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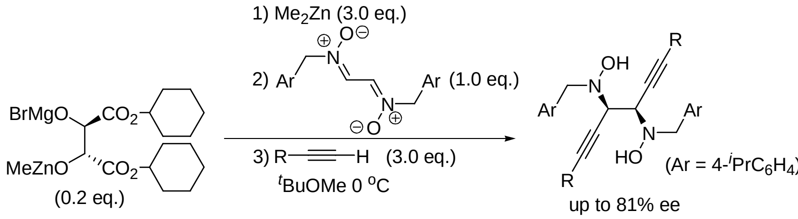

Catalytic Asymmetric Dialkynylation Reaction of α-Dinitrone by Utilizing Tartaric Acid Ester as a Chiral Auxiliary

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Abstract—The asymmetric addition of alkynylzinc reagents, prepared in situ from dimethylzinc and 1-alkynes, to α-dinitrones derived from glyoxal and *N*-(4-isopropylbenzyl)hydroxylamine was investigated by utilizing dicyclohexyl (*R*,*R*)-tartrate as a chiral auxiliary. Addition reaction of methyl(2-phenylethynyl)zinc afforded the corresponding optically active C_2-symmetric (*R*,*R*)-bis(hydroxylamine) derivative with enantioselectivities of 90% and 81% ee by utilizing a stoichiometric and a catalytic amount of the tartrate, respectively. Furthermore, the catalytic addition reaction of several alkynylzinc reagents also furnished the corresponding bis(hydroxylamine)s with moderate to good enantioselectivities.

1. Introduction

Optically active 1,2-diamine frameworks, which are contained in the numerous biologically active compounds and used as chiral auxiliaries, have been attracting a great deal of attention in organic synthesis.[1,2] The catalytic asymmetric C-C bond formation via nucleophilic addition of a *C*-nucleophile to imine functions provides one of the most important method for synthesizing optically active amines.[3] Especially, the addition of alkynyl nucleophile has a strategic advantage to produce more functionalized nitrogen-containing substances.[4] Recently, we have reported an enantioselective nucleophilic addition of alkynylzinc reagents to acyclic nitrones by utilizing tartaric acid ester as a chiral auxiliary.[5] Herein, we describe a catalytic asymmetric dialkynylation of α-dinitrone, derived from glyoxal, by utilizing tartaric acid ester as a chiral auxiliary to afford the corresponding optically active C_2-symmetric (*R*,*R*)-bis(hydroxylamine) derivatives, which are versatile building blocks for the chiral 1,2-diamino compounds.

2. Results and discussion

First, the addition reaction of an alkynylzinc reagent to an α-dinitrone **2a**, derived from glyoxal and *N*-(4-isopropylbenzyl)hydroxylamine, was examined in toluene at 0 ^{o}C as shown in Eq. 1, Table 1. In the presence of 0.2 molar amount of bis(methylzinc) salt of diisopropyl (*R*,*R*)-tartrate **1a**, prepared in situ from 0.2 molar amount of diisopropyl (*R*,*R*)-tartrate and 0.4 molar amount of dimethylzinc, the α-dinitrone **2a** was treated with dimethylzinc, followed by addition of phenylacetylene (**3A**). The corresponding (*S*,*S*)-bis(hydroxylamine) **4Aa** was obtained with low enantioselectivity of 21% ee and a small amount of *meso*-isomer **5Aa** was accompanied (Entry 1). On the contrary, the bis(bromomagnesium) salt **1b** afforded the opposite (*R*,*R*)-enantiomer with slightly enhanced optical yield (Entry 2). 2-Bromomagnesium 3-methylzinc salt **1c** realized a higher enantioselection for (*R*,*R*)-**4Aa** (Entry 3). In these reactions, α-dinitrone **2a** was scarcely soluble in toluene, so that the reaction mixture was heterogeneous and **2a** was supplied gradually into the reaction with the progress of the dialkynylation reaction. Next the influence of the ester groups in 2-bromomagnesium 3-methylzinc salt **1** was investigated (Entries 4-9). The use of the esters derived from primary alcohols afforded product **4Aa** with lower selectivity (Entries 4,5). In the case of the *t*-butyl ester, the enantioselectivity was also miserable (Entry 9). The esters derived from secondary alcohols were more effective and the cyclohexyl ester was the ester of choice to realize the highest selectivity of 70 % ee (Entry 8).

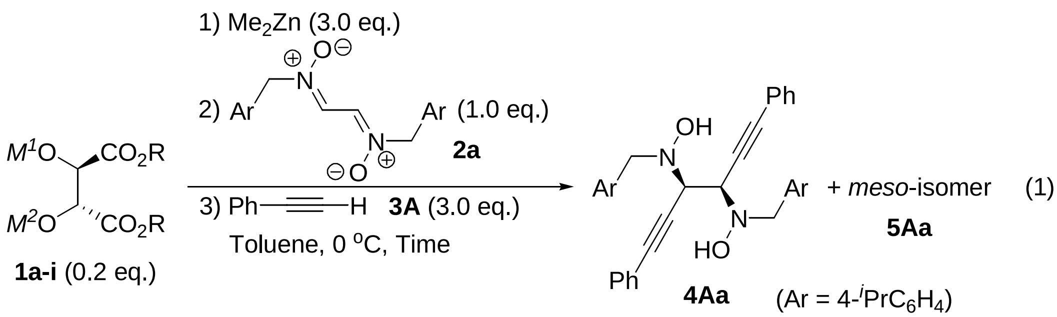
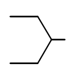
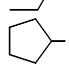
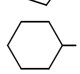
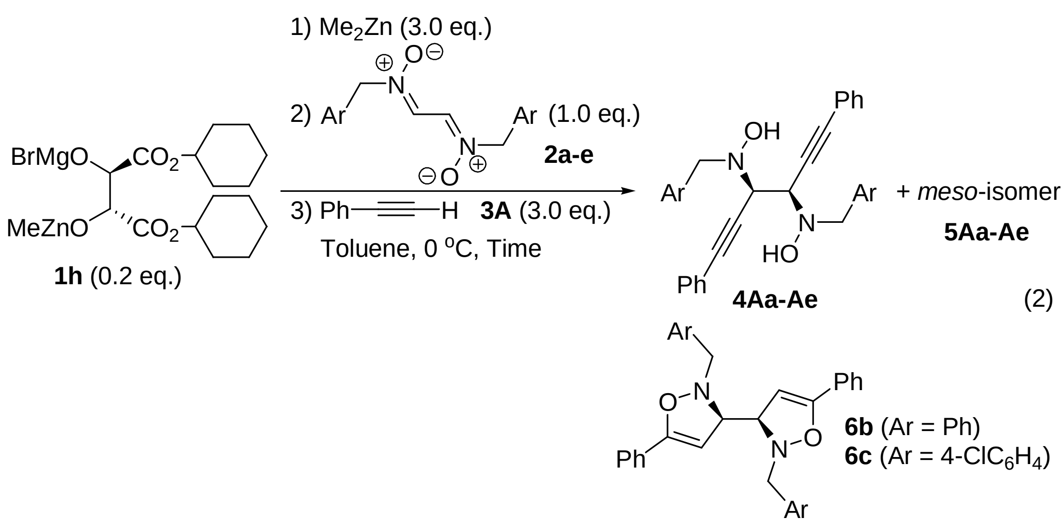


Table 1

Entry	M^1	M^2	R	**1**	Time/h	Yield of **4Aa**/%	ee of **4Aa**/%	Yield of **5Aa**/%
1	MeZn	MeZn	^{i}Pr	**a**	18	56	21[a)]	>5
2	BrMg	BrMg	^{i}Pr	**b**	5	70	47	>3
3	BrMg	MeZn	^{i}Pr	**c**	5	81	59	>3
4	BrMg	MeZn	Et	**d**	5	75	12	>3
5	BrMg	MeZn	Bn	**e**	5	67	7	>6
6	BrMg	MeZn		**f**	5	72	30	>6
7	BrMg	MeZn		**g**	5	74	51	>3
8	BrMg	MeZn		**h**	4	73	70	12
9	BrMg	MeZn	^{t}Bu	**i**	5	69	9	>4

a) A major product was the opposite (*S*,*S*)-enantiomer.

Furthermore, the enantioselectivity was found to be influenced by the substituents on nitrogen of α-dinitrones as shown in Eq. 2, Table 2. When the α-dinitrones **2b**-**d** were used, the alkynylation reactions proceeded slowly to afford the corresponding bis(hydroxylamine)s **4Ab**-**Ad** in low chemical yield and with poor enantioselectivity (Entries 2-4). On the other hand, the reaction of the 4-*t*-butylbenzyl substituted α-dinitrone **2e** proceeded smoothly to give the satisfactory amount of the product **4Ae**, however, the enantioselectivity decreased (Entry 5). These results might be due to the solubility of α-dinitrones. In the catalytic asymmetric alkynylation reaction of alkynylzinc reagent, solubility of α-dinitrones **2** could control the rate of supplying α-dinitrones into the reaction and the balance between the reaction rate and the supplying rate of α-dinitrone might be crucial. The nitrones **2b**-**d** are less soluble in toluene and *t*-butylbenzyl substituted nitrone **2e** is rather soluble, so that the amounts of the catalyst **1h** and α-dinitrones in the solution were not balanced in these cases to realize high enantioselectivity. In the case of less soluble α-dinitrones **2b**,**c**, the alkynylation reaction required longer time to consume the α-dinitrone and a part of the addition product further cyclized to give the corresponding biisoxazoles **6b**,**c** (Entries 2,3).



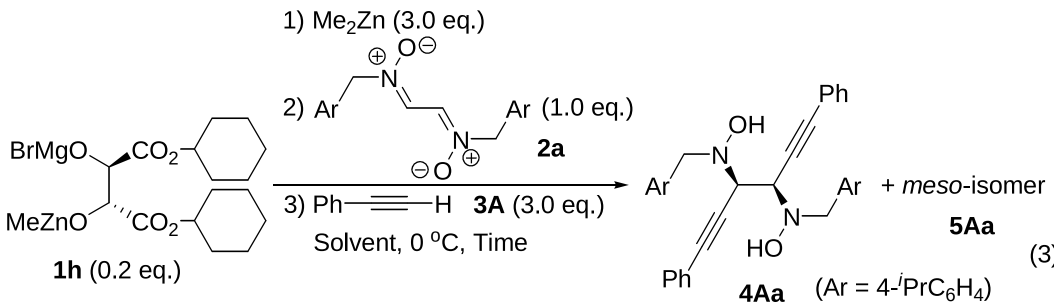
(2)

Table 2

Entry	$ArCH_2$	**2**	Time/h	**4** or **5**	Yield of **4**/%	ee of **4**/%	Yield of **5**/%	Yield of **6**/%
1	^{i}Pr–C_6H_4–CH_2	**a**	4	**Aa**	73	70	12	-
2	C_6H_5–CH_2	**b**	40	**Ab**	30	24	3	15
3	Cl–C_6H_4–CH_2	**c**	41	**Ac**	44	11	10	<10
4	$Me_2C_6H_3$–CH_2 (3,5-Me)	**d**	18	**Ad**	54	47	14	-
5	^{t}Bu–C_6H_4–CH_2	**e**	3	**Ae**	74	37	6	-

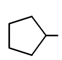
The effect of solvent was also examined and the results are listed in Eq. 3, Table 3. Dichloromethane afforded the bis(hydroxylamine) **4Aa** with slightly low enantioselectivity (Entry 2). The strongly coordinative solvents, such as MeCN or THF, decreased the enantioselectivity (Entries 3 and 4). On the other hand, when acyclic ethers were used, the optical yields were further improved (Entries 5-8). Especially, ^{t}BuOMe realized the enhanced enantioselectivity of 84% ee (Entry 6). In the case of the high-polar solvents, a part of the addition product cyclized to give the corresponding biisoxazole **6a** (Entries 3,4,9).

Unfortunately the enantioselectivities were varied depending on the Grignard reagent used for preparation of **1h**. It was found that the slightly excess amount of ^{n}BuMgBr was effective to realize reproducible high enantioselectivity (Entry 7). Probably a part of bromomagnesium salt in **1h** might be exchanged to the corresponding methylzinc salt in the presence of excess amount of methylzinc species to generate bis(methylzinc) salt **1i** (Eq. 4). As mentioned above, the addition reaction catalyzed by **1i** gave (*S*,*S*)-**4Aa**, which might decrease the enantioselectivity. When a slight excess amount of ^{n}BuMgBr was used, partially produced bis(bromomagnesium) salt **1j** could react with **1i** to regenerate **1h** (Eqs. 5,6).

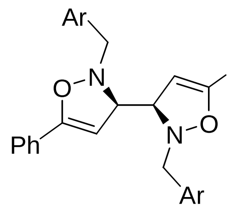


(3)

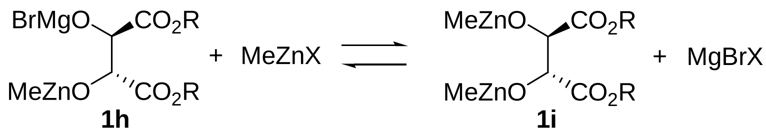
Table 3

Entry	Solvent	Time/h	Yield of **4Aa**/%	ee of **4Aa**/%	Yield of **5Aa**/%	Yield of **6a**/%
1	Toluene	4	73	70	12	-
2	CH_2Cl_2	1	67	57	15	-
3	MeCN	19	18	6	11	<17
4	THF	20	31	46	3	31
5	Et_2O	3	73	83	11	-
6	^{t}BuOMe	3	75	84	13	-
7[a)]	^{t}BuOMe	3	73	81	12	-
8	-OMe	3	74	79	14	-
9	DME	19	58	67	9	13

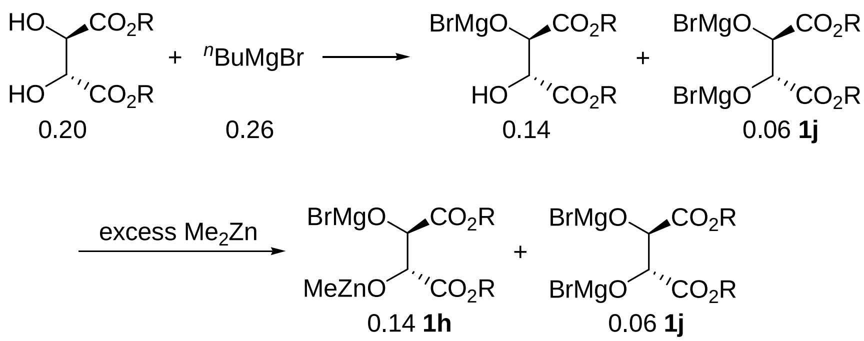
a) 0.20 Molar amount of dicyclohexyl (*R*,*R*)-tartrate was successively treated with 0.26 molar amount of ^{n}BuMgBr and 0.20 molar amount of Me_2Zn for the preparation of **1h** instead of using 0.20 molar amount of ^{n}BuMgBr.



6a (Ar = 4-^{i}PrC_6H_4)



(4)

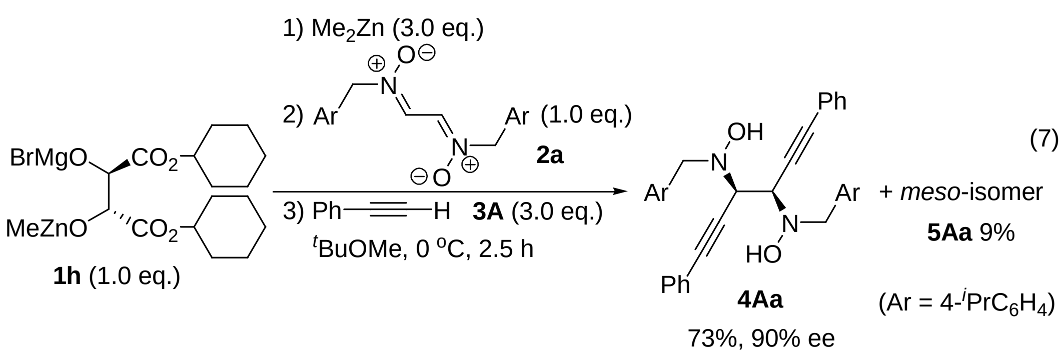


(5)

1i + **1j** $\longrightarrow$ 2 **1h** (6)

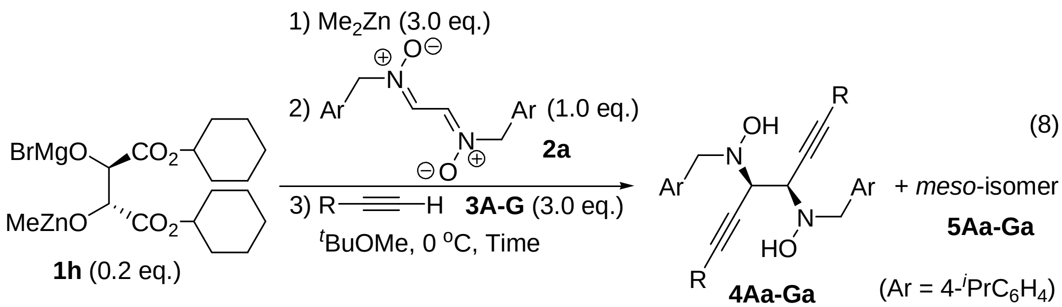
X = Me, C≡C−Ph or OR
R = Cyclohexyl

Furthermore, when the asymmetric dialkynylation reaction was carried out by using the stoichiometric amount of **1h**, bis(hydroxylamine) **4Aa** was obtained with higher enantioselectivity of 90% ee (Eq. 7), which indicated formation of the efficient chiral environment from dicyclohexyl tartrate.



(7)

The catalytic asymmetric addition of various alkynes **3B**-**G** were carried out under the optimized conditions to afford the corresponding bis(hydroxylamine)s **4Ba**-**Ga** with moderate to good enantioselectivities (Eq. 8, Table 4). In the cases of 1-hexyne (**3F**) and (trimethylsilyl)acetylene (**3G**), the alkynylation reactions proceeded slowly to afford the products **4Fa**,**Ga** in slightly lower chemical yields (Entries 6,7).



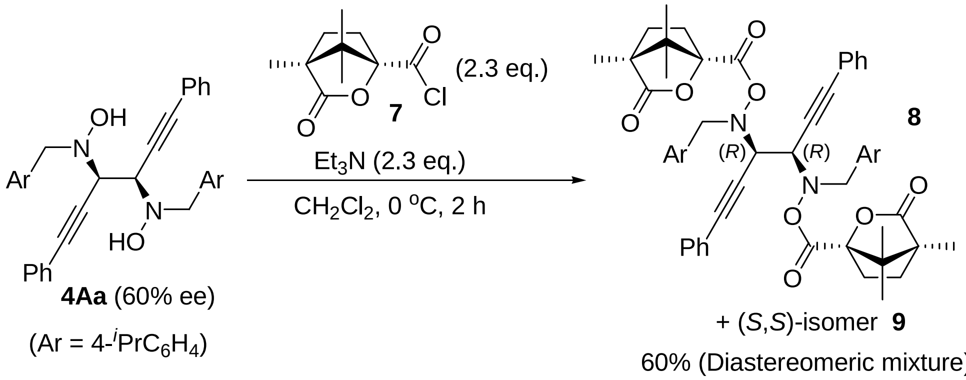
(8)

Table 4

Entry	R	**3**	Time/h	**4** or **5**	Yield of **4**/%	ee of **4**/%	Yield of **5**/%
1[a]	Ph	**A**	3	**Aa**	73	81	12
2[a]	4-^{n}PenC_6H_4	**B**	3	**Ba**	62	76	15
3[a]	4-MeOC_6H_4	**C**	3	**Ca**	63	72	12
4[a]	4-$CF_3C_6H_4$	**D**	3	**Da**	64	59	5
5[a]	2-FC_6H_4	**E**	6	**Ea**	78	74	10
6[a]	^{n}Bu	**F**	19	**Fa**	24	79	10
7[a]	TMS	**G**	24	**Ga**	57	70	15

a) 0.20 Molar amount of dicyclohexyl (*R*,*R*)-tartrate was treated with 0.26 molar amount of ^{n}BuMgBr and 0.2 molar amount of Me_2Zn for the preparation of **1h**.

The absolute configuration of the dialkynlyation product **4Aa** was determined to be *R*,*R* as follows: The enantiomerically rich **4Aa** (60% ee) was treated with (1*S*,4*R*)-camphanic chloride (**7**) and Et_3N to give the corresponding diastereomeric mixture of esters, **8** and **9**, in 60% yield (Eq. 9). Purification by recrystallization gave diastereomerically pure **8**, whose absolute configuration was determined to be *R*,*R* by X-ray crystallographic analysis (Figure 1). The absolute stereochemistries of other products were tentatively assigned to be also *R*,*R*.



(9)

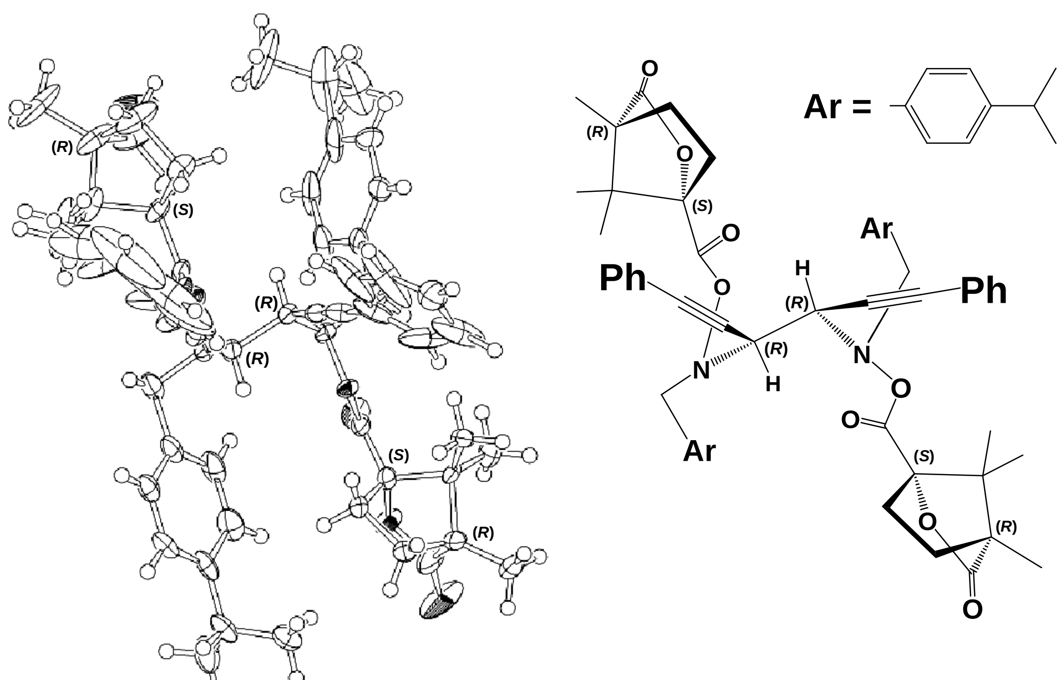
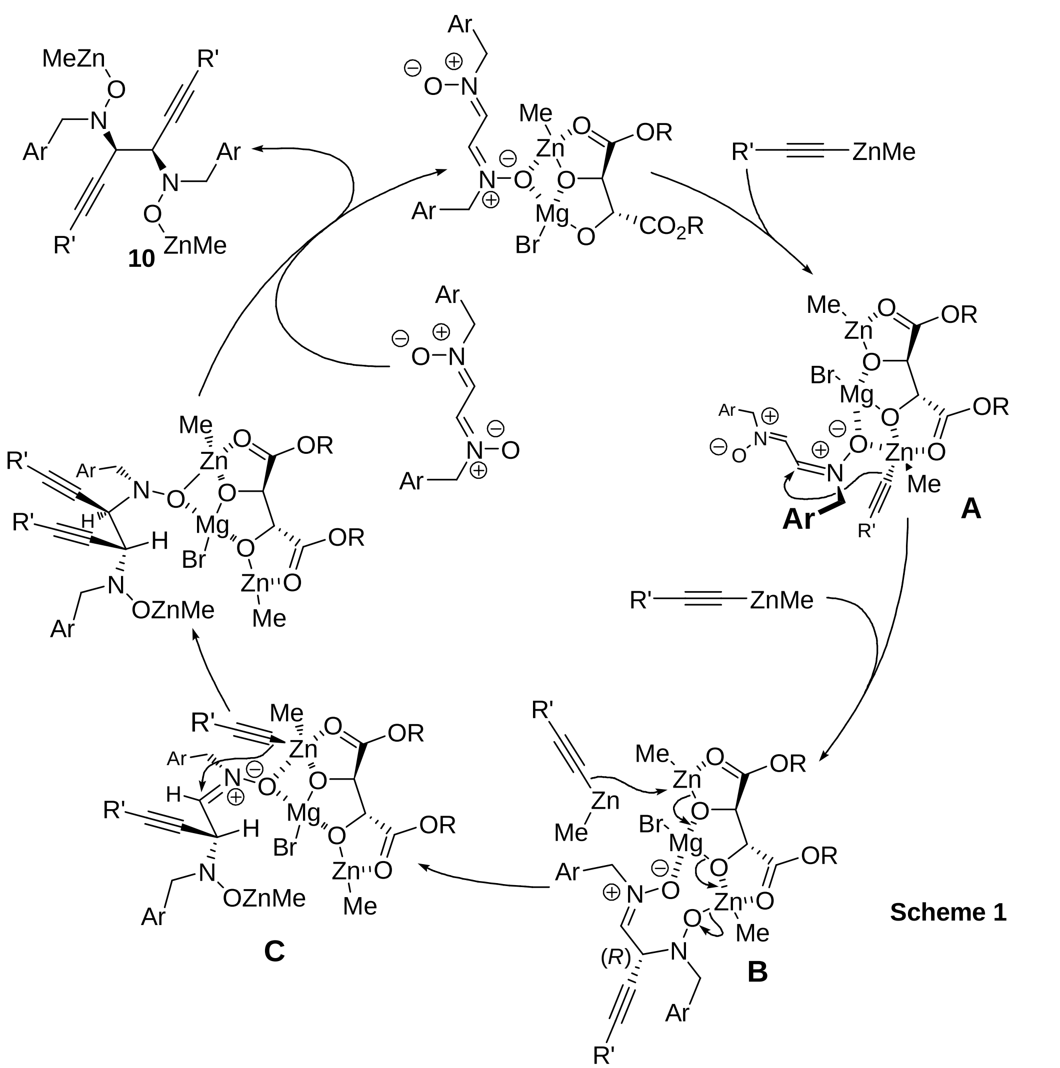


Figure 1

Although the precise reaction mechanism is still unclear, the plausible catalytic cycle is shown in Scheme 1. The first enantioselective alkynylation may proceed via the transition state **A** to afford the *R* configuration as confirmed above. The remaining nitrone moiety in the mono-adduct subsequently coordinates to Lewis acidic magnesium of the catalyst, followed by the transmetallation as depicted in **B**. The second enantioselective alkynylation may proceed via the transition state **C**, which is similar to the transition state **A** of the first alkynylation, to afford the (*R*,*R*)-product **10** .



3. Conclusion

In conclusion, we have developed enantio- and diastereoselective dialkynylation reaction of α-dinitrone by utilizing tartaric acid esters as a chiral auxiliary. This reaction provides a simple and attractive approach to optically active C_2-symmetric bis(hydroxylamine) derivatives.

4. Experimental

4.1 General

All of the melting points were determined by a micro melting apparatus (Yanagimoto-Seisakusho) and uncorrected. The ^{1}H NMR spectra were recorded on a JEOL Lambda 400 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 MS spectra were recorded with a JEOL SX-102A mass spectrometer. The specific optical rotations were recorded on JASCO DIP-370 spectrometer. THF and Et_2O were freshly distilled from sodium diphenylketyl. All other solvents were distilled according to the usual manner 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 α-Dinitrones

***N*,*N'*-(Ethane-1,2-diylidene)bis[(4-isopropylphenyl)methanamine oxide] (2a):** To a solution of 4-isopropylbenzaldehyde (6.72 g, 45.3 mmol) in MeOH (70 ml) was added a solution of hydroxyammonium chloride (4.73 g, 68.0 mmol) in H_2O (25 ml) and the mixture was stirred for 20 min at room temperature. To the mixture was added a solution of Na_2CO_3 (3.60 g, 34.0 mmol) in H_2O (25 ml) and the mixture was stirred for 19.5 h at room temperature. After most of the MeOH was evaporated under reduced pressure, the mixture was extracted with Et_2O. The combined extracts was washed with brine, dried over Na_2SO_4, and condensed under reduced pressure to give almost pure 4-isopropylbenzaldehyde oxime (7.33 g, 99%). The crude oxime was used in the following reaction without further purification. To a solution of 4-isopropylbenzaldehyde oxime (7.25 g, 44.4 mmol) in MeOH (35 ml) was added a solution of $NaBH_3CN$ (2.79 g, 44.4 mmol) in MeOH (30 ml) and two drops of an aqueous methyl orange solution as an indicator, then a 1 M aqueous HCl solution was added with stirring until the color turned red. The mixture was stirred for 2 h at room temperature adding a 1 M aqueous HCl solution to maintain the red color. The mixture was adjusted to pH 10 by adding a 6 M aqueous KOH solution and the mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure to give crude *N*-(4-isopropylbenzyl)hydroxylamine. To a solution of the crude hydroxylamine in THF (45 ml) was added a mixture of 40% aqueous glyoxal solution (3.22 g, 22.2 mmol) and THF (25 ml), followed by stirring for 4.5 h at room temperature. The precipitated crude α-dinitrone **2a** was filtered off. The product was purified by recrystallization from $CHCl_3$/hexane to give pure **2a** (5.38 g, 69%, 2 steps from 4-isopropylbenzaldehyde oxime). Mp 185–186 °C (decomp., recrystallized from $CHCl_3$/hexane); IR (KBr) 3099, 3054, 2961, 2871, 1525, 1466, 1443, 1421, 1373, 1323, 1307, 1282, 1195, 1151, 1058, 1019, 967, 893, 865, 845, 816, 755, 713, 663 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.23 (d, J = 6.83 Hz, 12H), 2.90 (sept, J = 6.83 Hz, 2H), 4.88 (s, 4H), 7.23 (d, J = 8.05 Hz, 4H), 7.31 (d, J = 8.05 Hz, 4H), 7.78 (s, 2H); Found: C, 75.14; H, 8.06; N, 7.89%. Calcd for $C_{22}H_{28}N_2O_2$: C, 74.96; H, 8.01; N, 7.95%.

In a similar manner, α-dinitrones **2b**–**2e** were synthesised using hydroxylamines prepared from the corresponding aldehydes.

***N*,*N'*-(Ethane-1,2-diylidene)bis(phenylmethanamine oxide) (2b):** Mp 205–206 °C (decomp., recrystallized from DMSO/H_2O); IR (KBr) 3100, 3056, 3033, 2984, 2921, 1527, 1495, 1456, 1443, 1375, 1337, 1315, 1291, 1197, 1149, 1028, 964, 925, 887, 863, 831, 756, 699, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.93 (s, 4H), 7.39 (s, 10H), 7.80 (s, 2H); Found: C, 71.50; H, 6.06; N, 10.46%. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%.

***N*,*N'*-(Ethane-1,2-diylidene)bis[(4-chlorophenyl)methanamine oxide] (2c):** Mp 213–214 °C (decomp., recrystallized from DMSO/H_2O); IR (KBr) 3101, 3056, 2985, 2923, 2849, 1599, 1577, 1526, 1494, 1443, 1408, 1374, 1330, 1304, 1281, 1197, 1153, 1145, 1097, 1019, 968, 893, 869, 847, 808, 737, 682 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.89 (s, 4H), 7.34 (d, J = 9.03 Hz, 4H), 7.37 (d, J = 9.03 Hz, 4H), 7.79 (s, 2H); Found: C, 57.11; H, 4.19; N, 8.31%. Calcd for $C_{16}H_{14}N_2O_2Cl_2$: C, 56.99; H, 4.19; N, 8.31%.

***N*,*N'*-(Ethane-1,2-diylidene)bis[(3,5-dimethylphenyl)methanamine oxide] (2d):** Mp 206–207 °C (decomp., recrystallized from $CHCl_3$/AcOEt); IR (KBr) 3098, 3057, 3022, 2955, 2917, 2867, 1606, 1530, 1469, 1369, 1321, 1307, 1280, 1192, 1153, 1038, 996, 925, 914, 891, 849, 740, 679 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.31 (s, 12H), 4.84 (s, 4H), 7.00 (s, 6H), 7.78 (s, 2H); Found: C, 74.19; H, 7.45; N, 8.69%. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64%.

***N*,*N'*-(Ethane-1,2-diylidene)bis[(4-*t*-butylphenyl)methanamine oxide] (2e):** Mp 159.5–160.5 °C (decomp., recrystallized from AcOE/hexane); IR (KBr) 3092, 3053, 2961, 2904, 2868, 1529, 1473, 1436, 1417, 1362, 1321, 1269, 1188, 1153, 1109, 1024, 949, 895, 842, 810, 751, 691, 658 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.30 (s, 18H), 4.89 (s, 4H), 7.32 (d, J = 8.29 Hz, 4H), 7.40 (d, J = 8.29 Hz, 4H), 7.79 (s, 2H); Found: C, 75.71; H, 8.51; N, 7.38%. Calcd for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36%.

4.3 Catalytic Asymmetric Dialkynylation Reaction

Representative Procedure for Catalytic Asymmetric Dialkynylation of an α-Dinitrone (Table 3, Entry 7): To a ^{t}BuOMe (1.0 ml) solution of dicyclohexyl (*R*,*R*)-tartrate (32 mg 0.10 mmol) was added butylmagnesium bromide (0.13 mmol, 0.25 ml of 0.536 M solution in THF) at 0 °C under an argon atmosphere, and the mixture was stirred for 10 min. After adding dimethylzinc (1.6 mmol, 1.6 ml of 1.0 M solution in hexane), the resulting suspension was stirred for 10 min at 0 °C. To the suspension, solid α-dinitrone **2a** (180 mg, 0.51 mmol) was added and the suspension was stirred for 10 min at 0 °C. To the reaction mixture, a ^{t}BuOMe (1.0 ml) solution of phenylacetylene (**3A**) (156 mg, 1.53 mmol) was added and the suspension was stirred for 3 h at 0 °C. The reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution. After warming to room temperature, the precipitate containing *meso*-isomer **5Aa** was separated by filtration through Celite to give the filtrate (F) and precipitate (P). The precipitate (P) was suspended in $CHCl_3$ and the mixture was heated to dissolve **5Aa**. The insoluble inorganic matter was filtered off through Celite and the filtrate was condensed under reduced pressure to give the *meso*-isomer **5Aa** (29 mg, 10%). The filtrate (F) was extracted with AcOEt and the combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure. The resulting residue was dissolved in a small amount of Et_2O, followed by addition of hexane to precipitate additional *meso*-isomer **5Aa**, which was separated by filtration (5 mg, 2%). The filtrate was condensed and the residue was purified by TLC (SiO_2, hexane/AcOEt = 5/1) to give *dl*-isomer **4Aa** (206 mg, 73%). The enantiomer ratio was determined by HPLC analysis (Daicel Chiralcel IA, hexane/^{i}PrOH = 30/1, detected at 254 nm) to be 81% ee.

In a similar way, the asymmetric addition reactions of alkynylzinc reagent to the α-dinitrones **2** were carried out to give the corresponding bis(hydroxylamine)s **4**. The physical and spectral data of **4**, **5**, and **6** are given in following.

***N*,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Aa):** Mp 125–126 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +14 (c 0.824, EtOH, 81% ee); IR (KBr) 3487, 3218, 3054, 3023, 2960, 2927, 2907, 2869, 2225, 1598, 1513, 1489, 1443, 1363, 1327, 1304, 1100, 1069, 1055, 1020, 959, 914, 805, 758, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.24 (d, J = 6.83 Hz, 12H), 2.90 (sept, J = 6.83 Hz, 2H), 3.98 (d, J = 12.69 Hz, 2H), 4.20 (d, J = 12.69 Hz, 2H), 4.25 (s, 2H), 5.48 (br, 2H), 7.20 (d, J = 8.05 Hz, 4H), 7.28–7.33 (m, 6H), 7.34 (d, J = 8.05 Hz, 4H), 7.47–7.55 (m, 4H); Found: C, 81.71; H, 7.28; N, 5.02%. Calcd for $C_{38}H_{40}N_2O_2$: C, 81.98; H, 7.24; N, 5.03%.

***N*,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(benzyl)hydroxylamine] (4Ab):** Mp 114.5–115.5 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +7 (c 0.73, EtOH, 24% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel OD-H, hexane/EtOH = 100/1, detected at 254 nm). IR (KBr) 3420, 3061, 3031, 2905, 2860, 2225, 1598, 1572, 1541, 1490, 1455, 1442, 1302, 1259, 1177, 1157, 1069, 1029, 967, 915, 822, 756, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.00 (d, J = 12.82 Hz, 2H), 4.23 (d, J = 12.82 Hz, 2H), 4.25 (s, 2H), 5.22 (s, 2H), 7.26–7.38 (m, 12H), 7.42 (d, J = 6.71 Hz, 4H), 7.47–7.56 (m, 4H); Found: C, 81.29; H, 6.02; N, 5.95%. Calcd for

$C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93%.

***N*,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-chlorobenzyl)hydroxylamine] (4Ac):** Mp 107.5–108.5 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +5 (c 0.488, EtOH, 11% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel OD-H, hexane/EtOH = 40/1, detected at 254 nm). IR (KBr) 3551, 3290, 3060, 2919, 2861, 2227, 1598, 1491, 1442, 1407, 1363, 1299, 1226, 1090, 1070, 1049, 1016, 967, 915, 851, 833, 801, 757, 724, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.96 (d, J = 12.93 Hz, 2H), 4.21 (d, J = 12.93 Hz, 2H), 4.24 (s, 2H), 5.32 (br, 2H), 7.28–7.38 (m, 14H), 7.47–7.53 (m, 4H); Found: C, 70.93; H, 4.82; N, 5.16%. Calcd for $C_{32}H_{26}N_2O_2Cl_2$: C, 70.98; H, 4.84; N, 5.18%.

***N*,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(3,5-dimethylbenzyl)hydroxylamine] (4Ad):** Mp 138–139 °C (decomp., recrystallized from EtOH/hexane); $[\alpha]_D^{25}$ +10 (c 0.584, EtOH, 47% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel OD-H, hexane/EtOH = 100/1, detected at 254 nm). IR (KBr) 3465, 3208, 3019, 2915, 2861, 2228, 1607, 1490, 1459, 1442, 1377, 1362, 1326, 1307, 1259, 1159, 1102, 1069, 1041, 981, 915, 853, 815, 756, 690, 668 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.30 (s, 12H), 3.92 (d, J = 12.69 Hz, 2H), 4.16 (d, J = 12.69 Hz, 2H), 4.26 (s, 2H), 5.55 (br, 2H), 6.92 (s, 2H), 7.04 (s, 4H), 7.28–7.34 (m, 6H), 7.48–7.54 (m, 4H); Found: C, 81.66; H, 6.87; N, 5.27%. Calcd for $C_{36}H_{36}N_2O_2$: C, 81.78; H, 6.86; N, 5.30%.

***N*,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-*t*-butylbenzyl)hydroxylamine] (4Ae):** Mp 106.5–107.5 °C (from EtOH/hexane); $[\alpha]_D^{25}$ +5 (c 0.884, EtOH, 37% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 60/1, detected at 254 nm). IR (KBr) 3285, 3057, 3031, 2962, 2903, 2867, 1598, 1509, 1490, 1474, 1459, 1442, 1413, 1395, 1363, 1296, 1269, 1109, 1069, 1048, 1023, 963, 914, 844, 809, 756, 690, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.31 (s, 18H), 3.99 (d, J = 12.69 Hz, 2H), 4.21 (d, J = 12.69 Hz, 2H), 4.26 (s, 2H), 5.44 (br, 2H), 7.29–7.34 (m, 6H), 7.35 (s, 8H), 7.49–7.53 (m, 4H); Found: C, 82.36; H, 7.72; N, 4.81%. Calcd for $C_{40}H_{44}N_2O_2$: C, 82.15; H, 7.58; N, 4.79%.

***N*,*N'*-[(*R*,*R*)-1,6-Bis(4-pentylphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Ba):** Mp 105–106 °C (decomp., recrystallized from EtOH/hexane); $[\alpha]_D^{25}$ +13 (c 0.892, EtOH, 76% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 15/1, detected at 254 nm). IR (KBr) 3276, 3083, 3026, 2958, 2928, 2857, 2227, 1611, 1509, 1460, 1420, 1382, 1362, 1317, 1182, 1115, 1081, 1055, 1020, 965, 834, 816, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.88 (t, 6.59 Hz, 6H), 1.24 (d, J = 6.83 Hz, 12H), 1.27–1.36 (m, 8H), 1.60 (quint, J = 7.56 Hz, 4H), 2.59 (t, J = 7.56 Hz, 4H), 2.89 (sept, J = 6.83 Hz, 2H), 3.96 (d, J = 12.69 Hz, 2H), 4.20 (d, 12.69 J = Hz, 2H), 4.23 (s, 2H), 5.23 (br, 2H), 7.12 (d, J = 8.05 Hz, 4H), 7.19 (d, J = 7.81 Hz, 4H), 7.33 (d, J = 8.05 Hz, 4H), 7.42 (d, J = 7.81 Hz, 4H); Found: C, 82.45; H, 8.78; N, 3.94%. Calcd for $C_{48}H_{60}N_2O_2$: C, 82.71; H, 8.68; N, 4.02%.

***N*,*N'*-[(*R*,*R*)-1,6-Bis(4-methoxyphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Ca):** Mp 125–126 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +12 (c 0.788, EtOH, 72% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/EtOH = 7/1, detected at 254 nm). IR (KBr) 3435, 3008, 2958, 2932, 2892, 2837, 2225, 1606, 1569, 1509, 1462, 1442, 1418, 1384, 1363, 1334, 1290, 1248, 1171, 1104, 1030, 970, 920, 831, 804, 764, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.24 (d, J = 6.83 Hz, 12H), 2.89 (sept, J = 6.83 Hz, 2H), 3.81 (s, 6H), 3.96 (d, J = 12.69 Hz, 2H), 4.19 (d, J = 12.69 Hz, 2H), 4.22 (s, 2H), 5.46 (br, 2H), 6.83 (d, J = 9.03 Hz, 4H), 7.19 (d, J = 8.05 Hz, 4H), 7.33 (d, J = 8.05 Hz, 4H), 7.44 (d, J = 9.03 Hz, 4H); Found: C, 77.77; H, 7.19; N, 4.61%. Calcd for $C_{40}H_{44}N_2O_4$: C, 77.89; H, 7.19; N, 4.54%.

***N*,*N'*-{(*R*,*R*)-1,6-Bis[4-(trifluoromethyl)phenyl]hexa-1,5-diyne-3,4-diyl}bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Da):** Mp 113.5–114.5 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +9 (c 0.912, EtOH, 59% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 20/1, detected at 254 nm). IR (KBr) 3296, 3055, 3025, 2962, 2929, 2871, 1615, 1515, 1463, 1420, 1405, 1385, 1363, 1324, 1168, 1129, 1105, 1067, 1017, 971, 843, 810, 732, 715, 659 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.24 (d, J = 6.83 Hz, 12H), 2.87 (sept, J = 6.83 Hz, 2H), 3.96 (d, J = 12.69 Hz, 2H), 4.19 (d, J = 12.69 Hz, 2H), 4.27 (s, 2H), 5.52 (s, 2H), 7.20 (d, J = 8.05 Hz, 4H), 7.32 (d, J = 8.05 Hz, 4H), 7.58 (d, J = 9.03 Hz, 4H), 7.60 (d, J = 9.03 Hz, 4H); Found: C, 69.35; H, 5.60; N, 3.98%. Calcd for $C_{40}H_{38}N_2O_2F_6$: C, 69.35; H, 5.53; N, 4.04%.

***N*,*N'*-[(*R*,*R*)-1,6-Bis(2-fluorophenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Ea):** Mp 108–109 °C (decomp., recrystallized from AcOEt/hexane); $[\alpha]_D^{25}$ +11 (c 0.948, EtOH, 74% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 10/1, detected at 254 nm). IR (KBr) 3241, 3060, 2960, 2927, 2870, 1612, 1574, 1514, 1493, 1448, 1420, 1384, 1363, 1303, 1271, 1255, 1216, 1104, 1055, 1031, 1021, 967, 944, 854, 827, 808, 758, 667 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.24 (d, J = 6.83 Hz, 12H), 2.89 (sept, J = 6.83 Hz, 2H), 4.01 (d, J = 12.69 Hz, 2H), 4.24 (d, J = 12.69 Hz, 2H), 4.31 (s, 2H), 5.43 (br, 2H), 7.04–7.12 (m, 4H), 7.19 (d, J = 8.05 Hz, 4H), 7.27–7.34 (m, 2H), 7.35 (d, J = 8.05 Hz, 4H), 7.46–7.53 (m, 2H); Found: C, 77.06; H, 6.60; N, 4.72%. Calcd for $C_{38}H_{38}N_2O_2F_2$: C, 77.00; H, 6.46; N, 4.73%.

***N*,*N'*-[(*R*,*R*)-Tetradeca-5,9-diyne-7,8-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (4Fa):** Obtained as an oil; $[\alpha]_D^{25}$ -10 (c 0.248, EtOH, 79% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 50/1, detected at 220 nm). IR (neat) 3230, 3093, 3053, 3012, 2958, 2931, 2871, 2233, 1614, 1567, 1514, 1464, 1421, 1381, 1362, 1328, 1301, 1237, 1142, 1103, 1056, 1020, 954, 809, 740, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.93 (t, J = 7.08 Hz, 6H), 1.24 (d, J = 6.83 Hz, 12H), 1.42–1.65 (m, 8H), 2.30 (t, 7.08 Hz, 4H), 2.88 (sept, J = 6.83 Hz, 2H), 3.82 (d, J

= 12.69 Hz, 2H), 3.87 (s, 2H), 4.07 (d, J = 12.69 Hz, 2H), 5.39 (br, 2H), 7.16 (d, J = 8.05 Hz, 4H), 7.28 (d, J = 8.05 Hz, 4H); HRMS (FAB$^+$), Found: *m/z* 517.37900. Calcd for $C_{34}H_{49}N_2O_2$: (M$^+$+H), 517.37941.

***N*,*N'*-[(*R*,*R*)-1,6-Bis(trimethylsilyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxyl amine] (4Ga):** Obtained as an oil; $[\alpha]_D^{25}$ -9 (c 0.536, EtOH, 70% ee). The enantiomer ratio was determined by HPLC (Daicel Chiralcel IA, hexane/^{i}PrOH = 100/1, detected at 220 nm). IR (neat) 3277, 3012, 2959, 2898, 2870, 2173, 1612, 1514, 1460, 1420, 1384, 1362, 1249, 1056, 1020, 982, 842, 808, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.22 (s, 18H), 1.24 (d, J = 6.83 Hz, 12H), 2.89 (sept, J = 6.83 Hz, 2H), 3.83 (d, J = 12.93 Hz, 2H), 3.96 (s, 2H), 4.09 (d, J = 12.93 Hz, 2H), 5.21 (br, 2H), 7.18 (d, J = 8.05 Hz, 4H), 7.28 (d, J = 8.05 Hz, 4H); HRMS (FAB$^+$), Found: *m/z* 549.33305. Calcd for $C_{32}H_{49}N_2O_2Si_2$: (M$^+$+H), 549.33327.

***N*,*N'*-[(*R*,*S*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Aa):** Mp 168.5–169.5 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3261, 3051, 2965, 2929, 2869, 2217, 1557, 1540, 1508, 1489, 1465, 1442, 1417, 1297, 1239, 1083, 1029, 998, 972, 919, 857, 832, 804, 758, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.24 (d, J = 6.83 Hz, 12H), 2.89 (sept, J = 6.83 Hz, 2H), 4.00 (d, J = 12.93 Hz, 2H), 4.27 (d, J = 12.93 Hz, 2H), 4.29 (s, 2H), 5.23 (br, 2H), 7.18 (d, J = 8.05 Hz, 4H), 7.31–7.36 (m, 6H), 7.37 (d, J = 8.05 Hz, 4H), 7.51–7.56 (m, 4H); Found: C, 81.71; H, 7.25; N, 4.94%. Calcd for $C_{38}H_{40}N_2O_2$: C, 81.98; H, 7.24; N, 5.03%.

***N*,*N'*-[(*R*,*S*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(benzyl)hydroxylamine] (5Ab):** Mp 172.5–173.5 °C (decomp., recrystallized from AcOEt); IR (KBr) 3240, 3084, 3063, 3030, 2934, 2879, 1598, 1492, 1454, 1443, 1344, 1296, 1236, 1215, 1079, 1031, 990, 971, 931, 915, 838, 818, 764, 742, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.04 (d, J = 13.17 Hz, 2H), 4.30 (d, J = 13.17 Hz, 2H), 4.30 (s, 2H), 5.17 (s, 2H), 7.28–7.37 (m, 12H), 7.43–7.48 (m, 4H), 7.51–7.57 (m, 4H); Found: C, 81.23; H, 6.02; N, 5.87%. Calcd for $C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93%.

***N*,*N'*-[(*R*,*S*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-chlorobenzyl)hydroxylamine] (5Ac):** Mp 169–170 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3253, 3064, 2876, 2216, 1598, 1541, 1507, 1490, 1465, 1457, 1442, 1405, 1339, 1298, 1236, 1177, 1091, 1029, 1017, 975, 948, 915, 856, 830, 801, 755, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.00 (d, J = 13.42 Hz, 2H), 4.25 (d, J = 13.42 Hz, 2H), 4.26 (s, 2H), 5.86 (br, 2H), 7.29 (d, J = 8.54 Hz, 4H), 7.33–7.41 (m, 10H), 7.49–7.55 (m, 4H); Found: C, 70.79; H, 5.05; N, 5.03%. Calcd for $C_{32}H_{26}N_2O_2Cl_2$: C, 70.98; H, 4.84; N, 5.18%.

***N*,*N'*-[(*R*,*S*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(3,5-dimethylbenzyl)hydroxylamine] (5Ad):** Mp 164–165 °C (decomp., recrystallized from $CHCl_3$/hexane); IR (KBr) 3232, 3019, 2914, 2873, 2225, 1606, 1489, 1458, 1442, 1379, 1349, 1299, 1235, 1166, 1088, 1071, 1029, 979, 928, 903, 859, 810, 756, 710, 691, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.28 (s, 12H), 3.97 (d, J = 12.93 Hz, 2H), 4.22 (d, J = 12.93 Hz, 2H), 4.30 (s, 2H), 5.16 (br, 2H), 6.91 (s, 2H), 7.07 (s, 4H), 7.31–7.37 (m, 6H), 7.51–7.58 (m, 4H); Found: C, 81.56; H, 6.97; N, 5.24%. Calcd for $C_{36}H_{36}N_2O_2$: C, 81.78; H, 6.86; N, 5.30%.

***N*,*N'*-[(*R*,*S*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-*t*-butylbenzyl)hydroxylamine] (5Ae):** Mp 186–187 °C (decomp., recrystallized from $CHCl_3$/hexane); IR (KBr) 3268, 3060, 3028, 2962, 2903, 2871, 2223, 1598, 1511, 1489, 1476, 1463, 1442, 1412, 1393, 1364, 1297, 1270, 1110, 1081, 1029, 995, 973, 860, 845, 824, 804, 755, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.31 (s, 18H), 4.01 (d, J = 13.17 Hz, 2H), 4.27 (d, J = 13.17 Hz, 2H), 4.30 (s, 2H), 5.25 (br, 2H), 7.31–7.40 (m, 14H), 7.50–7.56 (m, 4H); Found: C, 82.05; H, 7.84; N, 4.76%. Calcd for $C_{40}H_{44}N_2O_2$: C, 82.15; H, 7.58; N, 4.79%.

***N*,*N'*-[(*R*,*S*)-1,6-Bis(4-pentylphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Ba):** Mp 157.5–158.5 °C (decomp., recrystallized from Et_2O/hexane); IR (KBr) 3243, 3050, 3026, 2958, 2927, 2871, 2857, 1509, 1463, 1418, 1297, 1240, 1184, 1085, 1021, 855, 832, 804, 736, 715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.90 (t, 6.83 Hz, 6H), 1.24 (d, J = 7.07 Hz, 12H), 1.28–1.40 (m, 8H), 1.62 (quint, J = 7.56 Hz, 4H), 2.61 (t, J = 7.56 Hz, 4H), 2.89 (sept, J = 7.07 Hz, 2H), 3.99 (d, J = 12.93 Hz, 2H), 4.25 (d, 12.93 J = Hz, 2H), 4.26 (s, 2H), 5.24 (br, 2H), 7.15 (d, J = 8.05 Hz, 4H), 7.18 (d, J = 8.05 Hz, 4H), 7.36 (d, J = 8.05 Hz, 4H), 7.44 (d, J = 8.05 Hz, 4H); Found: C, 82.53; H, 8.76; N, 4.01%. Calcd for $C_{48}H_{60}N_2O_2$: C, 82.71; H, 8.68; N, 4.02%.

***N*,*N'*-[(*R*,*S*)-1,6-Bis(4-methoxyphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Ca):** Mp 197–198 °C (decomp., recrystallized from $CHCl_3$/hexane); IR (KBr) 3220, 3008, 2959, 2931, 2872, 2218, 1606, 1509, 1461, 1415, 1290, 1251, 1172, 1104, 1084, 1029, 857, 830, 805, 708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.24 (d, J = 7.07 Hz, 12H), 2.89 (sept, J = 7.07 Hz, 2H), 3.83 (s, 6H), 3.99 (d, J = 12.69 Hz, 2H), 4.25 (d, J = 12.69 Hz, 2H), 4.26 (s, 2H), 6.86 (d, J = 8.78 Hz, 4H), 7.18 (d, J = 8.05 Hz, 4H), 7.36 (d, J = 8.05 Hz, 4H), 7.46 (d, J = 8.78 Hz, 4H), Signals of the hydroxy proton (O<u>H</u>) was not observed clearly.; Found: C, 77.98; H, 7.29; N, 4.54%. Calcd for $C_{40}H_{44}N_2O_4$: C, 77.89; H, 7.19; N, 4.54%.

***N*,*N'*-{(*R*,*S*)-1,6-Bis[4-(trifluoromethyl)phenyl]hexa-1,5-diyne-3,4-diyl}bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Da):** Mp 161–162 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3232, 3055, 3024, 2961, 2928, 2894, 2873, 1614, 1568, 1514, 1462, 1406, 1326, 1300, 1258, 1169, 1131, 1105, 1088, 1068, 1017, 855, 842, 804, 730, 656 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.24 (d, J = 7.07 Hz, 12H), 2.90 (sept, J = 7.07 Hz, 2H), 4.00 (d, J = 12.93 Hz, 2H), 4.23 (d, J = 12.93 Hz, 2H), 4.32 (s, 2H), 5.29 (s, 2H), 7.19 (d, J = 8.05 Hz, 4H), 7.34 (d, J = 8.05 Hz, 4H), 7.60 (d, J = 8.54 Hz, 4H), 7.63 (d, J = 8.54 Hz, 4H); Found: C, 69.31; H, 5.55; N, 4.09%. Calcd for $C_{40}H_{38}N_2O_2F_6$: C, 69.35; H, 5.53; N, 4.04%.

***N*,*N'*-[(*R*,*S*)-1,6-Bis(2-fluorophenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Ea):** Mp 177–178 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3249, 3087, 3012, 2960, 2925, 2889, 1612, 1576, 1492, 1467, 1448, 1363, 1300, 1254, 1214, 1103, 1083, 1057, 1031, 997, 954, 856, 832, 822, 803, 759, 726 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.24 (d, J = 7.07 Hz, 12H), 2.89 (sept, J = 7.07 Hz, 2H), 4.03 (d, J = 12.93 Hz, 2H), 4.28 (d, J = 12.93 Hz, 2H), 4.33 (s, 2H), 5.19 (br, 2H), 7.05–7.15 (m, 4H), 7.18 (d, J = 8.05 Hz, 4H), 7.29–7.36 (m, 2H), 7.38 (d, J = 8.05 Hz, 4H), 7.49–7.55 (m, 2H); Found: C, 77.21; H, 6.46; N, 4.73%. Calcd for $C_{38}H_{38}N_2O_2F_2$: C, 77.00; H, 6.46; N, 4.73%.

***N*,*N'*-[(*R*,*S*)-Tetradeca-5,9-diyne-7,8-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Fa):** Mp 161–162 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3376, 3056, 3012, 2956, 2932, 2867, 2230, 1516, 1462, 1422, 1384, 1362, 1351, 1333, 1300, 1235, 1138, 1096, 1056, 1023, 1002, 956, 885, 852, 836, 813, 778, 737, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.94 (t, J = 7.08 Hz, 6H), 1.24 (d, J = 7.07 Hz, 12H), 1.41–1.63 (m, 8H), 2.32 (t, 6.83 Hz, 4H), 2.89 (sept, J = 7.07 Hz, 2H), 3.83 (d, J = 12.93 Hz, 2H), 3.91 (s, 2H), 4.13 (d, J = 12.93 Hz, 2H), 5.19 (br, 2H), 7.17 (d, J = 8.05 Hz, 4H), 7.30 (d, J = 8.05 Hz, 4H); Found: C, 79.12; H, 9.54; N, 5.38%. Calcd for $C_{34}H_{48}N_2O_2$: C, 79.02; H, 9.36; N, 5.42%.

***N*,*N'*-[(*R*,*S*)-1,6-Bis(trimethylsilyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (5Ga):** Mp 161.5–162.5 °C (decomp., recrystallized from AcOEt/hexane); IR (KBr) 3387, 3012, 2961, 2867, 2175, 1514, 1462, 1420, 1362, 1298, 1243, 1094, 1056, 1016, 996, 846, 811, 762, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.24 (s, 18H), 1.24 (d, J = 6.83 Hz, 12H), 2.89 (sept, J = 6.83 Hz, 2H), 3.85 (d, J = 12.93 Hz, 2H), 3.96 (s, 2H), 4.14 (d, J = 12.93 Hz, 2H), 5.08 (br, 2H), 7.17 (d, J = 8.05 Hz, 4H), 7.31 (d, J = 8.05 Hz, 4H); Found: C, 69.82; H, 8.91; N, 5.00%. Calcd for $C_{32}H_{48}N_2O_2Si_2$: C, 70.02; H, 8.81; N, 5.10%.

(3*R*,3'*R*)-2,2'-bis(4-isopropylbenzyl)-5,5'-diphenyl-2,2',3,3'-tetrahydro-3,3'-biisoxazole (6a): Obtained as an oil; IR (KBr) 3056, 3025, 2959, 2925, 2870, 1652, 1601, 1577, 1514, 1494, 1448, 1420, 1362, 1335, 1280, 1243, 1181, 1097, 1071, 1047, 1022, 1000, 917, 890, 822, 770, 724, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.27 (d, J = 6.83 Hz, 12H), 2.92 (sept, J = 6.83 Hz, 2H), 4.01 (d, J = 12.93 Hz, 2H), 4.19 (s, 2H), 4.20 (d, J = 12.93 Hz, 2H), 5.23 (s, 2H), 7.21 (d, J = 8.05 Hz, 4H), 7.29–7.33 (m, 6H), 7.36 (d, J = 8.05 Hz, 4H), 7.40–7.50 (m, 4H); HRMS (FAB^+), Found: *m/z* 557.31687. Calcd for $C_{38}H_{41}N_2O_2$: (M^++H), 557.31681.

(3*R*,3'*R*)-2,2'-Dibenzyl-5,5'-diphenyl-2,2',3,3'-tetrahydro-3,3'-biisoxazole (6b): Mp

113–114 °C (decomp., recrystallized from CH_2Cl_2/hexane); IR (KBr) 3106, 3085, 3061, 3031, 2877, 2839, 1653, 1600, 1577, 1494, 1449, 1360, 1342, 1316, 1278, 1248, 1219, 1043, 1024, 916, 889, 757, 726, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.07 (d, J = 13.42 Hz, 2H), 4.19 (s, 2H), 4.24 (d, J = 13.42 Hz, 2H), 5.24 (s, 2H), 7.26–7.40 (m, 12H), 7.41–7.45 (m, 4H), 7.45–7.50 (m, 4H); Found: C, 81.05; H, 5.93; N, 5.84%. Calcd for $C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93%.

(3*R*,3'*R*)-2,2'-Bis(4-chlorobenzyl)-5,5'-diphenyl-2,2',3,3'-tetrahydro-3,3'-biisoxazole (6c): Mp 134–135 °C (decomp., recrystallized from Et_2O/hexane); IR (KBr) 3112, 3084, 3065, 3036, 2925, 2900, 2846, 1659, 1598, 1577, 1491, 1447, 1406, 1331, 1243, 1228, 1089, 1042, 1015, 937, 919, 882, 817, 802, 761, 745, 735, 709, 689, 663 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.02 (d, J = 13.42 Hz, 2H), 4.14 (s, 2H), 4.20 (d, J = 13.42 Hz, 2H), 5.22 (s, 2H), 7.25–7.37 (m, 14H), 7.43–7.49 (m, 4H); Found: C, 70.69; H, 4.90; N, 5.01%. Calcd for $C_{32}H_{26}N_2O_2Cl_2$: C, 70.98; H, 4.84; N, 5.18%.

4.4 Determination of Absolute Configuration (Eq. 9): To a CH_2Cl_2 (3 ml) solution of *N*,*N'*-[(*R*,*R*)-1,6-diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine] (**4Aa**) (150 mg, 0.27 mmol, 60% ee) was added a CH_2Cl_2 (3 ml) solution of Et_3N (63 mg, 0.62 mmol) at 0 °C under a nitrogen atmosphere. To the mixture was added a CH_2Cl_2 (3 ml) solution of (1*S*,4*R*)-camphanic chloride (**7**) (134 mg, 0.62 mmol), and the mixture was stirred for 2 h at 0 °C. After quenching the reaction by addition of water, the mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over Na_2SO_4, and condensed under reduced pressure. The product was recrystallized from AcOEt/hexane to give the diastereomeric mixture of **8** and **9** (147 mg, 60%). The diastereomerically pure **8** (89 mg, 36%) was obtained by recrystallizing further twice (first: AcOEt/hexane, second: toluene/hexane).

***N*,*N'*-[(3*R*,4*R*)-1,6-diphenylhexa-1,5-diyne-3,4-diyl]bis{*N*-(4-isopropylbenzyl)-*O*-[(1*S'*,4*R'*)-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptane-3-one-1-carbonyl]hydroxylamine} (8):** Mp 148–149 °C (decomp., recrystallized from toluene/hexane); $[\alpha]_D^{25}$ +80 (c 0.14, EtOH, 100% ee); IR (KBr) 3053, 3018, 2962, 2934, 2871, 2230, 1781, 1599, 1513, 1490, 1443, 1398, 1381, 1332, 1309, 1254, 1227, 1167, 1103, 1051, 1018, 993, 956, 934, 847, 825, 756, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.55 (s, 6H), 0.70 (s, 6H), 0.97 (s, 6H), 1.21 (d, J = 6.83 Hz, 12H), 1.35–1.49 (m, 2H), 1.62–1.78 (m, 4H), 1.95–2.15 (m, 2H), 2.88 (sept, J = 6.83 Hz, 2H), 4.28 (d, J = 13.42 Hz, 2H), 4.46 (br, 2H), 4.86 (s, 2H), 7.17 (d, J = 8.05, 4H), 7.29–7.38 (m, 6H), 7.42 (d, J = 8.05 Hz, 4H), 7.45–7.51 (m, 4H); Found: C, 75.92; H, 6.96; N, 3.06%. Calcd for $C_{58}H_{64}N_2O_8$: C, 75.95; H, 7.03; N, 3.06%. Crystal data (Fig. 1): $C_{58}H_{64}N_2O_8$, FW 917.15, monoclinic, $P2_1$, a = 12.478(3) Å, b = 13.085(3) Å, c = 15.514(3) Å, β = 90.240(6)°, V = 2533.0(9) Å^3, Z = 2. D_{calcd} = 1.202 gcm^{-3}. R = 0.082 (R_w = 0.111) for 8489 reflections with $I > 3.00\sigma(I)$ and 613 variable parameters.

Acknowledgements

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Stereochemistry Abstract

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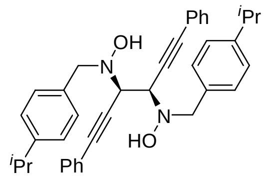
Yutaka Ukaji,* and Katsuhiko Inomata*



$C_{38}H_{40}N_2O_2$

N,*N*′-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

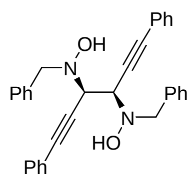
Ee = 81%

$[\alpha]_D^{25}$ +14 (c 0.824, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

Masakazu Serizawa, Shuhei Fujinami,
Yutaka Ukaji,* and Katsuhiko Inomata*



$C_{32}H_{28}N_2O_2$

N,*N*′-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(benzyl)hydroxylamine]

Ee = 24%

$[\alpha]_D^{25}$ +7 (c 0.73, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

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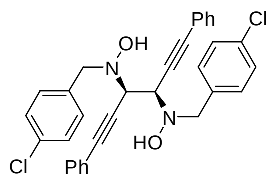
Yutaka Ukaji,* and Katsuhiko Inomata*



$C_{32}H_{26}N_2O_2Cl_2$

N,*N*′-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-chlorobenzyl)hydroxylamine]

Ee = 11%

$[\alpha]_D^{25}$ +5 (c 0.488, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

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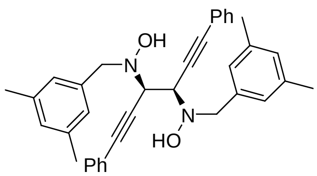
Yutaka Ukaji,* and Katsuhiko Inomata*



Ee = 47%

$[\alpha]_D^{25}$ +10 (c 0.584, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

$C_{36}H_{36}N_2O_2$

N,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(3,5-dimethylbenzyl)hydroxylamine]

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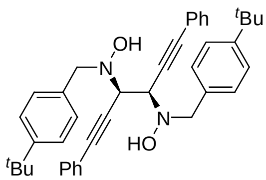
Yutaka Ukaji,* and Katsuhiko Inomata*



Ee = 37%

$[\alpha]_D^{25}$ +5 (c 0.884, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

$C_{40}H_{44}N_2O_2$

N,*N'*-[(*R*,*R*)-1,6-Diphenylhexa-1,5-diyne-3,4-diyl]bis[*N*-(4-*t*-butylbenzyl)hydroxylamine]

Masakazu Serizawa, Shuhei Fujinami,
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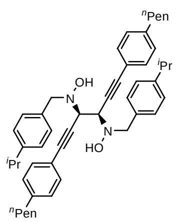

Ee = 76%

$[\alpha]_D^{25}$ +13 (c 0.892, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

$C_{48}H_{60}N_2O_2$

N,*N'*-[(*R*,*R*)-1,6-Bis(4-pentylphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

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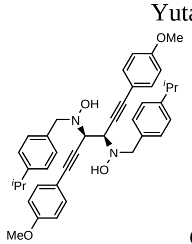

Ee = 72%

$[\alpha]_D^{25}$ +12 (c 0.788, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

$C_{40}H_{44}N_2O_4$

N,*N'*-[(*R*,*R*)-1,6-Bis(4-methoxyphenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

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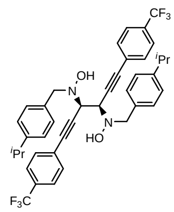


$C_{40}H_{38}N_2O_2F_6$

Ee = 59%

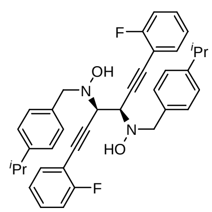
$[\alpha]_D^{25}$ +9 (c 0.912, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

N,*N′*-{(*R*,*R*)-1,6-Bis[4-(trifluoromethyl)phenyl]hexa-1,5-diyne-3,4-diyl}bis[*N*-(4-isopropylbenzyl)hydroxylamine]

Masakazu Serizawa, Shuhei Fujinami,
Yutaka Ukaji,* and Katsuhiko Inomata*



$C_{38}H_{38}N_2O_2F_2$

Ee = 74%

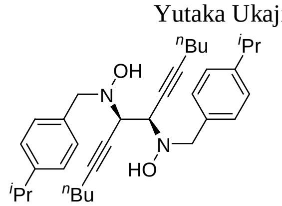
$[\alpha]_D^{25}$ +11 (c 0.948, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

N,*N′*-[(*R*,*R*)-1,6-Bis(2-fluorophenyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

Masakazu Serizawa, Shuhei Fujinami,
Yutaka Ukaji,* and Katsuhiko Inomata*



$C_{34}H_{48}N_2O_2$

Ee = 79%

$[\alpha]_D^{25}$ -10 (c 0.248, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

N,*N′*-[(*R*,*R*)-Tetradeca-5,9-diyne-7,8-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

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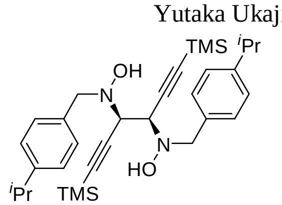

$C_{32}H_{48}N_2O_2Si_2$

Ee = 70%

$[\alpha]_D^{25}$ -9 (c 0.536, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate

Absolute configuration: (*R*,*R*)

N,*N′*-[(*R*,*R*)-1,6-Bis(trimethylsilyl)hexa-1,5-diyne-3,4-diyl]bis[*N*-(4-isopropylbenzyl)hydroxylamine]

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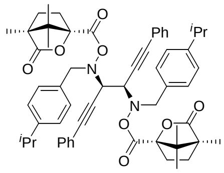

$C_{58}H_{64}N_2O_8$

N,*N*'-[(3*R*,4*R*)-1,6-diphenylhexa-1,5-diyne-3,4-diyl]

Ee = 100% $[\alpha]_D^{25}$ +80 (c 0.14, EtOH)

Source of Chirality: Dicyclohexyl (*R*,*R*)-tartrate,

(1*S*,4*R*)-camphanic chloride

Absolute configuration: (3*R*,4*R*,1*S*′,4*R*′)

bis{*N*-(4-isopropylbenzyl)-*O*-[(1*S*′,4*R*′)-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptane-3-one-1-carbonyl]hydroxylamine}