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Ring-Opening Reactions of Some Phosphoryl-Substituted Cyclopropanes by -NH and -SH Nucleophiles

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ABSTRACT

Reactions of (1-cyanocyclopropyl)diphenylphosphine oxide (1a) with -NH and -SH nucleophiles gave the anticipated ring-opened products, while those of (1-ethoxycarbonylcyclopropyl)diphenylphosphine oxide (1b) or diethyl 1-cyano- and 1-ethoxycarbonylcyclopropylphosphonates (1c–d) were often deflected by ester-exchange reactions. The ring-opened products of 1a by amines reacted with aromatic aldehydes under PTC conditions to produce homoallylic amines in good yields. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Electrophilic cyclopropanes can easily undergo ring-opening reactions under the attack of nucleophiles, and this reaction has been widely used in organic synthesis [1,2]. There are a few reports on the ring-opening reactions of some cyclopropylphosphonium salts with nucleophiles [1–7], but there is only one example of such a reaction of a phosphoryl-substituted cyclopropane, that with Me_2CuLi [8]. We report here a study of ring-opening reactions of some substituted cyclopropylphosphine oxides and cyclopropylphosphonates with -NH and -SH nucleophiles.

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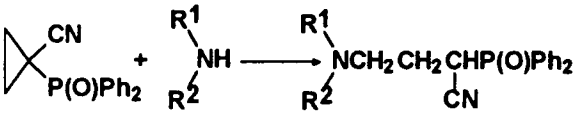
RESULTS AND DISCUSSION

Reaction of (1-Cyanocyclopropyl)diphenylphosphine Oxide (1a) with Primary and Secondary Amines

The ring-opening reaction of 1a by piperidine (2a) indicates that this reaction can take place in various solvents if the reaction temperature is higher than 78°C and that the reaction is markedly accelerated with the increase of the reaction temperature. This reaction can also proceed smoothly without solvent (Table 1).



1a 2a-k 3a-k

a: R^1R^2= ; b: R^1R^2=O ;
c: R^1R^2= ; d: R^1R^2= ;
e: R^1R^2= ; f: R^1=R^2= Et;
g: R^1=R^2= i-Pr; h: R^1=R^2= c-C_6H_{11};
i: R^1= H, R^2= n-pentyl; j: R^1=H, R^2=c-C_6H_{11};
k: R^1=H, R^2=Ph. (1)

However, the structure of the amine has a great influence on the ring-opening reaction of 1a (Equation 1, Table 1). In general, secondary amines are better ring-opening reagents than primary amines. Secondary amines, especially cyclic ones, such as piperidine (2a), morpholine (2b), and imidazole (2c), reacted with 1a at 150–160°C to produce the corre-

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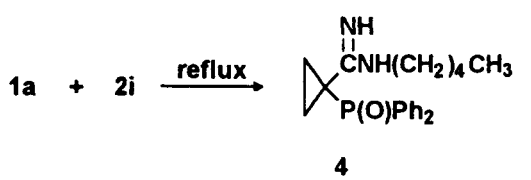
TABLE 1 Reaction of **1a** with Primary and Secondary Amines **(2)**

Nucleophiles (2)	*1a/2*[a]	*Solvent*	*Temperature* (°C)	*Duration* (*h*)	*Yield* (%)[b]
2a	1/3	xylene	reflux (138)	21	84.5
2a	1 mmol/5 mL	—	reflux (115)	10	84.9
2a	1/3	xylene	145–150[c]	10	95.9
2a	1 mmol/5 mL	—	145–150[c]	10	94.5
2b	1 mmol/3 mL	—	reflux (129)	24	75.3
2b	1 mmol/3 mL	—	160[c]	24	90.6
2c	1/5	xylene	160[c]	24	89.7
2d	1 mmol/5 mL	—	160[c]	24	*d*
2d	1/5	benzene	reflux (80)	36	73.3
2e	1 mmol/2 mL	—	160[c]	24	*e*
2f	1 mmol/2 mL	—	160[c]	24	*d*
2f	1/5	benzene	reflux (80)	25	47.6
2g	1 mmol/2 mL	—	160[c]	25	13.3
2h	1/1.1	xylene	reflux (138)	62	0
2i	1/2	EtOH	reflux (78)	71	17.0
2i	1 mmol/3 mL	—	160[c]	20	*e*
2i	1 mmol/3 mL	—	reflux (102)	30	*f*
2j	1 mmol/4 mL	—	160[c]	24	*e*
2k	1 mmol/4 mL	—	145[c]	24	*e*

[a]Molar ratio unless otherwise indicated.
[b]Isolated yield.
[c]Conducted in sealed tube.
[d]Decomposed and $Ph_2P(O)OH$ was isolated.
[e]The product was a complex mixture.
[f]**4** was isolated in a yield of 68.7%, see text.

sponding ring-opened products in high yields. Pyrrolidine (**2d**) and diethylamine (**2f**) reacted with **1a** under mild conditions to give good yields of the ring-opened products. However, when the reaction was performed in a sealed tube at a bath temperature of 160°C, decomposition products were isolated. With the rise of steric hindrance, the ring-opening ability of secondary amines decreases quickly. Diisopropylamine (**2g**) could give only a poor yield of the desired product, and dicyclohexylamine (**2h**) did not react at all.

Aliphatic and aromatic primary amines cannot undergo this reaction easily. n-Pentylamine (**2i**) reacted with **1a** under refluxing in ethanol for 72 hours to produce a low yield (17%) of the desired product. When this reaction was carried out by using excessive n-pentylamine as the solvent under refluxing, one isolated product indicated that the addition reaction of the amine to the cyano group was the main reaction (Equation 2).



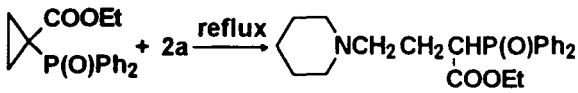
(2)

4

When this reaction was performed in a sealed tube at a bath temperature of 145°C, the products were too complex to be isolated. Reactions of n-hexylamine (**2j**), aniline (**2k**), and pyrrole (**2e**) with **1a** under similar conditions also led to complex mixtures.

Reactions of (1-Ethoxycarbonylcyclopropyl) diphenylphosphine Oxide (1b), *Diethyl (1-Cyanocyclopropyl)phosphonate* (1c) *and Diethyl (1-Ethoxycarbonylcyclopropyl) phosphonate* (1d) *with Amines*

When **1b** was refluxed with an excess of **2a** for 6 hours, the desired product was obtained in a yield of 72.6% (Equation 3).



(3)

1b **5**

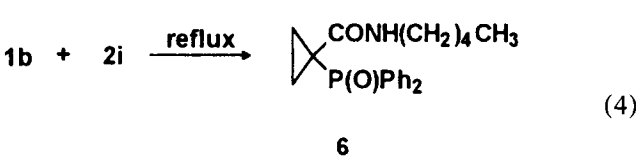
When the reaction time was prolonged, some ester-exchanged products were formed.

Reaction of **1b** with primary amines, such as n-pentylamine (**2i**), could only lead to a high yield of the ester-exchanged product (Equation 4).

TABLE 2 Reaction of **1a** with Thiophenol and Mercaptans **(7)**

Entry	RSH (7)	1/7	Pyridine	Solvent	Temp. (°C)	Yield (%)[a]
1	PhSH	0.5 mmol/0.5 mL	—	xylene	reflux	trace
2	PhSH	0.5 mmol/1.2 mL	0.1 mL	—	160[c]	83.7
3	C_2H_5SH	0.5 mmol/2 mmol	—	xylene	reflux	0
4	C_2H_5SH	0.5 mmol/0.6 mL	0.05 mL	—	165[c]	75.3
5	n-$C_6H_{13}SH$	0.5 mmol/2 mmol	—	xylene	reflux	0
6	n-$C_6H_{13}SH$	0.5 mmol/2 mmol	—[b]	xylene	reflux	trace
7	n-$C_6H_{13}SH$	0.5 mmol/1.0 mL	0.05 mL	—	165[c]	trace
8	n-$C_6H_{13}SH$	0.5 mmol/1.0 mL	0.05 mL[b]	—	165[c]	77.8

[a]Isolated yield.
[b]10 mol% DMAP was added as catalyst.
[c]Conducted in sealed tube.

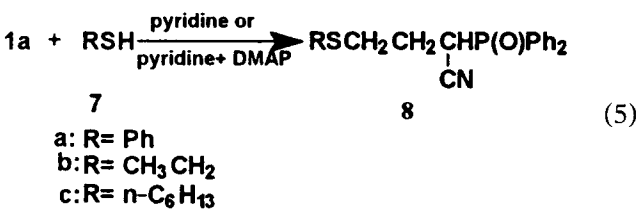


6 (4)

Ring-opening reactions of 1c and 1d with amines were seriously inhibited by the ester-exchange reactions. 1c or 1d reacted with 2a at various molar ratios and at different temperatures always to produce complex mixtures.

Reaction of 1a *with Mercaptans and Thiophenol*

Ring-opening reactions of 1a with mercaptans are more difficult to effect than those of secondary amines. When 1a and thiophenol were refluxed in xylene for 72 hours, only a trace amount of the ring-opened product was formed. This reaction could give a good yield of the product only when an excess of pyridine was added to the reaction mixture (Equation 5).



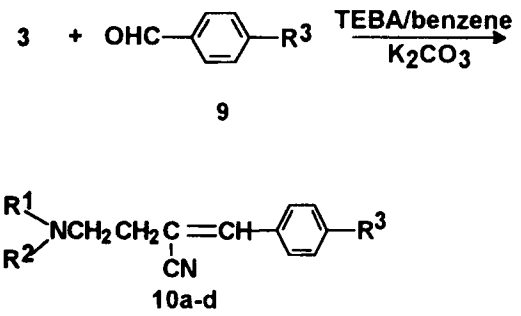
(5)

Ethyl mercaptan reacted with 1a under similar conditions, while n-hexyl mercaptan could only yield a trace amount of the product. The reaction of n-hexyl mercaptan produced good yield of the desired product but only after an additional catalytic amount of p-dimethylaminopyridine (DMAP) was added to the reaction mixture (Table 2).

Wittig-Horner Reaction of Some Ring-Opened Reaction Products 3 *with Aromatic Aldehydes under PTC Conditions*

Since unsaturated amines are important synthons and building blocks of various natural products, there are many reports of the syntheses of such compounds [9–11]. However, there is no systematic report on the syntheses of homoallylic amines. These compounds could be conveniently synthesized by the Wittig-Horner reaction of the ring-opened products of 1a by amines with aromatic aldehydes.

When the reaction was conducted by using solid K_2CO_3 as the base, triethylbenzylammonium chloride (TEBA) as the phase-transfer catalyst and benzene as the solvent, the desired homoallylic amines were obtained in good yields (Equation 6, Table 3).



(6)

a: R^1R^2= , R^3=H; b:R^1R^2=O , R^3=H;

c:R^1R^2=O , R^3=CH_3; d:R^1R^2= , R^3=H.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390L (90 M) spec-

TABLE 3 Reaction of **3** with Aromatic Aldehyes (**9**)

3	9	Temp.	10	Yield (%)[a]	e/z[b]
3a	**9a**	reflux	**10a**	89.6	39/61
3b	**9a**	r.t.	**10b**	88.3	43/57
3b	**9b**	reflux	**10c**	58.8	65/35
3d	**9a**	reflux	**10d**	77.3	73/27

[a]Isolated yield.
[b]Determined by integral of ^{1}H NMR.

trometer unless otherwise indicated, TMS being used as an internal standard. ^{31}P NMR spectra were recorded on a JEOL FX-90Q (90 M) spectrometer, 85% H_3PO_4 being used as an external standard. IR spectra were recorded on a Shimadzu IR-440 spectrometer. Elemental microanalyses were performed by the Analytical Laboratory of the Shanghai Institute of Organic Chemistry.

All reagents and solvents were purified by standard methods.

Materials

(1-Ethoxycarbonylcyclopropyl)diphenylphosphine oxide (**1b**) [12], diethyl (1-ethoxycarbonylcyclopropyl)phosphonate (**1d**) [12], and diethyl (1-cyanocyclopropyl)phosphonate (**1c**) [13] were prepared according to literature methods. (1-Cyanocyclopropyl)diphenylphosphine oxide (**1a**) was prepared in a similar way as **1c** from $Ph_2P(O)CH_2CN$ and $BrCH_2CH_2Br$. After recrystallization from benzene, white crystals were obtained in a yield of 67.3%, mp 172–173°C. ^{1}H NMR (300 M, $CDCl_3$) δ: 1.62 (m, 2H), 1.87 (m, 2H), 7.55 (m, 4H), 7.88 (m, 6H) ppm. IR (KCl wafer): 2210, 1585, 1440, 1310, 1250, 1200, 1125, 960, 850, 735 cm^{-1}. Anal. calcd for $C_{16}H_{14}NOP$ (267.27): C, 71.90; H, 5.28; N, 5.24; P, 11.59; found: C, 71.79; H, 5.27; N, 5.12; P, 11.20. ^{31}P NMR ($CDCl_3$) δ: 27.94 ppm.

$Ph_2P(O)CH_2CN$ was prepared according to the literature [14] or as described below: The crude product of Ph_2PCH_2CN [15], prepared from 25.8 g (0.1 mol) of Ph_2PSiMe_3 [16] and 8.3 g (0.1 mol) of $ClCH_2CN$, was dissolved in 50 mL of glacial acetic acid, and 17.0 g (0.15 mol) of 30% H_2O_2 was added dropwise with stirring. Upon completion of addition, the reaction mixture was stirred for an additional hour at 70–75°C and then poured into 200 mL of cold water with stirring. The white crystals were collected under suction and washed with water; 20.8 g (86.2%) of white crystals were obtained after recrystallization from benzene. Mp 148–150°C ([14]: 151–152°C).

Reaction of **1a** *with Piperidine* (**2a**)

1. Typical procedure A: 0.267 g (1 mmol) of **1a** and 0.255 g (3 mmol) of **2a** were refluxed in 5 mL of anhydrous xylene for 21 hours. The solvent was removed *in vacuo*, and the residue was dissolved in 10 mL of dilute aq. HCl (v/v = 1:1), washed with CH_2Cl_2 (2 × 2 mL), neutralized with solid Na_2CO_3, and then extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were washed with water (2 × 3 mL), dried (Na_2SO_4), and the solvent was removed. The crude product was chromatographed on silica gel ($CHCl_3/CH_3OH$ = 100/2 as eluent) to give 0.298 g of [1-cyano-3-(1-piperidinyl)propyl]diphenylphosphine oxide (**3a**) as a brown oil; yield, 84.5%. ^{1}H NMR (CCl_4) δ: 1.50 (brs, 8H), 2.35 (m, 6H), 3.60 (m, 1H), 7.40–8.00 (m, 10H) ppm. IR (film): 2220, 1440, 1190, 1115, 730, 700 cm^{-1}. Anal. calcd for $C_{21}H_{25}N_2OP$ (352.42); C, 71.57; H, 7.15; N, 7.95; P, 8.79; found: C, 71.28; H, 6.94; N, 8.01; P, 8.55.
2. According to procedure A, 5 mL of **2a** was used instead of xylene as the solvent and the mixture was refluxed for 10 hours; yield, 0.299 g (84.9%).
3. Typical procedure B: 0.267 g (1 mmol) of **1a**, 0.255 g (3 mmol) of **2a** and 5 mL of anhydrous xylene were stirred in a sealed tube at a bath temperature of 145–150°C for 10 hours. The tube was opened after having been cooled, and the reaction mixture was worked up as in procedure A; yield, 0.338 g (95.9%).
4. According to procedure B, 5 mL of **2a** was used instead of xylene as the solvent, and the mixture was stirred for 10 hours; yield, 0.333 g (94.5%).

Reaction of **1a** *with Morpholine* (**2b**)

1. A mixture of 0.267 g (1 mmol) of **1a** and 3 mL of **2b** was refluxed for 24 hours; 0.267 g of [1-cyano-3-(1-morpholinyl)propyl]diphenylphosphine oxide (**3b**) was obtained after a workup procedure as in procedure A. Yield, 75.3%, pale yellow oil. ^{1}H NMR (CCl_4) δ: 1.78 (m, 2H), 2.30 (m, 6H), 3.55 (t, 4H), 3.75 (m, 1H), 7.30–8.10 (m, 10H). IR (film): 2240, 1440, 1200, 1120, 730, 700 cm^{-1}. Anal. calcd for $C_{20}H_{23}N_2O_2P$ (354.39): C, 67.78; H, 6.54; N, 7.91; P, 8.74; found: C, 67.48; H, 6.69; N, 7.67; P, 8.49.
2. According to procedure B, 0.267 g (1 mmol)

of **1a** and 3 mL of **2b** were stirred in a sealed tube at a bath temperature of 160°C for 24 hours to yield 0.321 g (90.6%) of **3b**.

Reaction of **1a** *with Imidazole* (**2c**)

A mixture of 0.267 g (1 mmol) of **1a**, 0.340 g (5 mmol) of **2c**, and 5 mL of anhydrous xylene was stirred under a nitrogen atmosphere in a sealed tube at a bath temperature of 160°C for 24 hours. The solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with water until the water phase was neutral. The organic phase was dried over Na_2SO_4, and the solvent was evaporated. The crude product was recrystallized from ethanol to yield 0.301 g of [1-cyano-3-(1-imidazolyl)propyl]diphenylphosphine oxide (**3c**), white crystals, mp 168–170°C, yield, 89.7%. ^{1}H NMR (CCl_4) δ: 2.35 (brs, 6H), 4.10 (m, 1H), 4.46 (m, 2H) 7.20 (d, 3H), 7.58 (brs 6H), 7.70–8.10 (m, 4H). IR (KCl wafer): 2220, 1505, 1435, 1220, 1110, 830, 720 cm^{-1}. Anal. calcd for $C_{19}H_{18}N_3OP$ (335.35): C, 68.05; H, 5.41; N, 12.53; P, 9.24; found: C, 67.97; H, 5.60; N, 12.67; P, 8.97.

Reaction of **1a** *with Pyrrolidine* (**2d**)

A mixture of 0.267 g (1 mmol) of **1a** and 0.356 g (5 mmol) of **2d** was refluxed in 5 mL of benzene for 36 hours to yield 0.248 g of [1-cyano-3-(1-pyrrolidinyl)-propyl]diphenylphosphine oxide (**3d**), a pale yellow oil, yield, 73.3%. ^{1}H NMR (CCl_4) δ: 1.60 (brs 6H), 2.35 (brs, 4H), 2.70 (m, 2H), 3.74 (m, 1H), 7.25–8.10 (*m*, 10H). IR (film): 2220, 1440, 1190, 1120, 745, 725, 700 cm^{-1}. Anal. calcd for $C_{20}H_{23}N_2OP$ (338.39): C, 70.99; H, 6.85; N, 8.28; P, 9.15; found: C, 70.64; H, 6.91; N, 8.10; P, 9.38.

Reaction of **1a** *with Diethylamine* (**2f**)

A mixture of 0.267 g (1 mmol) of **1a** and 0.366 g (5 mmol) of **2f** was refluxed for 25 hours in 5 mL of anhydrous benzene to yield 0.128 g of [1-cyano-3-(N,N-diethylamino)propyl]diphenylphosphine oxide (**3f**), red oil, yield, 47.6%. ^{1}H NMR (CCl_4) δ: 1.00 (t, 6H), 1.60 (m, 2H), 3.45 (m, 6H), 3.61 (m, 1H), 7.33–8.20 (m, 10H). IR (film): 2210, 1440, 1220, 1120, 785, 725, 700 cm^{-1}. Anal. calcd for $C_{20}H_{25}N_2OP$ (340.41): C, 70.57; H, 7.40; N, 8.23; P, 9.10; found: C, 70.25; H, 7.29; N, 8.47; P, 8.93.

Reaction of **1a** *with Diisopropylamine* (**2g**)

A mixture of 0.267 g of **1a** and 2 mL of **2g** was reacted in a sealed tube at a bath temperature of 160°C for 25 hours to yield 0.049 g of [1-cyano-3-(N,N-diisopropylamino)propyl]diphenylphosphine oxide (**3g**), pale yellow oil, yield, 13.3%. ^{1}H NMR (CCl_4) δ: 1.00 (t, 12H), 1.55 (m, 2H), 2.60 (m, 2H), 2.90 (m, 2H), 3.65 (m, 1H), 7.20–8.05 (m, 10H). IR (film): 2220, 1440, 1200, 1125, 770, 725 cm^{-1}. Anal. calcd for $C_{22}H_{29}N_2OP$ (368.46): C, 71.72; H, 7.93; N, 7.60; found: C, 71.48; H, 8.05; N, 7.37.

Reaction of **1a** *with n-Pentylamine* (**2i**)

1. A mixture of 0.267 g (1 mmol) of **1a** and 0.174 g (2 mmol) of **2i** was refluxed in 5 mL of anhydrous ethanol for 71 hours to yield 0.060 g of [1-cyano-3-(n-pentylamino)propyl]diphenylphosphine oxide (**3i**), red oil, yield, 17.0%. ^{1}H NMR ($CDCl_3$) δ: 0.90 (t, 3H), 1.30 (brs, 7H), 2.30 (m, 2H), 3.30 (t, 4H), 4.05 (m, 1H), 7.20–7.95 (m, 10H). IR (film): 3340 (br), 2950, 2860, 2210, 1440, 1200, 1125, 760, 725 cm^{-1}. ^{31}P NMR ($CDCl_3$) δ: 32.55. Anal. calcd for $C_{21}H_{27}N_2OP$ (354.43): C, 71.17; H, 7.68; N, 7.90; found: C, 70.98; H, 7.75; N, 7.81.
2. A mixture of 0.267 g (1 mmol) of **1a** and 3 mL of **2i** was refluxed for 30 hours. The excess of **2i** was evaporated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3/CH_3OH$ = 20/1 as eluent) to give 0.243 g of N-n-pentyl 1-(diphenylphosphinyl)cyclopropylamidine (**4**), red oil, yield, 68.7%. ^{1}H NMR (300 M, $CDCl_3$) δ: 0.80 (t, 3H), 1.20 (brs, 10H), 3.00 (m, 2H), 6.06 (brs, 2H), 7.45 (mc, 10H). IR (film): 3300 (br), 3040, 2950, 2840, 1620 (br), 1440, 1340, 1180, 1120, 750 cm^{-1}. Anal. calcd for $C_{21}H_{27}N_2OP$ (354.43): C, 71.17; H, 7.68; N, 7.90; P, 8.74; found: C, 71.03; H, 7.43; N, 7.79; P, 8.52. This product has identical ^{1}H NMR and IR spectra with the authentic sample prepared from **1a** and **2i** under the catalysis of $AlCl_3$ [17].

Reaction of (1-ethoxycarbonylcyclopropyl) diphenylphosphine oxide (**1b**) *with piperidine* (**2a**)

A mixture of 0.157 g (0.5 mmol) of **1b** and 1.5 mL of **2a** was refluxed with stirring for 61 hours (controlled by TLC). The excess of **2a** was evaporated, and the residue was worked up in the same way as in procedure A; 0.145 g of [1-ethoxycarbonyl-3-(1-piperidinyl)propyl]diphenylphosphine oxide (**5**) was obtained as a yellow powder, mp 120–122°C, yield, 72.6%. ^{1}H NMR (CCl_4) δ: 0.75 (t, J = 6 Hz, 3H), 1.32 (brs, 4H), 1.65 (m, 4H), 2.12 (brs, 6H), 3.40 (m, 1H),

3.65 (q, J = 6 Hz, 2H), 7.10–8.05 (m, 10H). IR (KCl wafer): 1730, 1440, 1330, 1195, 1160, 1110, 1025, 730, 710, 700 cm^{-1}. Anal. calcd for $C_{23}H_{30}NO_3P$ (399.47): C, 69.15; H, 7.57; N, 3.51; P, 7.75; found: C, 69.29; H, 7.55; N, 3.27; P, 7.65.

Reaction of **1b** *with n-Pentylamine* (**2i**)

A mixture of 0.157 g (0.5 mmol) of **1b** and 1.5 mL of **2i** was refluxed with stirring for 30 hours. The excess of **2i** was evaporated under reduced pressure, and the residue was dissolved in CH_2Cl_2 (15 mL), washed with delute aq. HCl (v/v = 1:1) (2 × 3 mL) and H_2O, dried (Na_2SO_4), and the solvent was evaporated. The residue was recrystallized from benzene to give 0.162 g of N-n-pentyl [(1-diphenylphosphinyl)-cyclopropyl]formamide (**6**), white crystals, mp 104–105°C, yield, 91.2%. ^1H NMR (CCl_4) δ: 0.76 (t, 3H), 1.10 (brs, 6H), 2.20 (m, 2H), 2.95 (t, 4H), 3.38 (m, 1H), 7.00–8.15 (m, 10H). IR (KCl wafer): 3300 (br), 3040, 1680, 1435, 1265, 1185, 1115, 740, 720, 690 cm^{-1}. Anal. calcd for $C_{21}H_{26}NO_2P$ (355.42): C, 70.97; H, 7.37; N, 3.94; P, 8.72; found: C, 70.73; H, 7.43; N, 3.86; P, 8.59.

Reaction of **1a** *with Thiophenol* (**7a**)

A mixture of 0.134 g (0.5 mmol) of **1a**, 1.2 mL of **7a**, and 0.1 mL of pyridine was heated at a bath temperature of 160°C in a sealed tube under a nitrogen atmosphere for 24 hours. The excess of **7a** was evaporated *in vacuo*, and the residue chromatographed on silica gel ($CHCl_3$ as eluent) to give 0.158 g of (1-cyano-3-phenylthiopropyl)diphenylphosphine oxide (**8a**) as a pale yellow oil; yield, 83.7%. ^1H NMR (CCl_4) δ: 1.90 (m, 2H), 2.90 (m, 2H), 3.85 (m, 1H), 7.30 (mc, 15H). IR (film): 3070, 2870, 2230, 1590, 1485, 1445, 1200, 1120, 1070, 1025, 1000, 730, 700 cm^{-1}. Anal. calcd for $C_{22}H_{20}NOPS$ (377.45): C, 70.01; H, 5.34; N, 3.71; P, 8.21; S, 8.50; found: C, 69.65; H, 5.18; N, 3.60; P, 8.30; S, 8.33.

Reaction of **1a** *with Ethyl Mercaptan* (**7b**)

A mixture of 0.134 g (0.5 mmol) of **1a**, 0.6 mL of **7b** and 0.05 mL of pyridine was reacted in a sealed tube at 165°C for 24 hours to give 0.124 g of (1-cyano-3-ethylthiopropyl)diphenylphosphine oxide (**8b**) as a yellow oil; yield, 75.3%. ^1H NMR (CCl_4) δ: 1.10 (t, 3H), 1.95 (m, 2H), 2.35 (q, 2H), 2.60 (m, 2H), 3.80 (m, 1H), 7.55 (mc, 10H). IR (film): 2230, 1590, 1480, 1440, 1200, 1120, 730, 700 cm^{-1}. Anal. calcd for $C_{18}H_{20}NOPS$ (329.40): C, 65.63; H, 6.12; N, 4.25; P, 9.40; S, 9.73; found: C, 65.62; H, 6.11; N, 4.29; P, 9.67; S, 9.68.

Reaction of **1a** *with n-Hexyl Mercaptan* (**7c**)

A mixture of 0.134 g (0.5 mmol) of **1a**, 1.0 mL of **7c**, 0.05 mL of pyridine, and 0.006 g (0.05 mmol) of DMAP was reacted in a sealed tube at 165°C for 24 hours to give (1-cyano-3-n-hexylthiopropyl)diphenylphosphine oxide (**8c**) as a brown oil; yield, 77.8%. ^1H-NMR (CCl_4) δ: 0.75 (t, 3H), 1.20 (brs, 8H), 1.90 (m, 2H), 2.25 (q, 2H), 2.55 (m, 2H), 3.80 (m, 1H), 7.70 (mc, 10H). IR (film): 2210, 1590(d), 1440, 1200, 1120, 750, 730, 700 cm^{-1}. Anal. calcd for $C_{22}H_{28}NOPS$ (385.51): C, 68.54; H, 7.32; N, 3.63; P, 8.03; S, 8.32; found: C, 68.56; H, 7.43; N, 3.44; P, 8.25; S, 8.30.

Reaction of [1-Cyano-3-(1-piperidinyl) propyl]diphenylphosphine Oxide (**3a**) *with Benzaldehyde* (**9a**)

Typical procedure C: A mixture of 0.352 g (1 mmol) of **3a**, 3 mL of anhydrous benzene, 0.553 g (4 mmol) of anhydrous K_2CO_3, 0.016 g (0.07 mmol) of TEBA, and 0.318 g (3 mmol) of **9a** in 2 mL of benzene was refluxed with vigorous stirring for 9 hours (controlled by TLC). A precipitate was filtered off and washed with benzene. The filtrate was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel ($CHCl_3/CH_3OH$ = 100/1 as eluent) to give 0.215 g of 1-phenyl-2-cyano-4-(1-piperidinyl)-1-butene (**10a**) as a red oil; yield, 89.6%, e/z = 39/61. ^1H NMR (CCl_4) δ: 1.43 (brs, 6H), 2.40 (m, 8H), 6.77 (s, 0.61H), 7.07 (s, 0.39H), 7.25 (s, 3H), 7.58 (m, 2H). IR (film): 2220, 1440, 1115, 750, 700 cm^{-1}. Anal. calcd for $C_{16}H_{20}N_2$ (240.35): C, 79.96; H, 8.39; N, 11.65; found: C, 79.57; H, 8.39; N, 11.34.

Reaction of [1-Cyano-3-(1-morpholinyl)propyl]diphenylphosphine Oxide (**3b**) *with* **9a**

The reaction was carried out according to procedure C, but it was performed at room temperature for 30 hours, to yield 1-phenyl-2-cyano-4-(1-morpholinyl)-1-butene (**10b**) as a blue oil; yield, 88.3%, e/z = 43/57. ^1H NMR (CCl_4) δ: 2.42 (m, 8H), 3.55 (m, 4H), 6.82 (s, 0.57H), 7.12 (s, 0.43H), 7.30 (m, 4H), 7.60 (m, 1H). IR (film): 2190, 1440, 1115, 750, 690 cm^{-1}. Anal. calcd for $C_{15}H_{18}N_2O$ (242.32): C, 74.35; H, 7.49; N, 11.56; found: C, 74.61; H, 7.44; N, 11.20.

Reaction of **3b** *with p-Methylbenzaldehyde* (**9b**)

According to procedure C, the reaction was carried out under reflux for 7 hours to yield 1-(4-methylphenyl)-2-cyano-4-(1-morpholinyl)-1-butene (**10c**) as a brown oil; yield, 58.8%, e/z = 65/35. ^1H NMR

(CCl_4) δ: 2.42 (s, 3H), 2.80 (mc, 8H), 3.60 (m, 4H), 6.68 (s, 0.35H), 6.80 (s, 0.65H), 7.26 (m, 4H). IR (film): 2220, 1630, 1440, 1120, 815 cm^{-1}. Anal. calcd for $C_{16}H_{20}N_2O$ (256.35): C, 74.97; H, 7.86; N, 10.93; found: C, 74.62; H, 7.65; N, 10.70.

Reaction of [1-Cyano-3-(1-pyrrolidinyl)propyl]diphenylphosphine Oxide (3d) *with* 9a

According to procedure C, the reaction was carried out under reflux for 10 hours to yield 1-phenyl-2-cyano-4-(1-pyrrolidinyl)-1-butene (**10d**) as a red oil; yield, 77.3%, *e/z* = 73/27. ^1H NMR (CCl_4) δ: 1.02 (brs, 2H), 1.52 (brs, 4H), 2.39 (m, 6H), 6.54 (s, 0.27H), 6.92 (s, 0.73H), 7.10 (s, 5H). IR (film): 2210, 1445, 755, 730, 700 cm^{-1}. Anal. calcd for $C_{15}H_{18}N_2$ (226.32): C, 79.60; H, 8.02; N, 12.38; found: C, 79.75; H, 7.93; N, 12.05.

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