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Tetrahedron 63 (2007) 6358–6364
Tetrahedron

Conversion of tertiary alcohols to *tert*-alkyl azides by way of quinone-mediated oxidation–reduction condensation using alkyl diphenylphosphinites

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Received 27 January 2007; revised 30 March 2007; accepted 30 March 2007
Available online 6 April 2007

Abstract—A novel method for the preparation of alkyl azides from alcohols by way of oxidation–reduction condensation is described. In this reaction, the sterically-hindered *tert*-alkyl phosphinites that are prepared from the corresponding alcohols are converted into *tert*-alkyl azides with almost complete inversion of their stereochemistry: the obtained alkyl azides are then successfully reduced to afford the corresponding amines on treatment with $LiAlH_4$, thus, a versatile method for the preparation of chiral amines from the corresponding chiral alcohols is established.

1. Introduction

Since an azide[1] is frequently used for introducing an amino group and the construction of a heterocyclic skeleton, conversion of an alcohol to its corresponding azide is one of the most important functional group transformations in organic synthesis.[2] The most fundamental method for azidation is the Mitsunobu reaction,[3] using hydrogen azide as an azide source.[4] There are some more alternative methods using diphenyl phosphorazidate (DPPA),[5] zinc azide/bispyridine complex,[6] DPPA/DBU,[7] and so forth.[8] These methods are widely applied to primary and secondary alcohols, in which the reactions proceed via S_N2 manner and afford azides with complete inversion of their stereochemistries. However, only a few examples[8d,9] have been reported on the conversion of sterically-hindered tertiary alcohols to the corresponding azides, much less the azidation of chiral tertiary alcohols with inversion in their configurations.

Recently, a new type of oxidation–reduction condensation[10] of carboxylic acids with alkyl phosphinites that were readily prepared from the corresponding alcohols in the presence of 2,6-dimethyl-1,4-benzoquinone (DMBQ) was reported from our laboratory,[11] where almost complete stereochemical inversion was observed even in the case of bulky *tert*-alkyl phosphinites. This method was then successfully applied to the preparation of ethers,[12] sulfides,[13] cyanides[10b,14] or isocyanides,[14] and to the alkylation of $HC(CO_2Et)_3$.[15] Also, C–N bond forming reactions of alkyl phosphinites using phthalimide[16] or nitrobenzenesulfonamide[17] as a nitrogen nucleophile were reported. In the cases of *tert*-alkyl phosphinites, however, the yield of the corresponding *N*-alkyl phthalimides or *N*-alkyl sulfonamides was poor. Therefore, it was desired to develop a new and efficient method for the stereospecific conversion of *tert*-alkyl alcohols into the corresponding amine derivatives. Since the bulkiness of *N*-nucleophile is considered to retard the nucleophilic substitution to *tert*-alkyl phosphinites, less sterically demanding *N*-nucleophile should be required in order to perform this process. Therefore, an azide anion (N_3^-) was chosen as a small nucleophile. Treatment of the azide anion with phosphinites in the presence of quinone derivatives gives the zwitterionic intermediate **A** as shown in Scheme 1. This intermediate reacts with the azide anion to afford the inverted azide **2** together with the phosphinate **3**.

Recently, a novel method for a preparation of the *tert*-alkyl azides based on the oxidation–reduction condensation using a quinone derivative and trimethylsilyl azide ($TMSN_3$) as an azide source was reported from our laboratory.[18] In this paper, we would like to report our further study on this reaction to examine the scope and limitation.

Keywords: Oxidation–reduction condensation; Alkyl diphenylphosphinite; Quinone; Trimethylsilyl azide.
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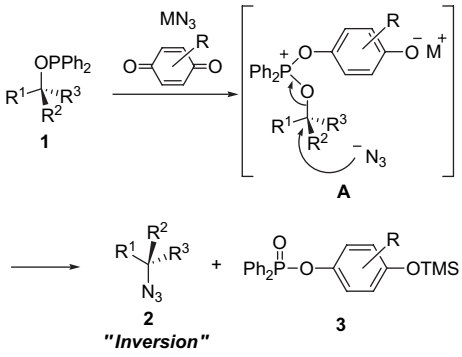
doi:10.1016/j.tet.2007.03.176



Scheme 1.

2. Results and discussion

2.1. Optimization of reaction conditions

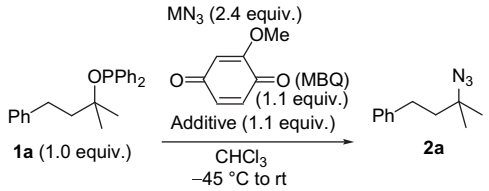
According to the above mentioned considerations, the reaction of *tert*-alkyl phosphinite **1a**, derived from 2-methyl-4-phenylbutan-2-ol, with tetrabutylammonium azide (Bu_4NN_3) in the presence of methoxybenzoquinone (MBQ) was examined first (Table 1, Entry 1) and the desired azide **2a** was produced in 22% yield. Since trapping of the anionic oxygen atom of intermediate **A** (Scheme 1) was considered necessary, addition of 1.1 equiv of tetraisopropyl orthotitanate ($Ti(O^iPr)_4$) was examined next: the reaction of **1a** with Bu_4NN_3 in the presence of MBQ and $Ti(O^iPr)_4$[19] gave **2a** in 22% yield (Entry 2). When trimethylsilyl azide ($TMSN_3$) was employed in place of Bu_4NN_3, the yield of **2a** increased to 61% (Entry 3). Since $TMSN_3$ was found to be an efficient azidation reagent, the effect of several Lewis acids was examined next (Entries 4–7). Whereas the reaction employing $Yb(O^iPr)_3$ afforded **2a** in a slightly better yield than other Lewis acids (Entry 5), the yield of **2a** remained almost the same in the reaction without any additives (63%, Entry 8).

The effect of the substituent(s) on various 1,4-benzoquinone derivatives was examined (Table 2). The reaction of phosphinite **1a** in the presence of 1,4-benzoquinone gave the corresponding azide (**2a**) in 61% yield (Entry 2). The reaction with 2,6-disubstituted-1,4-benzoquinone derivatives such as DMBQ and DBBQ afforded the desired product in low yield (Entries 3 and 4). 2,6-Dimethoxy-1,4-benzoquinone gave a better result (Entry 5) while electron-withdrawing substituents retarded the reaction (Entries 7 and 8). When 2,5-dimethoxy-1,4-benzoquinone was used, the desired product was not detected (Entry 6).

In the next stage, the effect of the solvent was examined at 0 °C (see Table 3). Whereas polar solvents such as THF or CH_3CN lowered the yield of the desired azide (Entries 1 and 2), toluene or halogenated solvents gave better results (Entries 3–5). As for the effect of concentration, no substantial increase in the yield was observed (Entries 5–7).

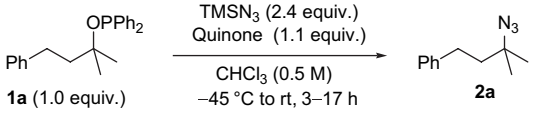
Further, the molar ratio of **1a**, MBQ and $TMSN_3$ was examined (see Table 4). As the amount of $TMSN_3$ increased, the yield of **2a** became slightly better (Entries 1–4). It is noted

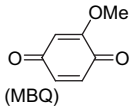
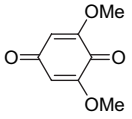
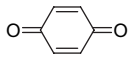
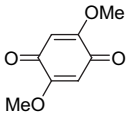
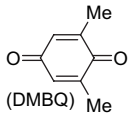
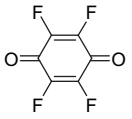
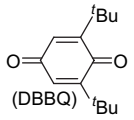
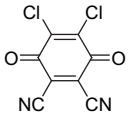
Table 1. Additive effect



Entry	MN_3	Additive	Yield/%
1	Bu_4NN_3	None	22
2		$Ti(O^iPr)_4$	22
3	$TMSN_3$	$Ti(O^iPr)_4$	61
4		$Y(O^iPr)_3$	51
5		$Yb(O^iPr)_3$	68
6		$Yb(OTf)_3$	55
7		TMSOTf	53
8		None	63

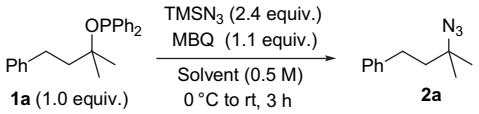
Table 2. Effect of quinone derivatives on azidation of **1a**



Entry	Quinone	Yield/%	Entry	Quinone	Yield/%
1	 (MBQ)	63	5		62
2		61	6		ND[b]
3	 (DMBQ)	37	7		<7[b]
4	 (DBBQ)	31[a,b]	8		ND[b]

[a] The reaction was carried out for 17 h.
[b] Reaction performed from 0 °C to rt.

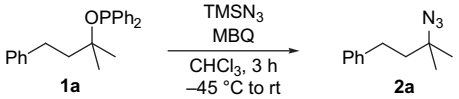
Table 3. Effect of solvent



Entry	Solvent	Yield/%
1	THF	30
2	CH_3CN	21
3	Toluene	55
4	CH_2Cl_2	51
5	$CHCl_3$ (0.5 M)	58 (63)[a]
6	$CHCl_3$ (0.2 M)	58
7	$CHCl_3$ (1.0 M)	56

[a] Reaction performed form −45 °C to rt.

Table 4. Optimization of the reaction conditions



Entry	**1a**/equiv	$TMSN_3$/equiv	MBQ/equiv	Yield/%
1	1.0	1.8	1.1	56
2	1.0	2.4	1.1	63
3	1.0	3.0	1.1	60
4	1.0	5.0	1.1	65
5	1.0	2.4	1.1	53[a]
6	1.0	2.4	1.1	20[b]
7	1.6	1.0	1.6	90[c]

[a] MBQ was slowly added to the reaction mixture for 1 h at rt.
[b] Compound **1a** was slowly added to the reaction mixture for 3.5 h.
[c] Yield based on $TMSN_3$.

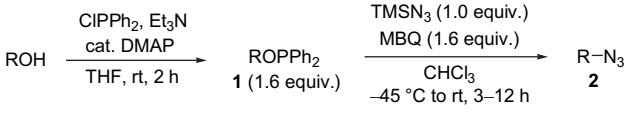
that substantial amounts of elimination products, 4-phenyl-2-methylbut-2-ene and 4-phenyl-2-methylbut-1-ene were formed[14c] under these conditions. In order to suppress the formation of alkenes, slow addition of either MBQ (Entry 5) or $TMSN_3$ (Entry 6) was further examined. However, no substantial effect on the formation of alkenes was observed irrespective of the rates of addition: i.e., **2a** was obtained in 53 and 20% yield, respectively. Finally, **2a** was obtained in 90% yield when 1.6 M amount of **1a** was used (Entry 7).

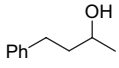
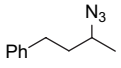
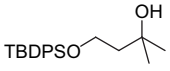
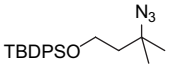
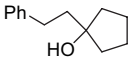
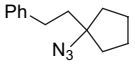
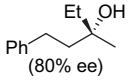
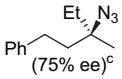
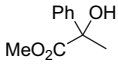
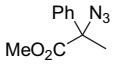
2.2. Generality of the azidation by $TMSN_3$

Alkyl diphenylphosphinites were prepared from the corresponding alcohols on treatment with chlorodiphenylphosphine ($ClPPh_2$) in the presence of triethylamine (Et_3N) and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) according to the reported procedure.[13b] The reactions of the obtained secondary and tertiary alkyl phosphinites were next examined under the optimized conditions (Table 5). The reaction of secondary phosphinite **1b** afforded the azide **2b** in high yield (Entry 1). *tert*-Alkyl phosphinite **1c** bearing *tert*-butyldiphenylsilyl group or cyclic phosphinite **1d** was successfully converted into the corresponding azides in good yields (Entries 2 and 3). Next, azidation of a chiral tertiary alkyl phosphinite **1e** that was prepared from (*S*)-3-methyl-1-phenylpentan-3-ol was carried out and the inverted product **2e** was obtained in high yield with almost complete inversion of stereochemistry. This suggests that the reaction proceeded basically via S_N2 mechanism. Further, the reaction of a chiral benzylic phosphinite **1f** gave the corresponding azide **2f** in good yield with slight lowering of the optical purity (Entry 5). It is considered that this reaction proceeded partially via S_N1 mechanism because the benzylic cation was generated more easily in this case. This reaction was also applicable to phosphinite **1g** bearing ester part (Entry 6).

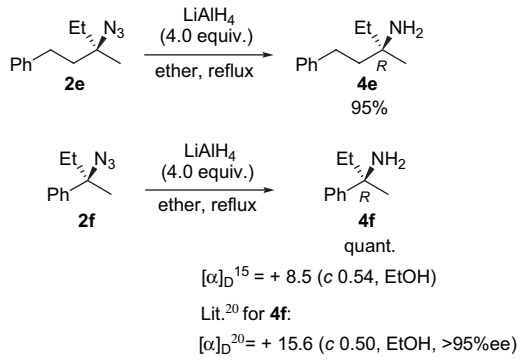
The chiral azides (**2e** or **2f**) obtained were converted into the corresponding chiral amine **4e** or **4f** in high yield by treating lithium aluminumhydride ($LiAlH_4$) in ether (Scheme 2). The chiral amine **4f** was shown dextrorotatory as reported in the literature[20] and thus the azide **2f** could be hypothesized to be (*R*)-configurated. The alleged stereospecificity of this azidation is thus also indicative of an inverted configuration for the azide **2e**. To the best of our knowledge, this is the first example of the stereospecific synthesis of an inverted chiral tertiary azide from a chiral tertiary alcohol via S_N2 displacement.

Table 5. Condensation of alcohols with $TMSN_3$



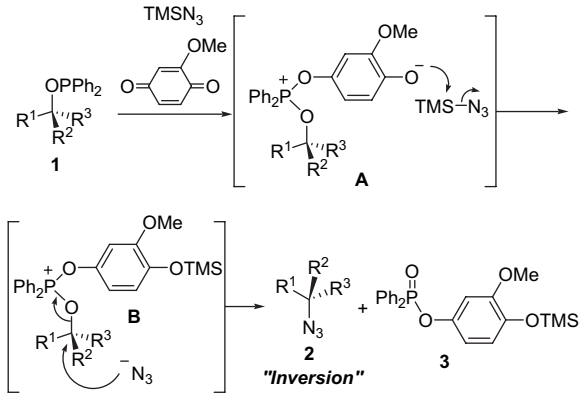
Entry	Alcohol	Yield/%	Product	Yield/%	Inversion[d]
1		**1b** (quant)		**2b** (92)[a]	—
2		**1c** (98%)		**2c** (67)[b]	—
3		**1d** (87%)		**2d** (79)[b]	—
4	 (80% ee)	**1e** (99%)	 (75% ee)[c]	**2e** (88)[b]	94%
5	 (98% ee)	**1f** (96%)	 (59% ee)[c]	**2f** (77)[b]	60%
6		**1g** (99%)		**2g** (52)[b]	—

[a] Compound **1** of 1.0 equiv, 2.4 equiv of $TMSN_3$, and 1.1 equiv of MBQ was used.
[b] Yield based on $TMSN_3$.
[c] The enantiomeric ratio was determined by HPLC analysis after reducing the azide to amine with $LiAlH_4$.
[d] Inversion (%) was defined as (% ee of **2**)/(% ee of SM).



Scheme 2.

The reaction mechanism is assumed[21] as follows (Scheme 3): reaction of phosphinite **1** with MBQ gives a zwitterionic intermediate **A** and following O-silylation by $TMSN_3$ results in the formation of intermediate **B** and azide anion (N_3^-). Subsequent nucleophilic attack of N_3^- to the phosphonium part in an S_N2 manner gives the phosphinate derivative **3** and the inverted azide **2**. It is noted that since O-silylation of the intermediate **A** is irreversible and is playing an important role in carrying out this transformation, an electron-donating substituent of the quinone derivative advantaged the nucleophilicity of the intermediate **A**.



Scheme 3.

3. Conclusion

Azidation of *tert*-alcohols by a new type of oxidation–reduction condensation via alkyl diphenylphosphinites was described. *tert*-Alkyl azides are synthesized under neutral and mild conditions by treating *tert*-alkyl phosphinites with $TMSN_3$ in the presence of MBQ. It is also noted that chiral *tert*-alkyl azides were formed from the corresponding chiral *tert*-alcohols with almost complete inversion in configuration. Thus, a concise method for preparation of chiral amines from the corresponding alcohols was established.

4. Experimental

4.1. General

All melting points were determined on a Yanagimoto micro melting point apparatus (Yanaco MP-S3) and remain uncorrected. 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 in $CDCl_3$ 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 ($CDCl_3$; δ=77.0 ppm). Carbon–^{31}P coupling constants are reported when possible. High-resolution mass spectral analysis (HRMS) was carried out on a Bruker LC/ESI-TOF MS or a JEOL JMS-700V. The optical rotations were measured with a JASCO P-1020 polarimeter. High-performance liquid chromatography (HPLC) was carried out using a Hitachi LC-Organizer, L-4000UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF_{254}, 0.25 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. All reactions were carried out under an argon atmosphere in dried glassware, unless otherwise noted. Dry solvents (CH_2Cl_2 and toluene) were prepared by distilling over appropriate drying agents. Dry solvents were purchased from Kanto (THF, $CHCl_3$, and Et_2O) and Kokusan (CH_3CN). Most organic chemicals were purchased from Tokyo Kasei Kogyo (TCI) unless otherwise noted. Lewis acids were purchased from TCI and Koujyundo. $LiAlH_4$ was purchased from Kanto.

4.2. Procedure for the preparation of tertiary alchohols

(*S*)-3-Methyl-5-phenylpentan-3-ol (Ref. 14c) and methyl α-phenyllactate (Ref. 13c) (Table 5, Entries 4 and 6) were prepared following the literature procedure. (*S*)-2-Phenylbutan-2-ol (Table 5, Entry 5) was prepared according to Walsh's procedure.[22,13c]

4.2.1. 4-(*tert*-Butyldiphenylsiloxy)-2-methylbutan-2-ol (Table 5, Entry 2). To a solution of 3-methylbutane-1,3-diol (1.56 g, 15 mmol) in DMF (60 mL) were added TBDPSCl (4.24 mL, 16.5 mmol) and imidazole (1.53 g, 22.5 mmol) at rt. After the reaction mixture was stirred for 2 days at rt, the reaction mixture was quenched with H_2O and diluted with ethyl acetate. It was extracted with ethyl acetate, and the organic layer was washed with brine and dried over anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography to afford 4-(*tert*-butyldiphenylsiloxy)-2-methylbutan-2-ol (4.00 g, 78%). Colorless oil; IR (ATR, cm^{-1}) 3441, 1107, 1079, 737, 700; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.72–7.65 (m, 4H), 7.48–7.36 (m, 6H), 3.90 (t, J=5.8 Hz, 2H), 3.82 (br, 1H), 1.75 (t, J=5.8 Hz, 2H), 1.27 (s, 6H), 1.05 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.4, 132.6, 129.7, 127.7, 70.9, 62.0, 43.0, 29.4, 26.8, 19.1. Anal. Calcd for $C_{21}H_{30}OSi$: C, 73.63; H, 8.83%. Found: C, 73.42; H, 8.55%.

4.2.2. 1-(3-Phenylethyl)cyclopentanol (Table 5, Entry 3). To a solution of cyclopentanone (3.22 mL, 36.4 mmol) in THF (15 mL) were added the Grignard reagent prepared

from magnesium turnings (972 mg, 40.0 mmol) and 2-chloroethylbenzene (4.78 mL, 36.4 mmol) in THF (15 mL) at 0 °C. After the reaction mixture was stirred for 2 h at rt, the reaction mixture was quenched with saturated aq ammonium chloride and diluted with ethyl acetate. It was extracted with ethyl acetate, and the organic layer was washed with brine and dried over anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography to afford 1-(3-phenylethyl)cyclopentanol (0.88 g, 13%). Colorless oil; IR (ATR, cm^{-1}) 740, 696; ^1H NMR (270 MHz, $CDCl_3$) δ 7.37–7.13 (m, 5H), 2.81–2.70 (m, 2H), 1.95–1.53 (m, 10H), 1.29 (br, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.5, 128.3, 128.2, 125.6, 82.4, 43.5, 39.8, 31.3, 23.9. HRMS (ESI^+) Calcd for $C_{13}H_{18}NaO$: $[M+Na]^+$ 213.1250. Found: 213.1242.

4.3. General procedure for the preparation of alkyl diphenylphosphinites

A typical procedure for the preparation of alkyl diphenylphosphinites (**1a–1g**) is described for **1a**. To a stirred solution of 2-methyl-4-phenylbutan-2-ol (1.64 g, 10 mmol) and DMAP (244 mg, 2 mmol) in dry THF (20 mL) were added Et_3N (1.67 mL, 12 mmol) followed by $ClPPh_2$ (2.02 mL, 11 mmol) under an argon atmosphere. After stirring at rt for 2 h, the resulting white slurry was concentrated by a rotatory evaporator. After dilution of the residue with hexane/ethyl acetate (v/v=9/1, ca. 100 mL, HPLC grade), the mixture was filtered through a pad of alumina (activated, 300 mesh; purchased from Wako Pure Chemical Industries, Ltd.) and Celite. The filtrate was concentrated under reduced pressure to give the desired phosphinite **1a** (3.48 g, quant), which required no further purification.

4.3.1. 2-Methyl-4-phenylbutan-2-yl diphenylphosphinite (1a). Spectral data were consistent with those of the literature.[13c,14c] Colorless oil; IR (ATR, cm^{-1}) 913, 739, 694; ^1H NMR (270 MHz, $CDCl_3$) δ 7.60–7.47 (m, 4H), 7.45–7.05 (m, 11H), 2.74–2.62 (m, 2H), 2.03–1.94 (m, 2H), 1.43 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.6 (d, J=15.6 Hz), 142.4, 130.0 (d, J=22.4 Hz), 128.6, 128.2, 128.2, 128.1 (d, J=6.7 Hz), 128.0, 125.6, 78.4 (d, J=11.2 Hz), 45.1 (d, J=5.6 Hz), 30.8, 28.1 (d, J=9.5 Hz).

4.3.2. 4-Phenylbutan-2-yl diphenylphosphinite (1b). Spectral data were consistent with those of the literature.[14c] White solid; mp 33–35 °C; IR (ATR, cm^{-1}) 940, 888, 741, 723, 695; ^1H NMR (270 MHz, $CDCl_3$) δ 7.71–7.02 (m, 15H), 4.22–4.02 (m, 1H), 2.81–2.55 (m, 2H), 2.12–1.72 (m, 2H), 1.31 (d, J=6.5 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.0 (d, J=16.7 Hz), 142.5 (d, J=16.1 Hz), 141.9, 130.6, 130.3, 130.1, 130.0, 129.2, 128.8, 128.2, 128.1, 128.1, 128.0, 125.6, 77.0 (d, J=20.6 Hz), 40.1 (d, J=5.6 Hz), 31.9, 22.4 (d, J=5.6 Hz).

4.3.3. 4-(*tert*-Butyldiphenylsiloxy)-2-methylbutan-2-yl diphenylphosphinite (1c). Colorless oil; IR (ATR, cm^{-1}) 1090, 937, 910, 738, 696; ^1H NMR (270 MHz, $CDCl_3$) δ 7.63–7.60 (m, 4H), 7.43–7.20 (m, 16H), 3.84–3.78 (m, 2H), 2.05–1.98 (m, 2H), 1.35 (s, 6H), 1.04 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.4 (d, J=16.2 Hz), 135.4, 133.9, 130.0 (d, J=22.4 Hz), 129.4, 128.6, 128.0 (d, J=7.3 Hz), 127.5, 77.8 (d, J=12.2 Hz), 60.5, 45.5 (d, J=4.1 Hz), 28.5 (d, J=9.5 Hz), 26.9, 19.2. HRMS (EI^+) Calcd for $C_{33}H_{39}O_2SiP$: $[M]^+$ 526.2457. Found: 526.2452.

4.3.4. 1-(3-Phenylethyl)cyclopentyl diphenylphosphinite (1d). Colorless oil; IR (ATR, cm^{-1}) 908, 739, 694; ^1H NMR (270 MHz, $CDCl_3$) δ 7.58–7.25 (m, 4H), 7.56–7.22 (m, 6H), 7.22–7.05 (m, 3H), 6.93–6.85 (m, 2H), 2.63–2.52 (m, 2H), 2.25–1.98 (m, 4H), 1.80–1.50 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.6 (d, J=15.7 Hz), 142.5, 130.0 (d, J=22.9 Hz), 128.7, 128.1, 128.1, 128.0, 125.5, 90.4 (d, J=10.6 Hz), 42.3 (d, J=8.4 Hz), 38.5 (d, J=8.9 Hz), 31.3, 23.8. HRMS (ESI^+) Calcd for $C_{25}H_{27}NaOP$: $[M+Na]^+$ 397.1692. Found: 397.1701.

4.3.5. (*S*)-3-Methyl-5-phenylpentan-3-yl diphenylphosphinite (1e). Spectral data were consistent with those of the literature.[14c] Colorless oil; $[\alpha]_D^{13}$ +4 (c 0.98, $CHCl_3$); IR (ATR, cm^{-1}) 908, 739, 693; ^1H NMR (270 MHz, $CDCl_3$) δ 7.58–7.47 (m, 4H), 7.32–7.02 (m, 11H), 2.63–2.57 (m, 2H), 2.03–1.93 (m, 2H), 1.81 (q, J=7.4 Hz, 2H), 1.37 (s, 3H), 0.90 (t, J=7.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.8, 143.8, 143.6, 143.6, 142.5, 130.2, 130.1, 130.0, 130.0, 128.6, 128.6, 128.2, 128.1, 128.1, 128.0, 125.5, 81.0 (d, J=10.6 Hz), 42.2 (d, J=6.7 Hz), 33.2 (d, J=7.3 Hz), 30.4, 25.3 (d, J=11.2 Hz), 8.7 (d, J=1.1 Hz).

4.3.6. (*S*)-2-Phenylbutan-2-yl diphenylphosphinite (1f). Spectral data were consistent with those of the literature.[13c] White solid; mp 78–80 °C; $[\alpha]_D^{16}$ −6 (c 0.95, $CHCl_3$); IR (ATR, cm^{-1}) 1053, 1017, 939, 746, 695; ^1H NMR (270 MHz, $CDCl_3$) δ 7.61–7.18 (m, 15H), 2.21–1.89 (m, 2H), 1.70 (s, 3H), 0.70 (t, J=7.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 145.8, 145.8, 143.6, 143.4, 143.2, 130.4, 130.3, 130.0, 130.0, 128.7, 128.6, 128.1, 128.1, 128.0, 128.0, 127.9, 126.6, 125.8, 125.8, 82.6 (d, J=12.9 Hz), 36.6 (d, J=6.2 Hz), 27.2 (d, J=12.9 Hz), 8.8.

4.3.7. Methyl 2-(diphenylphosphinoxy)-2-phenylpropanoate (1g). Spectral data were consistent with those of the literature.[13c] Colorless oil; IR (ATR, cm^{-1}) 1742, 1227, 1125, 1103, 692; ^1H NMR (270 MHz, $CDCl_3$) δ 7.61–7.49 (m, 6H), 7.39–7.24 (m, 9H), 3.63 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 173.2, 142.6, 142.4, 142.4, 142.2, 141.7, 141.7, 130.6, 130.4, 130.3, 130.1, 129.1, 128.8, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 125.4, 82.8 (d, J=16.8 Hz), 52.4, 26.5 (d, J=12.3 Hz).

4.4. General procedure for reaction of alkyl diphenylphosphinites with $TMSN_3$

A typical procedure for the preparation of azide (**2a–2g**) is described for **2f**. To a stirred solution of **1f** (232 mg, 0.64 mmol) in dry $CHCl_3$ (1.28 mL) were added MBQ (88.4 mg, 0.64 mmol) followed by $TMSN_3$ (54.6 μL, 0.40 mmol) at −45 °C under an Ar atmosphere. The reaction mixture was allowed to warm to rt and was stirred for 12 h. Direct purification by preparative TLC afforded **2f** (71.4 mg, 88%).

4.4.1. (3-Azido-3-methylbutyl)benzene (2a). Spectral data were consistent with those of the literature.[9d] Pale

yellow oil; IR (ATR, cm^{-1}) 2095, 1253, 743, 697; ^1H NMR (270 MHz, $CDCl_3$) δ 7.34–7.15 (m, 5H), 2.73–2.63 (m, 2H), 1.84–1.75 (m, 2H), 1.33 (s, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.7, 128.3, 128.2, 125.8, 61.4, 43.5, 30.8, 26.1.

4.4.2. (3-Azido-butyl)benzene (2b). Spectral data were consistent with those of the literature.[9d] Pale yellow oil; IR (ATR, cm^{-1}) 2095, 1247, 744, 698; ^1H NMR (270 MHz, $CDCl_3$) δ 7.34–7.15 (m, 5H), 3.50–3.35 (m, 1H), 2.82–2.58 (m, 2H), 1.90–1.67 (m, 2H), 1.28 (d, J=6.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.0, 128.4, 128.3, 126.0, 57.1, 37.9, 32.4, 19.5.

4.4.3. (3-Azido-3-methylbutoxy)*tert*-butyldiphenylsilane (2c). Spectral data were consistent with those of the literature.[9d] Pale yellow oil; IR (ATR, cm^{-1}) 2101, 1108, 905, 727, 704; ^1H NMR (270 MHz, $CDCl_3$) δ 7.71–7.63 (m, 4H), 7.45–7.34 (m, 6H), 3.77 (t, J=6.8 Hz, 2H), 1.79 (t, J=6.8 Hz, 2H), 2.82–2.58 (m, 2H), 1.25 (s, 6H), 1.05 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.4, 133.6, 129.6, 127.6, 60.6, 60.3, 43.5, 26.9, 26.6, 19.2.

4.4.4. [3-(1-Azidocyclopentyl)propyl]benzene (2d). Pale yellow oil; IR (ATR, cm^{-1}) 2093, 1254, 744, 698; ^1H NMR (270 MHz, $CDCl_3$) δ 7.32–7.13 (m, 5H), 2.77–2.68 (m, 2H), 1.98–1.50 (m, 10H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.8, 128.3, 128.1, 125.8, 73.4, 41.2, 37.0, 31.7, 23.8. Anal. Calcd for $C_{13}H_{17}N_3$: C, 72.52; H, 7.96; N, 19.52%. Found: C, 72.41; H, 7.90; N, 19.15%.

4.4.5. (*R*)-(3-Azido-3-methylbutyl)benzene (2e). Colorless oil; $[\alpha]_D^{12}$ +19 (c 1.10, $CHCl_3$); IR (ATR, cm^{-1}) 2088, 1254, 754, 740, 697; ^1H NMR (270 MHz, $CDCl_3$) δ 7.34–7.13 (m, 5H), 2.71–2.58 (m, 2H), 1.83–1.72 (m, 2H), 1.62 (q, J=7.5 Hz, 2H), 1.28 (s, 3H), 0.95 (t, J=7.5 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.8, 128.3, 128.2, 125.8, 64.3, 41.1, 32.1, 30.5, 22.8, 8.4. Anal. Calcd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67%. Found: C, 70.69; H, 8.63; N, 20.26%.

4.4.6. (*R*)-(1-Azido-1-methylpropyl)benzene (2f). Colorless oil; $[\alpha]_D^{13}$ +46 (c 0.95, $CHCl_3$); IR (ATR, cm^{-1}) 2092, 1248, 759, 697; ^1H NMR (270 MHz, $CDCl_3$) δ 7.43–7.23 (m, 5H), 1.97–1.77 (m, 2H), 1.66 (s, 3H), 0.79 (t, J=7.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.2, 128.3, 127.1, 125.5, 67.3, 35.1, 25.2, 8.8. Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98%. Found: C, 68.62; H, 7.13; N, 23.71%.

4.4.7. Methyl 2-azido-2-phenylpropanoate (2g). Pale yellow oil; IR (ATR, cm^{-1}) 2098, 1738, 1241, 1106, 697; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.30 (m, 5H), 3.80 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 138.8, 128.7, 128.4, 125.5, 69.3, 53.1, 24.5. HRMS (ESI^+) Calcd for $C_{10}H_{11}N_3NaO_2$: $[M+Na]^+$ 228.0743. Found: 228.0733.

4.4.8. (*R*)-3-Methyl-5-phenylpentan-3-ylamine (4e). $LiAlH_4$ (36 mg, 0.948 mmol) was added at rt to a solution of **2e** (48.0 mg, 0.236 mmol) in Et_2O (2 mL). After 5 h reflux, the reaction mixture was carefully quenched with H_2O (36 μL), 15% aq NaOH (108 μL), and H_2O (36 μL). After dilution of the residue with ethyl acetate, the mixture was filtered through Celite and anhydrous sodium sulfate. The filtrate was concentrated under reduced pressure to give the desired amine **4** (39.6 mg, 95%). Pale yellow oil; 75% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/i-PrOH/Et_2NH=100/1/0.1, flow rate=1.0 mL min^{-1}): t_R= 34.0 (*S*), 38.1 min (*R*); $[\alpha]_D^{16}$ +1 (c 1.19, EtOH); IR (ATR, cm^{-1}) 754, 723, 697; ^1H NMR (270 MHz, $CDCl_3$) δ 7.34–7.12 (m, 5H), 2.68–2.55 (m, 2H), 1.68–1.57 (m, 2H), 1.45 (q, J=7.4 Hz, 2H), 1.19 (br, 2H), 1.09 (s, 3H), 0.91 (t, J=7.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 142.7, 128.1, 128.1, 125.4, 51.4, 44.3, 35.1, 30.5, 27.5, 8.3. HRMS (ESI^+) Calcd for $C_{12}H_{20}N$: $[M+H]^+$ 178.1590. Found: 178.1596.

4.4.9. (*R*)-2-Phenylbutan-2-ylamine (4f). Spectral data were consistent with those of the literature.[20] Pale yellow oil; 59% ee; the ee value was determined by chiral HPLC analysis (DAICEL CHIRALCEL OD-H column, hexane/i-PrOH/Et_2NH=500/1/0.5, flow rate=1.0 mL min^{-1}): t_R= 15.0 (*R*), 20.0 min (*S*); $[\alpha]_D^{15}$ +9 (c 0.54, EtOH); IR (ATR, cm^{-1}) 760, 732, 699; ^1H NMR (270 MHz, $CDCl_3$) δ 7.50–7.39 (m, 2H), 7.39–7.16 (m, 3H), 1.90–1.62 (m, 2H), 1.53 (br, 2H), 1.45 (s, 3H), 0.74 (t, J=7.4 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 148.6, 128.0, 125.9, 125.2, 55.2, 37.7, 30.7, 8.8.

Acknowledgements

One of the present authors (K.K.) acknowledges useful discussions with Dr. H. Yamabe (The Kitasato Institute). This study was supported in part by the Grant of the 21st Century COE Program from Ministry of Education, Culture, Sports, Science, and Technology (MEXT), Japan. K.K. was granted a Research Fellowship of the Japan Society for the Promotion of Science for Young Scientist.

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