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Cyanation of Alcohols with Diethyl Cyanophosphonate and 2,6-Dimethyl-1,4-benzoquinone by a New Type of Oxidation–Reduction Condensation

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Cyanation of various alcohols by a new type of oxidation–reduction condensation is described. Primary alkyl diphenylphosphinites, 2,6-dimethyl-1,4-benzoquinone (DMBQ), and diethyl cyanophosphonate gave the corresponding nitriles in high yields. During the above experiment on cyanation of 4-phenylbutan-2-ol, the unexpected formation of a mixture of nitrile and isocyanide was observed. After careful examination of the reaction conditions, selective synthesis of isocyanides from secondary alcohols was successfully accomplished by the use of zinc oxide (ZnO) as an additive. Reaction of tertiary alcohols provided the corresponding isocyanides exclusively in the absence of an additive. Cyanation of optically active alcohols was tried in order to clarify the stereochemistry of this reaction, and the reaction was thus proved to proceed with the inversion of configuration.

The aliphatic nucleophilic substitution reaction is one of the most important processes in organic reactions.[1] Among the nucleophiles used in such substitution reactions, anions such as enolate, nitrite, and cyanide anions exhibit very characteristic behaviors. These anions are known as ambident nucleophiles[2] because they possess two different reactive sites within a single molecule. Although reactions with electrophiles proceed at either position of the nucleophiles, various factors such as their counter cations, solvents, and the nature of electrophiles influence the intrinsic reactivities of the nucleophiles. For example, alkali metal cyanides such as sodium and potassium cyanides react preferentially with alkyl halides at the C-position and form nitriles.[3] On the other hand, heavy metal cyanides such as silver and copper cyanides react at the N-position and form isocyanides predominantly.[4]

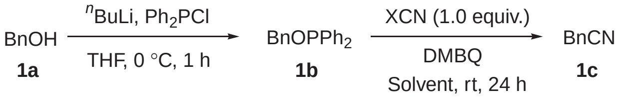
The oxidation–reduction condensation is recognized as one of the most convenient and useful synthetic methods in organic synthesis since the reaction is performed under neutral and mild conditions.[5] Recently, a newer type of oxidation–reduction condensation was reported from our laboratory; that is, a combination of alkyl diphenylphosphinites prepared readily from various alcohols, and quinones such as 2,6-dimethyl-1,4-benzoquinone (DMBQ) and 2,6-di-*t*-butyl-1,4-benzoquinone (DBBQ) made many kinds of organic transformations such as esterification,[6] etherification,[7] amination,[8] and thioetherification[9] possible. In order to extend the scope of this condensation reaction, the carbon–carbon bond-forming reaction using a cyanide ion, the simplest carbon nucleophile of all, was tried.

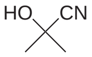
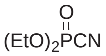
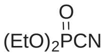
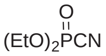
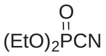
Introduction of a cyano group with nucleophilic displacement by a cyanide ion is considered a versatile method for carbon chain elongation and further functional group manipulation. In order to perform this transformation, a two-step procedure involving initial conversion of alcohols into the corresponding halides or sulfonates and the following substitution with inorganic cyanides has generally been employed. When secondary and tertiary alcohols were used in this reaction, however, high temperature or the presence of strong bases was needed in some cases, which often caused the undesirable elimination reaction. Therefore, procedures such as one-pot cyanation of alcohols according to the Mitsunobu reaction were employed for the transformation under mild conditions.[10] Further, the conversion of alcohols into nitriles by using a $PPh_3/DDQ/{}^nBu_4NCN$ system has also been reported recently.[11]

As described above, a cyanide ion is an ambident nucleophile that reacts alternatively at the C- or N-position in accordance with the reaction conditions. If a cyanide ion reacted at the N-position, isocyanides are formed instead of nitriles. Isocyanides are the compounds that formally possess divalent carbon with unique reactivities.[12] By making the best use of their characteristics, isocyanides are employed in multicomponent reactions such as Passerini[13] and Ugi[14] reactions, and synthesis of heterocycles[15] besides being used as ligands of transition-metal complexes.[16] There are various methods for the preparation of these isocyanides such as nucleophilic displacement of alkyl halides by silver cyanide,[4a,b] dehydration of formamides,[17] carbylamine reaction,[18] or reduction of isocyanates or isothiocyanates.[19] Since these reactions are often carried out under basic conditions or at high reaction temperatures, it is desired to develop more convenient synthetic reactions that proceed under mild conditions.

We would like to report here the syntheses of respective nitriles from primary alcohols and isocyanides from secondary and tertiary alcohols via the corresponding alkyl diphenylphosphinites by a new type of oxidation–reduction condensation using 2,6-dimethyl-1,4-benzoquinone and diethyl cyanophosphonate.[20]

Table 1. Cyanation of Benzyl Alcohol with Various Cyanides and DMBQ



Entry	$BnOPPh_2$ /equiv	XCN	DMBQ /equiv	Solvent /mL	Yield /%[a)]
1	1.0	TMSCN	1.0	CH_2Cl_2 /0.50	0
2	1.0		1.0	CH_2Cl_2 /0.50	20
3	1.0	 $(EtO)_2P(O)CN$	1.0	CH_2Cl_2 /0.50	35
4	1.0	 $(EtO)_2P(O)CN$	1.0	$CHCl_3$ /0.50	49
5	1.5	 $(EtO)_2P(O)CN$	1.5	$CHCl_3$ /0.50	73
6	1.5	 $(EtO)_2P(O)CN$	1.5	$CHCl_3$ /1.5	82

a) A small amount of DMBQ was contained. Yield was determined by ^{1}H NMR analysis.

Results and Discussion

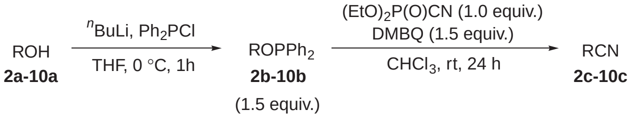
Cyanation of Primary Alcohols. In the first place, cyanation of benzyl diphenylphosphinite with DMBQ and TMSCN (trimethylsilyl cyanide) was tried in CH_2Cl_2. The desired nitrile, however, was not obtained at all (Table 1, Entry 1). Even in the case of using acetone cyanohydrin in place of TMSCN, the yield of nitrile was 20% (Table 1, Entry 2), whereas it increased up to 35% by using diethyl cyanophosphonate (Table 1, Entry 3). After screening several reaction conditions, the nitrile was eventually obtained in 82% yield when 1.5 equiv of benzyl diphenylphosphinite and 1.5 equiv of DMBQ were used in $CHCl_3$ (Table 1, Entries 4–6).

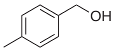
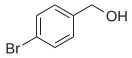
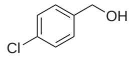
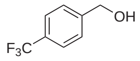
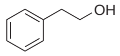
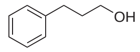
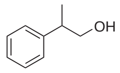
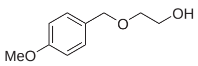
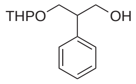
Next, cyanation of several primary alcohols was tried by using DMBQ and diethyl cyanophosphonate (Table 2). Benzyl alcohols having various substituents also afforded the corresponding nitriles in good yields (Table 2, Entries 1–4). In addition, non-benzylic, hindered primary alcohols and mono-protected diols having a *p*-methoxybenzyl group or a tetrahydropyranyl group also provided the desired nitriles in high yields (Table 2, Entries 5–9).

A proposed reaction mechanism is shown in Scheme 1: Alkyl diphenylphosphinite reacted initially with DMBQ to form the adduct **11**,[6a] which in turn transformed to the phosphonium cyanide **12** by reaction with diethyl cyanophosphonate. By the attack of the cyanide anion to the alkyl group of **12**, the corresponding nitrile was formed.

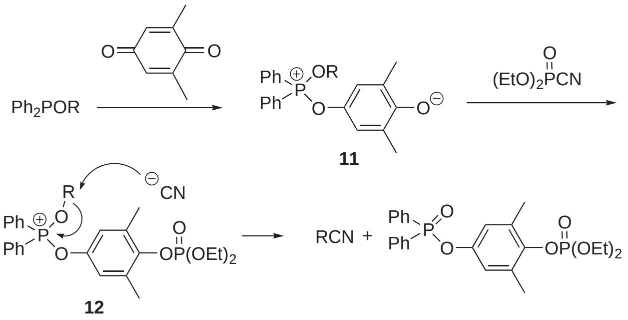
Cyanation of Secondary Alcohols. Next, cyanation of secondary alcohols was examined. It was unexpectedly found that the isocyanide **13c** was formed[21] in 23% yield along with the aimed nitrile **14** by the cyanation of 4-phenylbutan-2-ol (**13a**) with diethyl cyanophosphonate in $CHCl_3$ at room temperature (Scheme 2).

Table 2. Cyanation of Various Primary Alcohols with $(EtO)_2P(O)CN$ and DMBQ

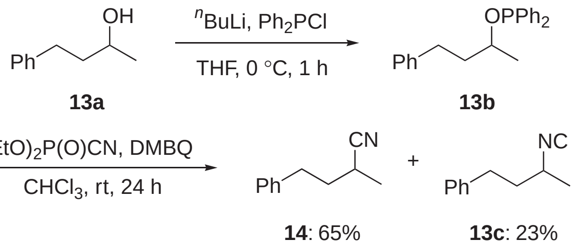


Entry	ROH		Yield/%	
			$ROPPh_2$	RCN
1		**2a**	99	64
2		**3a**	75[a)]	73
3		**4a**	96	86
4		**5a**	89	70
5		**6a**	quant.	97
6		**7a**	90	94
7		**8a**	94	81[b),c)]
8		**9a**	84[a)]	96
9		**10a**	78[a)]	83[b)]

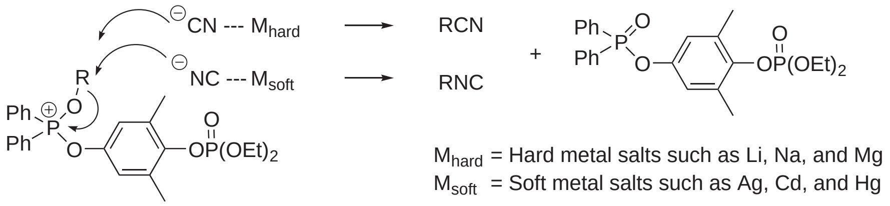
a) Preparation of alkyl diphenylphosphinite was carried out at −78 °C. b) The reaction was carried out in 5.0 mL of $CHCl_3$ for 48 h. c) A small amount of DMBQ was contaminated. Yield was determined by ^{1}H NMR analysis.



Scheme 1.

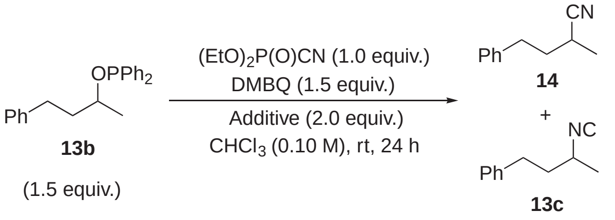


Scheme 2.



Scheme 3.

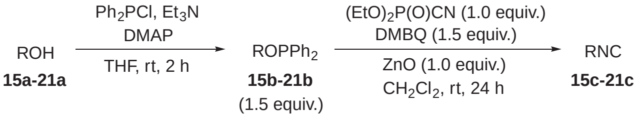
Table 3. Additive Effect

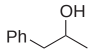
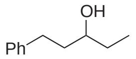
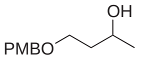
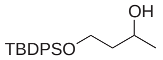
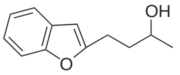
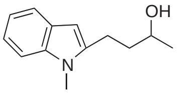
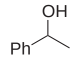


Entry	Additive	Yield (**14**:**13c**)/%[a]	Entry	Additive	Yield (**14**:**13c**)/%[a]
1	None	88 (74:26)	6	Ag_2O	0
2	Li_2SO_4	88 (79:21)	7	HgO	0
3	Na_2CO_3	80 (82:18)	8	CdO	68 (<5:>95)
4	$Mg(OTf)_2$	72 (84:16)	9	ZnO	57 (<5:>95)
5	CaO	48 (81:19)	10	ZnO	82[b),c)] (<5:>95)

a) Isolated as a mixture of isomers. Numbers in parentheses are ratios of isomers determined by comparing the peak of the methine proton of each isomer in ^{1}H NMR analysis. b) The reaction was carried out in CH_2Cl_2 (1.0 M). c) 1.0 equiv of ZnO was used.

Table 4. Selective Formation of Isocyanides from Various Secondary Alcohols with ZnO as an Additive



Entry	ROH		Yield/%	
			$ROPPh_2$	RNC
1		**15a**	quant.	63[a)]
2		**16a**	95	89
3		**17a**	82	63
4		**18a**	quant.	72
5		**19a**	71	78
6		**20a**	86	81
7		**21a**	99	40[b)]

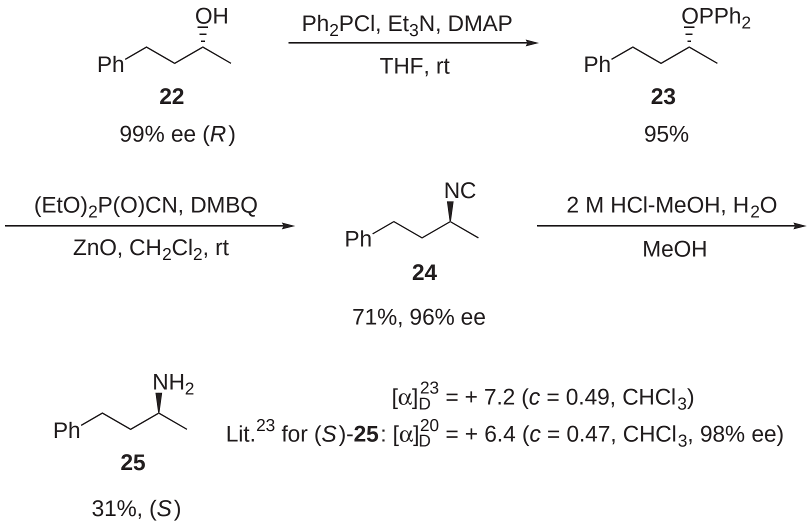
a) 1.5 mL of CH_2Cl_2 was used. b) The reaction time was 3 h.

Formation of isocyanides from secondary alcohols with cyanide ions has not been reported yet.[10] Since a cyanide anion worked as an ambident nucleophile, it was figured that either nitriles or isocyanides should be selectively formed in the presence of an additive such as an inorganic salt taking the Pearson's HSAB principle[22] into consideration: that is, hard metal salts interact preferentially at the harder N-position of the cyanide to form nitriles whereas soft metal salts interact at the C-position of softer character to afford isocyanides (Scheme 3).

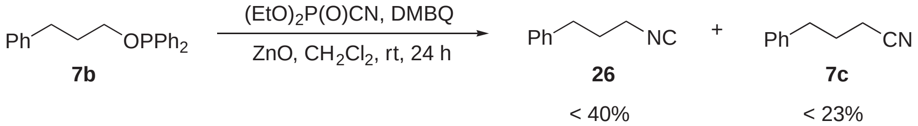
The effect of inorganic salts was then examined in order to selectively prepare either nitrile or isocyanide (Table 3). First, reactions were tried by using various alkali metal salts and alkaline earth metal salts (Table 3, Entries 2–5). Contrary to our expectation, the yield of the desired nitrile was not good. Then, the same reaction was tried in the presence of heavy metal salts (Table 3, Entries 6–9). At that time, it was strikingly found that only the isocyanide was obtained in the case when ZnO or CdO was used as an additive (Table 3, Entries 8 and 9). Although CdO afforded the isocyanide in higher yield, further optimization of the reaction conditions in the existence of ZnO was tried from the environmental-benign point of view. Under the optimized conditions (1.0 M of CH_2Cl_2 and 1.0 equiv of ZnO), the desired isocyanide was obtained in 82% yield (Table 3, Entry 10).

Next, the cyanation of several secondary alcohols was tried under the above optimized conditions (Table 4). Alkyl diphenylphosphinites derived from 1-phenylpropan-2-ol and 1-phenylpentan-3-ol provided the corresponding isocyanides in good yields (Table 4, Entries 1 and 2). Monoprotected diols having a *p*-methoxybenzyl group or a *t*-butyldiphenylsilyl group provided the desired isocyanides in satisfactory yields as well (Table 4, Entries 3 and 4). On the other hand, heterocyclic moieties contained in benzofuran and 1-methyl indole were not affected under the above conditions (Table 4, Entries 5 and 6). In the case of 1-phenylethanol, the corresponding isocyanide was obtained in 40% yield (Table 4, Entry 7).

Cyanation of an optically active secondary alcohol was next tried in order to examine the stereochemistry of this reaction. It was found that the inversion of configuration took place when (*R*)-4-phenylbutan-2-ol was used as the substrate. The absolute configuration of the isocyanide was determined by conversion to the known amine **25**[23] and comparison of the sign of specific rotation (Scheme 4).

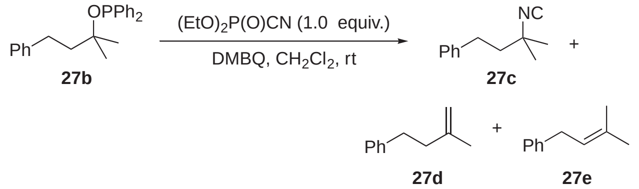


Scheme 4.



Scheme 5.

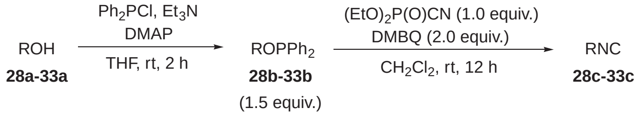
Table 5. Cyanation of Tertiary Alkyl Diphenylphosphinite

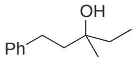
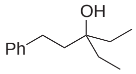
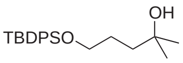
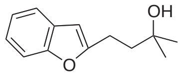
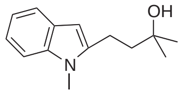
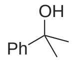


Entry	**27b** /equiv	DMBQ /equiv	Time /h	Yield/%	
				27c	**27d** + **27e**[c)]
1[a)]	1.5	1.5	24	40	39
2	1.5	1.5	24	44	29
3	1.5[b)]	1.5	12	50	33
4	1.5[b)]	2.0	12	70	26

a) 1.0 equiv of ZnO was used. b) Purified with basic silica-gel chromatography. c) Yield based on **27b**.

Table 6. Synthesis of Isocyanides from Various Tertiary Alcohols



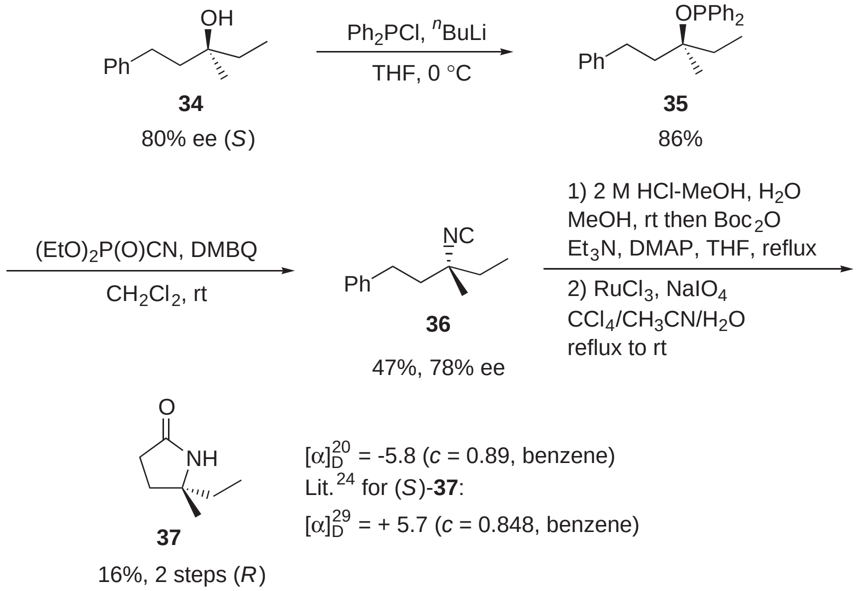
Entry	ROH		Yield/%	
			ROPPh$_2$	RNC
1		**28a**	82[a)]	59[c)]
2		**29a**	87[a)]	60[b)]
3		**30a**	98	71[c)]
4		**31a**	84	67
5		**32a**	85	43[b),c)]
6		**33a**	75	33

a) ROPPh$_2$ was prepared by using ^{n}BuLi as a base. b) 2.0 equiv of ROPPh$_2$ was used. c) The reaction time was 7 h.

When the cyanation of a primary alcohol was examined under the same conditions, however, a mixture of the corresponding isocyanide[21] and nitrile was obtained unexpectedly in a ca. 2:1 ratio in the cyanation of the alkyl diphenylphosphinite **7b** derived from 3-phenylpropan-1-ol (Scheme 5).

Cyanation of Tertiary Alcohols. Next, the cyanation of tertiary alcohols was tried (Table 5). Cyanation of 2-methyl-4-phenylbutan-2-ol gave the corresponding isocyanide in 40% yield when ZnO was used as an additive (Table 5, Entry 1). It was unexpected that the corresponding isocyanide would be obtained exclusively in the absence of ZnO (Table 5, Entry 2). However, the above reaction conditions were not reproducible. After intensive examination of reaction conditions, purification with basic silica-gel chromatography was found most effective for the reproduction of the reaction (Table 5, Entry 3). Finally, the corresponding isocyanide was obtained in 70% yield (Table 5, Entry 4).

The cyanation of several tertiary alcohols was further tried under the optimized conditions (Table 6) and alkyl diphenylphosphinites derived from 3-methyl-1-phenylpentan-3-ol and



Scheme 6.

3-ethyl-1-phenylpentan-3-ol was found to provide the corresponding isocyanides in good yields (Table 6, Entries 1 and 2). The desired products were obtained in high yields by using phosphinites having a *t*-butyldiphenylsilyl group and benzo[*b*]furan-2-yl group (Table 6, Entries 3 and 4). On the other hand, cyanation of an alcohol having a 1-methylindol-2-yl group and benzylic tertiary alcohol afforded the corresponding isocyanides in moderate yield (Table 6, Entries 5 and 6).

In order to examine the stereochemistry of this reaction, cyanation of an optically active tertiary alcohol, (*S*)-3-methyl-1-phenylpentan-3-ol (**34**), was tried and the inversion of configuration was confirmed similar to the case of a secondary alcohol such as (*R*)-4-phenylbutan-2-ol (Scheme 6). The absolute configurations of the isocyanide **36** were determined by leading to the known lactam **37**[24] to compare with the sign of specific rotation reported in the literature.

Conclusion

Cyanation of various alcohols via alkyl diphenylphosphinites was established by a new type of oxidation–reduction condensation. Although the cyanation of primary alcohols provided the corresponding nitriles, isocyanides were formed exclusively in the case when secondary alcohols were treated with ZnO and tertiary alcohols in the absence of an additive. Concerning the stereochemistry of the reaction, the inversion of configuration was confirmed when the cyanation of optically active alcohols was performed.

Experimental

General. Infrared (IR) spectra were recorded on a Shimadzu FT-IR 8900 spectrometer or a Sens*IR* Technologies Travel*IR*™ portable FT-IR spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard (CDCl$_3$; $\delta = 77.0$ ppm). Carbon–^{31}P coupling constants are reported when possible. The optical rotations were measured with a JASCO P-1020 polarimeter. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700V instrument unless otherwise noted. High-performance liquid chromatography (HPLC) was carried out using a Hitachi LC-Organizer, L-4000UV Detecter, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Column chromatography was carried out on Merck silica gel 60 (0.063–0.200 mm) or Fuji Silysia Chromatorex® NH (100–200 mesh). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. All reactions were carried out under an argon atmosphere unless otherwise noted. Dry solvents (Dichloromethane, MeOH, and EtOH) were prepared by distillation under appropriate drying agents. Dehydrated solvents (THF, Dioxane, and Chloroform) were purchased from KANTO KAGAKU and were used as received. ZnO (3N5) was purchased from KANTO KAGAKU and was dried by a heatgun for 5 min prior to use. *t*-Butyldimethylsilyl chloride was purchased from Shin-Etsu Chemical. 10% Pd/C was purchased from KAWAKEN Fine Chemicals. Other reagents were purchased from Tokyo Kasei Kogyo, KANTO KAGAKU, Kokusan Chemical, Wako Pure Chemical Industries, Acros Organics, or Aldrich Chemical, and were used as received unless otherwise noted.

Preparation of Primary Alkyl Diphenylphosphinites. To a stirred solution of alcohol (20 mmol) in dehydrated THF (60 mL) was added a hexane solution of ^{n}BuLi (20 mmol) at 0 °C dropwise under an argon atmosphere. After the solution was stirred for 1 h, PPh$_2$Cl (20 mmol) was added dropwise. The solution was further stirred for 1 h, then concentrated in vacuo. After the dilution of the residue with a mixed solution of hexane (180 mL) and ethyl acetate (20 mL), the suspension was filtered through a pad of alumina and Celite. The filtrate was concentrated in vacuo to afford the desired phosphinites.

Typical Experimental Procedure for Cyanation of Primary Alkyl Diphenylphosphinites. To a mixture of alkyl diphenylphosphinite (0.75 mmol) and diethyl cyanophosphonate (0.50

mmol) was added a chloroform solution (1.5 mL) of 2,6-dimethyl-1,4-benzoquinone (0.75 mmol) at room temperature under an argon atmosphere. After 24 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution and with brine, and then dried over anhydrous Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC to afford the corresponding nitrile.

Benzyl Diphenylphosphinite (1b):[6a] Colorless oil; IR (ATR) 3054, 3030, 2926, 2861, 1953, 1887, 1585, 1495, 1479, 1453, 1434, 1373, 1306, 1210, 1179, 1157, 1094, 1079, 1034, 1006, 994, 912, 832, 783, 733, 692 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.2 (15H, m), 4.88 (2H, d, $J = 9.5$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.52 (d, $J = 17.8$ Hz), 138.60 (d, $J = 8.4$ Hz), 130.52, 130.20, 129.23, 128.20 (d, $J = 7.3$ Hz), 127.61, 127.35, 71.54 (d, $J = 19.5$ Hz); HRMS (EI positive) Found: m/z 291.0941. Calcd for $C_{19}H_{17}OP - H$: 291.0939.

Phenylacetonitrile (1c):[25] Colorless oil; IR (KBr) 3067, 3034, 2922, 2343, 2251, 1956, 1603, 1587, 1497, 1456, 1416, 1339, 1186, 1157, 1078, 1030, 1003, 941, 899, 735, 696, 675, 615 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.2 (5H, m), 3.76 (2H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 129.74, 128.97, 127.88, 127.76, 117.77, 23.72; HRMS (EI positive) Found: m/z 117.0573. Calcd for C_8H_7N: 117.0578.

4-Methylbenzyl Diphenylphosphinite (2b): Colorless oil; IR (ATR) 3051, 3006, 2920, 2862, 1895, 1616, 1586, 1515, 1479, 1434, 1370, 1307, 1205, 1179, 1095, 1026, 1006, 991, 802, 785, 739, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.0 (14H, m), 4.81 (2H, d, $J = 9.2$ Hz), 2.27 (3H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.63 (d, $J = 17.9$ Hz), 137.15, 135.54 (d, $J = 8.3$ Hz), 130.41, 130.10, 129.06, 128.85, 128.09 (d, $J = 6.7$ Hz), 127.43, 71.39 (d, $J = 19.5$ Hz), 21.18; HRMS (EI positive) Found: m/z 305.1113. Calcd for $C_{20}H_{19}OP - H$: 305.1095.

4-Methylphenylacetonitrile (2c):[26] Colorless oil; IR (KBr) 3028, 3011, 2924, 2864, 2737, 2251, 1913, 1618, 1516, 1452, 1418, 1381, 1215, 1186, 1119, 1105, 1042, 1022, 953, 912, 839, 799, 752 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.18 (4H, m), 3.68 (2H, s), 2.34 (3H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 137.60, 129.57, 127.61, 126.66, 117.97, 23.18, 21.05; HRMS (EI positive) Found: m/z 131.0737. Calcd for C_9H_9N: 131.0735.

4-Bromobenzyl Diphenylphosphinite (3b): White solid; mp 50–51 °C; IR (ATR) 3069, 2868, 1966, 1898, 1588, 1480, 1454, 1434, 1402, 1360, 1307, 1280, 1242, 1205, 1128, 1098, 1067, 1006, 990, 944, 916, 834, 796, 743, 727, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.7–7.1 (14H, m), 4.86 (2H, d, $J = 9.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.26 (d, $J = 17.8$ Hz), 137.58 (d, $J = 7.8$ Hz), 131.30, 130.50, 130.18, 129.30, 128.94, 128.21 (d, $J = 7.3$ Hz), 121.47, 70.73 (d, $J = 20.1$ Hz); HRMS (EI positive) Found: m/z 369.0051. Calcd for $C_{19}H_{16}{}^{79}BrOP - H$: 369.0004.

4-Bromophenylacetonitrile (3c):[27] White solid; mp 48–49 °C (lit.[28] mp 47.5–48.5 °C); IR (KBr) 2963, 2926, 2249, 1591, 1487, 1460, 1412, 1315, 1103, 1067, 1013, 926, 905, 837, 824, 791 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50 (2H, d, $J = 8.4$ Hz), 7.10 (2H, d, $J = 8.1$ Hz), 3.71 (2H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 132.09, 129.44, 128.73, 121.99, 117.22, 23.20; HRMS (EI positive) Found: m/z 194.9686. Calcd for $C_8H_6{}^{79}BrN$: 194.9684.

4-Chlorobenzyl Diphenylphosphinite (4b): White solid; mp 39–41 °C; IR (ATR) 3069, 2943, 2866, 1898, 1593, 1484, 1454, 1434, 1404, 1360, 1307, 1275, 1241, 1206, 1090, 1068, 1008, 989, 944, 916, 837, 799, 743, 729, 712, 694 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.1 (14H, m), 4.83 (2H, d, $J = 9.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.32 (d, $J = 17.8$ Hz), 137.12 (d, $J = 7.8$ Hz), 133.37, 130.55, 130.22, 129.34, 128.69, 128.41, 128.29, 128.20, 70.78 (d, $J = 19.5$ Hz); HRMS (EI positive) Found: m/z 325.0555. Calcd for $C_{19}H_{16}{}^{35}ClOP - H$: 325.0549.

4-Chlorophenylacetonitrile (4c):[29] Colorless oil; IR (KBr) 2941, 2920, 2257, 1493, 1410, 1090, 1015, 912, 841, 799, 664 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35 (2H, d, $J = 8.6$ Hz), 7.26 (2H, d, $J = 8.6$ Hz), 3.72 (2H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 133.93, 129.14, 129.12, 128.21, 117.32, 23.12; HRMS (EI positive) Found: m/z 151.0185. Calcd for $C_8H_6{}^{35}ClN$: 151.0189.

4-(Trifluoromethyl)benzyl Diphenylphosphinite (5b): Colorless oil; IR (ATR) 3056, 2865, 1620, 1587, 1480, 1434, 1419, 1372, 1323, 1162, 1121, 1065, 1043, 1013, 820, 790, 740, 694 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.1 (14H, m), 4.90 (2H, d, $J = 9.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.66 (d, $J = 8.3$ Hz), 141.20 (d, $J = 17.9$ Hz), 130.59, 130.27, 129.45, 128.21 (d, $J = 6.7$ Hz), 127.24, 125.20 (q, $J = 270.6$ Hz), 70.66 (d, $J = 20.1$ Hz); HRMS (EI positive) Found: m/z 359.0811. Calcd for $C_{20}H_{16}F_3OP - H$: 359.0813.

4-(Trifluoromethyl)phenylacetonitrile (5c): Colorless oil; IR (KBr) 2928, 2252, 2000, 1938, 1717, 1620, 1420, 1327, 1165, 1109, 1067, 1016, 943, 924, 868, 847, 818, 752, 719 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.65 (2H, d, $J = 8.4$ Hz), 7.47 (2H, d, $J = 8.1$ Hz), 3.83 (2H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 133.76, 130.42 (q, $J = 32$ Hz), 128.23, 126.02 (q, $J = 3.9$ Hz), 125.66, 124.04 (q, $J = 323$ Hz), 23.40; HRMS (EI positive) Found: m/z 185.0453. Calcd for $C_9H_6F_3N$: 185.0452.

2-Phenylethyl Diphenylphosphinite (6b): Colorless oil; IR (ATR) 3055, 3027, 2942, 2868, 1951, 1885, 1811, 1603, 1586, 1495, 1479, 1453, 1434, 1377, 1305, 1180, 1156, 1092, 1054, 1016, 1001, 915, 886, 841, 737, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.5–7.2 (15H, m), 4.10 (2H, dt, $J = 8.4$, 7.3 Hz), 3.03 (2H, t, $J = 6.8$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.77 (d, $J = 18.4$ Hz), 138.13, 130.37, 130.05, 129.06, 128.94, 128.13 (d, $J = 8.9$ Hz), 126.16, 70.70 (d, $J = 19.0$ Hz), 38.01 (d, $J = 7.3$ Hz); HRMS (EI positive) Found: m/z 306.1180. Calcd for $C_{20}H_{19}OP$: 306.1174.

3-Phenylpropionitrile (6c):[25] Colorless oil; IR (neat) 2868, 2359, 2340, 2245, 1497, 1454, 1423, 1339, 1078, 1030, 976, 905, 746, 700, 669 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.2 (5H, m), 2.95 (2H, t, $J = 7.3$ Hz), 2.61 (2H, t, $J = 7.6$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 137.88, 128.73, 128.12, 127.10, 119.04, 31.58, 19.42; HRMS (EI positive) Found: m/z 131.0741. Calcd for C_9H_9N: 131.0735.

3-Phenylpropyl Diphenylphosphinite (7b): Colorless oil; IR (ATR) 3055, 2939, 2865, 2359, 1766, 1726, 1662, 1587, 1551, 1495, 1480, 1434, 1382, 1091, 1025, 938, 783, 738, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.1 (15H, m), 3.88 (2H, dt, $J = 8.9$, 6.5 Hz), 2.71 (2H, d, $J = 7.6$ Hz), 2.00 (2H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.03 (d, $J = 17.9$ Hz), 141.52, 130.05, 129.11, 128.34, 128.22, 128.13, 125.70, 69.37 (d, $J = 6.8$ Hz), 33.14 (d, $J = 7.8$ Hz), 32.20, 30.36; HRMS (EI positive) Found: m/z 320.1317. Calcd for $C_{21}H_{21}OP$: 320.1330.

4-Phenylbutyronitrile (7c):[30] Colorless oil; IR (KBr) 3086, 3063, 3028, 3005, 2939, 2866, 2247, 1603, 1497, 1456, 1423, 1350, 1082, 1030, 912, 845, 800, 748, 700 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 2.77 (2H, t, $J = 7.3$ Hz), 2.31 (2H, t, $J = 7.0$ Hz), 2.1–1.9 (2H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 139.53, 128.51, 128.30, 126.35, 119.39, 34.37, 26.93, 16.42; HRMS (EI positive) Found: m/z 145.0895. Calcd for $C_{10}H_{11}N$: 145.0891.

2-Phenylpropyl Diphenylphosphinite (8b): Colorless oil; IR (ATR) 3055, 3028, 2963, 2927, 2868, 1951, 1886, 1602, 1586, 1493, 1480, 1452, 1434, 1384, 1305, 1180, 1156, 1094, 1067, 1013, 1000, 907, 798, 739, 693 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.0 (15H, m), 4.0–3.7 (2H, m), 3.2–3.0 (1H, m), 1.30 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.53, 141.85 (d, $J = 17.9$ Hz), 130.32, 130.27, 129.99, 129.95, 129.01, 128.97, 128.18, 128.12, 128.09, 128.02, 128.00, 127.37, 126.27, 75.39 (d, $J = 18.4$ Hz), 41.44 (d, $J = 7.3$ Hz), 18.07; HRMS (EI positive) Found: m/z 320.1349. Calcd for $C_{21}H_{21}OP$: 320.1330.

3-Phenylbutyronitrile (8c):[31] Colorless oil; IR (KBr) 3063, 3030, 2968, 2932, 2878, 2835, 2247, 1954, 1881, 1811, 1602, 1583, 1497, 1454, 1421, 1383, 1358, 1329, 1312, 1097, 1067, 1016, 999, 914, 764, 700 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.2 (5H, m), 3.16 (1H, m), 2.59 (2H, m), 1.46 (3H, d, $J = 6.8$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 142.98, 128.74, 127.21, 126.42, 118.48, 36.57, 26.42, 20.74; HRMS (EI positive) Found: m/z 145.0895. Calcd for $C_{10}H_{11}N$: 145.0891.

2-(4-Methoxybenzyloxy)ethyl Diphenylphosphinite (9b): Colorless oil; IR (ATR) 3052, 3002, 2928, 2861, 1887, 1611, 1586, 1511, 1461, 1434, 1374, 1356, 1301, 1245, 1174, 1097, 1056, 1033, 922, 843, 817, 738, 695 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.2 (10H, m), 7.19 (2H, d, $J = 6.8$ Hz), 6.83 (2H, d, $J = 6.5$ Hz), 4.42 (2H, s), 4.1–3.9 (2H, m), 3.77 (3H, s), 3.7–3.6 (2H, m); ^{13}C NMR (68 MHz, CDCl$_3$) δ 158.96, 141.92 (d, $J = 17.8$ Hz), 130.39, 130.17, 130.07, 129.11, 129.07, 128.11 (d, $J = 6.6$ Hz), 113.62, 72.74, 70.02 (d, $J = 7.3$ Hz), 69.40 (d, $J = 19.0$ Hz), 55.24; HRMS (EI positive) Found: m/z 366.1378. Calcd for $C_{22}H_{23}O_3P$: 366.1385.

3-(4-Methoxybenzyloxy)propionitrile (9c): Colorless oil; IR (ATR) 2936, 2872, 2251, 1612, 1586, 1512, 1462, 1413, 1361, 1302, 1245, 1175, 1097, 1031, 913, 820, 754, 731 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.26 (2H, t, $J = 6.2$ Hz), 6.88 (2H, d, $J = 8.6$ Hz), 4.49 (2H, s), 3.79 (3H, s), 3.63 (2H, t, $J = 6.5$ Hz), 2.58 (2H, t, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 159.21, 129.20, 129.11, 117.70, 113.75, 72.82, 64.17, 55.21, 18.87; HRMS (EI positive) Found: m/z 191.0942. Calcd for $C_{11}H_{13}NO_2$: 191.0946.

2-Phenyl-3-(tetrahydropyran-2-yloxy)propyl Diphenylphosphinite (10b): Colorless oil; IR (ATR) 3055, 2939, 2869, 1737, 1603, 1494, 1479, 1453, 1434, 1380, 1352, 1322, 1280, 1260, 1200, 1182, 1156, 1133, 1121, 1073, 1024, 997, 970, 905, 869, 812, 739, 694 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.1–7.5 (15H, m), 4.6–4.5 (1H, m), 4.3–4.0 (3H, m), 3.7–3.6 (2H, m), 3.5–3.2 (2H, m), 1.9–1.3 (6H, m); ^{13}C NMR (68 MHz, CDCl$_3$) δ 142.00, 141.97, 141.95, 141.73, 141.69, 141.68, 140.35, 140.34, 140.28, 140.26, 130.41, 130.39, 130.30, 130.28, 130.26, 130.09, 130.07, 129.99, 129.95, 129.93, 129.05, 129.00, 128.94, 128.32, 128.11, 128.01, 128.00, 127.98, 126.58, 98.70, 98.47, 71.12, 71.08, 71.07, 70.84, 70.80, 68.19, 67.90, 67.88, 61.77, 61.64, 47.52, 47.50, 47.46, 47.45, 47.41, 47.38, 47.35, 47.33, 30.55, 30.52, 30.51, 25.51, 25.50; HRMS (EI positive) Found: m/z 420.1863. Calcd for $C_{26}H_{29}O_3P$: 420.1854.

3-Phenyl-4-(tetrahydropyran-2-yloxy)butyronitrile (10c): Colorless oil; IR (ATR) 2942, 2870, 2246, 1496, 1454, 1440, 1385, 1352, 1322, 1280, 1260, 1201, 1183, 1155, 1123, 1071, 1029, 977, 904, 869, 814, 759, 732, 700 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.2 (5H, m), 4.7–4.5 (1H, m), 4.1–3.9 (1H, m), 3.8–3.4 (3H, m), 3.3–3.2 (1H, m), 3.0–2.6 (2H, m), 1.9–1.4 (6H, m); ^{13}C NMR (68 MHz, CDCl$_3$) δ 139.07, 139.00, 128.66, 127.56, 127.36, 127.34, 118.45, 99.26, 98.47, 69.76, 69.27, 62.32, 62.03, 42.31, 42.28, 30.47, 30.43, 25.35, 21.28, 21.23, 19.43, 19.26; HRMS (EI positive) Found: m/z 245.1413. Calcd for $C_{15}H_{19}NO_2$: 245.1416.

Preparation of Secondary Alkyl Diphenylphosphinites. To a stirred solution of alcohol (20 mmol) and DMAP (4-dimethylaminopyridine) (6 mmol) in dehydrated THF (40 mL) was added Et_3N (24 mmol), and then PPh_2Cl (22 mmol) was dropped into the solution under an argon atmosphere. After stirring at rt for 2 h, the white slurry was concentrated in vacuo. After dilution of the residue with a mixed solution of hexane (180 mL) and ethyl acetate (20 mL), the suspension was filtered through a pad of alumina and Celite. To remove a trace amount of DMAP, the filtrate was concentrated and filtered through a pad of alumina and Celite again. The filtrate was concentrated in vacuo to afford the desired phosphinites.

Typical Experimental Procedure for Cyanation of Secondary Alkyl Diphenylphosphinites. To a stirred suspension of dry ZnO (0.50 mmol), alkyl diphenylphosphinite (0.75 mmol), and diethyl cyanophosphonate (0.50 mmol) was added a dichloromethane solution (0.50 mL) of 2,6-dimethyl-1,4-benzoquinone (0.75 mmol) at room temperature under an argon atmosphere. After 24 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution and with brine, and then dried over anhydrous Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC to afford the corresponding isocyanide.

4-Phenylbutan-2-yl Diphenylphosphinite (13b): White solid; mp 37–38 °C; IR (ATR) 3055, 3027, 2961, 2933, 2868, 1602, 1491, 1478, 1453, 1434, 1373, 1349, 1311, 1191, 1124, 1097, 1080, 1049, 1017, 937, 911, 886, 791, 741, 723, 696 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.7–7.0 (15H, m), 4.2–4.0 (1H, m), 2.8–2.5 (2H, m), 2.1–1.7 (2H, m), 1.31 (3H, d, $J = 6.5$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.01 (d, $J = 16.7$ Hz), 142.54 (d, $J = 16.1$ Hz), 141.89, 130.57, 130.25, 130.10, 129.79, 129.08, 128.83, 128.19, 128.14, 128.10, 128.03, 125.61, 76.96 (d, $J = 20.6$ Hz), 40.12 (d, $J = 5.6$ Hz), 31.89, 22.42 (d, $J = 5.6$ Hz); HRMS (EI positive) Found: m/z 334.1497. Calcd for $C_{22}H_{23}OP$: 334.1487.

4-Phenylbutan-2-yl Isocyanide (13c): Colorless oil; IR (ATR) 3063, 3028, 2984, 2936, 2862, 2137, 1734, 1717, 1699, 1684, 1650, 1604, 1558, 1541, 1521, 1496, 1454, 1382, 1347, 1185, 1129, 1052, 1031, 918, 858, 798, 775, 743, 698 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.1 (5H, m), 3.6–3.5 (1H, m), 2.9–2.6 (2H, m), 2.0–1.7 (2H, m), 1.38 (3H, dt, $J = 6.8$, 2.2 Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 154.57 (t, $J = 5.0$ Hz), 140.02, 128.41, 128.25, 126.14, 49.42 (t, $J = 5.6$ Hz), 38.31, 31.94, 21.69.

2-Methyl-4-phenylbutyronitrile (14):[32] Colorless oil; IR (ATR) 3028, 2981, 2936, 2863, 2239, 1603, 1496, 1454, 1383, 1123, 1051, 1030, 742, 699 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.1 (5H, m), 2.9–2.6 (2H, m), 2.6–2.5 (1H, m), 2.0–1.7 (2H, m), 1.32 (3H, d, $J = 7.0$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 139.98, 128.50, 128.27, 126.67, 122.65, 35.76, 33.21, 24.89, 18.06; HRMS (EI positive) Found: m/z 159.1049. Calcd for $C_{11}H_{13}N$: 159.1048.

1-Phenylpropan-2-yl Diphenyphosphinite (15b): Colorless oil; IR (ATR) 3055, 3027, 2970, 2927, 1951, 1587, 1495, 1480, 1452, 1434, 1376, 1351, 1303, 1212, 1180, 1126, 1093, 1068, 1061, 998, 948, 879, 859, 738, 693 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.1 (15H, m), 4.4–4.1 (1H, m), 3.02 (1H, dd, $J = 13.5$, 6.8 Hz), 2.81 (1H, dd, $J = 13.5$, 6.5 Hz), 1.28 (3H, d, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 142.86, 142.62, 142.36, 142.12, 138.24, 130.33, 130.24, 130.02, 129.91, 129.50, 128.91, 128.81, 128.12, 128.04, 127.94, 126.09, 78.26 (d, $J = 20.6$ Hz), 44.91 (d, $J = 5.6$ Hz), 22.00 (d, $J = 5.0$ Hz); HRMS (EI positive) Found: m/z 320.1315. Calcd for $C_{21}H_{21}OP$: 320.1330.

1-Phenylpropan-2-yl Isocyanide (15c): Colorless oil; IR (ATR) 3030, 2986, 2928, 2140, 1603, 1494, 1453, 1381, 1347, 1277, 1206, 1090, 1076, 1032, 909, 738, 699 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 3.9–3.7 (1H, m), 3.0–2.7 (2H, m), 1.37 (3H, dt, $J = 6.5$, 2.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 154.99 (t, $J = 5.0$ Hz), 135.89, 128.96, 128.24, 126.84, 51.31 (t, $J = 5.0$ Hz), 42.77, 21.05.

1-Phenylpentan-3-yl Diphenylphosphinite (16b): Colorless oil; IR (ATR) 3057, 3026, 2962, 2933, 2874, 1949, 1734, 1602, 1494, 1479, 1454, 1434, 1360, 1304, 1232, 1179, 1094, 1066, 1024, 963, 940, 828, 739, 694 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.0 (15H, m), 4.0–3.8 (1H, m), 2.7–2.4 (2H, m), 2.0–1.5 (4H, m), 0.87 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.08 (d, $J = 6.1$ Hz), 142.84 (d, $J = 6.7$ Hz), 142.05, 130.55, 130.24, 130.22, 129.92, 129.03, 128.83, 128.18, 128.17, 128.10, 128.08, 128.00, 125.58, 82.47 (d, $J = 19.0$ Hz), 37.31 (d, $J = 5.0$ Hz), 31.71, 28.84 (d, $J = 5.6$ Hz), 9.86; HRMS (EI positive) Found: m/z 348.1657 Calcd for $C_{23}H_{25}OP$: 348.1643.

1-Phenylpentan-3-yl Isocyanide (16c): Colorless oil; IR (ATR) 3028, 2970, 2935, 2136, 1603, 1495, 1454, 1384, 1355, 1179, 1114, 1059, 1029, 990, 917, 883, 847, 806, 749, 699 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 3.5–3.3 (1H, m), 3.0–2.6 (2H, m), 2.0–1.7 (2H, m), 1.7–1.5 (2H, m), 1.03 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.14 (t, $J = 5.6$ Hz), 140.11, 128.38, 128.23, 126.09, 55.82 (t, $J = 5.6$ Hz), 36.25, 31.95, 28.18, 10.12.

4-(4-Methoxybenzyloxy)butan-2-yl Diphenylphosphinite (17b): Colorless oil; IR (ATR) 3053, 2963, 2931, 2860, 1611, 1586, 1512, 1478, 1457, 1435, 1373, 1362, 1301, 1245, 1207, 1174, 1091, 1032, 971, 936, 883, 819, 738, 695 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.5–7.3 (10H, m), 7.19 (2H, d, $J = 8.6$ Hz), 6.84 (2H, d, $J = 8.6$ Hz), 4.26 (3H, s), 3.79 (3H, s), 3.46 (2H, d, $J = 6.2$ Hz), 2.0–1.7 (2H, m), 1.27 (3H, d, $J = 5.7$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 158.87, 143.00 (d, $J = 16.7$ Hz), 142.50 (d, $J = 16.7$ Hz), 130.61, 130.39, 130.28, 130.08, 129.76, 129.16, 129.04, 128.77, 128.14, 128.09, 128.04, 128.00, 113.60, 74.78 (d, $J = 21.2$ Hz), 72.57, 66.54, 55.26, 38.43 (d, $J = 5.6$ Hz), 22.66 (d, $J = 5.0$ Hz); HRMS (EI positive) Found: m/z 394.1711. Calcd for $C_{24}H_{27}O_3P$: 394.1698.

4-(4-Methoxybenzyloxy)butan-2-yl Isocyanide (17c): Colorless oil; IR (ATR) 2937, 2865, 2139, 1612, 1586, 1512, 1460, 1365, 1301, 1245, 1174, 1091, 1032, 816, 755, 708 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.25 (2H, d, $J = 8.4$ Hz), 6.88 (2H, d, $J = 8.6$ Hz), 4.46 (1H, d, $J = 11.3$ Hz), 4.41 (1H, d, $J = 11.3$ Hz), 4.0–3.8 (1H, m), 3.79 (3H, s), 3.7–3.5 (2H, m), 1.9–1.7 (2H, m), 1.36 (3H, dt, $J = 6.8$, 2.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 159.01, 154.28 (t, $J = 5.0$ Hz), 129.87, 129.12, 113.65, 72.85, 65.60, 55.19, 47.31 (t, $J = 5.6$ Hz), 36.91, 21.63.

4-(*t*-Butyldiphenylsilyloxy)butan-2-yl Diphenylphosphinite (18b): Colorless oil; IR (ATR) 3070, 3051, 2959, 2930, 2857, 1889, 1588, 1472, 1429, 1378, 1360, 1305, 1263, 1231, 1186, 1104, 1088, 1026, 994, 974, 932, 893, 822, 766, 737, 696 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.7–7.2 (20H, m), 4.4–4.2 (1H, m), 3.8–3.6 (2H, m), 2.0–1.7 (2H, m), 1.28 (3H, d, $J = 6.2$ Hz), 1.01 (9H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.62 (d, $J = 17.3$ Hz), 142.55 (d, $J = 16.2$ Hz), 135.42, 135.39, 133.81, 133.71, 130.41, 130.17, 130.08, 129.85, 129.42, 129.38, 128.89, 128.79, 128.13, 128.09, 128.03, 128.00, 127.49, 127.47, 77.20, 74.63 (d, $J = 21.2$ Hz), 60.60, 41.23 (d, $J = 5.6$ Hz), 26.90, 22.68, 19.26, 0.14; HRMS (EI positive) Found: m/z 512.2296. Calcd for $C_{32}H_{37}O_2PSi$: 512.2300.

4-(*t*-Butyldiphenylsilyloxy)butan-2-yl Isocyanide (18c): Colorless oil; IR (ATR) 3070, 2955, 2933, 2858, 2139, 1589, 1471, 1427, 1388, 1360, 1348, 1261, 1227, 1187, 1107, 1088, 995, 983, 937, 902, 874, 821, 765, 735, 700, 689 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.7–7.6 (4H, m), 7.5–7.3 (6H, m), 4.0–3.6 (3H, m), 2.8–2.7 (2H, m), 1.37 (3H, dt, $J = 6.5$, 2.2 Hz), 1.03 (9H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 154.46 (t, $J = 5.0$ Hz), 135.33, 135.28, 133.21, 133.01, 129.63, 129.61, 127.62, 127.59, 56.69, 46.95 (t, $J = 5.6$ Hz), 39.47, 26.84, 21.71, 19.23.

4-(Benzo[*b*]furan-2-yl)butan-2-yl Diphenylphosphinite (19b): Colorless oil; IR (ATR) 3054, 2968, 2926, 1600, 1587, 1478, 1454, 1434, 1376, 1349, 1305, 1252, 1194, 1169, 1127, 1096, 1063, 1005, 959, 935, 890, 822, 798, 736, 694 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.0 (14H, m), 6.20 (1H, m), 4.2–4.0 (1H, m), 2.9–2.6 (2H, m), 2.2–1.9 (2H, m), 1.32 (3H, d, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 158.87, 154.45, 142.84 (d, $J = 16.2$ Hz), 142.37 (d, $J = 16.7$ Hz), 130.64, 130.32, 130.11, 129.79, 129.17, 128.86, 128.75, 128.23, 128.13, 128.04, 123.00, 122.27, 120.10, 110.60, 102.02, 76.37 (d, $J = 20.7$ Hz), 36.12 (d, $J = 6.1$ Hz), 24.68, 22.32 (d, $J = 5.0$ Hz); HRMS (EI positive) Found: m/z 374.1420. Calcd for $C_{24}H_{23}O_2P$: 374.1436.

4-(Benzo[*b*]furan-2-yl)butan-2-yl Isocyanide (19c): Colorless oil; IR (ATR) 2985, 2939, 2137, 1725, 1602, 1588, 1453, 1383, 1347, 1252, 1194, 1169, 1130, 1104, 1067, 1008, 941, 880, 854, 805, 747 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.3 (2H, m), 7.3–7.1 (2H, m), 6.44 (1H, s), 3.8–3.5 (1H, m), 3.1–2.8 (2H, m), 2.1–1.9 (2H, m), 1.38 (3H, dt, $J = 6.8$, 2.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.11 (t, $J = 4.5$ Hz), 154.50, 128.42, 123.35, 122.47, 120.22, 110.63, 102.87, 49.43 (t, $J = 5.6$ Hz), 34.60, 24.89, 21.59.

4-(1-Methylindol-2-yl)butan-2-yl Diphenylphosphinite (20b): Colorless oil; IR (ATR) 3051, 2965, 2927, 1545, 1468, 1433, 1402, 1375, 1343, 1312, 1233, 1125, 1095, 1059, 1026, 1013, 955, 940, 888, 847, 770, 736, 695 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.0 (14H, m), 6.16 (1H, m), 4.3–4.1 (1H, m), 3.49 (3H, m), 2.9–2.6 (2H, m), 2.2–1.9 (2H, m), 1.37 (3H, d, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.81 (d, $J = 16.2$ Hz), 142.44 (d, $J = 16.2$ Hz), 140.44, 137.10, 130.78, 130.46, 129.98, 129.67, 129.24, 128.82, 128.13, 128.04, 127.66, 120.39, 119.59, 119.06, 108.56, 98.43, 76.96 (d, $J = 21.2$ Hz), 37.01 (d, $J = 5.6$ Hz), 22.99, 22.48 (d, $J = 4.5$ Hz); HRMS (EI positive) Found: m/z 387.1763. Calcd for $C_{25}H_{26}NOP$: 387.1752.

4-(1-Methylindol-2-yl)butan-2-yl Isocyanide (20c): Colorless oil; IR (ATR) 3052, 2982, 2936, 2137, 1611, 1546, 1467, 1341, 1313, 1233, 1206, 1165, 1128, 1098, 1062, 1011, 921, 843, 809, 776, 745, 681 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.5 (1H, m), 7.3–7.0 (3H, m), 6.25 (1H, s), 3.8–3.6 (1H, m), 3.64 (3H, s), 3.0–2.8 (2H, m), 2.1–1.8 (2H, m), 1.40 (3H, dt, $J = 7.0$, 1.9 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.01 (t, $J = 5.6$ Hz), 138.40, 137.19, 127.46, 120.78, 119.68, 119.29, 108.73, 99.0, 49.53 (t, $J = 5.6$ Hz), 35.45, 29.44, 22.99, 21.66.

1-Phenylethyl Diphenylphosphinite (21b): Colorless oil; IR (ATR) 3055, 2973, 2882, 1953, 1586, 1492, 1480, 1449, 1434, 1370, 1357, 1326, 1304, 1285, 1206, 1157, 1091, 1063, 1027, 1010, 995, 924, 780, 738, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.7–7.2 (15H, m), 5.1–4.9 (1H, m), 1.59 (3H, d, $J = 6.5$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.83, 143.77, 142.41 (d, $J = 17.8$ Hz), 141.94 (d, $J = 16.2$ Hz), 130.39, 130.34, 130.07, 130.02, 129.06, 128.89, 128.22, 128.17, 128.12, 128.05, 127.95, 127.35, 125.96, 78.50 (d, $J = 20.7$ Hz), 25.12 (d, $J = 5.6$ Hz);

HRMS (EI positive) Found: m/z 306.1188. Calcd for $C_{20}H_{19}OP$: 306.1174.

1-Phenylethyl Isocyanide (21c):[33] Colorless oil; IR (ATR) 3034, 2989, 2938, 2139, 1603, 1496, 1451, 1378, 1349, 1279, 1202, 1075, 1029, 993, 913, 856, 756, 696 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.5–7.2 (5H, m), 4.9–4.7 (1H, m), 1.68 (3H, dt, $J = 6.8$, 2.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 156.02 (t, $J = 5.6$ Hz), 138.37, 128.80, 128.14, 125.26, 53.81 (t, $J = 6.7$ Hz), 25.20.

(*R*)-4-Phenylbutan-2-yl Diphenylphosphinite (23): White solid; mp 53–54 °C; $[\alpha]_D^{17} = -40.9$ (c 1.0, $CHCl_3$); IR (ATR) 3069, 2961, 2933, 2869, 1602, 1492, 1479, 1453, 1434, 1373, 1349, 1312, 1191, 1124, 1097, 1080, 1049, 1017, 938, 912, 886, 791, 742, 723, 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.7–7.0 (15H, m), 4.2–4.0 (1H, m), 2.8–2.5 (2H, m), 2.1–1.7 (2H, m), 1.31 (3H, d, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.03 (d, $J = 16.7$ Hz), 142.57 (d, $J = 16.1$ Hz), 141.90, 130.59, 130.26, 130.12, 129.81, 129.08, 128.81, 128.27, 128.20, 128.14, 128.10, 128.04, 125.62, 76.96 (d, $J = 20.6$ Hz), 40.12 (d, $J = 6.2$ Hz), 31.89, 22.41 (d, $J = 5.6$ Hz); HRMS (EI positive) Found: m/z 334.1498. Calcd for $C_{22}H_{23}OP$: 334.1487.

(*S*)-4-Phenylbutan-2-yl Isocyanide (24): Colorless oil; $[\alpha]_D^{23} = +97.9$ (c 1.0, $CHCl_3$), 96% ee; IR (ATR) 3028, 2984, 2937, 2862, 2137, 1727, 1603, 1495, 1453, 1382, 1347, 1185, 1129, 1052, 1031, 918, 858, 775, 743, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 3.6–3.5 (1H, m), 2.9–2.6 (2H, m), 2.0–1.7 (2H, m), 1.38 (3H, dt, $J = 6.8$, 2.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 154.59 (t, $J = 5.0$ Hz), 140.04, 128.43, 128.27, 126.16, 49.44 (t, $J = 5.6$ Hz), 38.32, 31.96, 21.72; HPLC analysis: DALCEL CHIRALCEL OJ-H (ϕ4.6 × 250 mm), hexane/isopropyl alcohol = 1000/1, flow rate: 1.0 mL min^{-1}, Temp. 25 °C, detector: 254 nm, (*R*)-4-Phenylbutan-2-yl Isocyanide (**24′**) ($t_R = 21.6$ min), (*S*)-4-Phenylbutan-2-yl Isocyanide (**24**) ($t_R = 23.6$ min).

3-Phenylpropyl Isocyanide (26): Colorless oil; IR (ATR) 3062, 3027, 2930, 2861, 2147, 1735, 1603, 1496, 1452, 1350, 1243, 1178, 1084, 1030, 1006, 941, 912, 890, 853, 804, 744, 699 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 3.4–3.3 (2H, m), 2.79 (2H, t, $J = 7.0$ Hz), 2.1–1.9 (2H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.86 (t, $J = 5.6$ Hz), 139.54, 128.42, 128.24, 126.21, 40.60 (t, $J = 6.2$ Hz), 32.10, 28.02.

(*S*)-4-Phenylbutan-2-ylamine (25).[23] To a cooled (0 °C) solution of the isocyanide **24** (56.5 mg, 0.354 mmol) in MeOH (2.5 mL) was added dropwise 2 M HCl in MeOH (6.0 mL). Water (125 µL) was added and the resulting solution allowed to warm to rt and stirred for an additional 1 h. The solvent was removed in vacuo and 1 M aqueous NaOH solution was added. The mixture was extracted with AcOEt and the combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and then concentrated in vacuo. The resulting residue was purified by preparative TLC ($CHCl_3$/MeOH = 1/1) to afford **25** (16.2 mg, 31%) as a colorless oil. $[\alpha]_D^{23} = +7.2$ (c 0.49, $CHCl_3$) [Lit.[23] $[\alpha]_D^{20} = +6.4$ (c 0.47, $CHCl_3$), 98% ee]; IR (ATR) 3739, 3673, 3649, 3061, 3026, 2954, 2923, 2857, 1868, 1772, 1734, 1716, 1699, 1684, 1650, 1602, 1558, 1542, 1522, 1494, 1454, 1374, 1095, 1063, 1030, 838, 743, 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.3–7.1 (5H, m), 3.0–2.8 (1H, m), 2.8–2.5 (2H, m), 1.9–1.7 (2H, m), 1.8–1.6 (2H, m), 1.12 (3H, d, $J = 6.5$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.06, 128.24, 128.21, 125.64, 46.65, 41.64, 32.83, 23.86; HRMS (EI positive) Found: m/z 149.1194. Calcd for $C_{10}H_{15}N$: 149.1204.

Preparation of Tertiary Alkyl Diphenylphosphinites. The preparation of tertiary alkyl diphenylphosphinites was done by a similar method as for the secondary alkyl diphenylphosphinites except for the purification step. After concentration of the filtrate, it was subjected to basic silica-gel column chromatography and subsequent filtration through a pad of alumina and Celite to afford the desired phosphinites. The purification step was important for the reproducibility of the reaction.

Typical Experimental Procedure for Cyanation of Tertiary Alkyl Diphenylphosphinites. To a stirred mixture of alkyl diphenylphosphinite (0.75 mmol) and diethyl cyanophosphonate (0.50 mmol) was added a dichloromethane solution (0.50 mL) of 2,6-dimethyl-1,4-benzoquinone (1.0 mmol) at room temperature under an argon atmosphere. After 12 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution and with brine, and then dried over anhydrous Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC to afford the corresponding isocyanide.

2-Methyl-4-phenylbutan-2-yl Diphenylphosphinite (27b): Colorless oil; IR (ATR) 3055, 3026, 2969, 2932, 2863, 1948, 1603, 1494, 1479, 1454, 1434, 1381, 1366, 1303, 1242, 1204, 1170, 1124, 1094, 1070, 1027, 981, 913, 846, 801, 739, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.4 (4H, m), 7.4–7.0 (11H, m), 2.7–2.6 (2H, m), 2.1–1.9 (2H, m), 1.43 (6H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.56 (d, $J = 13.8$ Hz), 142.40, 130.10, 129.77, 128.64, 128.21 (d, $J = 1.2$ Hz), 128.06 (d, $J = 7.3$ Hz), 125.55, 78.44 (d, $J = 11.7$ Hz), 45.13 (d, $J = 5.6$ Hz), 30.76, 28.11 (d, $J = 9.5$ Hz); HRMS (EI positive) Found: m/z 348.1632 Calcd for $C_{23}H_{25}OP$: 348.1643.

2-Methyl-4-phenylbutan-2-yl Isocyanide (27c): Colorless oil; IR (ATR) 3028, 2984, 2937, 2866, 2131, 1604, 1496, 1468, 1454, 1391, 1372, 1283, 1218, 1170, 1134, 1074, 1030, 909, 881, 752, 697 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.4–7.1 (5H, m), 2.9–2.7 (2H, m), 1.9–1.8 (2H, m), 1.47 (6H, t, $J = 1.9$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 153.34 (t, $J = 5.0$ Hz), 140.69, 128.38, 128.18, 125.99, 57.24 (t, $J = 5.0$ Hz), 44.32, 30.71, 29.00.

2-Methyl-4-phenylbut-1-ene (27d)[34] **and 3-Methyl-1-phenylbut-2-ene (27e):**[35] Mixture of stereoisomers; Colorless oil; IR (ATR) 3063, 3027, 2970, 2916, 2857, 1649, 1604, 1494, 1451, 1376, 1102, 1073, 1029, 982, 886, 854, 773, 737, 696 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) **27d**: δ 7.3–7.1 (5H, m), 4.74 (1H, s), 4.71 (1H, s), 2.75 (2H, t, $J = 7.8$ Hz), 2.31 (2H, t, $J = 8.9$ Hz), 1.77 (3H, s); **27e**: δ 7.3–7.1 (5H, m), 5.33 (1H, tt, $J = 1.4$, 7.3 Hz), 3.34 (2H, d, $J = 7.6$ Hz), 1.74 (3H, s), 1.72 (3H, s); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.25, 142.07, 141.68, 132.38, 128.23, 128.20, 128.18, 128.17, 125.65, 125.58, 123.08, 110.11, 39.66, 34.41, 34.29, 25.83, 22.70, 17.90; HRMS (EI positive) Found: m/z 146.1095 Calcd for $C_{11}H_{14}$: 146.1096.

3-Methyl-1-phenylpentan-3-yl Diphenylphosphinite (28b): Colorless oil; IR (ATR) 3055, 3024, 2966, 2935, 2877, 1951, 1602, 1587, 1494, 1478, 1454, 1434, 1374, 1333, 1300, 1182, 1156, 1130, 1094, 1069, 1026, 998, 931, 908, 842, 804, 739, 693 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.6–7.4 (4H, m), 7.4–7.0 (11H, m), 2.7–2.5 (2H, m), 2.1–1.9 (2H, m), 1.81 (2H, q, $J = 7.0$ Hz), 1.38 (3H, s), 0.90 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.89, 143.85, 143.66, 143.61, 142.47, 130.19, 130.14, 129.85, 129.81, 128.64, 128.60, 128.19, 128.03 (d, $J = 7.3$ Hz), 125.55, 80.97 (d, $J = 10.0$ Hz), 42.18 (d, $J = 6.2$ Hz), 33.24 (d, $J = 7.3$ Hz), 30.42, 25.34 (d, $J = 11.1$ Hz), 8.74 (d, $J = 1.2$ Hz); HRMS (EI positive) Found: m/z 362.1798. Calcd for $C_{24}H_{27}OP$: 362.1800.

3-Methyl-1-phenylpentan-3-yl Isocyanide (28c): Colorless oil; IR (ATR) 3028, 2976, 2939, 2883, 2129, 1603, 1496, 1456, 1383, 1295, 1193, 1157, 1075, 1030, 1005, 928, 904, 864, 824, 751, 700 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.1 (5H, m), 2.9–2.7 (2H, m), 2.0–1.5 (4H, m), 1.40 (3H, t, $J = 1.6$ Hz), 1.04 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 153.69 (t, $J =$ 4.4 Hz), 140.80, 128.36, 128.15, 125.95, 60.87 (t, $J = 5.0$ Hz), 42.40, 33.79, 30.35, 25.73, 8.23.

3-Ethyl-1-phenylpentan-3-yl Diphenylphosphinite (29b): Colorless oil; IR (ATR) 3746, 3055, 3024, 2965, 2938, 2878, 1601, 1494, 1477, 1453, 1434, 1377, 1336, 1303, 1212, 1174, 1155, 1093, 1067, 1028, 995, 966, 923, 839, 820, 738, 694 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.4 (4H, m), 7.3–6.9 (11H, m), 2.6–2.4 (2H, m), 2.0–1.9 (2H, m), 1.9–1.7 (4H, m), 0.84 (6H, t, $J = 7.6$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.80 (d, $J = 15.6$ Hz), 142.53, 130.24, 129.90, 128.63, 128.16, 128.02 (d, $J = 7.3$ Hz), 125.52, 83.42 (d, $J = 8.9$ Hz), 39.54 (d, $J = 6.7$ Hz), 29.99 (d, $J = 1.2$ Hz), 29.79 (d, $J = 8.4$ Hz), 8.27 (d, $J = 1.7$ Hz); HRMS (EI positive) Found: m/z 376.1965. Calcd for $C_{25}H_{29}OP$: 376.1956.

3-Ethyl-1-phenylpentan-3-yl Isocyanide (29c): Colorless oil; IR (ATR) 3027, 2973, 2943, 2883, 2128, 1603, 1496, 1455, 1384, 1343, 1204, 1177, 1154, 1077, 1030, 998, 977, 907, 891, 828, 751, 700 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.1 (5H, m), 2.8–2.6 (2H, m), 1.9–1.8 (2H, m), 1.8–1.6 (4H, m), 1.00 (6H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 153.99 (t, $J =$ 4.5 Hz), 140.93, 128.26, 128.18, 126.00, 64.36 (t, $J = 5.0$ Hz), 39.15, 30.27, 30.05, 7.94.

5-(*t*-Butyldiphenylsilyloxy)-2-methylpentan-2-yl Diphenylphosphinite (30b): Colorless oil; IR (ATR) 3068, 3051, 2958, 2930, 2857, 1587, 1472, 1429, 1383, 1365, 1305, 1248, 1214, 1183, 1094, 1054, 1028, 998, 971, 931, 916, 822, 791, 738, 696 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.7–7.6 (4H, m), 7.5–7.2 (16H, m), 3.62 (2H, t, $J = 6.5$ Hz), 1.8–1.5 (4H, m), 1.35 (6H, s), 1.04 (9H, s); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.69 (d, $J =$ 16.1 Hz), 135.44, 133.91, 130.04, 129.71, 129.39, 128.52, 127.99 (d, $J = 6.7$ Hz), 127.48, 78.59 (d, $J = 11.7$ Hz), 39.40 (d, $J = 6.1$ Hz), 28.01 (d, $J = 10.0$ Hz), 27.69, 26.94, 19.32; HRMS (Recorded on a micromass Q-Tof-2 instrument, ESI positive) Found: m/z 541.2684. Calcd for $C_{34}H_{41}O_2PSi + H$: 541.2692.

5-(*t*-Butyldiphenylsilyloxy)-2-methylpentan-2-yl Isocyanide (30c): Colorless oil; IR (ATR) 3071, 2934, 2859, 2132, 1589, 1470, 1427, 1389, 1371, 1222, 1179, 1103, 1009, 975, 939, 822, 804, 755, 740, 701, 689 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.7–7.6 (4H, m), 7.5–7.3 (6H, m), 3.70 (2H, t, $J = 5.4$ Hz), 1.7–1.5 (4H, m), 1.38 (6H, s), 1.06 (9H, s); ^{13}C NMR (68 MHz, CDCl$_3$) δ 152.88 (t, $J = 3.9$ Hz), 135.38, 133.57, 129.49, 127.52, 63.34, 57.16 (t, $J = 5.0$ Hz), 38.90, 29.02, 27.45, 26.89, 19.24.

4-(Benzo[*b*]furan-2-yl)-2-methylbutan-2-yl Diphenylphosphinite (31b): Colorless oil; IR (ATR) 3054, 2970, 2928, 1600, 1588, 1477, 1454, 1434, 1382, 1366, 1303, 1252, 1205, 1166, 1129, 1098, 1068, 1025, 1007, 933, 909, 846, 817, 797, 739, 694 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.1 (14H, m), 6.28 (1H, m), 2.9–2.8 (2H, m), 2.2–2.1 (2H, m), 1.45 (6H, s). ^{13}C NMR (68 MHz, CDCl$_3$) δ 159.19, 154.43, 143.31 (d, $J = 15.7$ Hz), 130.18, 129.85, 128.80, 128.73, 128.09 (d, $J = 6.7$ Hz), 122.98, 122.28, 120.07, 110.57, 101.60, 78.00 (d, $J = 11.7$ Hz), 40.81 (d, $J = 5.0$ Hz), 27.95 (d, $J = 10.0$ Hz), 23.55; HRMS (EI positive) Found: m/z 388.1575. Calcd for $C_{25}H_{25}O_2P$: 388.1592.

4-(Benzo[*b*]furan-2-yl)-2-methylbutan-2-yl Isocyanide (31c): Colorless oil; IR (ATR) 2984, 2932, 2131, 1650, 1601, 1590, 1453, 1391, 1372, 1253, 1219, 1170, 1141, 1121, 1105, 1008, 945, 878, 800, 748, 682 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.3 (2H, m), 7.3–7.1 (2H, m), 6.42 (1H, s), 3.0–2.9 (2H, m), 2.1–1.9 (2H, m), 1.47 (6H, t, $J = 1.6$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 157.23, 154.45, 153.90 (t, $J = 4.5$ Hz), 128.51, 123.30, 122.43, 120.23, 110.60, 102.29, 56.98 (t, $J = 5.0$ Hz), 40.04, 28.93, 23.75.

4-(1-Methylindol-2-yl)-2-methylbutan-2-yl Diphenylphosphinite (32b): White solid; mp 81 °C; IR (ATR) 3052, 2965, 1742, 1548, 1467, 1432, 1401, 1384, 1367, 1337, 1317, 1303, 1275, 1248, 1233, 1164, 1138, 1093, 1067, 1023, 1009, 937, 912, 856, 838, 780, 740, 728, 696 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.0 (14H, m), 6.20 (1H, s), 3.53 (3H, s), 2.9–2.7 (2H, m), 2.2–2.0 (2H, m), 1.48 (6H, s); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.36 (d, $J = 15.7$ Hz), 140.98, 137.18, 130.15, 129.82, 128.76, 128.11 (d, $J = 7.3$ Hz), 127.72, 120.39, 119.60, 119.08, 108.58, 98.30, 78.17 (d, $J = 11.7$ Hz), 41.83 (d, $J = 5.6$ Hz), 29.32, 28.12 (d, $J = 9.5$ Hz), 21.66; HRMS (EI positive) Found: m/z 401.1917. Calcd for $C_{26}H_{28}NOP$: 401.1909.

4-(1-Methylindol-2-yl)-2-methylbutan-2-yl Isocyanide (32c): Yellow solid; mp 95–97 °C; IR (ATR) 3055, 2986, 2947, 2132, 1936, 1600, 1541, 1466, 1436, 1410, 1391, 1372, 1355, 1334, 1311, 1280, 1222, 1180, 1143, 1130, 1098, 1007, 997, 928, 909, 876, 844, 788, 753, 700, 662 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.52 (1H, d, $J = 7.6$ Hz), 7.26 (1H, d, $J = 8.1$ Hz), 7.16 (1H, dt, $J = 10.5$, 1.4 Hz), 7.07 (1H, dt, $J = 7.6$, 1.1 Hz), 6.24 (1H, s), 3.67 (3H, s), 3.0–2.8 (2H, m), 2.1–1.9 (2H, m), 1.50 (6H, t, $J = 1.9$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 153.94 (t, $J = 5.0$ Hz), 139.10, 137.26, 127.57, 120.80, 119.74, 119.31, 108.75, 98.70, 57.17 (t, $J = 4.5$ Hz), 41.12, 29.53, 29.06, 21.87.

2-Phenylpropan-2-yl Diphenylphosphinite (33b): Colorless oil; IR (ATR) 3061, 2981, 2968, 2923, 1739, 1599, 1493, 1476, 1460, 1446, 1431, 1380, 1363, 1303, 1261, 1192, 1144, 1097, 1067, 1027, 1000, 946, 901, 887, 757, 745, 694 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.4 (6H, m), 7.4–7.2 (9H, m), 1.74 (6H, d, $J = 1.9$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 147.32 (d, $J = 2.8$ Hz), 143.17 (d, $J = 15.7$ Hz), 130.29, 129.96, 128.69, 128.05 (d, $J = 7.3$ Hz), 126.85, 125.31 (d, $J = 1.6$ Hz), 79.58 (d, $J = 13.9$ Hz), 30.43 (d, $J = 10.0$ Hz); HRMS (EI positive) Found: m/z 320.1315. Calcd for $C_{21}H_{21}OP$: 320.1330.

2-Phenylpropan-2-yl Isocyanide (33c):[36] Colorless oil; IR (ATR) 3064, 2988, 2937, 2133, 1603, 1497, 1447, 1390, 1369, 1257, 1167, 1107, 1079, 1030, 934, 912, 823, 762, 697 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.5–7.3 (5H, m), 1.79 (6H, t, $J =$ 1.9 Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 154.84 (t, $J = 4.4$ Hz), 141.98, 128.48, 127.55, 123.93 (d, $J = 1.7$ Hz), 60.56 (t, $J =$ 6.2 Hz), 31.92.

(*S*)-3-Methyl-1-phenylpentan-3-yl Diphenylphosphinite (35): Colorless oil; $[\alpha]_D^{20} = +3.8$ (c 1.0, CHCl$_3$); IR (ATR) 3056, 3025, 2967, 2935, 2878, 1603, 1587, 1495, 1479, 1454, 1434, 1375, 1333, 1301, 1182, 1157, 1131, 1095, 1067, 1026, 998, 931, 908, 842, 804, 739, 693 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 7.6–7.4 (4H, m), 7.4–7.0 (11H, m), 2.7–2.5 (2H, m), 2.1–1.9 (2H, m), 1.81 (2H, q, $J = 7.3$ Hz), 1.38 (3H, s), 0.90 (3H, t, $J = 7.6$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 143.87, 143.82, 143.63, 143.59, 142.48, 130.18, 130.13, 129.84, 129.80, 128.63, 128.60, 128.20, 128.04 (d, $J = 7.2$ Hz), 125.54, 80.98 (d, $J = 10.6$ Hz), 42.16 (d, $J = 6.1$ Hz), 33.22 (d, $J = 7.8$ Hz), 30.42, 25.33 (d, $J = 11.2$ Hz), 8.74 (d, $J = 1.2$ Hz); HRMS (EI positive) Found: m/z 362.1806. Calcd for $C_{24}H_{27}OP$: 362.1800.

(*R*)-3-Methyl-1-phenylpentan-3-yl Isocyanide (36): Colorless oil; $[\alpha]_D^{22} = +14.7$ (c 1.0, CHCl$_3$), 78% ee; IR (ATR) 3027, 2976, 2940, 2883, 2128, 1603, 1496, 1456, 1383, 1294, 1193, 1157, 1075, 1030, 1004, 928, 904, 864, 825, 751, 700 cm^{-1};

^{1}H NMR (270 MHz, CDCl$_3$) δ 7.4–7.1 (5H, m), 2.9–2.7 (2H, m), 2.0–1.5 (4H, m), 1.41 (3H, t, $J = 1.9$ Hz), 1.04 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 153.58 (t, $J = 4.4$ Hz), 140.77, 128.33, 128.12, 125.92, 60.84 (t, $J = 5.0$ Hz), 42.36, 33.77, 30.31, 25.70, 8.19; HPLC analysis: DALCEL CHIRALCEL OD-H (ϕ4.6 × 250 mm), hexane/isopropyl alcohol = 500/1, flow rate: 1.0 mL min^{-1}, Temp. 25 °C, detector: 254 nm, (*R*)-3-methyl-1-phenylpentan-3-yl isocyanide (**36**) ($t_R = 18.6$ min), (*S*)-3-methyl-1-phenylpentan-3-yl isocyanide (**36′**) ($t_R = 24.1$ min).

Preparation of (*R*)-5-Ethyl-5-methyltetrahydropyrrol-2-one (37). To a cooled (0 °C) solution of the isocyanide **36** (200.0 mg, 1.07 mmol) in MeOH (4.0 mL) was added dropwise 2 M HCl in MeOH (8.0 mL). Water (200 µL) was added and the resulting solution was allowed to warm to rt and further stirred for 11 h. The solvent was removed in vacuo and 1 M aqueous NaOH solution was added. The mixture was extracted with AcOEt and the combined organic extracts were washed with water and brine, dried over anhydrous Na$_2$SO$_4$, filtered, and then concentrated in vacuo to afford (*R*)-3-methyl-1-phenylpentane-3-ylamine as a crude product.

To a stirred solution of the crude amine, DMAP (13.4 mg, 0.11 mmol), and Et$_3$N (0.45 mL, 3.21 mmol) in THF (5.0 mL) was added di-*t*-butyl dicarbonate (0.49 mL, 2.14 mmol) dropwise at 0 °C, and the reaction mixture was heated at reflux for 5 h. The solvent was evaporated in vacuo, and saturated aqueous NaHCO$_3$ solution was added. The mixture was extracted with diethyl ether and the combined organic extracts were washed with water and brine, dried over anhydrous Na$_2$SO$_4$, filtered, and then concentrated in vacuo. The obtained crude product was purified by preparative TLC (hexane/AcOEt = 5/1) to give (*R*)-3-methyl-1-phenylpentan-3-ylcarbamic acid *t*-butyl ester (239 mg, 81%) as a colorless oil. $[\alpha]_D^{20} = +6.8$ (*c* 1.0, CHCl$_3$); IR (ATR) 3362, 3025, 2970, 2933, 2880, 2128, 1716, 1603, 1495, 1455, 1387, 1365, 1247, 1165, 1078, 1032, 1002, 937, 870, 778, 749, 723, 698 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) 6.5:1 mixture of rotamers. Major rotamer: δ 7.3–7.1 (5H, m), 4.36 (1H, brs), 2.55 (2H, t, $J = 9.5$ Hz), 2.1–1.5 (4H, m), 1.45 (9H, s), 1.23 (3H, s), 0.87 (3H, t, $J = 7.6$ Hz); Minor rotamer: δ 7.3–7.1 (5H, m), 4.36 (1H, brs), 2.76 (2H, t, $J = 8.6$ Hz), 2.1–1.5 (4H, m), 1.45 (9H, s), 1.23 (3H, s), 1.04 (3H, t, $J = 7.6$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 153.96, 142.35, 128.34, 128.16, 128.11, 125.96, 125.43, 78.47, 77.10, 55.00, 42.33, 40.20, 33.73, 31.30, 30.34, 28.68, 28.40, 25.66, 24.02, 8.20, 7.97; HRMS (Recorded on a micromass Q-Tof-2 instrument, ESI positive) Found: m/z 278.2122. Calcd for C$_{17}$H$_{27}$NO$_2$ + H: 278.2120.

To a stirred biphasic solution of (*R*)-3-methyl-1-phenylpentan-3-ylcarbamic acid *t*-butyl ester (143.3 mg, 0.52 mmol) in carbon tetrachloride (1.1 mL), acetonitrile (1.1 mL), and water (1.7 mL), NaIO$_4$ (2.45 g, 11.4 mmol) and RuCl$_3$ (5.2 mg, 0.025 mmol) were added. After the mixture was heated at reflux for 10 h and stirred at room temperature for 19 h, it was filtrated through a pad of Celite. The filtrate was azeotroped three times with toluene and it was purified by column chromatography (silica gel, hexane/AcOEt = 2/1 to 1/1) to give **37** (13.3 mg, 20%) as a colorless oil. $[\alpha]_D^{20} = -5.8$ (*c* 0.89, benzene) [Lit.[24] for (*S*)-isomer: $[\alpha]_D^{29} = +5.7$ (*c* 0.848, benzene)]; IR (ATR) 3205, 2966, 2928, 2881, 1685, 1538, 1460, 1422, 1380, 1334, 1288, 1236, 1210, 1164, 1116, 1058, 999, 918, 789, 751 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) δ 6.36 (1H, brs), 2.5–2.3 (2H, m), 2.1–1.7 (2H, m), 1.55 (2H, q, $J = 7.0$ Hz), 1.25 (3H, s), 0.92 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, CDCl$_3$) δ 177.16, 59.54, 34.66, 32.98, 30.61, 26.82, 8.64; HRMS (Recorded on a micromass Q-Tof-2 instrument, ESI positive) Found: m/z 128.1071. Calcd for C$_7$H$_{13}$NO + H: 128.1075.

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Supporting Information

Experimental procedures, characterization data, and references to known compounds for **9a**, **10a**, **16a**–**20a**, **29a**–**32a**, and **34**. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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