Copper-Catalyzed Reaction of Terminal Alkynes with Nitrones. Selective Synthesis of 1-Aza-1-buten-3-yne and 2-Azetidinone Derivatives

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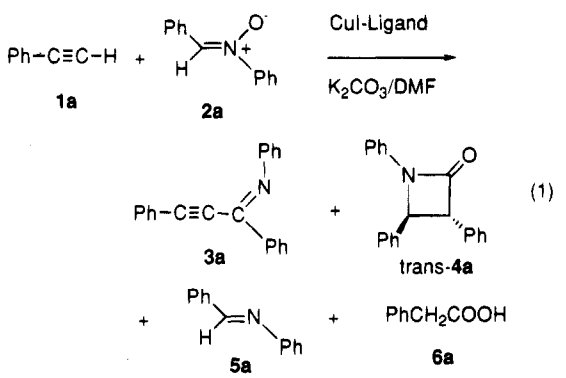
Reaction of arylacetylenes with *C,N*-diarylnitrones using a catalyst system of CuI–dppe (dppe = 1,2-bis(diphenylphosphino)ethane) in the presence of potassium carbonate in DMF predominantly affords the corresponding 1,2,4-triaryl-1-aza-1-buten-3-ynes in good yields. In contrast, the catalytic reaction using CuI in the presence of an excess amount of pyridine as the ligand gives 1,3,4-triaryl-2-azetidinones as the major products. The reaction with aliphatic terminal alkynes in place of arylacetylenes produces the latter products irrespective of the catalyst system used. Asymmetric induction is also observed in the reaction of phenylacetylene with α,*N*-diphenylnitrone to give 1,2,4-triphenyl-2-azetidinone in the presence of chiral bisoxazoline-type ligands.

Introduction

Alkynes that are activated by electron-withdrawing groups undergo [3 + 2] cycloaddition reactions with nitrones to give isoxazoline derivatives.[1-4] While simple terminal alkynes cannot react with nitrones, reaction of copper(I) acetylides with nitrones interestingly affords 2-azetidinone (β-lactam) derivatives.[5-7] On the other hand, we have recently reported that the coupling reaction of terminal alkynes with aryl and vinyl iodides efficiently proceeds in the presence of copper(I) iodide and triphenylphosphine using potassium carbonate as base.[8] In the course of these studies, we have found that terminal alkynes can also react with nitrones in the presence of a catalytic amount of CuI to give two kinds of coupling products, 1-aza-1-buten-3-ynes and 2-azetidinones, along with redox products, i.e., carboxylic acids and imines. The product composition was influenced by the ligand added as well as the substituents on the acetylene employed.[9] Subsequently, we have carried out a detailed study of the scope and limitations of the catalytic coupling of terminal alkynes with nitrones. Asymmetric induction in the formation of 1,2,4-triphenyl-2-azetidinone, as a representative example, has also been undertaken using chiral bisoxazoline-type ligands. The results are described herein.

Results and Discussion

Reaction of Phenylacetylene (1a) with α,*N*-Diphenylnitrone (2a). The reaction of **1a** (1 mmol) with **2a** (1 mmol) using CuI (0.1 mmol), K_2CO_3 (1.1 mmol), and water (2 mmol) was carried out in DMF at 80 °C, under nitrogen, in the presence of a number of phosphines and nitrogen-containing compounds as the ligands (eq 1 and Table 1). The products, *N*-(1,3-diphenyl-2-propynylidene)aniline (**3a**), *trans*-1,3,4-triphenyl-2-azetidinone (*trans*-**4a**), *N*-benzylideneaniline (**5a**), and phenylacetic acid (**6a**) were detected and the product composition varied with the specific ligand. The reaction using dppe (1,2-bis(diphenylphosphino)ethane) selectively afforded the azenyne **3a**. In contrast, only a trace amount of **3a** (less than 1%) was formed from 1,10-phenanthroline, which yielded *trans*-**4a** (28%) together with **5a** (51%) and **6a** (40%). It was also found that the yield of **4a** could be significantly increased by using an excess amount of pyridine as the ligand at a lower temperature. Thus, **4a** was obtained in a yield of 71% at 0 °C in the presence of pyridine. In this case, the product was a mixture of *trans*-**4a** and its cis-isomer in a ratio of 31:69. It was confirmed that the reaction using dppe or pyridine did not proceed without either CuI or K_2CO_3, suggesting that copper(I) phenylacetylide coordinated by the ligand added is involved as a key intermediate.[8] Although the reaction occurred without the addition of a ligand at 80 °C, the rate of consumption of the substrates was considerably reduced, giving **3a**, **4a**, and **5a** in comparable relative amounts.



(1)

Reaction of Various Terminal Alkynes with Nitrones using CuI–dppe. The reactions of **1a** (2 mmol) with various α,*N*-diarylnitrones **2b-i** (2 mmol) in the presence of 0.2 mmol of each of CuI and dppe afforded

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Table 1. Reaction of 1a with 2a[a]

ligand	time (h)	% yield[b] 3a	4a (trans/cis)[c]	5a	6a[d]
none	10	40	18	25	11
none[e]	6	26	13	26	12
PPh_3	3	53	19	27	
Ph_2Bu^n	4	26	19	36	22
PBu_3^n	5	13	36	44	33
dppe[f]	4	74	3	7	9
dppp[f]	4	68	7	11	
dppb[f]	24	10	7	30	
bpy[g]	5	15	6	38	
phen[h]	3	tr	28	51	40
phen[h,i]	3		55 (56:44)	41	23
py[i,j]	3		65 (34:66)	26	16
py[j,k]	8		71 (31:69)	22	11

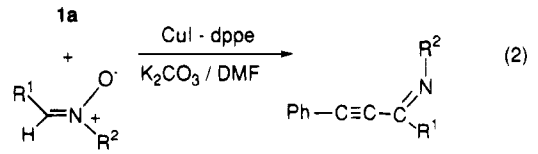
[a] Reaction conditions; [1]:[2]:[CuI]:[K_2CO_3]:[H_2O] = 1:1:0.1:1.1:2 (in mmol), in DMF at 80 °C under N_2. [b] Determined by GLC analysis. [c] The product has trans-configuration unless otherwise noted. [d] Unless a value is given, the yield was not determined. [e] Reaction without water. [f] $Ph_2P(CH_2)_nPPh_2$:dppe; n = 2, dppp; n = 3, dppb; n = 4. [g] bpy = α,α′-dipyridyl. [h] phen = 1,10-phenanthroline. [i] Reaction at room temperature. [j] py = pyridine (1.5 mL). [k] Reaction at 0 °C.

Table 2. Reaction of 1a with Various Nitrones 2a-n and 1b-e with 2a using CuI–dppe[a]

alkyne	nitrone	time (h)	product(s), % yield[b]
1a	**2a**	4	**3a**, 74
1a	**2b**	5	**3b**, 77
1a	**2c**	5	**3c**, 80
1a	**2d**	4	**3d**, 62
1a	**2e**	2	**3e**, 65
1a	**2f**	5	**3f**, 71
1a	**2g**	3	**3g**, 76
1a	**2h**	21	**3h**, 70
1a	**2i**	2	**3i**, 83
1a	**2j**	24	**3i**, 66
1a	**2k**	3	**3k**, 65
1a[c]	**2l**	16	**3l**, 32
1a[c]	**2m**	16	**3m**, 42
1b	**2a**	6	**7**, 74
1c	**2a**	3	**8**, 72
1d	**2a**	4	**9**, 24; **5a**, 65
1e	**2a**	3	**10**, 28; **5a**, 65

[a] The reaction was carried out using **1** (2 mmol), **2** (2 mmol), CuI (0.2 mmol), dppe (0.2 mml), K_2CO_3 (2.2 mmol), and H_2O (4 mmol) in DMF at 80 °C under nitrogen. [b] Isolated yield. [c] **1a** (4 mmol) was used.

the corresponding 1,2-diaryl-3-phenyl-1-aza-1-buten-3-ynes (**3b-i**) in 57–83% isolated yields, as did that of **1a** with **2a** (eq 2 and Table 2). The alkyne **1a** also reacted

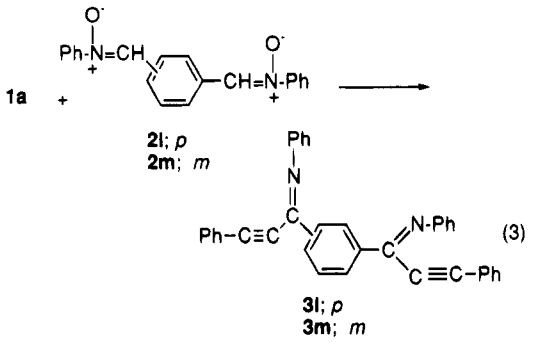


(2)

2b; R^1=4-MeC_6H_4, R^2=Ph
2c; R^1=4-ClC_6H_4, R^2=Ph
2d; R^1=Ph, R^2=4-MeC_6H_4
2e; R^1=Ph, R^2=4-ClC_6H_4
2f; R^1=1-naphthyl, R^2=Ph
2g; R^1=2-naphthyl, R^2=Ph
2h; R^1=2-thienyl, R^2=Ph
2i; R^1=3-pyridyl, R^2=Ph
2j; R^1=Ph, R^2=Me
2k; R^1=(E)-styryl, R^2=Ph

3b; R^1=4-MeC_6H_4, R^2=Ph
3c; R^1=4-ClC_6H_4, R^2=Ph
3d; R^1=Ph, R^2=4-MeC_6H_4
3e; R^1=Ph, R^2=4-ClC_6H_4
3f; R^1=1-naphthyl, R^2=Ph
3g; R^1=2-naphthyl, R^2=Ph
3h; R^1=2-thienyl, R^2=Ph
3i; R^1=3-pyridyl, R^2=Ph
3j; R^1=Ph, R^2=Me
3k; R^1=(E)-styryl, R^2=Ph

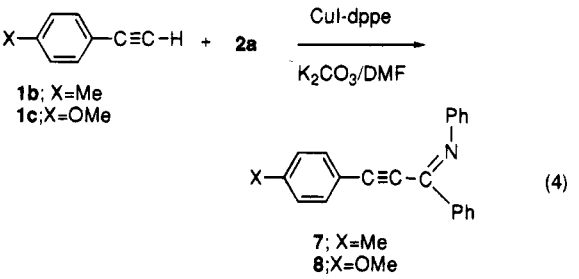
with α-phenyl-*N*-methylnitrone (**2j**) and α-(*E*)-styryl-*N*-phenylnitrone (**2k**) to give compounds **3j** and **3k**, respectively. From the reactions of **1a** with dinitrones **2l** and **2m**, products **3l** and **3m** were isolated in 42% and 32% yields, respectively (eq 3). α-Phenyl-*N*-benzylnitrone and



(3)

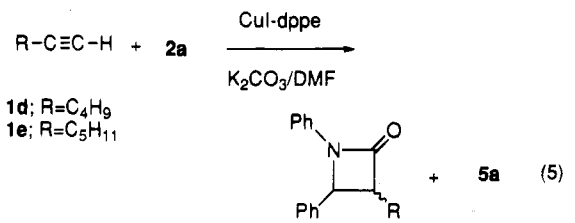
3l; *p*
3m; *m*

α-phenyl-*N*-*tert*-butylnitrone, however, did not react with **1a**; only the starting materials were recovered. As expected, the reaction of 4-methyl- and 4-methoxyphenylacetylenes (**1b,c**) with **2a** gave azaenynes **7** and **8** (eq 4). In contrast, no azaenynes were formed in the reac-



(4)

7; X=Me
8;X=OMe



(5)

9; $R=C_4H_9$
10; $R=C_5H_{11}$

tions of 1-hexyne (**1d**) and 1-heptyne (**1e**), azetidin-2-ones **9** and **10** being instead formed in 24% and 28% yields, together with *N*-benzylideneaniline (**5a**) (eq 5). Treatment of propargyl alcohol **1g** or methyl propiolate **1f** with **2a** gave no coupled products; only **5a** was detected.

While relevant methods for the preparation of 2,4-diaryl-1-aza-1-buten-3-ynes employing the corresponding imidoyl chlorides and terminal alkynes have been reported,[10-12] the present route has the advantage of being carried out with less expensive, more easily handled reagents.

Reaction of Various Terminal Alkynes with Nitrones Using CuI–Pyridine. The reaction of **1a** (2 mmol) with a series of α,*N*-diarylnitrones, **2a** and its derivatives **2b-e** and **2n-p** (2 mmol), each of which has a substituent at the 4-position of one of the two phenyl rings, was carried out using 0.2 mmol of CuI and 2 mL of pyridine in DMF at room temperature for 2–5 h (Table 3). As expected, the corresponding 1,4-diaryl-3-phenyl-

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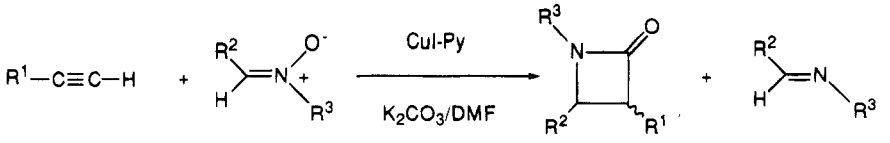
Table 3. Reaction of 1a with 2a-e,h-i, o-t and 1e-k with 2a using CuI–Pyridine[a]



alkyne R^1	nitrone R^2	R^3	time (h)	% yield[b] 2-azetidinone (trans/cis)	% yield[b] imine
Ph (**1a**)	Ph	4-(MeOOC)C_6H_4 (**2n**)	2	**4n**, 82 (54:46)	**5n**, 11
Ph (**1a**)	Ph	4-ClC_6H_4 (**2e**)	2	**4e**, 73 (30:70)	**5e**, 25
Ph (**1a**)	Ph	Ph (**2a**)	3	**4a**, 65 (34:66)	**5a**, 26
Ph (**1a**)	Ph	4-MeC_6H_4 (**2d**)	4	**4d**, 54 (35:65)	**5d**, 35
Ph (**1a**)	Ph	4-$MeOC_6H_4$ (**2o**)	5	**4o**, 21 (40:60)	**5o**, 72
Ph (**1a**)	4-ClC_6H_4	Ph (**2c**)	3	**4c**, 69 (38:62)	**5c**, 27
Ph (**1a**)	4-MeC_6H_4	Ph (**2b**)	3	**4b**, 65 (34:66)	**5b**, 31
Ph (**1a**)	4-$MeOC_6H_4$	Ph (**2p**)	5	**4p**, 32 (55:45)	**5p**, 58
Ph (**1a**)[c]	2-thienyl	Ph (**2h**)	72	**4h**, 48 (92:8)	**5h**, 28
Ph (**1a**)	3-pyridyl	Ph (**2i**)	2	**4i**, 52 (35:65)	**5i**, 31
Ph (**1a**)	PhCO	Ph (**2q**)	5	**4q**, 50 (46:54)	*c*
Ph (**1a**)	*n*-Pr	Ph (**2r**)	8	**4r**, 52 (52:48)	
Ph (**1a**)	*i*-Pr	Ph (**2s**)	4	**4s**, 26 (50:50)	
C_5H_{11} (**1e**)	Ph	Ph (**2a**)	7	**10**, 59 (26:74)	**5a**, 32
COOMe (**1f**)	Ph	Ph (**2a**)	2	**11**, 35 (100:0)	**5a**, 44
CH_2OH (**1g**)	Ph	Ph (**2a**)	2	**12**, 32 (20:80)	**5a**, 52
CH(Me)OH (**1h**)	Ph	Ph (**2a**)	2	**13**, 58 (29:71)	**5a**, 39
(*E*)-styryl (**1i**)	Ph	Ph (**2a**)	4	**14**, 69 (40:60)	**5a**, 29
1-cyclohexenyl (**1j**)	Ph	Ph (**2a**)	2	**15**, 67 (47:53)	**5a**, 27
MeOCH=CH (**1k**)	Ph	Ph (**2a**)	5	**16**, 39 (26:74)	**5a**, 41

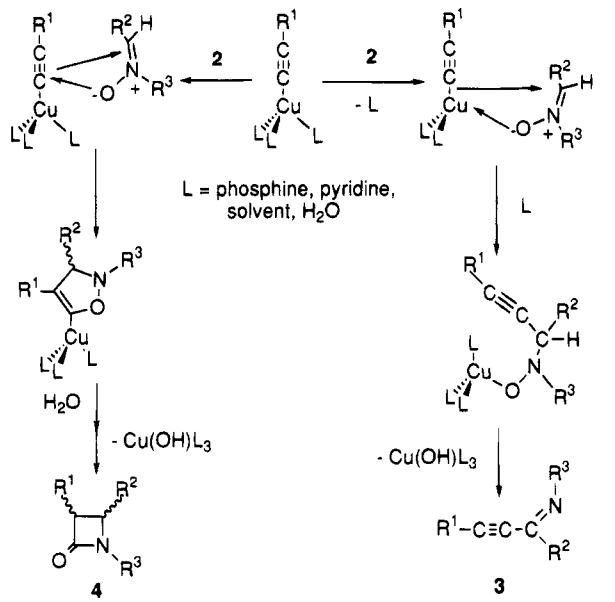
[a] The reaction was carried out using **1** (2 mmol), **2** (2 mmol), CuI (0.2 mmol), and K_2CO_3 (2.2 mmol) in the presence of pyridine (2 mL) in DMF at room temperature under nitrogen. [b] Isolated yield. [c] Not Determined. [c] Reaction at 80 °C.

2-azetidinones **4a-e** and **4n-p**, which were mixtures of the trans- and cis-isomers in ratios of 1:1–2:3, along with imines **5** (plus phenylacetic acid) were obtained. No azaenyne product was detected. It was also observed that the product composition was significantly affected by the electronic nature of the 4-substituent. The ratio of **4** to **5** increases as the substituent on either the α- or *N*-phenyl ring becomes more electron-withdrawing. This is in contrast to the reaction using CuI–dppe where the yield of azaenyne products was less sensitive to substituent variation. The reaction rate also appeared to be a function of the substituent, being reduced by electron-donating substituents.

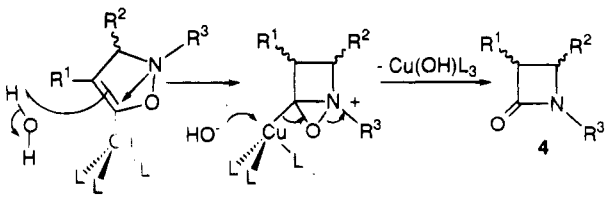
α-Heteroaryl-, α-benzoyl-, and α-alkyl-*N*-phenylnitrones, **2h,i**, **2q**, and **2r,s**, reacted with **1a** to give the corresponding 2-azetidinones, **4h,i**, **4q**, and **4r,s**, in 26–73% yields. It is noted that the nitrones **2r,s** were generated in situ and used without isolation because of their instability (see Experimental Section). From the reactions of alkynes **1e-k** with **2a**, azetidinones **10–16** were isolated. The formation of azetidinones **11** and **12** is of interest, since the reaction of **1f** and **1g** with **2a** using CuI–dppe gave no coupled products.

Reaction Scheme. A possible mechanism to rationalize the formation of azaenynes **3** and azetidinones **4**, based on the observed results is illustrated in Scheme 1. The key intermediate that reacts with nitrone to lead to the coupled products may be copper(I) acetylide coordinated by the ligand added, solvent, and H_2O.[8] The phosphine and pyridine type ligands appear to stabilize the monomeric acetylide intermediate. Indeed, precipitation of copper(I) phenyl acetylide, which is polymeric, was confirmed when the reaction using **1a** was carried out without addition of the ligands. Attack of the acetylide on the electrophilic carbon of **2** followed by elimination of a copper hydroxide species may give **3**. Addition of the intermediate to **2** in a [2 + 3] manner may also occur to give **4**. A possible route for the transformation of the

Scheme 1



Scheme 2



[2 + 3] adduct to **4** is shown in Scheme 2 and is similar to that proposed previously.[6]

The observed effectiveness of the phosphine ligands in for the reaction of **1a** with **2a** to give **3a** followed the sequence dppe > dppb > PPh_3 > PPh_2Bu^n > dppb (Table 1). This suggests that a bidentate ligand that can tightly

Scheme 3

$$RC{\equiv}C\text{-}CuL_3 \xrightarrow[-5]{2} RC{\equiv}C\text{-}O\text{-}CuL_3 \xrightarrow[-Cu(OH)L_3]{2H_2O} RCH_2COOH$$

ligate to the copper metal center is essential for a selective reaction. The fact that the reaction using CuI–dppe requires a relatively higher temperature than that with CuI–pyridine suggests that dppe suppresses the reaction, especially the [2 + 3] addition. One of the possible reasons for this could be that the ligand makes the terminal carbon of the acetylide intermediate relatively negative, and, therefore, it becomes less reactive toward the oxygen of **2**. The coordination of the ligand could also increase the nucleophilic character of the terminal carbon, and hence, the intermediate preferentially attacks the electrophilic carbon of **2** to give **3** when arylacetylenes are employed as the starting materials. In the case of aliphatic terminal alkynes, however, formation of **3** could not be detected, only **4** along with **5**. This would imply that copper alkylacetylides tend to act as dipolarophiles rather than nucleophiles, possibly because of their good frontier orbital interaction with **2**. To establish this, further investigation is required.

Pyridine in DMF appears to effectively stabilize monomeric copper acetylide, as considered above to enhance the reaction leading to **4**. In the case using CuI–pyridine, the relative yield of **5** from **4** was markedly influenced by the reaction temperature and the substituents of the *C*,*N*-diarylnitrones. Higher reaction temperature and electron-donating substituents enhanced the formation of byproduct **5**. A possible mechanism for the formation of **5** together with carboxylic acids is described in Scheme 3. Coordination of the oxygen of the nitrone, followed by insertion of it into the Cu–C bond, gives imine and an (alkynyloxy)copper species. The latter undergoes hydrolysis to give acids. At a relatively high temperature, the N–O bond could be easily broken. It should be noted that the electron-donating substituents were also found to suppress the rate of the consumption of **1**. Thus, they seem to retard the cycloaddition more strongly than the oxygen atom transfer reaction.

The trans/cis ratio of **4** appears to be determined in the reaction of the five membered cyclic adduct with H_2O as proposed previously.[6] Approach of H_2O to the adduct from the less hindered side may favorably afford the cis-isomer of **4**. Selective formation of *trans*-**4a** at a higher temperature (Table 1) may imply isomerization of the *cis*-compound to the thermodynamically more stable trans-isomer. It was confirmed that *cis*-1,2,4-triaryl-2-azetidinones are easily transformed into the corresponding trans-isomers by treating them with K_2CO_3 in DMF at 80 °C.

The reaction of **1h** with **2a** gave a mixture of *trans*-**13a**, *cis*-**13a**, *trans*-**13b**, and *cis*-**13b** in a ratio of 11:60:17:12 (eq 6). Structural assignments were made by

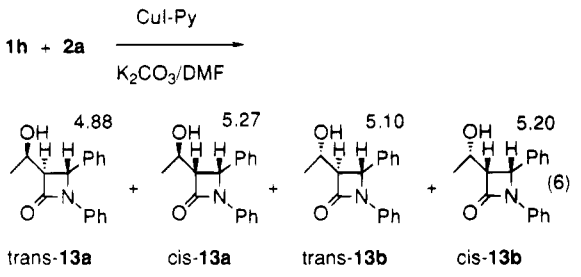


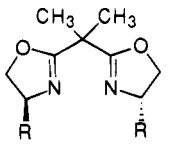
Table 4. Reaction of 1a with 2a in the Presence of Chiral Ligands 17a-c and (−)-Sparteine[a]

ligand	CuI:ligand[b]	time (h)	yield of *trans*-**4a** (%)	ee (%)
17a	0.1:0.2	5	5	c
17a	0.1:1	2	45	40
17a	1:1	1	54	68
17a[d]	0.1:0.2	2	50	57
17b	1:1	1	53	67
17c	1:1	2	40	45
(−)-sparteine	0.1:1	2	47	23

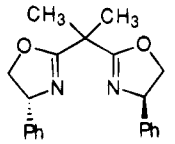
[a] The reaction was carried out using **1a** (1 mmol) and **2a** (1 mmol) at room temperature, and the product was treated with K_2CO_3 (see Experimental Section). [b] In mmol. [c] Not determined. [d] Alkyne **1a** was added to the reaction mixture in 10 portions.

comparison of the ^1H NMR spectrum of the mixture with that reported previously[13] and the composition was determined by the ratio of the peak areas of the H-4 protons (the δ values are indicated in eq 6). The product ratio of (*trans*-**13a** + *cis*-**13a**)/(*trans*-**13b** + *cis*-**13b**) may be determined in the cycloaddition step. Molecular models suggest that steric repulsion between the methyl group in **1h** and the *C*-phenyl group in **2a** may be the major reason for in the preferential formation of **13a**.

Reaction of 1a with 2a in the Presence of Chiral Ligands. The results of the reaction of **1h** with **2a** may also suggest that asymmetric induction in the formation of **4** is possible, if the reaction of **1** with **2** is carried out in the presence of certain chiral ligands. While for the normal reaction an excess of pyridine was usually used, the reaction also proceeded with a catalytic amount of 1,10-phenanthroline (Table 1). Therefore, chiral nitrogen-containing bidentate ligands could be suitable for the purpose. The reaction of **1a** with **2a** was, thus, conducted as a model using bisoxazoline type ligands **17a-c**. They have been reported to show good enantiodifferentiation ability in some catalytic reactions.[14-16] The reaction at room temperature using 1 mmol each of **1a** and **2a** in the presence of CuI (0.1 mmol) and **17a** (0.2 mmol), which



17a; R=i-Pr
17b; R=t-Bu



17c

was prepared using (*S*)-(+)-valinol, did not proceed well. Precipitation of copper(I) phenylacetylide was observed. Thus, the reaction using 1 mmol of **17a** was carried out. It gave **4a** (45%) in a trans/cis ratio of 35:65 (Table 4). The ^1H NMR spectrum of the product in the presence of Eu(tfc)$_3$ (tfc = tris(3-(trifluoromethyl)hydroxymethylenecamphorato)europium) indicated that the enantiomeric excess was 40% in both the trans- and cis-isomers. Treatment of the trans–cis mixture with K_2CO_3 in DMF at 80 °C quantitatively gave *trans*-**4a** with 40% ee. These results are consistent with stereo-differentiation in the

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cycloaddition step (Scheme 1). A higher ee of 68% was obtained by increasing the amount of CuI to 1 mmol. The optical rotation $[\alpha]_D$ of **4a** after treatment with K_2CO_3 (i.e., *trans*-**4a**) was 36.8° (c = 1.0, $CHCl_3$). The reactions using **17b** and **17c** afforded enantiomeric excesses of 67% and 45%, respectively. The product *trans*-**4a** obtained using **17c** which was prepared with (*R*)-(−)-2-phenylglycinol, showed an optical rotation $[\alpha]_D$ of −25.7° (c = 1.3, $CHCl_3$). This indicates that the measurement of ee by ^1H NMR is adequate, and both (+)- and (−)-**4** rich samples can be prepared by the present method. The reaction using (−)-sparteine also gave a (−)-*trans*-**4a** rich product.

The above results suggest that in the catalytic reaction, complete chelation of the ligands to the copper acetylide intermediate may be hindered by the alkyne substrate, which has generally high affinity for copper(I) species, since it exists in high concentration in the early stage. Consequently, the alkyne **1a** was gradually added to the reaction using CuI (0.1 mmol) and **17a** (0.2 mmol). The reaction proceeded smoothly to afford a fairly good ee of 57%. This method was also applied to the reaction using **17b** or **17c**. However, copper(I) phenylacetylide precipitated within 10 min. This may imply that the complexation affinities of **17b** and **17c** are lower than that of **17a**.

Experimental Section

^1H NMR spectra were recorded at 400 MHz for $CDCl_3$ solutions. MS data were obtained by EI. GC analysis was carried out using a silicone OV-17 glass column (i.d. 2.6 mm × 1.5 m) or a CBP-1 capillary column (i.d. 0.5 mm × 25 m). Alkynes **1b**, **1c**, and **1i** were prepared by the methods reported previously.[17] Nitrones **2a-q** were prepared by condensation of the corresponding aldehydes with hydroxylamines in ethanol.[4] Nitrones **2r** and **2s** were generated by addition of *n*- and isobutylaldehydes (2.4 mmol, 173 mg) in ether (3 mL) to a mixture of *N*-phenylhydroxylamine (2.4 mmol, 262 mg) and K_2CO_3 (5 mmol, 690 mg) in ether (3 mL) at 0 °C in a period of ca. 1 h, and the resulting solution was directly subjected to the reaction with alkynes. Bisoxazolines **17a-c** were prepared by the reported method.[15] Other starting materials were commercially available. Solvents were purified by standard methods before use. The following experimental details given below may be regarded as typical in methodology and scale.

Reaction of Phenylacetylene (1a) with α,*N*-Diphenylnitrone (2a) Using CuI−dppe. To a mixture of **2a** (2 mmol, 394 mg), CuI (0.2 mmol, 38 mg), dppe (0.2 mmol, 80 mg), and potassium carbonate (2.2 mmol, 300 mg) was added a solution of **1a** (2 mmol, 204 mg) and water (4 mmol, 72 mg) in DMF (8 mL), and the resulting mixture was stirred under nitrogen at 80 °C for 4 h. Then, the mixture was poured into water, extracted with ether, and dried over Na_2SO_4. Product **3a** (416 mg, 74%) was isolated by column chromatography on silica gel using hexane−benzene (3:1, v/v) as eluant.

Reaction of Phenylacetylene (1a) with α,*N*-Diphenylnitrone (2a) using CuI−Pyridine. To a mixture of **2a** (2 mmol, 394 mg), CuI (0.2 mmol, 38 mg), and K_2CO_3 (2.2 mmol, 300 mg) was added a solution of **1a** (2 mmol, 204 mg) in DMF (6 mL)−pyridine (2 mL), and the resulting mixture was stirred at rt under nitrogen for 3 h. Then, the mixture was poured into water, extracted with ether, and dried over Na_2SO_4. The product mixture was chromatographed on silica gel. Elution with hexane−benzene (1:1, v/v) gave **5a** (94 mg, 26%). The next fraction obtained by eluting with hexane−benzene (1:3, v/v) contained **4a** (389 mg, 65%).

Reaction of Phenylacetylene (1a) with α,*N*-Diphenylnitrone (2a) in the Presence of Ligand 17a. A mixture of CuI (0.1 mmol, 19 mg) and **17a** (1 mmol, 266 mg) in DMF (2 mL) was stirred for 30 min at rt under nitrogen. Then, **2a** (1 mmol, 197 mg), potassium carbonate (1.1 mmol, 150 mg), and **1a** (1 mmol, 102 mg) in DMF (3 mL) was added, and the resulting mixture was stirred for a further 2 h. Column chromatography on silica gel of the product mixture using hexane−benzene as above gave **4a** (135 mg, 45%). ^1H NMR of the product in $CDCl_3$ in the presence of Eu(tfc)$_3$ (0.8 equiv) indicated that the trans/cis ratio was 35:65 and ee of both the isomers was 40%. Treatment of the product (100 mg) with potassium carbonate (100 mg) in DMF (5 mL) at 80 °C for 1 h afforded *trans*-**4a** quantitatively. Its ee was also determined to be 40%.

Products. Compounds **3a**,[12] **3j**,[18] **3k**,[19] **4a-d**,[6] **4e**,[20] **4h**,[7] **4o**,[21] **4p**,[6] **4q**,[7] **4s**,[22] and **9**,[6] are known and were compared with those authentic specimens. The analytical data of other products **3** and **4** are as follows. It is noted that boiling points were determined using a Kugelrohr distillation apparatus.

***N*-[1-(4-Methylphenyl)-3-phenyl-2-propynylidene]-aniline (3b):** mp 75−76 °C; ^1H NMR δ 2.43 (s, 3H), 7.16−7.20 (m, 3H), 7.28−7.34 (m, 6H), 7.37−7.42 (m, 3H), 8.14 (d, 2H, J = 8.3 Hz); MS m/z 295 (M^+). Anal. Calcd for $C_{22}H_{17}N$: C, 89.44; H, 5.81; N, 4.74. Found: C, 89.17; H, 5.81; N, 4.76.

***N*-[1-(4-Chlorophenyl)-3-phenyl-2-propynylidene]-aniline (3c):** mp 113−115 °C; ^1H NMR δ 7.17−7.22 (m, 3H), 7.31−7.48 (m, 9H), 8.18−8.21 (m, 2H); MS m/z 315, 317 (M^+). Anal. Calcd for $C_{21}H_{14}NCl$: C, 79.86; H, 4.48; N, 4.44; Cl, 11.23. Found: C, 80.08; H, 4.48; N, 4.38; Cl, 11.33.

***N*-(1,3-Diphenyl-2-propynylidene)-4-methylaniline (3d):** mp 62−64 °C; ^1H NMR δ 2.40 (s, 3H), 7.14−7.17 (m, 2H), 7.21−7.25 (m, 2H), 7.32−7.39 (m, 5H), 7.47−7.50 (m, 3H), 8.24−8.27 (m, 2H); MS m/z 295(M^+). Anal. Calcd for $C_{22}H_{17}N$: C, 89.44; H, 5.81; N, 4.74. Found: C, 89.19; H, 5.78; N, 4.73.

***N*-(1,3-Diphenyl-2-propynylidene)-4-chloroaniline (3e):** mp 117−118 °C; ^1H NMR δ 7.12−7.16 (m, 2H), 7.34−7.41 (m, 7H), 7.48−7.53 (m, 3H), 8.23−8.26 (m, 2H); MS m/z 315, 317 (M^+). Anal. Calcd for $C_{21}H_{14}NCl$: C, 79.86; H, 4.48; N, 4.44; Cl, 11.23. Found: C,79.74, H, 4.39, N, 4.46, Cl, 11.22.

***N*-[1-(1-Naphthyl)-3-phenyl-2-propynylidene]aniline (3f):** bp 186 °C/3 mmHg; ^1H NMR δ 7.23−7.32 (m, 8H), 7.45−7.48 (m, 2H), 7.52−7.61 (m, 3H), 7.90−7.99 (m, 2H), 8.14−8.16 (m, 1H), 8.97 (d, 1H, J = 8.8 Hz); MS m/z 331(M^+). Anal. Calcd for $C_{25}H_{17}N$: C, 90.60; H, 5.17; N, 4.23. Found: C, 90.60; H, 5.06; N, 4.19.

***N*-[1-(2-Naphthyl)-3-phenyl-2-propynylidene]aniline (3g):** mp 104−105 °C; ^1H NMR δ 7.21−7.25 (m, 3H), 7.33−7.40 (m, 5H), 7.41−7.46 (m, 2H), 7.52−7.58 (m, 2H), 7.89−7.94 (m, 2H), 7.98−8.00 (m, 1H), 8.38−8.41 (m, 1H), 8.71 (s, 1H); MS m/z 331 (M^+). Anal. Calcd for $C_{25}H_{17}N$: C, 90.60; H, 5.17; N, 4.23. Found; C, 90.58; H, 5.03; N, 4.20.

***N*-(1-(2-Thienyl)-3-phenyl-2-propynylidene)aniline (3h):** bp 170 °C/2 mmHg;^1H NMR δ 7.13−7.15 (m, 1H), 7.21−7.24 (m, 2H), 7.32−7.42 (m, 8H), 7.49−7.51 (m, 1H), 7.81−7.83 (m, 1H); MS m/z 287 (M^+). Anal. Calcd for $C_{19}H_{13}NS$: C, 79.41; H, 4.56; N, 4.88; S, 11.16. Found: C, 79.27; H, 4.60; N, 4.91; S, 11.02.

***N*-[1-(3-Pyridyl)-3-phenyl-2-propynylidene)aniline (3i):** bp 141 °C/2 mmHg; ^1H NMR δ 7.21−7.26 (m, 3H), 7.31−7.36 (m, 4H), 7.41−7.46 (m, 4H), 8.52−8.54 (m, 1H), 8.75 (s, 1H), 9.46 (s, 1H); MS m/z 282 (M^+). Anal. Calcd for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.62; H, 5.04; N, 9.84.

1,4-Bis(1,4-diphenyl-1-aza-1-buten-3-yn-2-yl)benzene (3l): mp 107−108 °C; ^1H NMR δ 7.20−7.25 (m, 10H), 7.31−7.34 (m, 6H), 7.41−7.45 (m, 4H), 7.43 (t, 1H, J = 7.8 Hz), 8.43 (dd, 2H, J = 7.8, 1.5 Hz), 9.16 (d, 1H, J = 1.9 Hz); MS m/z

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484 (M^+). Anal. Calcd for $C_{36}H_{24}N_2$: C, 89.23; H, 4.99; N, 5.78. Found: C, 88.86; H, 4.86; N, 5.67.

1,3-Bis(1,4-diphenyl-1-aza-1-buten-3-yn-2-yl)benzene (3m): mp 174–176 °C; ^{1}H NMR δ 7.20–7.25 (m, 6H), 7.33–7.39 (m, 10H), 7.42–7.46 (m, 4H), 8.39 (s, 4H); MS *m/z* 484 (M^+). Anal. Calcd for $C_{36}H_{24}N_2$: C, 89.23; H, 4.99; N, 5.78. Found: C, 89.29; H, 4.97; N, 5.58.

1,3-Diphenyl-4-(3-pyridyl)-2-azetidinone (4i): ^{1}H NMR (trans/cis = 35:65) δ 4.22 (d, 1H, J = 2.4 Hz; trans), 4.93 (d, 1H, J = 2.4 Hz; trans), 5.00 (d, 1H, J = 6.1 Hz; cis), 5.43 (d, 1H, J = 6.1 Hz; cis), 6.92–7.32 (m, 13H), 8.31 (m, 1H; cis), 8.60 (m, 1H; trans); MS *m/z* 300 (M^+); mp 160–161 °C (trans). Anal. Calcd for $C_{20}H_{16}N_2O$: C, 79.97; H, 5.37; N, 9.33. Found: C, 79.76; H, 5.07; N, 9.17.

3,4-Diphenyl-1-[4-(methoxycarbonyl)phenyl]-2-azetidinone (4n): ^{1}H NMR (trans/cis = 54:46) δ 3.86 (s, 3H; trans), 3.87 (s, 3H; cis), 4.33 (d, 1H, J = 2.5 Hz; trans), 5.00 (d, 1H, J = 2.5 Hz; trans), 5.05 (d, 1H, J = 6.4 Hz; cis), 5.50 (d, 1H, J = 6.4 Hz; cis), 7.03–7.98 (m, 14H); MS *m/z* 357(M^+); mp 144–145.5 °C (trans). Anal. Calcd for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 76.77; H, 5.28; N, 3.98.

1,3-Diphenyl-4-propyl-2-azetidinone (4r): bp 157 °C/2 mmHg; ^{1}H NMR (trans/cis = 52:48) δ 0.65 (t, 3H, J = 7.3 Hz; cis), 0.99 (t, 3H, J = 7.3 Hz, trans), 1.30–1.40 (m, 2H), 1.50–1.57 (m, 2H), 1.80–1.88 (m, 2H), 2.17–2.27 (m, 2H), 4.04–4.08 (m, 1H; trans), 4.09 (d, 1H, J = 2.4 Hz; trans), 4.30–4.35 (m, 1H; cis), 4.68 (d, 1H, J = 6.3 Hz; cis), 7.10–7.47 (m, 10H); MS *m/z* 265 (M^+). Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.14; H, 7.20; N, 5.22.

***N*-[3-(4-Methylphenyl)-1-phenyl-2-propynylidene]-aniline (7):** bp 156 °C/2 mmHg; ^{1}H NMR δ 2.35 (s, 3H), 7.11–7.25 (m,7H), 7.39–7.43 (m,2H), 7.48–7.51 (m, 3H), 8.25–8.28 (m, 2H). MS *m/z* 295 (M^+). Anal. Calcd for $C_{22}H_{17}N$: C, 89.44; H, 5.81; N, 4.74. Found: C, 89.71; H, 5.96; N, 5.04.

***N*-[3-(4-Methoxyphenyl)-1-phenyl-2-propynylidene]-aniline (8):** bp 175 °C/2mmHg; ^{1}H NMR δ 3.81 (s, 3H), 6.81–6.85 (m, 2H), 7.17–7.19 (m, 3H), 7.24–7.27 (m, 2H), 7.39–7.43 (m, 2H), 7.48–7.51 (m, 3H), 8.24–8.27 (m, 2H); MS *m/z* 311 (M^+). Anal. Calcd for $C_{22}H_{17}NO$: C, 84.85; H, 5.51; N, 4.50. Found: C, 84.37; H, 5.82; N, 4.50.

1,4-Diphenyl-3-pentyl-2-azetidinone (10): ^{1}H NMR (trans/cis = 26:74) δ 0.76 (t, 3H, J = 6.8 Hz; cis), 0.88 (t, 3H, J = 6.8 Hz; trans), 1.08–1.18 (m, 6H; cis), 1.30–1.36 (m, 6H; trans), 1.43–1.53 (m, 2H; cis), 1.79–1.88 (m, 1H; trans), 1.92–1.99 (m, 1H; trans), 3.08 (m, 1H; trans), 3.55 (dt, 1H, J = 5.9, 7.8 Hz; cis), 4.65 (d, 1H, J = 2.4 Hz; trans), 5.18 (d, 1H, J = 5.9 Hz; cis), 7.03–7.39 (m, 10H); MS *m/z* 293(M^+); mp 74–74.5 °C (trans). Anal. Calcd for $C_{20}H_{23}NO$: C, 81.86; H, 7.92; N, 4.77. Found: C, 81.71; H, 7.95; N, 4.77.

***trans*-3-(Methoxycarbonyl)-1,4-diphenyl-2-azetidinone (11):** 160 °C/2 mmHg; ^{1}H NMR δ 3.83 (s, 3H), 3.99 (d, 1H, J = 2.9 Hz), 5.33 (d, 1H, J = 2.4 Hz), 7.06 (t, 1H, J = 6.8 Hz), 7.24–7.40 (m, 10H); MS *m/z* 281 (M^+). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.18; H, 5.47; N, 4.85.

1,4-Diphenyl-3-(hydroxymethyl)-2-azetidinone (12): ^{1}H NMR (trans/cis = 20:80) δ 3.28 (dd, 1H, J = 6.8, 4.4 Hz; trans), 3.57 (dd, 1H, J = 11.7, 8.3 Hz; cis), 3.75 (dd, 1H, J = 8.7 Hz, 5.4 Hz; cis), 3.85–3.90 (m, 1H; cis), 4.02 (dd, 1H, J = 11.7, 3.9 Hz; trans), 4.14 (m, 1H; trans), 5.04 (d, 1H, J = 2.4 Hz; trans), 5.28 (d, 1H, J = 5.9 Hz; cis), 7.03–7.08 (m, 1H), 7.26–7.41 (m, 9H); MS *m/z* 253 (M^+); Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97, N, 5.53. Found: C, 75.69; H, 6.00; N, 5.41. mp 118–121 °C (trans/cis = 20:80).

3(*E*)-Styryl-1,4-diphenyl-2-azetidinone (14): ^{1}H NMR (trans/cis = 40:60) δ 3.89–3.91 (m, 1H; trans), 4.43–4.47 (m, 1H; cis), 4.88 (d, 1H, J = 2.4 Hz; trans), 5.34 (d, 1H, J = 5.9 Hz; cis), 5.57–5.60 (m, 1H; cis), 6.39 (dd, 1H, J = 15.6, 8.3 Hz; trans), 6.65–6.69 (m, 1H), 7.03–7.40 (m, 15H); MS *m/z* 325 (M^+); mp 163–165 °C (cis). Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.31. Found: C, 84.72; H, 5.77; N, 4.24.

3-(1-Cyclohexenyl)-1,4-diphenyl-2-azetidinone (15): ^{1}H NMR (trans/cis = 47:53) δ 0.88–2.08 (m, 8H), 3.62–3.63 (m, 1H; trans), 4.18 (d, 1H, J = 5.9 Hz; cis), 4.81 (d, 1H, J = 2.9 Hz; trans), 5.21 (d, 1H, J = 5.9 Hz; cis), 5.78 (d, 1H, J = 1.5 Hz; trans), 5.86 (d, 1H, J = 1.5 Hz; cis), 7.03–7.35 (m, 10H); MS *m/z* 303 (M^+); mp 99–100 °C (trans). Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.00; H, 6.89; N, 4.58.

1,4-Diphenyl-3-(2-methoxyethylene)-2-azetidinone (16): ^{1}H NMR (trans/cis = 26:74) δ 3.54 (s, 3H; cis), 3.60 (s, 3H; trans), 3.99–4.03 (m, 1H), 4.61 (dd, 1H, J = 6.4, 4.4 Hz; trans), 4.73–4.75 (m, 1H; cis), 4.80 (d, 1H, J = 2.4 Hz; trans), 5.25 (d, 1H, J = 6.4 Hz; cis), 5.87 (dd, 1H, J = 5.4, 1.0 Hz; cis), 6.14–6.16 (m, 1H; trans), 7.00–8.41 (m, 10H); MS *m/z* 279 (M^+); mp 120–123 °C (trans/cis = 13:87). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.52; H, 5.98; N, 4.90.

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