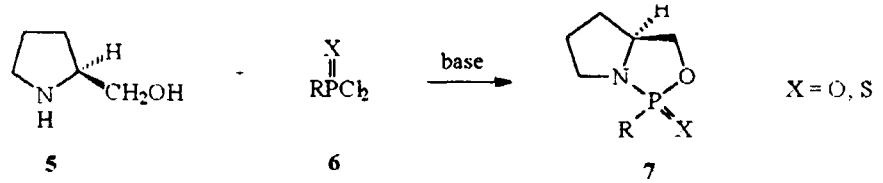
(+)-1 2 3 (+)-4

prolinol **5** derived from L-proline with phosphoro(-no)dichloridate **6** (X = O) or its thio-analogue **6** (X = S) is described, which gives 1,2,3-azaphosphaoxabicyclo[3.3.0]octane **7** as an unequal mixture of diastereoisomers.

RESULTS AND DISCUSSION

The cyclizations of (+)-**5** with **6** were performed in the presence of triethylamine at 60 ~ 65°C for 3 ~ 5 h in chloroform solvent. After the reactions were complete, the ratios of diastereoisomers of the crude products **7** were determined by ^{31}P NMR technique and then the percentages of diastereoisomeric excess (%de) were calculated from the intensities of ^{31}P NMR resonances (Table I). Products 1,2,3-azaphosphaoxabicyclo[3.3.0]octanes **7** were obtained in moderate to fair yields with low to good %de values. Generally, every product **7** (X = O) except 7e has a relatively better %de value compared with its thio-analogue (X = S). This result is presumbly due to the higher reactivities of phosphoro(-no)dichloridates **6** (X = O) than those of their corresponding thiophosphoro(-no)dichloridates **6** (X = S). The crude products **7** were easily purified by vaccum liquid chromatography (VLC) on silica gel or by recrystallization. Their structures were confirmed by IR, ^1H NMR spectra and elemental analyses (Table II). In some cases, product **7** as a mixture of a pair of diastereoisomers was successfully resolved by VLC in excellent resolved yield, e.g., 7f ~ h, 7j ~ l (Table III). These asymmetric cyclizations may provide a possibility for preparation of chiral phosphorus reagents with known absolute configuration.

In a preliminarily investigation, the influences of reaction temperature, solvent and substrate concentration upon stereochemical outcome of the cyclizations



5 **6** **7**

TABLE I Data of 7 as diastereoisomeric mixture prepared

								Elemental Analyses					
			n_D^{25} or	^{31}P NMR		de	Yield	C%		H%		N%	
7	R	X	mp(°C)	δ (ppm)*		(%)	(%)	Calc.	Found	Calc.	Found	Calc.	Found
a	EtO	O	1.4685	25.98	21.94	12.8	84.6	44.00	43.95	7.38	7.32	7.33	7.31
b	EtO	S	1.5170	83.33	90.87	8.5	92.6	40.58	40.32	6.81	6.84	6.76	6.68
c	EtS	O	1.5249	49.00	41.32	36.3	67.6	40.58	40.48	6.81	6.97	6.76	6.58
d	EtS	S	1.5749	109.98	99.75	5.5	75.9	37.65	37.53	6.32	6.15	6.27	6.22
e	PhO	O	1.5338	21.67	16.42	11.4	83.3	55.23	54.94	5.90	5.85	5.86	5.69
f	PhO	S	78~79	74.85	83.33	23.0	78.9	51.95	51.82	5.46	5.46	5.50	5.30
g	Et_2N	O	1.4808	23.69	30.55	34.1	64.2	49.54	49.41	8.78	8.38	12.84	12.74
h	Et_2N	S	50~51	75.92	89.52	23.2	76.9	46.14	46.13	8.17	7.83	11.96	11.68
i	Me	O	1.4790	51.42	45.09	48.3	78.6	44.77	44.58	7.50	7.55	8.69	8.45
j	Me	S	1.5488	109.58	100.15	8.0	84.3	40.67	40.72	6.83	6.94	7.90	7.94
k	Ph	O	110~112	38.09	33.79	80.3	80.7	59.19	59.03	6.32	6.22	6.28	6.29
l	Ph	S	86~87	100.96	91.81	11.9	75.3	55.32	55.26	5.88	5.88	5.84	5.91

*The first δ value corresponds to that of the major diastereoisomer

TABLE II IR and ^1H NMR data of **7** as diastereoisomeric mixture

	IR (film or KBr tablet) $\nu(cm^{-1})$			
7	P=O	P-N	P-O-C_{ring}	^1H NMR, δ(ppm), J_{PH} (Hz)
a	1236	960	1196, 1000	1.28(t,3H), 1.46~2.14(m,4H), 2.72~3.42(m,1H), 3.98(m,6H)
b		957	1197, 1002	1.28(t,3H), 1.46~2.14(m,4H), 2.72~3.42(m,1H), 4.04 (m,6H)
c	1236	960	1195, 1000	1.34(t,3H), 1.52~2.14(m,4H), 2.86(m,3H), 3.56~4.62(m,4H)
d		957	1195, 999	1.34(t,3H), 1.52~2.14(m,4H), 2.86(m,3H), 3.58~4.62(m,4H)
e	1222	960	1157, 1004	1.48~2.20(m,4H), 2.78~3.26(m,1H), 3.32~4.62(m,4H), 7.16(m,5H)
f		953	1158, 995	1.48~2.24(m,4H), 2.84~3.28(m,1H), 3.34~4.68(m,4H), 7.14(m,5H)
g	1236	949	1179, 1009	1.14(t,3H), 1.46~2.14(m,4H), 3.02(m,5H), 3.52~4.46(m,4H)
h		970	1166, 1005	1.14(t,6H), 1.46~2.14(m,4H), 3.08(m,5H), 3.54~4.48(m,4H)
i	1227	961	1199, 1007	1.60(d,3H,J=18.0), 1.46~2.14(m,4H), 2.66~3.38(m,1H), 3.48~4.44(m,4H)
j		958	1197, 1001	1.96(d,3H,J=17.2), 1.46~2.18(m,4H), 2.70~3.38(m,1H), 3.58~4.62(m,4H)
k	1228	960	1197, 1003	1.46~2.24(m,4H), 2.28~3.34(m,1H), 3.76~4.70(m,4H), 7.42~8.10(m,5H)
l		965	1168, 1001	1.46~2.18(m,4H), 2.84~3.30(m,1H), 3.66~4.78(m,4H), 7.18~7.96(m,5H)

have been disclosed. The results indicate that reaction temperature (room temperature or reflux in chloroform) has a little effect on the %de values of products **7**. Reflux temperature in chloroform is preferable in all cyclization experiments in order to shorten reaction times. Solvent and substrate concentration have significant influences upon the asymmetric induction of the cyclizations. Chloroform solvent of moderate polarity is preferably used to obtain higher %de

TABLE III Data of the resolved diastereoisomers of **7**

7	*n_D^{25} or mp (°C)*	*^{31}P NMR, δ (ppm)*	*$[\alpha]_D$ (in $CHCl_3$)*	*Resolved yield (%)*
f	95~96	74.98	−66.3	90.0
	61~62	83.83	+36.5	89.9
g	1.4848	23.69	+25.1	86.6
	1.4768	30.42	+85.3	85.3
h	70~71	76.06	+69.5	81.0
	24~25	89.92	+100.0	87.1
j	1.5440	109.58	+95.6	87.2
	88~89	100.15	+72.5	85.2
k	112~113	38.50	+85.6	95.0
l	91~93	100.15	+117.6	86.5
	71~72	91.00	−2.5	87.9

values in the cyclizations. For exemples, 7a was prepared separately in acetonitrile, chloroform and petroleum ether with %de values of 16.4, 62.4 and 23.7, respectively. Additionally, low substrate concentration can facilitate producing **7** with a relatively high %de value. For instances, five selected compounds 7a~b, 7d, 7f, 7l have prepared from a same amount of (+)-**5** (0.1 mol) in 30 ml. and 50 ml. of chloroform, respectively. Their %de values are illustrated as follows:

Compounds	*7a*	*7b*	*7d*	*7f*	*7l*
%de obtained in 30 ml. of $CHCl_3$	12.8	8.5	5.5	23.0	11.9
%de obtained in 50 ml of $CHCl_3$	62.4	62.4	32.5	43.4	100

The above data clearly show that cyclizations proceeding in lower concentrations can afford much higher %de values.

Experimental

Melting points were determined with Yanaco MP-500 apparatus. ^1H and ^{31}P NMR spectra were measured in $CDCl_3$ on a JEOL FX-90Q instrument at 90 MHz, using TMS as internal standard and 85% H_3PO_4 as external standard. IR spectra were recorded on Shimadzu IR-435 spectrophotometer as thin film or KBr tablet. Optical rotations were measured on a Perkin-Elmer 241MC polarimeter. All temperatures were uncorrected.

Preparation of L-(+)-prolinol 5: As described previously in the literatures,[3,4] L-proline (11.5 g, 100 mmol) was reduced by $LiAlH_4$ in THF to give (+)-**5** with b.p. 54~56°C/1 mm, n_D^{25} 1.4848, $[\alpha]_D$ +38.6° (c = 1, $CHCl_3$); yield: 7.0 g (70.0%).

Preparation of (thio)phosphorodichloridates 6a~h: According to general method, phosphorus oxychloride or thiophosphoryl chloride reacted with equiv-

TABLE IV Data of (Thio)phosphoro(-no)dichloridates **6** prepared

6	*R*	*X*	*mp (°C) or bp (°C/mm)*	n_D^{25}	*Yield (%)*	*6*	*R*	*X*	*mp (°C) or bp (°C/mm)*	n_D^{25}	*Yield (%)*
a	EtO	O	58 ~ 62/10	1.4338	78.5	g	Et_2N	O	46 ~ 50/0.2	1.4620	66.3
b	EtO	S	66 ~ 68/20	1.5026	87.0	h	Et_2N	S	50 ~ 54/0.5	1.5248	73.6
c	EtS	O	40 ~ 42/1	1.5226	83.2	i	Me	O	32 ~ 35		92.8
d	EtS	S	58 ~ 62/2	1.5881	81.6	j	Me	S	30 ~ 40/15	1.5430	62.2
e	PhO	O	62 ~ 64/0.1	1.5208	70.1	k	Ph	O	126 ~ 127/12	1.5575	64.2
f	PhO	S	82 ~ 84/0.5	1.5720	74.5	l	Ph	S	70 ~ 72/0.1	1.6221	75.6

alent amounts of alcohol, phenol, mercaptan or diethylamine in organic solvent to give 6a ~ h conveniently. Data of **6** prepared are listed in Table IV .

Preparation of methyl(thio)phosphonodichlorides 6i,j: As described previously in the literatures,[5,6] O,O-dimethyl methylphosphonate reacted with $SOCl_2$ to give methylphosphonodichloride **6i**, which was then treated with P_2S_5 to produce **6j**.

Preparation of phenyl(thio)phosphonodichlorides 6k,l: As described previously in the literatures,[7,8,9] phosphorus trichloride reacted with benzene in the presence of $AlCl_3$ to give $PhPCl_2$, which was then sulfurized with sulfur or oxidized with P_2O_5 and chlorine to produce **6l** and **6k**, respectively.

Cyclization of (+)-5 with 6e (Typical procedure): To a mixture of (+)-**5** (1.01 g, 10 mmol), Et_3N (2.22 g, 22 mmol) and $CHCl_3$ (20 ml.), a solution of **6e** (2.11 g, 10 mmol) in $CHCl_3$ (10 ml.) was added dropwise with stirring at 60°C. The reaction mixture was refluxed for 3 h, then cooled to room temperature. A sample (1 ml.) was removed from the reaction mixture to measure ^{31}P NMR spectra. The remaining reaction mixture was washed with water (30 ml.) and then dried. After removal of solvent, the crude product (3.20 g) was purified by VLC on silica gel (300 ~ 400 mesh, petroleum ether/EtOAc gradient elution) to give product **7e** with n_D^{25} 1.5338; yield: 2.00 g (83.3%).

Resolution of a pair of diastereoisomers in 7f (Typical procedure): The crude product **7f** obtained from the reaction of (+)-**5** with **6f** was preliminarily purified by recrystallization with a mixture solvent (10 ml. of petroleum ether and 4 ml. of EtOAc) to give a white solid, which was further resolved by VLC on silica gel (300 ~ 400 mesh, petroleum ether/EtOAc gradient elution) to give two fractions, the first with a chemical shift δ 74.98 ppm and the second with 83.83 ppm in ^{31}P NMR spectra.

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References

[1] C. C. Tang, H. F. Lang, L. G. Wu, Z. J. He, R. Y . Chen, *Chinese Chem. Lett.*, **7**(3), 705 (1997).
[2] C. C. Tang, H. F. Lang, Z. J. He, R. Y . Chen, *Phosphorus, Sulfur and Silicon*, **104**, 123 (1996).
[3] R. G. Kostyanovsky, L. M. Gella, et al., *Tetrahedron*, **30**, 39 (1974).
[4] U. Schmidt, R. Scholm, *Angew. Chem. Int. Ed. Engl.*, **28**(2), 752 (1989).
[5] K. Vasu, N. K. Roy, *Agric. Biol. Chem.*, **47**(11), 2657 (1983).

[6] J. Grosse, W. Pieper, H. Neumaier, et al., *Angew. Chem. Int. Ed. Engl.*, **21**(7), 542 (1982).
[7] N. K. Roy, H. K. Taneja, *J. Indian Chem. Soc.*, **69**, 42 (1992).
[8] E. H. Amonoo-Neizer, et al., *J. Chem. Soc.*, 4296 (1965).
[9] A. D. F. Toy, *J. Am. Chem. Soc.*, **70**, 186 (1948).