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Asymmetric addition of phenylzinc reagents to *C*-alkynyl nitrones. Enantiomeric enhancement by a product-like additive

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Abstract—Asymmetric addition of diphenylzinc to *C*-alkynyl nitrones was achieved by utilizing di(*t*-butyl) (*R*,*R*)-tartrate as a chiral auxiliary to afford the corresponding optically active (*S*)-*N*-(1-phenyl-3-substituted prop-2-ynyl)hydroxylamines. By the addition of a product-like additive, enantiomeric enhancement was observed. A mixed zinc reagent, PhZnMe, improved the enantioselection to afford hydroxylamines in up to 92% ee.

1. Introduction

Chiral amines are synthetically important target compounds, since they can be found in natural products, pharmaceuticals, and other bioactive molecules.[1] For example, chiral benzylic amines are found in such biologically active compounds and their building blocks.[2] One of the most attractive approaches to the syntheses of benzylic amines is the enantioselective addition of phenylmetal reagents to imine derivatives.[3,4] Although various methods for the enantioselective synthesis of chiral benzylic amines are known, including the reduction and alkylation of aromatic imines, the direct asymmetric addition of phenyl reagents to a C=N bond is still one of the more challenging problems, especially in terms of the availability of chiral auxiliaries. Very recently, we reported an enantioselective nucleophilic addition of alkynylzinc reagents to nitrones by utilizing a tartaric acid ester as a chiral auxiliary and unprecedented enantiomeric enhancement by a racemic product-like additive was realized.[5] Herein, we report an enantioselective addition of phenylzinc reagents to acyclic nitrones bearing an alkynyl substituent on the carbon by utilizing the tartaric acid ester as a chiral auxiliary to produce *N*-(1-phenyl-3-substituted prop-2-ynyl)hydroxylamines. The enantiomeric enhancement by the addition of a product-like additive was again observed.

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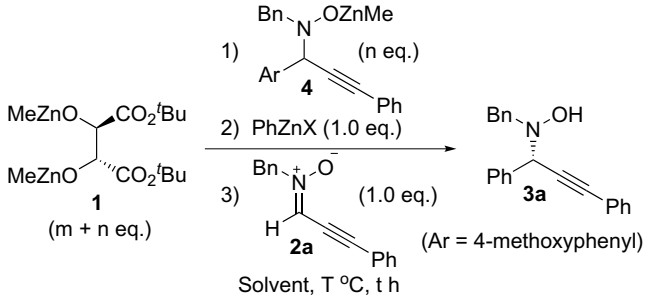
2. Results and discussion

An asymmetric addition reaction of diphenylzinc to *N*-benzyl *C*-alkynyl nitrone **2a** was first examined (Table 1). To a solution of 1.0 equiv of bis(methylzinc) salt of di(*t*-butyl) (*R*,*R*)-tartrate **1**, prepared in situ from 1.0 equiv of di-(*t*-butyl) (*R*,*R*)-tartrate [(*R*,*R*)-DTBT] and 2.0 equiv of dimethylzinc in CH_2Cl_2, diphenylzinc (X = Ph) and nitrone **2a** were successively added at 0 °C (Scheme 1, $m = 1.0$, $n = 0$). After the usual workup, the corresponding *N*-(propargylic)hydroxylamine **3a** was obtained in 53% yield and with an enantioselectivity of 70% ee (entry 1). The addition predominantly occurred from the *si*-face of nitrone **2a**, and the sense of the enantiofacial differentiation was the same as that in our previous addition reactions of alkynylzinc reagents to *C*-(phenyl-substituted) nitrones.[5] When the reaction temperature was increased to 25 °C or 40 °C, the reaction proceeded smoothly to give the desired product **3a** with enantioselectivities of 76% ee and 79% ee, respectively (entries 2 and 3). Previously, we observed enantiomeric enhancement by a product-like additive in the addition of alkynylzinc reagents.[5] Thus, the effect of the addition of a product-like additive **4**, prepared in situ from 0.2 equiv of racemic *N*-benzyl-*N*-[1-(4-methoxyphenyl)-3-phenylprop-2-ynyl]hydroxylamine and 0.2 equiv of dimethylzinc, was also investigated in the present reaction at 0 °C, 25 °C and 40 °C, respectively (Scheme 1, $m = 1.0$, $n = 0.2$).[5a] To our delight, the enantioselectivity was enhanced remarkably (entries 4–6). When the reaction was carried out at 25 °C and 40 °C, **3a** was obtained with

Table 1. Asymmetric addition of phenylzinc reagents to nitrone **2a**

Entry	*m* (equiv)	*n* (equiv)	X	Solvent	*T* (°C)	*t* (h)	Yield (%)	ee[a] (%)
1	1.0	0	Ph	CH_2Cl_2	0	16	53	70
2	1.0	0	Ph	CH_2Cl_2	25	0.5	68	76
3	1.0	0	Ph	CH_2Cl_2	40	0.5	54	79
4	1.0	0.2	Ph	CH_2Cl_2	0	16	50	82
5	1.0	0.2	Ph	CH_2Cl_2	25	0.5	65	88
6	1.0	0.2	Ph	CH_2Cl_2	40	0.5	67	88
7	1.0	0.2	Ph	$CHCl_3$	25	0.5	72	88
8	1.0	0.2	Ph	Et_2O	25	0.5	67	82
9	1.0	0.2	Ph	Toluene	25	0.5	63	81
10	1.0	0.2	Ph	Benzene	25	0.5	60	80
11	0.2	0	Ph	$CHCl_3$	25	0.5	34	36
12	0.2	0.2	Ph	$CHCl_3$	25	0.5	63	56
13	1.0	0.2	Me[b]	CH_2Cl_2	25	1	75	91
14	1.0	0.2	Me[b]	$CHCl_3$	25	1	75	92

[a] Enantiomer ratios were determined by HPLC analysis (Daicel Chiralcel OD-H).
[b] PhZnMe was prepared in situ from 0.5 equiv of Ph_2Zn and 0.5 equiv of Me_2Zn.



Scheme 1.

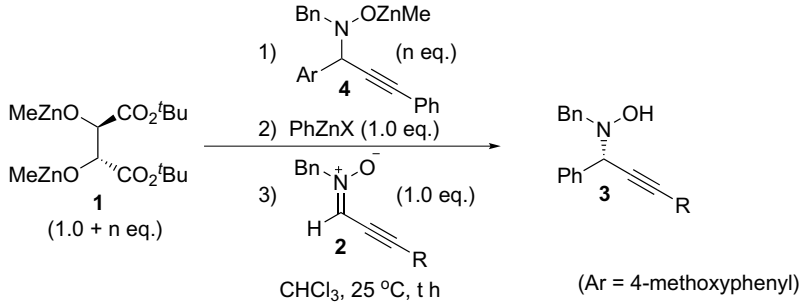
high enantioselectivity of 88% ee. The effect of the solvent was also investigated for further optimization at 25 °C. (entries 5, 7–10). Although the enantioselectivity did not remarkably change depending on the solvent used, higher yields resulted in $CHCl_3$. When 0.2 equiv of **1** was used, the enantioselectivity was not satisfactory (entry 11). However, enantiomeric enhancement was still observed by the addition of the product-like additive **4** to give **3a** with improved enantioselectivity (entry 12). Finally, it was found that utilization of a mixed zinc species PhZnMe, prepared in situ from Ph_2Zn and Me_2Zn,[6] achieved the highest enantioselectivity of 92% ee (entry 14).

Asymmetric additions of phenylzinc reagents to several other nitrones **2** were then performed (Scheme 2) to furnish the corresponding *N*-(propargylic)hydroxylamines **3** with high enantioselectivities (Table 2). It was confirmed that the addition of the product-like additive **4** was effective in improving the enantioselectivity, as shown in the column of $n = 0.2$ in Table 2. Not only in the case of *C*-(aryl-substituted alkynyl) nitrones **2a**–**c**, but also in the case of *C*-(alkyl-substituted alkynyl) nitrone **2d**, was the enantiomeric excess remarkably enhanced in the presence of additive **4**. Furthermore, higher enantioselectivities were achieved by the use of PhZnMe (entries 2 and 8).

It has now been confirmed that enantiomeric enhancement occurs in the preparation of **3** by both the phenylation of *C*-alkynyl nitrones and the alkynylation of *C*-aromatic nitrones.[5] To scope such an intriguing enantiomeric enhancement,[7] asymmetric phenylation of a *C*-alkenyl nitrone **5** was examined next. The addition reaction proved sluggish to afford the corresponding *N*-(allylic)hydroxylamine **6** with poor enantioselectivity, however, the enantioselectivity was also enhanced to 49% ee in the presence of the additive **4** (Scheme 3).[8]

3. Conclusion

As described above, the asymmetric addition of phenylzinc reagents to *C*-alkynyl nitrones has been developed utilizing tartaric acid esters as a chiral auxiliary. By the addition of a product-like substrate, high enantioselectivities were

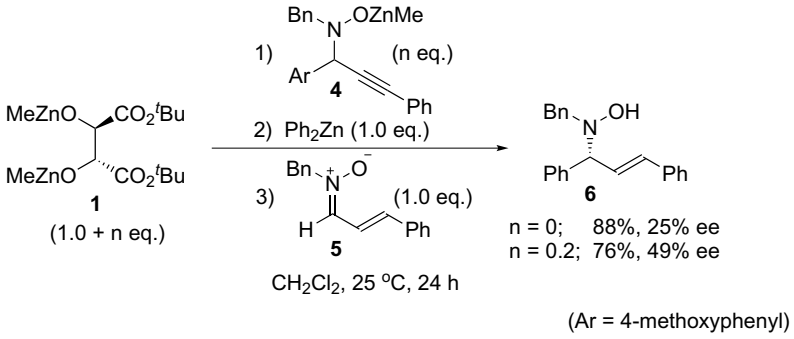


Scheme 2.

Table 2. Asymmetric addition of phenylzinc reagents to nitrones **2** in the presence of a racemic product-like additive **4**

Entry	**2**		X	t (h)	$n = 0.2$		$n = 0$	
	R				Yield (%)	ee (%)	Yield (%)	ee (%)
1	Ph	**a**	Ph	0.5	72	88[a]	70	64[a]
2			Me[c]	1	75	92[a]		
3	$^{p}CH_3C_6H_4$	**b**	Ph	1	75	87[a]	80	77[a]
4			Me[c]	1	66	87[a]		
5	$^{p}BrC_6H_4$	**c**	Ph	1	64	90[a]	68	53[a]
6			Me[c]	1	70	90[a]		
7	$^{n}C_6H_{13}$	**d**	Ph	1	67	82[b]	61	52[b]
8			Me[c]	1	67	87[b]		

[a] Enantiomeric ratio was determined by HPLC analysis (Daicel Chiralcel OD-H).
[b] Enantiomeric ratio was determined by HPLC analysis (Daicel Chiralcel OJ-H).
[c] PhZnMe was prepared in situ from 0.5 equiv of Ph_2Zn and 0.5 equiv of Me_2Zn.



Scheme 3.

realized. Furthermore, the enantiomeric enhancement by the addition of *N*-(propargylic)hydroxylamine derivative **4** was also achieved in the case of *C*-alkenyl nitrones. Further investigation on the present peculiar enantiomeric enhancement by the product-like additive is currently in progress in our laboratory.

4. Experimental

4.1. General

All of the melting points were determined by a micro melting apparatus (Yamagimoto–Seisakusho) and are uncorrected. The ^{1}H NMR spectra were recorded on JEOL Lambda 400 and JEOL Lambda 300 spectrometers. The chemical shifts were determined in the δ-scale relative to tetramethylsilane (δ 0) as an internal standard. The IR spectra were measured by JASCO FT/IR-230 spectrometer. The specific optical rotations were recorded on JASCO DIP-370 spectrometer. $CHCl_3$ was treated with Merck's aluminum oxide 90 active basic (0.063–0.200 mm, activity stage I, Art. 101076) and dried over MS 4 Å just before use. Et_2O was freshly distilled from sodium diphenylketyl. All other solvents were distilled and stored over drying agents. Flash column chromatography and thin-layer chromatography (TLC) were performed on Cica-Merck's Silica Gel 60 (No. 9385-5B) and Merck's Silica Gel 60 PF_{254} (Art. 107749), respectively.

4.2. Preparation of aldehydes

Phenylpropynal was prepared according to the procedure described in Ref. 9. Other aldehydes were prepared in a similar manner.

4.2.1. Phenylpropynal.[9] Obtained as an oil, IR (neat) 3297, 3061, 2856, 2189, 1660, 1489, 1444, 1388, 1261, 1174, 1027, 1002, 978, 758, 688 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36–7.40 (m, 2H), 7.44–7.49 (m, 1H), 7.52–7.64 (m, 2H), 9.47 (s, 1H, CHO); HRMS (FAB$^+$), found: m/z 131.04970. Calcd for C_9H_7O: (M^++H), 131.05015.

4.2.2. *p*-Tolylpropynal. Obtained as an oil, IR (neat) 3295, 3033, 2922, 2856, 2185, 1657, 1605, 1508, 1448, 1408, 1385, 1266, 1180, 1020, 982, 817, 711 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, 3H, CH_3), 7.20 (d, $J = 8.06$ Hz, 2H), 7.49 (d, $J = 8.06$ Hz, 2H), 9.41 (s, 1H, CHO); HRMS (FAB$^+$), found: m/z 145.06581. Calcd for $C_{10}H_9O$: (M^++H), 145.06535.

4.2.3. (4-Bromophenyl)propynal. Mp 95–97 °C (from hexane/AcOEt; unstable on storage); IR (KBr) 3283, 3087, 2922, 2890, 2191, 1654, 1581, 1475, 1392, 1264, 1067,

1009, 988, 822, 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46 (d, $J = 8.61$ Hz, 2H), 7.56 (d, $J = 8.61$ Hz, 2H), 9.41 (s, 1H, CHO); HRMS (FAB^+), found: m/z 208.96006. Calcd for C_9H_6OBr: (M^++H), 208.96020.

4.2.4. Non-2-ynal. Obtained as an oil, IR (neat) 2931, 2859, 2201, 1671, 1457, 1387, 1226, 1137, 824, 790, 726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, $J = 7.14$ Hz, 3H, CH_3), 1.31 (m, 4H, $(CH_2)_2$), 1.39 (quin, $J = 7.14$ Hz, 2H, CH_2), 1.60 (quin, $J = 7.14$ Hz, 2H, CH_2), 2.41 (t, $J = 7.14$ Hz, 2H, C≡CCH_2), 9.17 (s, 1H, CHO); HRMS (FAB^+), found: m/z 139.11263. Calcd for $C_9H_{15}O$: (M^++H), 139.11230.

4.3. Preparation of nitrones

4.3.1. (*Z*)-1-Phenyl-*N*-(3-phenylprop-2-ynylidene)methanamine oxide 2a. To a solution of phenylpropynal (262 mg, 2.0 mmol) in CH_2Cl_2 (3 ml) with MS 3 Å (342 mg) was added a CH_2Cl_2 (3 ml) solution of *N*-(benzyl) hydroxylamine (246 mg, 2.0 mmol) at 0 °C under an argon atmosphere. The reaction mixture was stirred at 0 °C overnight. After filtration to remove the MS 3Å, the solvent was removed in vacuo and the residue was partitioned between ethyl acetate and water. The organic extract was washed successively with water, brine, and dried over sodium sulfate. After evaporation of the solvent, the residue was separated by silica gel [treated with 10% (w/w) water in advance to deactivate] column chromatography (eluted with $CHCl_3$) to afford **2a** (170 mg) in 36% yield. The nitrone was so labile that it was partially decomposed during purification even by treatment with deactivated silica gel. Obtained as an oil, IR (neat) 3062, 3030, 2923, 2215, 1654, 1578, 1541, 1495, 1451, 1238, 1178, 1072, 1027, 754, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.37 (s, 2H, CH_2Ph), 7.10 (s, 1H, ArHC=N), 7.29–7.39 (m, 6H), 7.47–7.55 (m, 4H); HRMS (FAB^+), found: m/z 236.10799. Calcd for $C_{16}H_{14}NO$: (M^++H), 236.10754.

In a similar manner, nitrones **2b**–**2d** were prepared from the corresponding aldehydes and *N*-(benzyl)hydroxylamine.

4.3.2. (*Z*)-1-Phenyl-*N*-(3-*p*-tolylprop-2-ynylidene)methanamine oxide 2b. Obtained as an oil, IR (neat) 3029, 2921, 2188, 1655, 1606, 1541, 1507, 1454, 1240, 1178, 816, 753, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3H, CH_3), 5.31 (s, 2H, CH_2Ph), 7.11 (s, 1H, ArHC=N), 7.20 (d, $J = 8.01$ Hz, 2H), 7.38 (d, $J = 8.01$ Hz, 2H), 7.30–7.38 (m, 3H), 7.53–7.40 (m, 2H); HRMS (FAB^+), found: m/z 250.12306. Calcd for $C_{17}H_{16}NO$: (M^++H), 250.12319.

4.3.3. (*Z*)-1-Phenyl-*N*-[3-(4-bromophenyl)prop-2-ynylidene]methanamine oxide 2c. Mp 90–91 °C (from hexane/AcOEt), IR (KBr) 3060, 3029, 2922, 2186, 1640, 1584, 1536, 1485, 1452, 1395, 1355, 1290, 1241, 1173, 1071, 1008, 952, 824, 771, 736, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.31 (s, 2H, CH_2Ph), 6.19 (s, 1H, ArHC=N), 7.32–7.41 (m, 4H), 7.50–7.54 (m, 5H); HRMS (FAB^+), found: m/z 314.01786. Calcd for $C_{16}H_{13}NOBr$: (M^++H), 314.01805.

4.3.4. (*Z*)-1-Phenyl-*N*-(non-2-ynylidene)methanamine oxide 2d. Obtained as an oil, IR (neat) 3030, 2928, 2857, 2232, 1654, 1496, 1455, 1353, 1078, 1028, 754, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, $J = 7.14$ Hz, 3H, CH_3), 1.35 (m, 4H, $(CH_2)_2$), 1.43 (quin, $J = 7.14$ Hz, 2H, CH_2), 1.59 (quin, $J = 7.14$ Hz, 2H, CH_2), 2.50 (t, $J = 7.14$ Hz, 2H, C≡CCH_2), 5.21 (s, 2H, CH_2Ph), 6.89 (s, 1H, ArHC=N), 7.30–7.39 (m, 3H), 7.40–7.56 (m, 2H); HRMS (FAB^+), found: m/z 244.16954. Calcd for $C_{16}H_{22}NO$: (M^++H), 244.17014.

4.3.5. (*Z*)-1-Phenyl-*N*-[(*E*)-3-phenylallylidene]methanamine oxide 5. To a solution of cinnamaldehyde (925 mg, 7.0 mmol) in CH_2Cl_2 (4.5 ml) was added a CH_2Cl_2 (4.5 ml) solution of *N*-(benzyl)hydroxylamine (865 mg, 7.0 mmol) at 25 °C under an argon atmosphere. The reaction mixture was stirred at 0 °C overnight. The solvent was removed in vacuo and the residue was recrystallized from hexane/AcOEt to give nitrone **5** (1.229 g) in 74% yield. Mp 124–125 °C (from hexane/AcOEt); IR (KBr) 3051, 1545, 1494, 1457, 1424, 1347, 1319, 1291, 1199, 1177, 1122, 1072, 1026, 961, 941, 915, 861, 821, 764, 747, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.96 (s, 2H, CH_2Ph), 6.94 (d, $J = 16.34$ Hz, 1H), 7.21 (d, $J = 9.76$ Hz, 1H), 7.28–7.36 (m, 3H), 7.38–7.50 (m, 8H). Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.00; H, 6.37; N, 5.90.

4.4. Preparation of *N*-benzyl-*N*-[1-(4-methoxyphenyl)-3-phenylprop-2-ynyl]hydroxylamine

To a toluene (9 ml) solution of phenyl acetylene (337 mg, 3.3 mmol) was added dimethylzinc (3.3 ml of 1.0 M solution in hexane, 3.3 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred for 30 min. To the solution, a toluene (9 ml) solution of *N*-(4-methoxybenzylidene)-1-phenylmethanamine oxide (732 mg, 3.0 mmol) was added. The resulting solution was stirred at 0 °C for 14 h and quenched by the addition of a saturated aq $NaHCO_3$ solution. After filtration of the precipitate, the filtrate was extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure. The residue was separated by TLC on SiO_2 to isolate the corresponding hydroxylamine (hexane/AcOEt = 3:1) in 97% yield (1.00 g). Mp 116–117 °C (from hexane/AcOEt), IR (KBr) 3235, 2924, 1608, 1509, 1489, 1456, 1333, 1303, 1246, 1172, 1077, 1033, 801, 753, 699, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (s, 3H, OCH_3), 3.97 (d, $J = 13.06$ Hz, 1H, CH_2Ph), 4.06 (d, $J = 13.06$ Hz, 1H, CH_2Ph), 4.90 (s, 1H, OH), 4.97 (s, 1H, ArCHNBn), 6.91 (d, $J = 8.61$ Hz, 2H) 7.28–7.41 (m, 8H), 7.54–7.58 (m, 4H); HRMS (FAB^+), found: m/z 344.1650. Calcd for $C_{23}H_{22}NO$: (M^++H), 344.1652.

4.5. Asymmetric phenylation

4.5.1. Representative procedure for asymmetric phenylation of *N*-benzyl *C*-alkynyl nitrone 2a (Table 2, entry 2). To a $CHCl_3$ (3 ml) solution of (*R*,*R*)-DTBT (157 mg, 0.6 mmol) was added dimethylzinc (1.55 ml of 1.0 M solution in hexane, 1.55 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred for 10 min. To the solution, a $CHCl_3$ (3 ml) solution of racemic *N*-benzyl-*N*-[1-(4-methoxyphenyl)-3-phenylprop-2-ynyl]hydroxylamine

(34 mg, 0.1 mmol) was added. After stirring for 10 min, diphenylzinc (1.95 ml of 0.128 M solution in toluene, 0.25 mmol) was added to the solution. The reaction mixture was warmed to 25 °C and stirred for 1 h, then a $CHCl_3$ (3 ml) solution of nitrone **2a** (117 mg, 0.5 mmol) was added. The resulting solution was stirred at 25 °C for 1 h and quenched by the addition of a saturated aq NH_4Cl solution. After filtration of the precipitate, the filtrate was extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure. The residue was separated by TLC on SiO_2 to isolate **3a** (hexane/AcOEt = 3:1) in 75% yield (117 mg).

4.5.2. (*S*)-*N*-Benzyl-*N*-(1,3-diphenylprop-2-ynyl)hydroxylamine 3a.[10] Mp 133–134 °C (from EtOH); $[\alpha]_D^{25} = -42$ (*c* 1.23, EtOH, 92% ee); IR (KBr) 3239, 3029, 2905, 1597, 1488, 1452, 1331, 1298, 1179, 1070, 1026, 1003, 988, 916, 826, 812, 757, 729, 690 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.89 (d, $J = 12.69$ Hz, 1H, CH_2Ph), 3.99 (d, $J = 12.69$ Hz, 1H, CH_2Ph), 4.87 (s, 1H, ArCHNBn), 5.69 (s, 1H, OH), 7.28–7.37 (m, 10H), 7.59–7.61 (m, 5H). Calcd for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 84.31; H, 6.15; N, 4.43. The enantiomer ratio was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/^{i}PrOH = 45:1, detected at 254 nm).

4.5.3. (*S*)-*N*-Benzyl-*N*-(1-phenyl-3-*p*-tolylprop-2-ynyl)hydroxylamine 3b. Mp 135–136 °C (from EtOH); $[\alpha]_D^{25} = -45$ (*c* 1.23, EtOH, 87% ee); IR (KBr) 3236, 3028, 2918, 1600, 1542, 1508, 1495, 1453, 1353, 1289, 1075, 1029, 1020, 985, 913, 861, 815, 757, 738, 696 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.37 (s, 3H, CH_3), 3.99 (s, 2H, CH_2Ph), 4.93 (s, 1H, ArCHNBn), 5.25 (s, 1H, OH), 6.87–7.86 (m, 14H). Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.47; N, 4.28. Found: C, 84.09; H, 6.50; N, 4.34. The enantiomer ratio was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/^{i}PrOH = 60:1, detected at 254 nm).

4.5.4. (*S*)-*N*-Benzyl-*N*-[3-(4-bromophenyl)-1-phenylprop-2-ynyl]hydroxylamine 3c. Mp 166–167 °C (from EtOH); $[\alpha]_D^{25} = -69$ (*c* 0.50, EtOH, 90% ee); IR (KBr) 3339, 3063, 3030, 2971, 2894, 1602, 1485, 1453, 1393, 1297, 1272, 1070, 1049, 1011, 880, 824, 736, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.98 (d, $J = 13.17$ Hz, 1H, CH_2Ph), 4.06 (d, $J = 13.17$ Hz, 1H, CH_2Ph), 4.98 (s, 1H, ArCHNBn), 5.05 (s, 1H, OH), 7.28–7.49 (m, 12H), 7.57–7.63 (m, 2H). Calcd for $C_{22}H_{18}NOBr$: C, 67.35; H, 4.60; N, 3.57. Found: C, 67.51; H, 4.70; N, 3.52. The enantiomer ratio was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/^{i}PrOH = 45:1, detected at 254 nm).

4.5.5. (*S*)-*N*-Benzyl-*N*-(1-phenylnon-2-ynyl)hydroxylamine 3d. Obtained as an oil, $[\alpha]_D^{25} = -43$ (*c* 1.14, EtOH, 87% ee); IR (neat) 3256, 3086, 3063, 3030, 2930, 2857, 2227, 1603, 1585, 1558, 1494, 1454, 1330, 1180, 1074, 1050, 879, 831, 813, 755, 735, 699 cm^{-1};^1H NMR ($CDCl_3$): δ 0.90 (t, $J = 6.69$ Hz, 3H, CH_3), 1.23–1.35 (m, 4H, $(CH_2)_2$), 1.43–1.51 (m, 2H, CH_2), 1.58–1.74 (m, 2H, CH_2), 2.38 (t, $J = 5.04$ Hz, 2H, $C{\equiv}CCH_2$), 3.90 (d, $J = 13.11$ Hz, 1H, CH_2Ph), 4.00 (d, $J = 13.11$ Hz, 1H, CH_2Ph), 4.77 (s, 1H, ArCHNBn), 4.89 (s, 1H, OH), 7.14–7.39 (m, 8H), 7.52–7.58 (m, 2H); HRMS (FAB^+), found: *m*/*z* 322.21737. Calcd for $C_{22}H_{28}NO$: (M^++H), 322.21709. The enantiomer ratio was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/EtOH = 75:1, detected at 254 nm).

4.5.6. Asymmetric phenylation of (*Z*)-1-phenyl-*N*-[(*E*)-3-phenylallylidene]methanamine oxide 5 (Scheme 3). To a CH_2Cl_2 (1.8 ml) solution of (*R*,*R*)-DTBT (95 mg, 0.36 mmol) was added dimethylzinc (0.78 ml of 1.0 M solution in hexane, 0.78 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred for 10 min. To the solution, a CH_2Cl_2 (1.8 ml) solution of racemic *N*-benzyl-*N*-[1-(4-methoxyphenyl)-3-phenylprop-2-ynyl]-hydroxylamine (21 mg, 0.06 mmol) was added. After stirring for 10 min, diphenylzinc (2.3 ml of 0.129 M solution in toluene, 0.30 mmol) was added to the solution. Then a CH_2Cl_2 (1.8 ml) solution of nitrone **5** (72 mg, 0.30 mmol) was added. The resulting solution was stirred at 25 °C for 24 h and then quenched by the addition of a saturated aq $NaHCO_3$ solution. After filtration of the precipitate, the filtrate was extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure. The residue was separated by TLC on SiO_2 to isolate **6** (hexane/AcOEt = 10:1) in 76% yield (73 mg).

4.5.7. (*R*,*E*)-*N*-Benzyl-*N*-(1,3-diphenylallyl)hydroxylamine 6. Obtained as an oil, $[\alpha]_D^{25} = +7$ (*c* 0.73, EtOH, 49% ee); IR (neat) 3529, 3082, 3059, 3027, 2923, 2850, 1599, 1494, 1452, 1246, 1072, 1028, 966, 744, 697 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.81 (d, $J = 13.42$ Hz, 1H, CH_2Ph), 3.95 (d, $J = 13.42$ Hz, 1H, CH_2Ph), 4.44 (d, $J = 8.04$ Hz, 1H), 4.75 (s, 1H, OH), 6.54 (m, 1H), 6.65 (d, $J = 11.20$ Hz, 1H), 7.27–7.58 (m, 15H); HRMS (FAB^+), found: *m*/*z* 316.16955. Calcd for $C_{22}H_{22}NO$: (M^++H), 316.17014. The enantiomeric ratio was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/^{i}PrOH = 20:1, detected at 254 nm).

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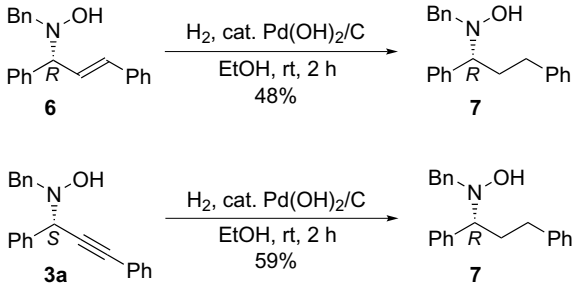
8. The absolute configuration of hydroxylamine **6** was confirmed to be (*R*) by chemical correlation. Namely, the double bond in **6** (38% ee) was reduced to give a saturated *N*-hydroxylamine **7**. Furthermore, (*S*)-**3a** (92% ee) was also reduced to **7**. Although the value of the specific rotation of **7** was too small to be compared, the major peaks in HPLC analyses (Daicel Chiralcel OD-H, hexane/EtOH = 4:1) were identical to each other.



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